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(54) Title: COMBINATORIAL ANTIBODY LIBRARIES AND USES THEREOF

(57) Abstract: Methods for making a combinatorial antibody library from human germline segments are provided. Also provided are libraries of nucleic acid molecules compiled from germline segments encoding VL chains and libraries of nucleic acid molecules encoding VH chains, and resulting antibody libraries. The libraries are provided as addressable libraries. Methods for screening antibody libraries against a target protein antigen, and the identified or selected antibodies are provided.

COMBINATORIAL ANTIBODY LIBRARIES AND USES THEREOF

RELATED APPLICATIONS

Benefit of priority is claimed to U.S. Provisional Application Serial No. 61/198,764, entitled "Combinatorial Antibody Libraries and Uses Thereof," filed November 07, 2008, and to U.S. Provisional Application Serial No. 61/211,204, entitled "Combinatorial Antibody Libraries and Uses Thereof," filed March 25, 2009. Where permitted, the subject matter of the above-noted applications are incorporated by reference in its entirety.

This application also is related to International PCT Application No. (Attorney Dkt. No. 3800016-00087/703PC), entitled "Anti-DLL4 Antibodies and Uses Thereof," filed the same day herewith, which claims priority to U.S. Provisional Application No. 61/198,764 and to U.S. Provisional Application No. 61/211,204.

This application also is related to U.S. Provisional Application No. (Attorney Dkt. No. 3800016-00004/p702), entitled "Methods for Affinity-Maturation-Based Antibody Optimization," filed the same day herewith.

Where permitted, the subject matter of each of the above-noted related applications is incorporated by reference in its entirety.

Incorporation by reference of Sequence Listing provided electronically

An electronic version of the Sequence Listing is filed herewith, the contents of which are incorporated by reference in their entirety. The electronic file is 2.92 mega bytes in size, and titled 701seq.PC1.txt.

FIELD OF THE INVENTION

Methods for making a combinatorial antibody library from human germline segments are provided. Also provided are libraries of nucleic acid molecules compiled from germline segments encoding VL chains and libraries of nucleic acid molecules encoding VH chains, and resulting antibody libraries. The libraries are provided as addressable libraries. Methods for screening antibody libraries against a target protein antigen, and the identified or selected antibodies are provided.

BACKGROUND

Numerous therapeutic and diagnostic monoclonal antibodies (MAbs) are used in the clinical setting to treat and diagnose human diseases, for example, cancer and autoimmune diseases. For example, exemplary therapeutic antibodies include Rituxan (Rituximab), Herceptin (Trastuzumab), Avastin (Bevacizumab) and Remicade (Infliximab). In designing antibody therapeutics, it is desirable to create antibodies, for example, antibodies that modulate a functional activity of a target, and/or improved antibodies such as antibodies with

higher specificity and/or affinity and/or and antibodies that are more bioavailable, or stable or soluble in particular cellular or tissue environments.

Available techniques for generating antibody therapeutics are limited. Current methods include using antibody libraries to select variant proteins with desired properties *in vitro*. The libraries are generated to contain mutational diversity by targeted and non-targeted methods (*e.g.,* Marks *et al., J. Mol. Biol.* (1991) 222, 581-597; Winters *et al.* (1994) Annu Rev. Immunol. 12:433-55; Rosok *et al.* (1996) J. Biol. Chem., 271:22611-22618; Kim *et al.* (2005) Mol. Cells 20:17-29; Mondon *et al.* (2008) Frontiers in Bioscience, 13:1117-1129; Benhar *et al.* (2007) Expert Opin. Biol. Ther., 7:763-779; and Knappik *et al.* (2000) J. Mol. Biol., 296:57-86) . Each of these antibody libraries has its limitations. Accordingly, it is among the objects herein is to provide methods for making antibody libraries, and antibodies produced by the methods.

SUMMARY

Provided herein are human combinatorial antibody libraries generated by rearrangement of human germline segments. Included among the combinatorial antibody libraries provided herein are libraries containing a plurality of antibodies, whereby each member antibody in the library contains a varable light (VL) chain and a variable heavy (VH) chain or a sufficient portion thereof to form an antigen binding site. Each VL chain of the antibodies in the library are encoded by a nucleic acid molecule that contains V_κ and a J_κ human germline segment or degenerate codons thereof, or a V_λ and a J_λ human germline segment or degenerate codons thereof, whereby the segments are linked in-frame. Each VH chain of the antibodies in the library are encoded by a nucleic acid molecule that contains a human V_H and a human J_H germline segment and any sequence of nucleotides between the V_H and a J_H germline segments, whereby the segments are linked in-frame. The human combinatorial antibody libraries contain at least about or 50 or 100 more different members. Each member in the library contains an antigen binding site and is a functional and productive antibody.

In such an example of a human combinatorial antibody library, the V_H germline segment, the sequence of nucleotides between the V_H and J_H and the J_H germline segment of the nucleic acid molecule encoding a VH chain are linked such that the V_H segment is 5' to the sequence of nucleotides between the V_H and J_H which is 5' to the J_H segment; and the V_κ and J_κ or V_λ and J_λ germline segments of the nucleic acid molecule encoding a VL chain are linked such that the V_κ segment is 5' to the J_κ segment or the V_λ segment is 5' to the J_λ segment. The sequence of nucleotides between the V_H and J_H germline segments is at or is

about 5, 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 nucleotides in length. In some examples, the sequence of nucleotides between the V_H and J_H germline segments encodes a peptide mimetic.

Also provided herein is a human combinatorial antibody library containing a plurality of antibodies, whereby each member antibody contains a modified variable light (VL) chain and/or a modified variable heavy chain (VH) chain or a sufficient portion thereof to form an antigen binding site. The VL chain in each library is encoded by a nucleic acid molecule that contains a V_κ and a J_κ human germline segment or degenerate codons thereof, or a V_λ and a J_λ human germline segment or degenerate codons thereof, whereby the segments are linked in-frame. Each VH chain of antibodies in the library are encoded by a nucleic acid molecule that contains a V_H, D_H and a J_H human germline segment or degenerate codons thereof, whereby the segments are linked in-frame. The resultant protein of the VL chain and the VH chain are modified by amino acid replacement or insertion of amino acids into a CDR. The CDR can be any one or more up to all of a CDRH1, CDRH2, CDRH3, CDRL1, CDRL2 or a CDRL3, for example, a CDRH3. The amino acids that can be inserted or replaced correspond to a peptide mimetic.

In all of the examples above, the peptide mimetic can be a TPO, EPO, G-CSF, IL-5, human brain natriuretic peptide (hBNP-32), exendin 4, GLP-1, GLP-2, glucagon, PACAP-38, CD209L, TNF, VEGF, MMP inhibitor, or CTLA-4 peptide mimetic. In particular of a peptide mimietic is a mimetic that mimics Epo activiation of its receptor. The peptide mimetic futher can include a flanking sequence at the carboxy and/ot N-terminal end, such as an amino acid or amino acids. For example, the flanking sequence can include glycine or a proline. Exemplary of peptide mimetics are any set forth in any of SEQ ID NOS: 891, and 987-1014.

In the libraries provided above, the nucleotides between the V_H and J_H germline segments is a human germline D_H segment or degenerate codons thereof. Hence, a human combinatorial antibody library provided herein includes a library containing a plurality of antibodies, each member antibody contains a variable light (VL) chain and a variable heavy (VH) chain or a sufficient portion thereof to form an antigen binding site. Each VL chain of the antibodies in the library are encoded by a nucleic acid molecule that contains a V_κ and a J_κ human germline segment or degenerate codons thereof, or a V_λ and a J_λ human germline segment or degenerate codons thereof, whereby the segments are linked in-frame. Each VH chain of the antibodies in the library are encoded by nucleic acid molecule that contains a V_H, D_H and a J_H germline segment, whereby the segments are linked in-frame. The human combinatorial antibody library contains at least about or 50 or 100 more different members.

In such examples of a human combinatorial antibody library, the V_H, D_H and J_H segments of the nucleic acid molecule encoding a VH chain are linked such that the V_H segment is 5' to the D_H segment which is 5' to the J_H segment; and the V_κ and J_κ or V_λ and J_λ germline segments of the nucleic acid molecule encoding a VL chain are linked such that the V_κ segment is 5' to the J_κ segment or the V_λ segment is 5' to the J_λ segment.

In all of the human combinatorial antibody libraries provided herein , the libraries can be provided as addressable libraries. In such addressable libraries, the antibody within each address is the same antibody and is different from the antibodies at all other addresses. For example, the addressable antibodies in the library are arranged in a spatial array. The spatial array can be a multiwall plate, wherein each individual locus of the plate corresponds to a different antibody member. The antibody members can be immobilized to the surface of the wells of the plate or can be present in solution. In another example, the addressable antibodies are attached to a solid support. In such an example, the solid support can be a filter, chip, slide, bead or cellulose, and the different antibody members are immobilized to the surface thereof. In some examples, the solid support is a biacore chip. In any of the addressable libaries provided herein, the members can be identifiably labled. For example, the label can be colored, chromogenic, luminescent, chemical, fluorescent or electronic.

The human combinatorial libraries provided herein include members whereby a plurality of nucleic acid molecules encode a VH chain and a plurality of nucleic acid molecules encode a VL chain such that the plurality of nucleic acid molecules encoding the VH chain and the VL chain are sufficient to generate at least about or 50 or 100 different antibodies. Hence, in the libraries provided herein, in the nucleic acid molecules encoding a VH chain all or a subset of germline V_H segments are linked with all or a subset of D_H segments which are linked with all or a subset of germline J_H segments to generate the plurality of nucleic acid molecules encoding a VH chain; and in the nucleic acid molecules encoding a VL chain all or a subset of germline V_κ segments are linked with all or a subset of germline J_κ segments, or all or a subset of germline V_λ segments are linked to all or a subset of germline J_λ segments to generate a plurality of nucleic acid molecules encoding a VL chain.

In the libraries provided herein, the VH chains in the members in the library are encoded by rearranged nucleic acid sequences combined by joining a human V_H germline segment, a D_H germline segment and a J_H germline segment. The human V_H germline segment is an IGHV1, IGHV2, IGHV3, IGHV4, IGHV5, IGHV6 or IGHV7 and genes and alleles thereof, for example, any set forth in any of SEQ ID NOS: 10-238. In examples of the combinatorial antibody libraries provided herein, the V_H gene segment can have one

nucleiotide added or removed at the V-D joint of the nucleic acid molecule encoding the VH chain to maintain the reading frame of the VH chain. For example, a nucleotide is inserted at the 3' end of a V_H nucleotide sequence to add a nucleotide between the V_H and D_H. The nucleotide can be any nucleotide, in particular, the nucleotide is a guanine (G). The D_H segment is an IGHD1, IGHD2, IGHD3, IGHD4, IGHD5, IGHD6, or IGHD7 and genes and alleles thereof, for example, any set forth in any of SEQ ID NOS:239-272. In the examples of the combinatorial antibody libraries provided herein, the D_H gene segment can have one nucleotide inserted or deleted at the V-D joint and/or the D-J joint of the nucleic acid encoding the VH chain to maintain the reading frame of the VH chain. The nucleotide insertion or deletion is chosen to maximize the hydrophilicity of the D_H. For example, a nucleotide from the 5' end of a D_H is deleted and/or a nucleotide from the 3' end of a D_H is deleted. In another example, a nucleotide is inserted at the 3' end of a D_H sequence to add a nucleotide between the D_H and J_H. The added nucleotide can be any nucleotide, in particular a guanine (G). The J_H germline segment is an IGHJ1, IGHJ2, IGHJ3, IGHJ4, IGHJ5 or IGHJ6 and genes and alleles thereof, for example, any set forth in any of SEQ ID NOS:273-285. In examples of the human combinatorial antibody library provided herein, the J_H gene segment can have one or more nucleotides inserted or deleted at the D-J joint of the nucleic acid sequence encoding a VH chain to maintain the reading frame of the VH chain. For example, the nucleotide insertion or deletion is chosen to maintain the reading frame of the J_H. In one examples, a nucleotide from the 5' end of the the J_H is deleted. In another example, a nucleotide from the 3' end of the J_H is deleted.

In the libraries provided herein, the VL chains in the members in the library are encoded by rearranged nucleic acid sequences encoding a kappa light chain combined by joining a human V_κ germline segment and a J_κ germline segment or are encoded by rearranged nucleic acid sequences encoding a lambda light chain combined by joining a human V_λ germline segment and a J_λ germline segment. The human V_κ is an IGKV1, IGKV2, IGKV3, IGKV4, IGKV5 and IGKV6, and genes or alleles thereof, for example, any set forth in any of SEQ ID NOS: 286-355 and 868. In examples of the combinatorial antibody libraries provided herein, the V_κ gene segment can have one or more nucleiotides inserted or deleted at the V-J joint of the nucleic acid molecule encoding the VL chain to maintain the reading frame of the VL chain. For example, a nucleotide is deleted at the 3' end of a V_κ. In another example, a nucleotide is inserted at the 3' end of a of a V_κ nucleotide sequence to add a nucleotide between the V_κ and J_κ. The nucleotide can be any nucleotide, in particular, the nucleotide is a guanine (G). The human J_κ is an IGKJ1, IGKJ2, IGKJ3, IGKJ4

or IGKJ5 and genes and alleles thereof, for example, any set forth in any of SEQ ID NOS: 356-364. In examples of the combinatorial antibody libraries provided herein, the J_κ gene segment has one or more nucleotides inserted or deleted at the V-J joint of the nucleic acid sequence encoding a VL chain to maintain the reading frame of the VL chain. The nucleotide insertion or deletion is chosen to maintain the reading frame of the J_κ. In some examples, a nucletode from the 5' end of the J_κ is deleted. The human V_λ is an IGLV1, IGLV2, IGLV3, IGLV4, IGLV5, IGLV6, IGLV7, IGLV8, IGLV9, IGLV10 or IGLV11 and genes and alleles thereof, for example, any set forth in any of SEQ ID NOS:365-441. In examples of the combinatorial antibody libraries provided herein, the V_λ has one or more nucleotides inserted or deleted at the V-J joint of the nucleic acid sequence encoding a VL to maintain the reading frame of the VL chain. For example, a nucleotide from the 3' end of a V_λ nucleotide sequence is deleted. In another example, a nucleotide is inserted at the 3' end of a V_λ nucleotide sequence to add a nucleotide between the V_λ and J_λ. The nucleotide can be any nucleotide, in particular a guanine (G). The human J_λ is an IGLJ1, IGLJ2, IGLJ3, IGLJ4, IGLJ5, IGLJ6 or IGLJ7 and genes and alleles thereof, for example, any set forth in any of SEQ ID NOS:442-451. In examples of the combinatorial antibody library provided herein, the J_λ has one nucleotide inserted or deleted at the V-J joint of the nucleic acid sequence encoding a VL chain to maintain the reading frame of the VL chain. The nucleotide insertion or deletion can be chosen to maintain the reading frame of the J_λ. For example, a nucleotide from teh 5' end of the J_λ is deleted.

The human combinatorial antibody libraries contain a plurality of members each encoded by a plurality of nucleic acid molecules encoding a VH chain and a plurality of nucleic acid molecules encoding a VL chain. The plurality of nucleic acid molecules can correspond to all combinations or permuations of rearranged germline segments or a subset thereof. Generally, the libraries provided herein include libraries containing at or about 50, 10^2, 10^3, 10^4, 2×10^4, 3×10^4, 4×10^4, 5×10^4, 6×10^4, 7×10^4, 8×10^4, 9×10^4, 10^5, 10^6, 10^7,10^8 , 10^9 or more different members. For example, libraries provided herein include those that contain 10^3, 2×10^3, 3×10^3 , 4×10^3, 5×10^3, 6×10^3, 4×10^3, 7×10^3, 8×10^3, 9×10^3, 10^4, 2×10^4, 3×10^4, 4×10^4, 5×10^4, 6×10^4, 7×10^4, 8×10^4, 9×10^4 or more different members.

For example, the plurality of nucleic acid molecules encoding a VH chain are generated from a subset of germline segments selected based on sequence similarities or differences, gene family, length, composition, CDR length or composition, species, functionality, specificity, group or subgroup. In one example, the plurality of nucleic acid

molecules encoding a VH chain are generated from a subset of germline segments selected based on CDR and the CDR is CDR3. In another example, the plurality of nucleic acid molecules encoding a VH chain are selected based on gene family, whereby one germline segment from each of a V_H, D_H, and/or J_H gene family is selected or one germline segment from a subset of a V_H, D_H, and/or J_H gene family is selected. In such an example, the V_H gene family is selected from among a IGHV1-18, IGHV1-2, IGHV1-24, IGHV1-3, IGHV1-45, IGHV1-46, IGHV1-58, IGHV1-69, IGHV1-8, IGHV2-26, IGHV2-5, IGHV2-70, IGHV3-11, IGHV3-13, IGHV3-15, IGHV3-16, IGHV3-20, IGHV3-21, IGHV3-23, IGHV3-30, IGHV3-33, IGHV3-35, IGHV3-38, IGHV3-43, IGHV3-48, IGHV3-49, IGHV3-53, IGHV3-64, IGHV3-66, IGHV3-7, IGHV3-72, IGHV3-73, IGHV3-74, IGHV3-9, IGHV4-28, IGHV4-31, IGHV4-34, IGHV4-39, IGHV4-4, IGHV4-59, IGHV4-61, IGHV5-51, IGHV6-1 and IGHV7-81; the D_H gene family is selected from among a IGHD1-1, IGHD1-14, IGHD1-20, IGHD1-26, IGHD1-7, IGHD2-15, IGHD2-2, IGHD2-21, IGHD2-8, IGHD3-10, IGHD3-16, IGHD3-22, IGHD3-3, IGHD3-9, IGHD4-11, IGHD4-17, IGHD4-23, IGHD4-4, IGHD5-12, IGHD5-18, IGHD5-24, IGHD5-5, IGHD6-13, IGHD6-19, IGHD6-25, IGHD6-6 and IGHD7-27; and the J_H gene family is selected from among a IGHJ1, IGHJ2, IGHJ3, IGHJ4, IGHJ5 and IGHJ6.

For example, the plurality of nucleic acid molecules encoding a VL chain are generated from a subset of germline segments selected based on sequence similarities or differences, gene family, length, composition, CDR length or composition, species, functionality, specificity, group, subgroup. In one example, the plurality of nucleic acid molecules encoding a VL chain are generated from a subset of germline segments selected based on CDR and the CDR is CDR3. In another example, the plurality of nucleic acid molecules encoding a VH chain are selected based on gene family, whereby one germline segment from each of a V_κ and/or J_κ or V_λ and/or J_λ gene family is selected or one germline segment from a subset of a V_κ and/or J_κ or V_λ and/or J_λ gene family is selected. In such an example, the V_κ gene family is selected from among a IGKV1-12, IGKV1-12, IGKV1-16, IGKV1-17, IGKV1-27, IGKV1-33, IGKV1-37, IGKV1-39, IGKV1-5, IGKV1-6, IGKV1-8, IGKV1-9, IGKV1-NL1, IGKV1/OR2, IGKV1D-12, IGKV1D-13, IGKV1D-16, IGKV1-D-17, IGKV1D-33, IGKV1D-37, IGKV1D-39, IGKV1D-42, IGKV1D-43, IGKV1D-8, IGKV2-24, IGKV2-28, IGKV2-29, IGKV2-30, IGKV2-30, IGKV2-40, IGKV2D-24, IGKV2D-26, IGKV2D-28, IGKV2D-29, IGKV2-D-30, IGKV2D-40, IGKV3-11, IGKV3-15, IGKV3-20, IGKV3-7, IGKV3-NL1, IGV3-NL2, IGKV3-NL3, IGKV3-NL4, IGKV3-NL5, IGKV3/OR2-268, IGKV3D-11, IGKV3D-15, IGKV3D-20, iGKV3D-7, IGKV4-1, IGKV5-2, IGKV6-21,

IGKV6D-21, IGKV6D-41, and IGKV1-39; the J_κ gene family is selected from among a IGKJ1, IGKJ2, IGKJ3, IGKJ4 and IGKJ5; the V_λ gene family is selected from among a IGLV1-36, IGLV1-40, IGLV1-41, IGLV1-44, IGLV1-47, IGLV1-50, IGLV1-51, IGLV10-54, IGLV11-55, IGLV2-11, IGLV2-14, IGLV2-18, IGLV2-23, IGLV2-33, IGLV2-8, IGLV3-1, IGLV3-10, IGLV3-12, IGLV3-16, IGLV3-19, IGLV3-21, IGLV3-22, IGLV3-25, IGLV3-27, IGLV3-32, IGLV3-9, IGLV4-3, IGLV4-60, IGLV4-69, IGLV5-37, IGLV5-39, IGLV5-45, IGLV5-8, IGLV5-52, IGLV6-57, IGLV7-43, IGLV7-46, IGLV8-61, IGLV8-61 and IGLV9-49; and the J_λ gene family is selected from among a IGLJ1, IGLJ2, IGLJ4, IGLJ5, IGLJ6 and IGLJ7.

In any of the combinatorial antibody libraries provided herein, each antibody member in the library is productive and functional. Hence, in some examples, member antibodies in the library contains a VH chain and/or a VL chain that is encoded by a nucleic acid molecule that is modified to remove stop codons and/or restriction enzyme sites.

In any of the combinatorial antibody libraries provided herein, the VH chain is encoded by a nucleic acid molecule having a sequence of nucleotides set forth in any of SEQ ID NOS: 1059-1410, or a subset thereof and the VL chain is encoded by a nucleic acid molecule having a sequence of nucleotides set forth in any of SEQ ID NOS: 1411-1422, 1424-1439 and 1441-1471, or a subset thereof. The antibody libraries provided herein include libraries containing members whereby the VH chain has a sequence of amino acids set forth in any of SEQ ID NOS: 1475-1826 or a subset thereof and the VL chain has a sequence of amino acids set forth in any of SEQ ID NOS: 1827-1838, 1840-1855 and 1857-1888 or a subset thereof.

The human combinatorial antibody libraries provided herein include those having members that are full length antibodies or are fragments or portions thereof of antibodies, whereby the fragment or portion of the antibody is sufficient to form an antigen binding site. Thus, any of the the combinatorial antibody libraries provided herein can further contain all of a portion of a constant region, such that the portion of a constant region is sufficient to permit association of a heavy and light chain. Included among fragments or portions of antibody members in the libraries provided herein are a Fab, Fab', $F(ab')_2$, single-chain Fvs (scFv), Fv, dsFv, diabody, Fd and Fd' fragments Fab fragments, Fd fragments, scFv fragments, or a scFab fragments. For example, combinatorial antibody libraries provided herein are Fab libriaries, whereby antibody members of the library are Fabs.

Provided herein is a library of nucleic acid molecules containing a plurality of addressable nucleic acid molecules encoding a variable light (VL) chain. In such libraries,

each VL chain is encoded by a nucleic acid molecule containing a V_κ and a J_κ human germline segment or a V_λ and a J_λ human germline segment linked in-frame, whereby the nucleic acid molecule within each address is the same and is different from the nucleic acid molecules at all other addresses. Each nucleic acid member are formed from combination of germline segments such that the V_κ and J_κ or V_λ and J_λ germline segments of the nucleic acid molecule encoding a VL chain are linked such that the V_κ segment is 5' to the J_κ segment or the V_λ segment is 5' to the J_λ segment. The library includes a plurality of nucleic acid members that can include all permuations of all combinations of germline segments. In some examples, the plurality of nucleic acid members includes a subset of all germline segments such that a subset of germline V_κ segments are linked with all or a subset of germline J_κ segments, or all or a subset of germline V_λ segments are linked to all or a subset of germline J_λ segments to generate a plurality of nucleic acid molecules encoding a VL chain.

In the VL nucleic acid libraries provided herein, nucleic acid molecules encoded a VL chain are generated by by rearranged nucleic acid sequences combined by joining a human V_κ germline segment and a J_κ germline segment. The V_κ is an IGKV1, IGKV2, IGKV3, IGKV4, IGKV5 or IGKV6, and genes and alleles thereof, for example any set forth in any of SEQ ID NOS:286-355 and 868. Included among the V_κ germline segment contained in nucleic acid members in the libraries provded herein are any where the V_κ has one or more nucleotides inserted or deleted a the V-J joint in the nucleic acid molecule encoding a VL to maintain the reading frame of the VL chain. For example, one or more nucleotides at the 3' end of the V_κ nucleotide sequence is deleted. In other examples, one or more nucleotides is inserted at the 3' end of a V_κ nucleotide sequence to add a nucleotide between the V_κ and J_κ germline segments. The nucleotide can be any nucleotide, and in particular is a guanine (G). The J_κ germline segment is an IGKJ1, IGKJ2, IGKJ3, IGKJ4 and IGKJ5 and genes and alleles thereof, for example, any set forth in any of SEQ ID NOS: 356-364. Included among the J_κ germline segment contained in nucleic acid members in the libraries provided herein are any where the J_κ has one or more nucleotides inserted or deleted at the V-J joint to maintain the reading frame of the VL chain. The insertion or deletion is typically chosen to maintain the reading frame of the J_κ. For example, one or more nucleotides from the 5' end of the J_κ is deleted.

In some examples, the VL nucleic acid libraries provided herein, nucleic acid molecules encoded a VL chain are generated by by rearranged nucleic acid sequences combined by joining a human V_λ germline segment and a J_λ germline segment. The V_λ

germline segment is an IGLV1, IGLV2, IGLV3, IGLV4, IGLV5, IGLV6, IGLV7, IGLV8, IGLV9, IGLV10 and IGLV11 and genes and alleles thereof, for example, any set forth in any of SEQ ID NOS: 365-441. Included among the V_λ germline segment contained in nucleic acid members in the libraries provided herein are any where the V_λ has one or more nucleotides inserted or deleted at the V-J joint of the nucleic acid molecule encoding a VL to maintain the reading frame of the VL chain. For example, one or more nucleotides is from the 3' end of a V_λ nucleotide sequence is deleted. In another example, one or more nucleotides is inserted at the 3' end of a V_λ nucleotide sequence to add a nucleotide between the V_λ and J_λ. The nucleotide can be any nucleotide, in particular a guanine (G). The J_λ germline segment is an IGLJ1, IGLJ2, IGLJ3, IGLJ4, IGLJ5, IGLJ6 and IGLJ7 and genes and alleles thereof, for example, any set forth in any of SEQ ID NOS: 442-451. Included among J_λ germline segments contained in nucleic acid members in the libraries provided herein are any where the J_λ has one or more nucleotides inserted or deleted at the V-J join of the nucleic acid molecule encoding a VL to maintain the reading frame of the VL chain. The insertion or deletion is typically chosed to maintain the reading frame of the J_λ .For example, a nucleotide from the 5' end of the J_λ is deleted.

Any of the plurality of nucleic acid molecules encoding a VL chain in the libraries provided herein can be generated from a subset of germline segments selected based on sequence similarities or differences, gene family, length, composition, CDR length or composition, species, functionality, specificity, group, subgroup. For example, the plurality of nucleic acid molecules encoding a VL chain are generated from a subset of germline segments selected based on CDR and the CDR is CDR3. In another example, the plurality of nucleic acid molecules encoding a VL chain are selected based on gene family, whereby one germline segment from each of a V_κ and/or J_κ or V_λ and/or J_λ gene family is selected or one germline segment from a subset of a V_κ and/or J_κ or V_λ and/or J_λ gene family is selected. In such an example, a V_κ germline segment can include any one or more germline segments from a IGKV1-12, IGKV1-12, IGKV1-16, IGKV1-17, IGKV1-27, IGKV1-33, IGKV1-37, IGKV1-39, IGKV1-5, IGKV1-6, IGKV1-8, IGKV1-9, IGKV1-NL1, IGKV1/OR2, IGKV1D-12, IGKV1D-13, IGKV1D-16, IGKV1-D-17, IGKV1D-33, IGKV1D-37, IGKV1D-39, IGKV1D-42, IGKV1D-43, IGKV1D-8, IGKV2-24, IGKV2-28, IGKV2-29, IGKV2-30, IGKV2-30, IGKV2-40, IGKV2D-24, IGKV2D-26, IGKV2D-28, IGKV2D-29, IGKV2-D-30, IGKV2D-40, IGKV3-11, IGKV3-15, IGKV3-20, IGKV3-7, IGKV3-NL1, IGV3-NL2, IGKV3-NL3, IGKV3-NL4, IGKV3-NL5, IGKV3/OR2-268, IGKV3D-11, IGKV3D-15, IGKV3D-20, IGKV3D-7, IGKV4-1, IGKV5-2, IGKV6-21, IGKV6D-21, IGKV6D-41, or

IGKV1-39 gene family; a J_κ germline segments can include any one or more germline segments from a IGKJ1, IGKJ2, IGKJ3, IGKJ4 and IGKJ5 gene family; a V_λ germline segment can include any one or more germline segments from a IGLV1-36, IGLV1-40, IGLV1-41, IGLV1-44, IGLV1-47, IGLV1-50, IGLV1-51, IGLV10-54, IGLV11-55, IGLV2-11, IGLV2-14, IGLV2-18, IGLV2-23, IGLV2-33, IGLV2-8, IGLV3-1, IGLV3-10, IGLV3-12, IGLV3-16, IGLV3-19, IGLV3-21, IGLV3-22, IGLV3-25, IGLV3-27, IGLV3-32, IGLV3-9, IGLV4-3, IGLV4-60, IGLV4-69, IGLV5-37, IGLV5-39, IGLV5-45, IGLV5-8, IGLV5-52, IGLV6-57, IGLV7-43, IGLV7-46, IGLV8-61, IGLV8-61 and IGLV9-49 gene family; and/or a J_λ germline segment can include any one or more germline segments from a IGLJ1, IGLJ2, IGLJ4, IGLJ5, IGLJ6 and IGLJ7 gene family.

In all of the nucleic acid libraries encoding a VL chain provided herein, the nucleic acid molecule encoding a VL chain can be modified to remove stop codons and/or restriction enzyme sites. Exemplary of nucleic acid molecules in the libraries provided herein include any of SEQ ID NOS:1411-1422, 1424-1439 and 1441-1471, or a subset thereof.

Provided herein is a library of nucleic acid molecules containing a plurality of addressable nucleic acid molecules encoding a variable light (VH) chain. In such libraries, each VH chain is encoded by a nucleic acid molecule containing a a V_H, a D_H and a J_H human germline segment linked in-frame, whereby the nucleic acid molecule within each address is the same and is different from the nucleic acid molecules at all other addresses. Each nucleic acid member is formed from combination of germline segments such that the V_H, a D_H and a J_H human germline segment of the nucleic acid molecule encoding a VH chain are linked such that the V_H segment is 5' to the D_H segment which is 5' to the J_H segment. The library includes a plurality of nucleic acid members that can include all permuations of all combinations of germline segments. In some examples, the plurality of nucleic acid members includes a subset of all germline segments such that a subset of germline V_H segment are linked with all or a subset of germline D_H segments which are linked with all or a subset of germline J_H segments to generate the plurality of nucleic acid molecules encoding a VH chain.

In the VH nucleic acid libraries provided herein, nucleic acid molecules encoded a VH chain are generated by by rearranged nucleic acid sequences combined by joining a human V_H,D_H and J_H germline segments. The V_H is an IGHV1, IGHV2, IGHV3, IGHV4, IGHV5, IGHV6 and IGHV7 and genes and alleles thereof, for example any set forth in any of SEQ ID NOS: 10-238. Included among the V_H germline segment contained in nucleic acid members in the libraries provded herein are any where the V_H has one or more nucleotides

added or removed at the V-D joint in the nucleic acid molecule encoding a VH to maintain the reading frame of the VH chain. For example, one or more nucleotides at the 3' end of the V_H nucleotide sequence is deleted. In other examples, one or more nucleotides is inserted or added at the 3' end of a V_H nucleotide sequence to add a nucleotide between the V_H and D_H germline segments. The nucleotide can be any nucleotide, and in particular is a guanine (G). The D_H germline segment is an IGHD1, IGHD2, IGHD3, IGHD4, IGHD5, IGHD6, and IGHD7 and genes and alleles thereof, for example, any set forth in any of SEQ ID NOS: 239-272. Included among the D_H germline segment contained in nucleic acid members in the libraries provided herein are any where the D_H has one or more nucleotides inserted or deleted at the V-D and/or the D-J joint to maintain the reading frame of the VH chain. The nucleotide insertion or deletion can be any nucleotide, but typically is chosen to maximize the hydrophilicity of the D_H. For example, one or more nucleotides from the 5' end of the D_H is deleted. In other examples, a nucleotide from the 3' end of a D_H is deleted. In further examples, a nucleotide is inserted at the 3' end of a D_H sequence to add a nucleotide been the D_H and J_H. The nucleotide can be any nucleotide, but typically is a guanine (G). The germline segment is an IGHJ1, IGHJ2, IGHJ3, IGHJ4, IGHJ5, and IGHJ6 and genes and alleles thereof, for example, any set forth in any of SEQ ID NOS:273-285. Included among the J_H germline segment contained in nucleic acid members in the libraries provided herein are any where the J_H has one or more nucleotides inserted or deleted at the D-J joint to maintain the reading frame of the VH chain. Typically, the nucleotide insertion or deletion is chosen to maintain the reading frame of the J_H. For example, one or more nucleotides from the 5' end of the J_H is deleted. In another example, one or more nucleotides from the 3' end of the J_H is deleted.

Any of the plurality of nucleic acid molecules encoding a VH chain in the libraries provided herein can be generated from a subset of germline segments selected based on sequence similarities or differences, gene family, length, composition, CDR length or composition, species, functionality, specificity, group, subgroup. For example, the plurality of nucleic acid molecules encoding a VH chain are generated from a subset of germline segments selected based on CDR and the CDR is CDR3. In another example, the plurality of nucleic acid molecules encoding a VH chain are selected based on gene family, whereby one germline segment from each of a V_H, D_H, and/or J_H gene family is selected or one germline segment from a subset of a V_H, D_H, and/or J_H gene family is selected. In such an example, a V_H germline segment can include any one or more germline segments from a IGHV1-18, IGHV1-2, IGHV1-24, IGHV1-3, IGHV1-45, IGHV1-46, IGHV1-58, IGHV1-69, IGHV1-8,

IGHV2-26, IGHV2-5, IGHV2-70, IGHV3-11, IGHV3-13, IGHV3-15, IGHV3-16, IGHV3-20, IGHV3-21, IGHV3-23, IGHV3-30, IGHV3-33, IGHV3-35, IGHV3-38, IGHV3-43, IGHV3-48, IGHV3-49, IGHV3-53, IGHV3-64, IGHV3-66, IGHV3-7, IGHV3-72, IGHV3-73, IGHV3-74, IGHV3-9, IGHV4-28, IGHV4-31, IGHV4-34, IGHV4-39, IGHV4-4, IGHV4-59, IGHV4-61, IGHV5-51, IGHV6-1 and IGHV7-81 gene family; a the D_H germline segment can include any one ore more germline segments from a IGHD1-1, IGHD1-14, IGHD1-20, IGHD1-26, IGHD1-7, IGHD2-15, IGHD2-2, IGHD2-21, IGHD2-8, IGHD3-10, IGHD3-16, IGHD3-22, IGHD3-3, IGHD3-9, IGHD4-11, IGHD4-17, IGHD4-23, IGHD4-4, IGHD5-12, IGHD5-18, IGHD5-24, IGHD5-5, IGHD6-13, IGHD6-19, IGHD6-25, IGHD6-6 and IGHD7-27 gene family; and/or a J_H germline segment can include any one or more germline segments from a IGHJ1, IGHJ2, IGHJ3, IGHJ4, IGHJ5 and IGHJ6 gene family.

In all of the nucleic acid libraries encoding a VH chain provided herein, the nucleic acid molecule encoding a VH chain can be modified to remove stop codons and/or restriction enzyme sites. Exemplary of nucleic acid molecules in the libraries provided herein include any of SEQ ID NOS: 1059-1410, or a subset thereof.

Also provided herein are libraries of addressable vectors containing any of the above nucleic acid molecules encoding a variable light (VL) chain or a variable heavy (VH) chain. Also provided herein are addressable cells, whereby each cell in the library contains any of the above different vectors.

Also provided herein are a library of nucleic acid molecules containing a plurality of addressable nucleic acid molecules encoding a variable light (VL) chain and a plurality of addressable nucleic acid molecules encoding a variable heavy (VH) chain (i.e. paired nucleic acid libraries). In such libraries, each VL chain is encoded by a nucleic acid molecule that contains a V_κ and a J_κ human germline segments or V_λ and J_λ germline segments linked in-frame and each VH chain is encoded by a nucleic acid molecule that contains a V_H, a D_H and a J_H human germline segment. The resulting nucleic acid members in the the nucleic acid molecule encoding the VL chain can be any provided herein and the nucleic acid molecule encoding the VH chain can be any provided herein. In such addressable libraries, each locus contains a nucleic acid molecule encoding a VH chain and a nucleic acid molecule encoding a VL chain, such that the combination of VH nucleic acid molecules and VL nucleic acid molecules within each address is different from the combination of nucleic acid molecules at all other addresses, i.e. the pairs of nucleic acid libraries at each locus are different.

Provided herein is a method of generating human combinatorial antibody libraries. The method includes the steps of a) combining a V_H, a D_H and a J_H human germline segment

or portion thereof in frame to generate a sequence of a nucleic acid molecule encoding a VH chain or a portion thereof and b) combining a V_κ and a J_κ human germline segment or portion thereof, or a V_λ and a J_λ germline segment or portion thereof in frame to generate a sequence of a nucleic acid molecule encoding a VL chain or a portion thereof. In the method provided herein each of the portions of the V_H, D_H, J_H, V_κ , J_κ, V_λ or J_λ in step a) and b) are sufficient to produce an antibody or portion thereof containing a VH or VL or portion thereof that forms a sufficient antigen binding site. In the methods, steps a) and b) are repeated a plurality of times to generate sequences of a plurality of different nucleic acid molecules. The nucleic acid molecules are synthesized to produce two libraries, whereby the first library contains nucleic acid molecules encoding a VH chain or portion thereof and the the second library contains nucleic acid molecules encoding a VL chain or a portion thereof. In the method, a nucleic acid molecule from the first library and from the second library are introduced into a cell (e.g. together such as by co-transformation). The step of introducing nucleic acids into cells is repeated a plurality of times with different pairs of nucleic acid molecules from the first library and the second library resulting in that contain nucleic acid molecules encoding a VH chain and a nucleic acid molecule encoding a VL chain such that the nucleic acid molecules encode a different combination of VH and VL chains from every other cell. The cells are grown to express the antibodies or portions thereof in each cell, thereby producing a plurality of antibodies or portion thereof. The plurality of produced antibody or portion thereof contains a VH and a VL or a sufficient portion thereof to form an antigen binding site and the antibodies or portions thereof are different from those at every other antibody or portions thereof in the library.

The human combinatorial library produced by the method provided herein can be provided as an addressable library. In such methods, each of the various steps can be performed in an addressed format so that throughout the steps of the method the identity of the germline segments, the recombined nucleic acid sequence and/or produced antibody or portion thereof are known by their address. For example, the synthesized nucleic acid sequences are individually addressed, thereby generating a first addressed nucleic acid library and a second addressed nucleic acid library. The nucleic acid molecules can be introduced into addressed cells, whereby each locus contains a cell that contains nucleic acid molecules encoding a different combination of a VH and a VL from every other cell in the addressed library of cells. Upon expression of the antibodies, addressed antibodies are produced whereby each locus contains an antibody containing a VH chain and a VL chain or a portion thereof sufficient to form an antigen binding site. The antibodies or portions thereof at each

locus is the same and is different from those at each and every other locus. Hence, the identify of the antibody or protion thereof is known by its address.

In the method of generating a human combinatorial antibody library provided herein, in step a) the V_H, D_H and J_H germline segments or portions thereof of the nucleic acid molecule encoding a VH chain are combined such that the V_H segment is 5' to the D_H segment which is 5' to the J_H segment; and in step b) the V_κ and J_κ or V_λ and J_λ germline segments or portions thereof of the nucleic acid molecule encoding a VL chain are linked such that the V_κ segment is 5' to the J_κ segment or the V_λ segment is 5' to the J_λ segment. Steps a) and/or b) can be performed manually or can be performed *in silico*, such as by a computer or computer system capable of or programmed to execute computer-readable instructions based on an algorithm for performing a method of combining human germline segments.

In the method provided herein for generating a human combinatorial antibody library, step a) includes the steps of selecting a V_H, a D_H and a J_H germline segment or portion thereof, generating a V-D joint by modifying the germline sequence of the V_H and/or D_H germline segments by insertion or deletion of one or more nucleotides in order to maximize the hydrophilicity of the D_H germline segment, generating a D-J joint by modifying the germline sequence of the D_H and/or J_H germline segments by insertion or deletion of one or more nucleotides to maintain the reading frame of the J_H, and combining the resulting V_H, D_H, and J_H, to generate a sequence of a nucleic acid molecule encoding a VH chain. In such a method, the V-D joint can be generated by deletion of one or more, for example one, nucleotide from the 5' end of the D_H germline segment. In another example, the V-D joint can be generated by deleting one or more nucleotides from the 3' end of the V_H germline segment. In a further example, the V-D joint can be generated by inserting one or more nucleotides at the 5' end of the D_H germline segment. For example, the inserted or added nucleotide or nucleotides can be any nucleotide, and in particular is a guanine (G). Further, the D-J joint can be generated by deletion of one or more nucleotides from the 5' end of the J_H. In another example, the D-J joint is generated by inserting a nucleotide from the 3' end of the D_H germline segment. The inserted or added nucleotide or nucleotides can be any nucleotide, and in particular is a guanine (G).

In the method provided herein for generating a human combinatorial antibody library, step b) includes the steps of selecting V_κ and J_κ or V_λ and J_λ germline segment or portion thereof, generating a V-J joint by modifying the germline sequence of the V_κ or J_κ by insertion or deletion of one or more nucleotides to maintain the reading frame of the J_κ, or by modifying

the germline sequence of the V_λ or J_λ by insertion or deletion of one or more nucleotides to maintain the reading frame of the J_λ, and combining the resulting V_κ and J_κ or V_λ and J_λ to generate a sequence of a nucleic acid molecule encoding a VL chain. In such a method, the V-J joint can be generated by deletion of one or more, for example one, nucleotide from the 5' end of the of the J_κ or J_λ germline segment. In another example, the V-J joint can be generated by deleting one or more nucleotides from the 3' end of the V_κ or V_λ germline segment. In a further example, the V-J joint can be generated by inserting one or more nucleotides at the 5' end of the J_κ or J_λ germline segment. For example, the inserted or added nucleotide or nucleotides can be any nucleotide, and in particular is a guanine (G).

In the methods of generating a combinatorial library provided herein, steps a) and b) are repeated a plurality of times. Repeating step a) a plurality of times includes selecting N1 (i.e. a first number) of different V_H germline segments, selecting N2 (i.e. a second number) of different D_H germline segments and selecting N3 (a third number) of different J_H sequences. The N1, N2 and N3 numbers can be the same or different, and can include all respective germline segments or a subset thereof. Generally, the N1, N2 and N3 are a number of germline segments that can be all or a subset of V_H, D_H or J_H germline segments, respectively. In the method of repeating step a) a plurality of times, all possible combination of V_H, D_H and J_H combinations are made to generate N1 x N2 x N3 different nucleic acid sequences encoding a VH chain.

For example, in the method of generating a human combinatorial antibody library provided herein, a V_H germline segment (including N1 different V_H germline segments) can be selected from all or a subset of an IGHV1, IGHV2, IGHV3, IGHV4, IGHV5, IGHV6 or IGHV7 and genes and alleles thereof, for example, a V_H germline segment set forth in any of SEQ ID NOS: 10-238. A D_H germline segment can be selected from all or a subset of an IGHD1, IGHD2, IGHD3, IGHD4, IGHD5, IGHD6, or IGHD7 and genes and alleles thereof, for example, a D_H germline segment set forth in any of SEQ ID NOS: 239-272. A J_H germline segment can be selected from all or a subset of IGHJ1, IGHJ2, IGHJ3, IGHJ4, IGHJ5, or IGHJ6 and genes and alleles thereof, for example, a J_H germline segment set forth in any of SEQ ID NOS: 273-285.

In any of the above examples, the method can include in step a) selecting a subset of germline segments based on sequence similarities or differences, gene family, length, composition, CDR length or composition, species, functionality, specificity, group or subgroup. For example, the subset of germline segments can be seleced based on gene family. In the methods, germline segments can be selected such that one germline segment

from each of a a V_H, D_H, and/or J_H gene family is selected or one germline segment from a subset of a V_H, D_H, and/or J_H gene family is selected. V_H gene families include, but are not limited to, a IGHV1-18, IGHV1-2, IGHV1-24, IGHV1-3, IGHV1-45, IGHV1-46, IGHV1-58, IGHV1-69, IGHV1-8, IGHV2-26, IGHV2-5, IGHV2-70, IGHV3-11, IGHV3-13, IGHV3-15, IGHV3-16, IGHV3-20, IGHV3-21, IGHV3-23, IGHV3-30, IGHV3-33, IGHV3-35, IGHV3-38, IGHV3-43, IGHV3-48, IGHV3-49, IGHV3-53, IGHV3-64, IGHV3-66, IGHV3-7, IGHV3-72, IGHV3-73, IGHV3-74, IGHV3-9, IGHV4-28, IGHV4-31, IGHV4-34, IGHV4-39, IGHV4-4, IGHV4-59, IGHV4-61, IGHV5-51, IGHV6-1 and IGHV7-81 gene families including genes and alleles thereof. D_H gene families include, but are not limited to, a IGHD1-1, IGHD1-14, IGHD1-20, IGHD1-26, IGHD1-7, IGHD2-15, IGHD2-2, IGHD2-21, IGHD2-8, IGHD3-10, IGHD3-16, IGHD3-22, IGHD3-3, IGHD3-9, IGHD4-11, IGHD4-17, IGHD4-23, IGHD4-4, IGHD5-12, IGHD5-18, IGHD5-24, IGHD5-5, IGHD6-13, IGHD6-19, IGHD6-25, IGHD6-6 and IGHD7-27 gene families including genes and alleles thereof. The J_H gene families include, but are not limited to, a IGHJ1, IGHJ2, IGHJ3, IGHJ4, IGHJ5 and IGHJ6 gene families including genes and alleles thereof.

In the methods of generating a combinatorial library provided herein, steps a) and b) are repeated a plurality of times. Repeating step b) a plurality of times includes selecting N1 (i.e. a first number) of different V_λ germline segments and selecting N2 (i.e. a second number) different J_λ germline segments or selecting N3 (a third number) of different V_κ germline segments and selecting N4 (i.e. a fourth number) of different J_κ germline segments. The N1, N2, N3 and N4 numbers can be the same or different, and can include all respective germline segments or a subset thereof. Generally, the N1, N2, N3 and N4 are a number of germline segments that can be all or a subset of V_λ, J_λ, V_κ, J_κ germline segments, respectively. In the method of repeating step b) a plurality of times, all possible combination of V_λ, J_λ, V_κ, J_κ combinations are made to generate N1 x N2 or N3 x N4 different nucleic acid sequences encoding a VL chain.

For example, in the method of generating a human combinatorial antibody library provided herein, a V_λ germline segment (including N1 different V_λ germline segments) can be selected from all or a subset of an IGLV1, IGLV2, IGLV3, IGLV4, IGLV5, IGLV6, IGLV7, IGLV8, IGLV9, IGLV10 and IGLV11 and genes and alleles thereof, for example, a V_λ germline segment set forth in any of SEQ ID NOS: 365-441. A J_λ germline segment can be selected from all or a subset of an IGLJ1, IGLJ2, IGLJ3, IGLJ4, IGLJ5, IGLJ6 and IGLJ7 and genes and alleles thereof, for example, a J_λ germline segment set forth in any of SEQ ID NOS: 442-451. A V_κ germline segment can be selected from all or a subset of IGKV1,

IGKV2, IGKV3, IGKV4, IGKV5 and IGKV6, and genes and alleles thereof, for example, a V_κ germline segment set forth in any of SEQ ID NOS: 286-355 and 868. A J_κ germline segment can be selected from all or a subset of a IGKJ1, IGKJ2, IGKJ3, IGKJ4 and IGKJ5 and genes and alleles thereof, for example, a J_κ germline segment set forth in any of SEQ ID NOS: 356-364.

In any of the above examples, the method can include in step b) selecting a subset of germline segments based on sequence similarities or differences, gene family, length, composition, CDR length or composition, species, functionality, specificity, group or subgroup. For example, the subset of germline segments can be seleced based on gene family. In the methods, germline segments can be selected such that one germline segment from each of a V_κ and/or J_κ or V_λ and/or J_λ gene family is selected or one germline segment from a subset of a V_κ and/or J_κ or V_λ and/or J_λ gene family is selected. V_κ gene families include, but are not limited to, a IGKV1-12, IGKV1-12, IGKV1-16, IGKV1-17, IGKV1-27, IGKV1-33, IGKV1-37, IGKV1-39, IGKV1-5, IGKV1-6, IGKV1-8, IGKV1-9, IGKV1-NL1, IGKV1/OR2, IGKV1D-12, IGKV1D-13, IGKV1D-16, IGKV1-D-17, IGKV1D-33, IGKV1D-37, IGKV1D-39, IGKV1D-42, IGKV1D-43, IGKV1D-8, IGKV2-24, IGKV2-28, IGKV2-29, IGKV2-30, IGKV2-30, IGKV2-40, IGKV2D-24, IGKV2D-26, IGKV2D-28, IGKV2D-29, IGKV2-D-30, IGKV2D-40, IGKV3-11, IGKV3-15, IGKV3-20, IGKV3-7, IGKV3-NL1, IGV3-NL2, IGKV3-NL3, IGKV3-NL4, IGKV3-NL5, IGKV3/OR2-268, IGKV3D-11, IGKV3D-15, IGKV3D-20, IGKV3D-7, IGKV4-1, IGKV5-2, IGKV6-21, IGKV6D-21, IGKV6D-41, and IGKV1-39 gene families including genes and alleles thereof. V_λ gene families include, but are not limited to, a IGLV1-36, IGLV1-40, IGLV1-41, IGLV1-44, IGLV1-47, IGLV1-50, IGLV1-51, IGLV10-54, IGLV11-55, IGLV2-11, IGLV2-14, IGLV2-18, IGLV2-23, IGLV2-33, IGLV2-8, IGLV3-1, IGLV3-10, IGLV3-12, IGLV3-16, IGLV3-19, IGLV3-21, IGLV3-22, IGLV3-25, IGLV3-27, IGLV3-32, IGLV3-9, IGLV4-3, IGLV4-60, IGLV4-69, IGLV5-37, IGLV5-39, IGLV5-45, IGLV5-8, IGLV5-52, IGLV6-57, IGLV7-43, IGLV7-46, IGLV8-61, IGLV8-61 and IGLV9-49 gene families including genes and alleles thereof. The J_λ gene families include, but are not limited to, a IGLJ1, IGLJ2, IGLJ4, IGLJ5, IGLJ6 and IGLJ7 gene families including genes and alleles thereof.

In any of the methods above of generating a human combinatorial antibody library, the germline segments can be included in a user-created database, for example, to provide convenient access to such sequences. In practicing the method, the sequences of the J_H, J_κ, and J_λ germline segment in the database are set forth in their correct reading frame (e.g., such as is set forth in Table 13).

The methods provided herein can further include a step after steps a) and/or b) of modifying the nucleic acid sequences encoding a VH chain or a portion thereof and/or modifying the nucleic acid sequences encoding a VL chain or a portion thereof. For example, the nucleic acid sequences can be modified by removing any internal stop codons. Generally, modification of stop codon(s) is made by making only one or two nucleotide changes to the nucleic acid sequences. The codon triplet for a stop codon can be changed to any other codon triplet encoding an amino acid. For example, the stop codon TAA can be modified to be TAT, the stop codon TAG can be modified to be TAT and the stop codon TGA can be modified to be TCA. In another example, the nucleic acid sequences can be modified by removing any internal restriction sites. The nucleotides recognized by a restriction enzyme can be modified to any other nucleotide sequence so long as the sequence is not recognized by a restriction enzyme of interest, i.e. one used in subsequent cloning steps. Generally, only one or two nucleotides changes are made. Typically, modification of restriction sites are made to maximize codon usage in *E. coli*.

In the methods of generating a human combinatorial antibody library provided herein, the plurality of nucleic acid sequences encoding a VH chain include, but are not limited to, any set forth in any of SEQ ID NOS: 1059-1410, or a subset thereof. The plurality of nucleic acid sequences encoding a VL chain include, but are not limited to, any set forth in any of SEQ ID NOS: 1411-1422, 1424-1439 and 1441-1471, or a subset thereof.

In any of the methods provided herein of generating a human combinatorial antibody library, the plurality of nucleic acid sequences encoding a VH chain and/or the plurality of nucleic acid sequences encoding a VL chain can be ranked. For example, the sequences can be ranked based on sequence similarity (e.g. performed by sequence alignment or other methods known in the art and described herein). The sequence similarity between and among the plurality of different nucleic acid molecules encoding a VH chain and/or the sequence similarity between and among the plurality of different nucleic acid molecules encoding a VL chain can be determined. A subset of nucleic acid sequences encoding a VH chain and/or a VL chain can be selected (*e.g.* for synthesis and subsequent expression) such that the selected sequences include those that are the most similar or are the most different from other selected sequences.

In the method provided herein for generating a combinatorial antibody library, the synthesized nucleic acid sequences in the addressed libraries are contained in vectors. Hence, a vector from a first vector library containing nucleic acid sequences encoding a VH chain and a vector from a second vector library containing nucleic acid sequences encoding a VL

chain are introduced into addressed cells for generation and production of antibody members of the library. The vector can further contain all or a portion of a constant region sufficient to permit association of heavy and light chains. For example, the vector can contain a C_{H1} and C_L such that the resulting encoded antibody is a Fab. In the methods provided herein, the cells include prokaryotic or eukaryotic cells. For example, cells include *E.coli* cells. In the methods of generating a combinatorial antibody library provided herein, the addressed cells can be arranged in a spatial array. The spatial array includes, for example, a multi-well plate such that each individual locus of the plate corresponds to a cell that contains nucleic acid molecules encoding a different combination of a VH and a VL compared to every other cell in the addressed library of cells.

The antibody or portions thereof that are expressed in the method provided herein include a full length antibody or a fragment or portion thereof sufficient to form an antigen binding site. For example, the expressed antibody is a Fab. The methods provided herein, further can include a step of purifying the antibodies or portions thereof. The antibodies or portion thereof in the libraries include those that are 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% pure. Hence, the addressable library includes antibody members that are purified such that the purified antibodies or portions thereof are addressed, and the antibody within each address is the same antibody and is different from all other antibodies at all other addresses in the library.

Also provided herein, is an addressable combinatorial antibody library produced by the method provide herein of generating a combinatorial antibody library. Such an antibody library includes members each containing a VH chain having a sequence of amino acids selected from among any of SEQ ID NOS: 1475-836 and a VL chain having a sequence of amino acids selected from among any of SEQ ID NOS: 1827-1838, 1840-1855 and 1857-1888.

Provided herein is a method of screening a human combinatorial antibody library for binding or activity against a target protein to identify antibodies or portions thereof that bind to a target protein and/or modulate an activity of a target protein. In such methods, a human combinatorial antibody library is provided. The library includes any human combinatorial antibody library provided herein or any human combinatorial antibody library produced by the methods provided herein. In such methods, the an antibody or portion thereof in the library is contacted with a target protein and binding of the antibody or portion thereof with the target protein and/or modulation of a functional activity by an antibody or portion thereof in the library is assessed. Antibodies or portions thereof that bind to the target protein and/or

modulate an activity of the target protein are identified, whereby the identified antibody or portion thereof is designated as a "HIT." In such methods, for example, the human combinatorial antibody library is an addressable library and contacting is performed in an addressable array, such that the identity of the "Hit" is known by its address. For example, screening is performed in a spatial array, such as a microwell plate.

In the methods of screening provided herein, the target protein is a membrane-bound protein, a cell surface receptor (CSR) or a CSR ligand. The membrane-bound protein or CSR includes, but is not limited to, a cytokine receptor, a receptor kinase, a receptor phosphatase, a receptor involved in cell-cell interactions or a cellular adhesion molecule. For example, the target protein includes, but is not limited to, VEGFR-1, VEGFR-2, VEGFR-3, a epidermal growth factor receptor (EGFR), ErbB-2, ErbB-b3, IGF-R1, C-Met, TNF-R1, TNF-R2, BTLA, HVEM, LT-βR, CD20, CD3, CD25, NOTCH, DLL4, G-CSF-R, GM-CSF-R, EPO-R, a cadherin, an integrin, CD52 and CD44, a VEGF-A, VEGF-B, VEGF-C, VEGF-D, PIGF, EGF, HGF, TNF-α, LIGHT, lymphotoxin (LT), IgE, G-CSF, GM-CSF and EPO.

In some examples, the binding of the antibody or portion thereof to the target protein is assessed. In other examples, modulation of a functional activity of the target protein by an antibody or portion thereof is assessed. The functional activity includes, but is not limited to, cellular proliferation, lymphoma apoptosis, chemotaxis, cancer cell invasion, matrigel, endothelial proliferation, tube formation and signal transduction.

In the methods of screening provided herein, binding can be assessed on cells and/or a functional activity can be assessed in a cell-based activity. In such examples, the cells express the target protein, typically on their surface as a membrane-bound or extracellular receptor, ligand or adhesion protein. For example, the cells can be transiently or stably expressed with a nucleic acid molecule encoding the target protein.

Provided herein is a method of screening that includes after identifying a "Hit", for example, in a previous iteration of the method of screening as provided above, a second library combinatorial antibody library is provided. In such examples, the second combinatorial antibody library is based on the identified "Hit." For example, the second library is generated by selecting V_H, D_H and J_H human germline segments that are related by sequence similarity to the germline segments of the identified HIT(s), and combining all possible V_H, D_H and J_H human germline segments or portions thereof in frame to generate a plurality of sequences of nucleic acid molecules each encoding a different VH chain or a portion thereof and selecting V_κ and a J_κ or V_λ and a J_λ human germline segments that are related by sequence similarity to the germline segments of the identified HIT(s), and

combining all possible V_κ and a J_κ human germline segments or portions thereof, or all possible V_λ and a J_λ germline segment or portions thereof in frame to generate a plurality of sequences of nucleic acid molecule each encoding a different VL chain or a portion thereof. The portions of the V_H, D_H, J_H, V_κ , J_κ, V_λ or J_λ are sufficient to produce an antibody containing a VH or VL or portion thereof that is sufficient to bind to an antigen. Upon combination of the germline segments, the nucleic acid molecules are synthesized to produce a first library that contains nucleic acid molecules encoding a VH chain or a portion thereof and a second library that contains nucleic acid molecules encoding a VL chain or a portion thereof. A nucleic acid molecule from the first library and from the second library is introduced into a cell and the steps are repeated a plurality of times to produce a library of cells such that each cell contains nucleic acid molecules encoding a different combination of VH and VL from every other cell in the library of cells. The cells are grown to express the antibodies in each cell, thereby producing a plurality of antibodies or portion thereof such that each produced antibody or portion thereof in the library contains a different combination of a VH and a VL chain or a sufficient portion thereof to form an antigen binding site from all other antibodies or portions thereof in the library. The antibodies are further purified to generate a second human combinatorial antibody library. In such examples, the second human combinatorial antibody library is generated such that the sequence similarity between and among related germline segments is or is about 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more.

In another example, a second combinatorial antibody library is provided that is generated by selecting a plurality of nucleic acid molecules encoding a VH chain that contain a V_H, a D_H or a J_H human germline segment that is the same as contained in the nucleic acid molecule encoding the identified HIT and selecting a plurality of nucleic acid molecules encoding a VL chain that contains a V_κ and a J_κ or a V_λ and a J_λ human germline segment that is the same as contained in the nucleic acid molecule encoding the identified HIT. A nucleic acid molecule from the plurality of nucleic acid molecules encoding a VL and a nucleic acid molecule from the plurality of nucleic acid molecules encoding a VH are introduced into a cells and the cells are grown. This is repeated a plurality of times to produce a library of cells, whereby each cells contains nucleic acid molecules encoding a different combination of a VH and a VL chain from every other cell in the library. Upon expression of the antibodies in each cell, a plurality of antibodies or portions thereof is produced. Each antibody or portion thereof in the library contains a different combination of a VH and a VL chain or a sufficient portion thereof to form an antigen binding site from all other antibodies or portions

thereof in the library. The antibodies or portions thereof are purified to generate a second combinatorial antibody library.

In additional examples, a second combinatorial library is provided based on the identified HIT(s) that is generated by introducing amino acid mutations into the "HIT" to generate a plurality of antibodies or portions thereof. Each antibody member or portion thereof in the second combinatorial antibody library differs from the identified "HIT" by one or more amino acid mutations in its primary sequence. In such examples, the amino acid mutations are in the complementarity determining regions (CDRs) of the identified HIT.

In each of the methods above, the second human combinatorial library is contacted with a target protein and binding of the antibody or portion thereof with the target protein and/or modulation of a functional activity by an antibody or portion thereof in the library is assessed. Antibodies or portions thereof that bind to the target protein and/or modulate an activity of the target protein are identified, whereby the identified antibody or portion thereof is designated as a further "HIT." In some examples, the second combinatorial antibody library is an addressable library such that the purified antibodies or portions thereof are addressed and each purified antibody within each address is the same antibody and is different from the antibodies at all other addresses. In such examples, contacting is performed in an addressable array, such that the identity of the "Hit" is known by its address. For example, screening is performed in a spatial array, such as a microwell plate.

In any of the examples of screening provided above, the method is repeated iteratively until a further "HIT" is identified having an optimized binding affinity for a target protein and/or having an activity that is optimized against a target protein compared to previous "HITS" in earlier iterations of the method.

Provided herein is an anti-DLL4 antibody that contains a VH chain encoded by a sequence of nucleotides compiled from a V_H, D_H and J_H germline segment and a VL chain encoded by a sequence of nucleotides compiled from a V_κ and J_κ or V_λ and J_λ germline segments. The V_H germline segment is an IGHV1, and IGHV5 or an IGHV6 or genes and alleles thereof; the D_H germline segment is an IGHD6, and IGHD5 or an IGHD3 or genes and alleles thereof; and the J_H germline segment is an IGHJ1 or an IGHJ4 or genes and alleles thereof. The V_κ germline segment is a IGKV3 and the Jκ is a IGKJ1 or genes and alleles thereof; the V_λ germline segment is a IGLV8 or an IGLV5 and the J_λ germline segment is a IGLJ1 or a IGLJ4 or genes and alleles thereof. The anti- DLL4 antibodies provided herein bind DLL4 and/or modulates an activity of DLL4.

In some examples, the V_H germline segment is an IGHV1-46*01, IGHV1-46*02 or an IGHV1-46*03 or an IGHV6-1*01 or an IGHV6-1*02. The D_H germline segment is an IGHD6-6*01, IGHD5-18*01, IGHD3-3*01 or IGHD3-3*02. The J_H germline segment is an IGHJ1*01, IGHJ4*01, IGHJ4*02 or IGHJ4*03. The Vκ germline segment is an IGKV3-11*01 or IGKV3-11*02. The Jκ germline segment is a IGKJ1*01. The V_λ germline segment is a IGLV8-61*01, IGLV8-61*02, IGLV8-61*03 or IGLV5-48*01. The J_λ germline segment that is a IGLJ1*01 or IGLJ4*01. For example, The anti-DLL4 antibody provided herein is an antibody or portion thereof containing a a VH chain encoded by a sequence of nucleotides compiled from an IGHV1-46*01, IGHD6-6*01 and IGHJ1*01 and a VL chain encoded by a sequence of nucleotides compiled from IGKV3-11*01 and IGKJ1*01 germline segments; a VH encoded by a sequence of nucleotides compiled from IGHV5-51*03, IGHD5-18*01 and IGHJ4*01 germline segments and a VL chain encoded by a sequence of nucleotides compiled from an IGLV8-61*01 and IGLJ1*01 germline segments; or a VH chain encoded by a sequence of nucleotides compiled from an IGHV6-1*01, and IGHD3-3*01 and an IGHJ4*01 germline segments and a VL chain encoded by a sequence of nucleotides compiled from an IGLV5-48*01 and a IGLJ4*01 germline segments. Anti-DLL4 antibodies provided herein include, but are not limited to, antibodies containing a VH chain having a sequence of amino acids set forth in SEQ ID NO: 1513 and a VL chain having a sequence of amino acids set forth in SEQ ID NO:1850; a VH chain having a sequence of amino acids set forth in SEQ ID NO: 1803 and a VL chain having a sequence of amino acids set forth in SEQ ID NO:1881; or a VH chain having a sequence of amino acids set forth in SEQ ID NO: 1812 and a VL chain having a sequence of amino acids set forth in SEQ ID NO:1884. For example, exemplary of an anti-DLL4 antibody provided herein is an antibody containing a VH chain having a sequence of amino acids set forth in SEQ ID NO: 1513 and a VL chain having a sequence of amino acids set forth in SEQ ID NO:1850 Antibodies that include portions of any of the above antibodies that form a sufficient antigen binding site that bind to anti-DLL4 and/or modulate an activity of DLL4 also are provided. Also provided are any antibodies that contain conservative amino acid changes in their sequence compared to any of the antibodies provided herein.

Provided herein is an anti-EpoR antibody containing a VH chain encoded by a sequence of nucleotides compiled from a V_H, D_H and J_H germline segment and a VL chain encoded by a sequence of nucleotides compiled from a V_κ and J_κ germline segments. The V_H germline segment is an IGHV1or genes and alleles thereof. The D_H germline segment is an IGHD6 or an IGHD3 or genes and alleles thereof. The J_H germline segment is an IGHJ1 or

genes and alleles thereof. The V_κ germline segment is an IGKV4. The Jκ is an IGKJ1. The anti-EpoR antibodies provided herein bind EpoR and/or modulate an activity of EpoR.

In some examples, the V_H germline segment is an IGHV1-46*01, IGHV1-46*02 or an IGHV1-46*03. The the D_H germline segment is an IGHD6-6*01, IGHD3-10*01 or IGHD3-10*02. The J_H germline segment is an IGHJ1*01, IGHJ4*01, IGHJ4*02 or IGHJ4*03. The Vκ germline segment is an IGKV4-1*01. theJκ germline segment that is a IGKJ1*01. For example, the anti-EpoR antibody provided herein contains a VH chain encoded by a sequence of nucleotides compiled from an IGHV1-46*01, IGHD3-10*01 and IGHJ4*01 and a VL chain encoded by a sequence of nucleotides compiled from IGKV4-1*01 and IGKJ1*01 germline segments or contains a VH chain encoded by a sequence of nucleotides compiled from IGHV1-46*01, IGHD6-6*01 and IGHJ1*01 germline segments and a VL chain encoded by a sequence of nucleotides compiled from an IGKV4-1*01 and IGKJ1*01 germline segments. Anti-EpoR antibodies provided herein include, but are not limited to, an antibody containing a VH chain having a sequence of amino acids set forth in SEQ ID NO: 1509 and a VL chain having a sequence of amino acids set forth in SEQ ID NO:1838; or a VH chain having a sequence of amino acids set forth in SEQ ID NO: 1513 and a VL chain having a sequence of amino acids set forth in SEQ ID NO:1838. Antibodies that include portions of any of the above antibodies that form a sufficient antigen binding site that bind to anti-EpoR and/or modulate an activity of EpoR also are provided. Also provided are any antibodies that contain conservative amino acid changes in their sequence compared to any of the antibodies provided herein.

Provided herein is an anti-ErbB2 antibody containing a VH chain encoded by a sequence of nucleotides compiled from a V_H, D_H and J_H germline segment and a VL chain encoded by a sequence of nucleotides compiled from a V_κ and J_κ germline segments. The V_H germline segment is an IGHV4 or an IGHV1or genes and alleles thereof. the D_H germline segment is an IGHD6 or an IGHD1 or genes and alleles thereof. The J_H germline segment is an IGHJ1 or an IGHJ2 or genes and alleles thereof. The V_κ germline segment is a IGKV3 or IGKV4. The Jκ is an IGKJ1 or genes and alleles thereof The anti-ErbB2 antibodies provided herein bind ErbB2 and/or modulate an activity of ErbB2.

In some examples, the V_H germline segment is an the V_H germline segment is an IGHV1-46*01, IGHV1-46*02 or an IGHV1-46*03 or an IGHV4-31*01, IGHV4-31*02, IGHV4-31*03, IGHV4-31*04, IGHV4-31*05, IGHV4-31*06, IGHV4-31*07, IGHV4-31*08, IGHV4-31*09, IGHV4-31*10. The D_H germline segment is an IGHD6-6*01 or IGHD1-26*01. The J_H germline segment is an IGHJ1*01 or an IGHJ2*01. The Vκ germline segment

is an IGHV3-20*01, IGHV3-20*02 or IGKV4-1*01. The Jκ germline segment that is a IGKJ1*01. For example, the anti-ErbB2 antibody provided herein a VH chain encoded by a sequence of nucleotides compiled from an IGHV4-31*02, IGHD1-26*01 and IGHJ2*01and a VL chain encoded by a sequence of nucleotides compiled from IGKV3-20*01 and IGKJ1*01 germline segments or contains a VH encoded by a sequence of nucleotides compiled from IGHV1-46*01, IGHD6-6*01 and IGHJ1*01 germline segments and a VL chain encoded by a sequence. Anti-ErbB2 antibodies provided herein include, but are not limited to, an antibody containing a VH chain having a sequence of amino acids set forth in SEQ ID NO: 1760 and a VL chain having a sequence of amino acids set forth in SEQ ID NO:1833; or a VH chain having a sequence of amino acids set forth in SEQ ID NO: 1513 and a VL chain having a seqene of amino acids set forth in SEQ ID NO:1838. Antibodies that include portions of any of the above antibodies that form a sufficient antigen binding site that bind to anti-ErbB2 and/or modulate an activity of ErbB2 also are provided. Also provided are any antibodies that contain conservative amino acid changes in their sequence compared to any of the antibodies provided herein.

Any of the antibodies provided herein can further contain a constant region or a portion of a constant region sufficient to permit association of a heavy and light chain. For example, antibodies provided herein include Fab antibodies. In addition, any of the antibodies provided herein include antibodies having a binding affinity that is or is about 10^{-6}M, 10^{-7}M, 10^{-8}M, 10^{-9}M, 10^{-10}M, 10^{-11}M or 10^{-12}M or lower. For example, any of the antibodies provided herein have a binding affinity that is or is about 1 x 10^{-9}M, 2 x 10^{-9}M, 3 x 10^{-9}M, 4 x 10^{-9}M, 5 x 10^{-9}M, 6 x 10^{-9}M, 7 x 10^{-9}M, 8 x 10^{-9}M, 9 x 10^{-9}M, 1 x 10^{-10}M, 2 x 10^{-10}M, 3 x 10^{-10}M, 4 x 10^{-10}M, 5 x 10^{-10}M, 6 x 10^{-10}M, 7 x 10^{-10}M, 8 x 10^{-10}M, 9 x 10^{-10}M or less.

Provided herein are methods of treatment using any of the antibodies provided herein, including any of the antibodies identified in the screening method provided herein. Such antibodies can be used to treat diseases or disorders associated with epression and/or activity of the target protein. In one example, provided herein are methods of treatment or uses of treating or formulating a medicament with any of the anti-DLL4 antibodies provided herein for treating a disease or disorder associated with expression and/or activity of DLL4. In another example, provided herein are methods of treatment or uses of treating or formulation of a medicament with any of the anti-EpoR antibodies provided herein for treating a disease or disorder associated with expression and/or activity of EpoR. In an additional example,

provided herein are methods of treatment using anti-ErbB2 antibodies provided herein for treating a disease or disorder associated with expression and/or activity of ErbB2.

Provided herein is a computer system or a computer readable medium that contains computer-readable instructions executable by a computer device for performing a method of combining human germline segments. The method of combinaing human germline segments includes thes steps of (a) accessing a user-created *in silico* database of all available human antibody germline segments (V_H, D_H, J_H, V_κ, J_κ, V_λ and J_λ); (b) applying an algorithm to generate a collection of every possible recombined full length nucleic acid sequence encoding a heavy chain (5'-V_H-D_H-J_H-3'); (c) applying an algorithm to generate a collection of every possible recombined full length nucleic acid sequence encoding a kappa light chains (5'-V_κ-J_κ-3') and/or every possible recombined full length nucleic acid sequence encoding a lambda light chains (5'-V_λ-J_λ-3'); (d) applying an algorithm to modify nucleotides at the V-D and/or D-J joints of the nucleic acid sequences of (b) and at the V-J joints of the nucleic acid sequences of (c) so that the resulting nucleic acids sequences are in frame; (e) modifying the nucleic acid sequences of (d) to remove any inadvertently generated stop codons; (f) assigning each recombined nucleic acid sequence to a unique locus of an addressable format; and (g) generating an output file that identifies the address of each recombined nucleic acid sequences. The method executed by the computer system or computer readable medium can further include (h) after step (e) adding nucleotides at the 5' and 3' termini of the recombined nucleic acid sequences containing a sequence recognized by a restriction enzyme; and (i) modifying the recombined nucleic acid sequence by nucleotide replacement to remove internal nucleotides that are recognized by a restriction enzyme. The method can further modify the recombined nucleic acid sequences to optimize codon usage for bacterial expression. In some examples, the method executed by the computer system or computer readable medium can include before step (f) selecting recombined nucleic acid sequence(s) from the library of recombined nucleic acid sequences based on sequence similarities or differences and assigning only the selected sequences to a locus in an addressable format in step f).

Provided herein is a method that includes execution of computer-readable instructions for performing a method of combining human germline segments by a computer device, whereby the method includes the steps of (a) accessing a user-created *in silico* database of all available human antibody germline segments (V_H, D_H, J_H, V_κ, J_κ, V_λ and J_λ); (b) applying an algorithm to generate a collection of every possible recombined full length nucleic acid sequence encoding a heavy chain (5'-V_H-D_H-J_H-3'); (c) applying an algorithm to generate a

collection of every possible recombined full length nucleic acid sequence encoding a kappa light chains (5'-V_κ-J_κ-3') and/or every possible recombined full length nucleic acid sequence encoding a lambda light chains (5'-V_λ-J_λ-3'); (d) applying an algorithm to modify nucleotides at the V-D and/or D-J joints of the nucleic acid sequences of (b) and at the V-J joints of the nucleic acid sequences of (c) so that the resulting nucleic acids sequences are in frame; (e) modifying the nucleic acid sequences of (d) to remove any inadvertently generated stop codons; (f) assigning each recombined nucleic acid sequence to a unique locus of an addressable format; and (g) generating an output file that identifies the address of each recombined nucleic acid sequences. The method further includes DNA synthesis of the recombined nucleic acid sequences encoding a heavy chain, encoding a kappa light chain, and/or encoding a lambda light chain, or DNA synthesis of a subset of recombined nucleic acid sequences encoding a heavy chain, encoding a kappa light chain, and/or encoding a lambda light chain.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1: Schematic illustration of the method for generating antibody diversity

Figure 1 illustrates how antibody diversity is generated, including combinatorial diversity, pairing diversity, and junctional diversity.

Figure 2: Schematic illustration of iterative methods of antibody discovery

Figure 2a is a depiction of the methods of 1) combining heavy and light germ line segments to generate nucleic acid sequences encoding a variable heavy and light chain; 2) synthesizing the nucleic acid molecules; 3) generating a plurality of antibodies by expression and association of the heavy and light chains; purifying the antibodies (*e.g.* using Piccolo and FLPC purification) and screening the antibodies for an activity (*e.g.* binding or a functional activity). Figure 2b is a depiction of iterative methods to identify additional related antibodies involving repeating the method based on identified "HITS" to identify HITs that are optimized or improved for the activity.

Figure 3: Plasmid A vector map

Figure 3 is an illustrative vector map of plasmid A, provided and described in detail herein.

Figure 4: Plasmid D vector map

Figure 4 is an illustrative vector map of plasmid D, provided and described in detail herein.

Figure 5: Plasmid C vector map

Figure 5 is an illustrative vector map of plasmid C, provided and described in detail herein.

Figure 6: Plasmid E vector map

Figure 6 is an illustrative vector map of plasmid E, provided and described in detail herein.

Figure 7: Schematic illustration of DNA Sequence Compilation Software modules

Figure 7 illustrates the 10 modules that are contained within the DNA Sequence Compilation Software. As illustrated, there are four layers, including the GUI (Graphical User Interface), the GUI Controls, the Compilation rules and the NCBI tools. In addition, the associations between the modules are illustrated.

Figure 8: Algorithm for heavy and light chain combinations

Figure 8 is a schematic diagram of the algorithm for generating recombined nucleic acid sequences from germline segments encoding a variable heavy chain or a variable light chain.

Figure 9: Algorithm for sequence compilation

Figure 9 is a flow chart for modifying recombined nucleic acid sequences encoding a functional variable heavy chain or a variable light chain.

Figure 10: Algorithm for ranking sequences

Figure 10 is a flow chart for ranking recombined variable heavy and light chains based on diversity score and cluster information.

Figure 11: Schematic illustration of sequence database file format

Figure 11 illustrates the format of the sequence database file. Illustrated are exemplary sequences, including VH1-18 (SEQ ID NO:10), VH1-2 (SEQ ID NO:13), IGHD1-1*01 (SEQ ID NO:239), IGHJ1*01 (SEQ ID NO:273), AI (SEQ ID NO:330), A10 (SEQ ID NO:354), IGKJ1*01 (SEQ ID NO:356), V1-11 (SEQ ID NO:365), V1-13 (SEQ ID NO:366), IGLJ1*01 (SEQ ID NO:442), IGLJ2*01 (SEQ ID NO:443), and Mfe I restriction site (SEQ ID NO:1900).

Figure 12: DNA Sequence Compilation Software initial startup screen

Figure 12 depicts the initial startup screen for the DNA Sequence Compilation Software. Illustrated are 5' End sequence CCATGGCA (SEQ ID NO:1901), 5' End sequence CCATGGCG, (SEQ ID NO:1902), 3' End sequence CTAGC (SEQ ID NO:1903) and 3' End sequence GTACT (SEQ ID NO:1904).

Figure 13: DNA Sequence Compilation Software splash screen

Figure 13 depicts the splash screen that appears upon application startup.

Figure 14: DNA Sequence Compilation Software 96-well plate screen

Figure 14 depicts a model 96-well plate screen containing compiled sequences. The sequence of gnl|Fabrus|V3-4_IGLJ7*01 (SEQ ID NO:1906) is illustrated in the sequence information box.

Figure 15: DNA Sequence Compilation Software light chain manual compilation screen

Figure 15 depicts a model manual compilation screen, which allows the user to compile either a kappa or lambda light chain. Selected in the VL sequence box is V1-11 (SEQ ID NO:365). Selected in the JL sequence box is IGLJ1*01 (SEQ ID NO:442). The full length sequence (SEQ ID NO:1914) is depicted in the Dna sequence box.

Figure 16: DNA Sequence Compilation Software heavy chain manual compilation screen

Figure 16 depicts a model manual compilation screen, which allows the user to compile a heavy chain. Selected in the VH sequence box is VH1-18 (SEQ ID NO:10). Selected in the DH sequence box is IGHD1-1*01 (SEQ ID NO:239). Selected in the JH sequence box is IGHJ1*01 (SEQ ID NO:373). The full length sequence (SEQ ID NO:1915) is depicted in the Dna sequence box.

Figure 17: DNA Sequence Compilation Software light chain auto compilation screen

Figure 17 depicts a model light chain auto compilation screen. Illustrated are exemplary sequences of variable light chains set forth in SEQ ID NOS:1880-1881, 1883, 1905-1913 and 1916-1940.

Figure 18: Light chain BLAST grid

Figure 18 depicts a model BLAST grid for a light chain sequence. Illustrated are exemplary sequences of variable light chains set forth in SEQ ID NOS:1880-1881, 1883, 1905-1913, 1916-1939.

Figure 19: DNA Sequence Compilation Software heavy chain auto compilation screen

Figure 19 depicts a model heavy chain auto compilation screen. Illustrated are exemplary sequences of variable heavy chains set forth in SEQ ID NOS:1556, 1760, 1769, 1821, 1941-1973.

Figure 20: Heavy chain BLAST grid

Figure 20 depicts a model of the BLAST grid for a heavy chain sequence. Illustrated are exemplary sequences of variable heavy chains set forth in SEQ ID NOS:1530, 1539, 1974-1995.

DETAILED DESCRIPTION

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A. DEFINITIONS

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of skill in the art to which the invention(s) belong. All patents, patent applications, published applications and publications, Genbank sequences, databases, websites and other published materials referred to throughout the entire disclosure herein, unless noted otherwise, are incorporated by reference in their entirety. In the event that there are a plurality of definitions for terms herein, those in this section prevail. Where reference is made to a URL or other such identifier or address, it understood that such identifiers can change and particular information on the internet can come and go, but equivalent information can be found by searching the internet. Reference thereto evidences the availability and public dissemination of such information.

As used herein, "combinatorial library" refers to collections of compounds formed by reacting different combinations of interchangeable chemical "building blocks" to produce a collection of compounds based on permutations of the building blocks. For an antibody combinatorial library, the building blocks are the component V, D and J regions (or modified forms thereof) from which antibodies are formed. For purposes herein, the terms "library" or "collection" are used interchangeably.

As used herein, a combinatorial antibody library is a collection of antibodies (or portions thereof, such as Fabs), where the antibodies are encoded by nucleic acid molecules produced by the combination of V, D and J gene segments, particularly human V, D and J germline segments. The combinatorial libraries herein typically contain at least 50 different antibody (or antibody portions or fragment) members, typically at or about 50, 100, 500, 10^3, 2×10^3, 3×10^3, 4×10^3, 5×10^3, 6×10^3, 7×10^3, 8×10^3, 9×10^3, 1×10^4, 2×10^4, 3×10^4, 4×10^4, 5×10^4, 6×10^4, 7×10^4, 8×10^4, 9×10^4, 1×10^5, 2×10^5, 3×10^5, $4x\ 10^5$, 5×10^5, 6×10^5, 7×10^5, 8×10^5, 9×10^5, 10^6, 10^7, 10^8, 10^9, 10^{10}, or more different members. The resulting libraries or collections of antibodies or portions thereof, can be screened for binding to a target protein or modulation of a functional activity.

As used herein, a human combinatorial antibody library is a collection of antibodies or portions thereof, whereby each member contains a VL and VH chains or a sufficient portion thereof to form an antigen binding site encoded by nucleic acid containing human germline segments produced as described herein.

As used herein, germline gene segments refer to immunoglobulin (Ig) variable (V), diversity (D) and junction (J) or constant (C) genes from the germline that encode immunoglobulin heavy or light (kappa and lambda) chains. There are multiple V, D, J and C

gene segments in the germline, but gene rearrangement results in only one segment of each occurring in each functional rearranged gene. For example, a functionally rearranged heavy chain contains one V, one D and one J and a functionally rarrangend light chain gene contains one V and one J. Hence, these gene segments are carried in the germ cells but cannot be transcribed and translated into heavy and light chains until they are arranged into functional genes. During B-cell differentiation in the bone marrow, these gene segments are randomly shuffled by a dynamic genetic system capable of generating more than 10^{10} specificities. For purposes herein, the gene segments are rearranged *in vitro* by combination or compilation of the individual germline segments.

Reference to a variable germline segment herein refers to V, D and J groups, subgroups, genes or alleles thereof. Gene segment sequences are accessible from known database (e.g., National Center for Biotechnology Information (NCBI), the international ImMunoGeneTics information system® (IMGT), the Kabat database and the Tomlinson's VBase database (Lefranc (2003) *Nucleic Acids Res.*, 31:307-310; Martin *et al.*, Bioinformatics Tools for Antibody Engineering in Handbook of Therapeutic Antibodies, Wiley-VCH (2007), pp. 104-107). Tables 3-5 list exemplary human variable germline segments. Sequences of exemplary V_H, D_H, J_H, V_κ, J_κ, V_λ and or J_λ, germline segments are set forth in SEQ ID NOS: 10-451 and 868. For purposes herein, a germline segment includes modified sequences thereof, that are modified in accord with the rules of sequence compilation provided herein to permit practice of the method. For example, germline gene segments include those that contain one amino acid deletion or insertion at the 5' or 3' end compared to any of the sequences of nucleotides set forth in SEQ ID NOS:10-451, 868.

As used herein, modified form with reference to a germline segment refers to a sequence of nucleotides that is substantially the same as the sequence of nucleotides of a human germline segment (e.g. a V_H, D_H, J_H, V_κ, J_κ, V_λ and J_λ.) except that the sequence of nucleotides contains one or a few nucleotide differences, for example, 2, 3, 4, 5, 6, 7 , 8, 9 or 10 nucleotide differences compared to the corresponding sequence in a germline segment sequence. In some instances, modified germline sequences are modified in accord with the rules herein to remove stop codons, restriction enzyme sites, or to add or delete nucleotides to maintain reading frames.

As used herein, inverted sequence with reference to nucleotides of a germline segment means that the gene segment has a sequence of nucleotides that is the reverse complement of a reference sequence of nucleotides. For purposes herein, the reference sequence of nucleotides is a germline segment, typically a D_H germline segment.

As used herein, "compilation," "compile," "combine," "combination," "rearrange," "rearrangement," or other similar terms or grammatical variations thereof refers to the process by which germline segments are ordered or assembled into nucleic acid sequences representing genes. For example, variable heavy chain germline segments are assembled such that the V_H segment is 5' to the D_H segment which is 5' to the J_H segment, thereby resulting in a nucleic acid sequence encoding a VH chain. Variable light chain germline segments are assembled such that the V_L segment is 5' to the J_L segment, thereby resulting in a nucleic acid sequence encoding a VL chain. A constant gene segment or segments also can be assembled onto the 3' end of a nucleic acid encoding a VH or VL chain.

As used herein, "linked," or "linkage" or other grammatical variations thereof with reference to germline segments refers to the joining of germline segments. Linkage can be direct or indirect. Germline segments can be linked directly without additional nucleotides between segments, or additional nucleotides can be added to render the entire segment in-frame, or nucleotides can be deleted to render the resulting segment in-frame. It is understood that the choice of linker nucleotides is made such that the resulting nucleic acid molecule is in-frame and encodes a functional and productive antibody.

As used herein, "in-frame" or "linked in-frame" with reference to linkage of human germline segments means that there are insertions and/or deletions in the nucleotide germline segments at the joined junctions to render the resulting nucleic acid molecule in-frame with the 5' start codon (ATG), thereby producing a "productive" or functional full-length polypeptide. The choice of nucleotides inserted or deleted from germline segments, particularly at joints joining various VD, DJ and VJ segments, is in accord with the rules provided in the method herein for V(D)J joint generation. For example, germline segments are assembled such that the V_H segment is 5' to the D_H segment which is 5' to the J_H segment. At the junction joining the V_H and the D_H and at the junction joining the D_H and J_H segments, nucleotides can be inserted or deleted from the individual V_H, D_H or J_H segments, such that the resulting nucleic acid molecule containing the joined VDJ segments are in-frame with the 5' start codon (ATG).

As used herein, a "functional antibody" or "productive antibody" with reference to a nucleic acid encoding an antibody or portion thereof refers to an antibody or portion thereof, such as Fab, that is encoded by the nucleic acid molecule produced by the methods as described herein. In a functional or productive antibody, the V(D)J germline segments are compiled (i.e. rearranged) such that the encoded antibody or portion thereof is not truncated and/or the amino acid sequence is not out of frame. This means that the nucleic acid

molecule does not contain internal stop codons that result in the protein translation machinery terminating protein assembly prematurely.

As used herein, a portion of an antibody includes sufficient amino acids to form an antigen binding site.

As used herein, a reading frame refers to a contiguous and non-overlapping set of three-nucleotide codons in DNA or RNA. Because three codons encode one amino acid, there exist three possible reading frames for given nucleotide sequence, reading frames 1, 2 or 3. For example, the sequence ACTGGTCA will be ACT GGT CA for reading frame 1, A CTG GTC A for reading frame 2 and AC TGG TCA for reading frame 3. Generally for practice of the method described herein, nucleic acid sequences are combined so that the V sequence has reading frame 1.

As used herein, a stop codon is used to refer to a three-nucleotide sequence that signals a halt in protein synthesis during translation, or any sequence encoding that sequence (e.g. a DNA sequence encoding an RNA stop codon sequence), including the amber stop codon (UAG or TAG)), the ochre stop codon (UAA or TAA)) and the opal stop codon (UGA or TGA)). It is not necessary that the stop codon signal termination of translation in every cell or in every organism. For example, in suppressor strain host cells, such as amber suppressor strains and partial amber suppressor strains, translation proceeds through one or more stop codon (e.g. the amber stop codon for an amber suppressor strain), at least some of the time.

As used herein, reference to a variable heavy (VH) chain or a variable light (VL) chain (also termed VH domain or VL domain) refers to the polypeptide chains that make up the variable domain of an antibody. For purposes herein, heavy chain germline segments are designated as V_H, D_H and J_H, and compilation thereof results in a nucleic acid encoding a VH chain. Light chain germline segments are designated as V_L or J_L, and include kappa and lambda light chains (V_κ and J_κ; V_λ and J_λ) and compilation thereof results in a nucleic acid encoding a VL chain. It is understood that a light chain chain is either a kappa or lambda light chain, but does not include a kappa/lambda combination by virtue of compilation of a V_κ and J_λ.

As used herein, a "degenerate codon" refers to three-nucleotide codons that specifies the same amino acid as a codon in a parent nucleotide sequence. One of skill in the art is familiar with degeneracy of the genetic code and can identify degenerate codons.

As used herein, a "group" with reference to a germline segment refers to a core coding region from an immunoglobulin, i.e. a variable (V) gene, diversity (D) gene, joining

(J) gene or constant (C) gene encoding a heavy or light chain. Exemplary of germline segment groups include V_H, D_H, J_H, V_κ, J_κ, V_λ and J_λ.

As used herein, a "subgroup" with reference to a germline segment refers to a set of sequences that are defined by nucleotide sequence similarity or identity. Generally, a subgroup is a set of genes that belong to the same group [V, D, J or C], in a given species, and that share at least 75% identity at the nucleotide level. Subgroups are classified based on IMGT nomenclature (imgt.cines.fr; see e.g., Lefranc *et al.* (2008) Briefings in Bioinformatics, 9:263-275). Generally, a subgroup represent a multigene family.

As used herein, an allele of a gene refer to germline sequences that have sequence polymorphism due to one or more nucleotide differences in the coding region compared to a reference gene sequence (e.g. substitutions, insertions or deletions). Thus, IG sequences that belong to the same subgroup can be highly similar in their coding sequence, but nonetheless exhibit high polymorphism. Subgroup alleles are classified based on IMGT nomenclature with an asterisk(*) followed by a two figure number. Exemplary allelic subgroup germline segments for V_H, D_H, J_H, V_κ, J_κ, V_λ and J_λ are set forth in Tables 3-5.

As used herein, a "family" with reference to a germline segment refers to sets of germline segment sequences that are defined by amino acid sequence similarity or identity. Generally, a germline family includes all alleles of a gene.

As used herein, a "segment designated D_H" refers to any sequence of nucleotides of at least or about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90 or 100 nucleotides in length. The sequence of nucleotides is sufficient to code for part of the CDR3 region of the VH chain.

As used herein, reference to a V, D or J gene segment "derived from a germline segment" refers to the corresponding nucleotides in a VH or VL nucleic acid sequence, that by recombination events, derived from a V, D or J germline gene.

As used herein, reference to a V region, D region or J region in an antibody or portion or fragment thereof refers to amino acids encoded by nucleotides that, by recombination events, derive from a corresponding V, D or J germline segment gene.

As used herein, "diversity" with respect to members in a collection refers to the number of unique members in a collection. Hence, diversity refers to the number of different amino acid sequences or nucleic acid sequences, respectively, among the analogous polypeptide members of that collection. For example, a collection of polynucleotides having a diversity of 10^4 contains 10^4 different nucleic acid sequences among the analogous polynucleotide members. In one example, the provided collections of polynucleotides and/or

polypeptides have diversities of at least at or about 10^2, 10^3, 10^4, 10^5, 10^6, 10^7, 10^8, 10^9, 10^{10} or more.

As used herein, "a diversity ratio" refers to a ratio of the number of different members in the library over the number of total members of the library. Thus, a library with a larger diversity ratio than another library contains more different members per total members, and thus more diversity per total members. The provided libraries include libraries having high diversity ratios, such as diversity ratios approaching 1, such as, for example, at or about 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 0.91, 0.92, 0.93, 0.94, 0.95, 0.96, 0.97, 0.98, or 0.99.

As used herein, "sequence diversity" refers to a representation of nucleic acid sequence similarity and is determined using sequence alignments, diversity scores, and/or sequence clustering. Any two sequences can be aligned by laying the sequences side-by-side and analyzing differences within nucleotides at every position along the length of the sequences. Sequence alignment can be assessed *in silico* using Basic Local Alignment Search Tool (BLAST), an NCBI tool for comparing nucleic acid and/or protein sequences. The use of BLAST for sequence alignment is well known to one of skill in the art. The Blast search algorithm compares two sequences and calculates the statistical significance of each match (a Blast score). Sequences that are most similar to each other will have a high Blast score, whereas sequences that are most varied will have a low Blast score.

As used herein, antibody refers to immunoglobulins and immunoglobulin portions, whether natural or partially or wholly synthetic, such as recombinantly, produced, including any portion thereof containing at least a portion of the variable region of the immunoglobulin molecule that is sufficient to form an antigen binding site. Hence, an antibody or portion thereof includes any protein having a binding domain that is homologous or substantially homologous to an immunoglobulin antigen binding site. For example, an antibody refers to an antibody that contains two heavy chains (which can be denoted H and H') and two light chains (which can be denoted L and L'), where each heavy chain can be a full-length immunoglobulin heavy chain or a portion thereof sufficient to form an antigen binding site (e.g. heavy chains include, but are not limited to, VH, chains VH-CH1 chains and VH-CH1-CH2-CH3 chains), and each light chain can be a full-length light chain or a protion thereof sufficient to form an antigen binding site (e.g. light chains include, but are not limited to, VL chains and VL-CL chains). Each heavy chain (H and H') pairs with one light chain (L and L', respectively). Typically, antibodies minimally include all or at least a portion of the variable heavy (VH) chain and/or the variable light (VL) chain. The antibody also can include all or a portion of the constant region.

For purposes herein, the term antibody includes full-length antibodies and portions thereof including antibody fragments, such as, but not limited to, Fab, Fab', $F(ab')_2$, single-chain Fvs (scFv), Fv, dsFv, diabody, Fd and Fd' fragments Fab fragments, Fd fragments and scFv fragments. Other known fragments include, but are not limited to, scFab fragments (Hust *et al.*, *BMC Biotechnology* (2007), 7:14). Antibodies include members of any immunoglobulin class, including IgG, IgM, IgA, IgD and IgE.

As used herein, a full-length antibody is an antibody having two full-length heavy chains (e.g. VH-CH1-CH2-CH3 or VH-CH1-CH2-CH3- CH4) and two full-length light chains (VL-CL) and hinge regions, such as human antibodies produced by antibody secreting B cells and antibodies with the same domains that are produced synthetically.

As used herein, antibody fragment or antibody portion refers to any portion of a full-length antibody that is less than full length but contains at least a portion of the variable region of the antibody sufficient to form an antigen binding site (e.g. one or more CDRs) and thus retains the a binding specificity and/or an activity of the full-length antibody; antibody fragments include antibody derivatives produced by enzymatic treatment of full-length antibodies, as well as synthetically, e.g. recombinantly produced derivatives. Examples of antibody fragments include, but are not limited to, Fab, Fab', $F(ab')_2$, single-chain Fvs (scFv), Fv, dsFv, diabody, Fd and Fd' fragments (see, for example, *Methods in Molecular Biology*, Vol 207: *Recombinant Antibodies for Cancer Therapy Methods and Protocols* (2003); Chapter 1; p 3-25, Kipriyanov). The fragment can include multiple chains linked together, such as by disulfide bridges and/or by peptide linkers. An antibody fragment generally contains at least about 50 amino acids and typically at least 200 amino acids.

As used herein, an Fv antibody fragment is composed of one variable heavy domain (VH) and one variable light (VL) domain linked by noncovalent interactions.

As used herein, a dsFv refers to an Fv with an engineered intermolecular disulfide bond, which stabilizes the VH-VL pair.

As used herein, an Fd fragment is a fragment of an antibody containing a variable domain (VH) and one constant region domain (CH1) of an antibody heavy chain.

As used herein, "Fab fragment" is an antibody fragment that contains the portion of the full-length antibody that results from digestion of a full-length immunoglobulin with papain, or a fragment having the same structure that is produced synthetically, e.g. recombinantly. A Fab fragment contains a light chain (containing a VL and CL portion) and another chain containing a variable domain of a heavy chain (VH) and one constant region domain portion of the heavy chain (CH1); it can be recombinantly produced.

As used herein, a $F(ab')_2$ fragment is an antibody fragment that results from digestion of an immunoglobulin with pepsin at pH 4.0-4.5, or a synthetically, e.g. recombinantly, produced antibody having the same structure. The $F(ab')_2$ fragment contains two Fab fragments but where each heavy chain portion contains an additional few amino acids, including cysteine residues that form disulfide linkages joining the two fragments; it can be recombinantly produced.

A Fab' fragment is a fragment containing one half (one heavy chain and one light chain) of the $F(ab')_2$ fragment.

As used herein, an Fd' fragment is a fragment of an antibody containing one heavy chain portion of a F(ab')2 fragment.

As used herein, an Fv' fragment is a fragment containing only the V_H and V_L domains of an antibody molecule.

As used herein, a scFv fragment refers to an antibody fragment that contains a variable light chain (VL) and variable heavy chain (VH), covalently connected by a polypeptide linker in any order. The linker is of a length such that the two variable domains are bridged without substantial interference. Exemplary linkers are $(Gly\text{-}Ser)_n$ residues with some Glu or Lys residues dispersed throughout to increase solubility.

As used herein, diabodies are dimeric scFv; diabodies typically have shorter peptide linkers than scFvs, and they preferentially dimerize.

As used herein, hsFv refers to antibody fragments in which the constant domains normally present in a Fab fragment have been substituted with a heterodimeric coiled-coil domain (see, e.g., Arndt *et al.* (2001) *J Mol Biol.* 7:312:221-228).

As used herein, a polypeptide domain is a part of a polypeptide (a sequence of three or more, generally 5 or 7 or more amino acids) that is a structurally and/or functionally distinguishable or definable. Exemplary of a polypeptide domain is a part of the polypeptide that can form an independently folded structure within a polypeptide made up of one or more structural motifs (e.g. combinations of alpha helices and/or beta strands connected by loop regions) and/or that is recognized by a particular functional activity, such as enzymatic activity or antigen binding. A polypeptide can have one, typically more than one, distinct domains. For example, the polypeptide can have one or more structural domains and one or more functional domains. A single polypeptide domain can be distinguished based on structure and function. A domain can encompass a contiguous linear sequence of amino acids. Alternatively, a domain can encompass a plurality of non-contiguous amino acid portions, which are non-contiguous along the linear sequence of amino acids of the

polypeptide. Typically, a polypeptide contains a plurality of domains. For example, each heavy chain and each light chain of an antibody molecule contains a plurality of immunoglobulin (Ig) domains, each about 110 amino acids in length.

As used herein, an Ig domain is a domain, recognized as such by those in the art, that is distinguished by a structure, called the Immunoglobulin (Ig) fold, which contains two beta-pleated sheets, each containing anti-parallel beta strands of amino acids connected by loops. The two beta sheets in the Ig fold are sandwiched together by hydrophobic interactions and a conserved intra-chain disulfide bond. Individual immunoglobulin domains within an antibody chain further can be distinguished based on function. For example, a light chain contains one variable region domain (VL) and one constant region domain (CL), while a heavy chain contains one variable region domain (VH) and three or four constant region domains (CH). Each VL, CL, VH, and CH domain is an example of an immunoglobulin domain.

As used herein, a "variable domain" with reference to an antibody is a specific Ig domain of an antibody heavy or light chain that contains a sequence of amino acids that varies among different antibodies. Each light chain and each heavy chain has one variable region domain (VL, and, VH). The variable domains provide antigen specificity, and thus are responsible for antigen recognition. Each variable region contains CDRs that are part of the antigen binding site domain and framework regions (FRs).

As used herein, "hypervariable region," "HV," "complementarity-determining region" and "CDR" and "antibody CDR" are used interchangeably to refer to one of a plurality of portions within each variable region that together form an antigen binding site of an antibody. Each variable region domain contains three CDRs, named CDR1, CDR2, and CDR3. The three CDRs are non-contiguous along the linear amino acid sequence, but are proximate in the folded polypeptide. The CDRs are located within the loops that join the parallel strands of the beta sheets of the variable domain.

As used herein, framework regions (FRs) are the domains within the antibody variable region domains that are located within the beta sheets; the FR regions are comparatively more conserved, in terms of their amino acid sequences, than the hypervariable regions.

As used herein, a constant region domain is a domain in an antibody heavy or light chain that contains a sequence of amino acids that is comparatively more conserved among antibodies than the variable region domain. Each light chain has a single light chain constant region (CL) domain and each heavy chain contains one or more heavy chain constant region

(CH) domains, which include, CH1, CH2, CH3 and CH4. Full-length IgA, IgD and IgG isotypes contain CH1, CH2 CH3 and a hinge region, while IgE and IgM contain CH1, CH2 CH3 and CH4. CH1 and CL domains extend the Fab arm of the antibody molecule, thus contributing to the interaction with antigen and rotation of the antibody arms. Antibody constant regions can serve effector functions, such as, but not limited to, clearance of antigens, pathogens and toxins to which the antibody specifically binds, e.g. through interactions with various cells, biomolecules and tissues.

As used herein, humanized antibodies refer to antibodies that are modified to include "human" sequences of amino acids so that administration to a human does not provoke an immune response. Methods for preparation of such antibodies are known. For example, the antibody in which the amino acid composition of the non-variable regions can be based on human antibodies. Computer programs have been designed to identify such regions.

As used herein, "antigen-binding site" refers to the interface formed by one or more complementary determining regions (CDRs; also called hypervariable region). Each antigen binding site contains three CDRs from the heavy chain variable region and three CDRs from the light chain variable region. An antibody molecule has two antigen combining sites, each containing portions of a heavy chain variable region and portions of a light chain variable region. The antigen combining sites can contain other portions of the variable region domains in addition to the CDRs.

As used herein, reference to an "antibody or portion thereof that is sufficient to form an antigen binding site" means that the antibody or portion thereof contains at least 1 or 2, typically 3, 4, 5 or all 6 CDRs of the VH and VL sufficient to retain at least a portion of the binding specificity of the corresponding full-length antibody containing all 6 CDRs. Generally, a sufficient antigen binding site at least requires CDR3 of the heavy chain (CDRH3). It typically futher requires the CDR3 of the light chain (CDRL3). As described herein, one of skill in the art knows and can identify the CDRs based on kabat or Chothia numbering (see e.g., Kabat, E.A. *et al.* (1991) *Sequences of Proteins of Immunological Interest*, Fifth Edition, U.S. Department of Health and Human Services, NIH Publication No. 91-3242, and Chothia, C. *et al.* (1987) *J. Mol. Biol.* 196:901-917). For example, based on Kabat numbering, CDR-LI corresponds to residues L24-L34; CDR-L2 corresponds to residues L50-L56; CDR-L3 corresponds to residues L89-L97; CDR-H1 corresponds to residues H31 – H35, 35a or 35b depending on the length; CDR-H2 corresponds to residues H50-H65; and CDR-H3 corresponds to residues H95-H102.

As used herein, a "peptide mimetic" is a peptide that mimics the activity of a polypeptide. For example, an erythropoietin (EPO) peptide mimetic is a peptide that mimics the activity of Epo, such as for binding and activation of the EPO receptor.

As used herein, an optimized antibody refers to an antibody, or portion thereof, that has an improved binding affinity for a target protein and/or an improved functional activity compared to a reference antibody. Typically, the antibody is optimized by virtue of one or more amino acid modifications (amino acid deletion, replacement or insertion) compared to a parent antibody not containing the one or more amino acid modifications. Generally, an activity or binding affinity is increased by at or about 1.5-fold, 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, 10-fold, 20-fold, 30-fold, 40-fold, 50-fold, 60-fold, 70-fold, 80-fold, 90-fold, 100-fold, 200-fold, 300-fold, 400-fold, 500-fold, 600-fold, 700-fold, 800-fold, 900-fold, 1000-fold or more compared to an activity or binding affininity of the parent antibody (e.g. germline Hit not containing the modification(s)).

As used herein, corresponding with reference to corresponding residues, for example "amino acid residues corresponding to", referes to residues compared among or between two polypeptides that are related sequences (e.g. allelic variants, genes of the same family, species variants). One of skill in the art can readily identify residues that correspond between or among polypeptides. For example, by aligning the sequence of regions encoded by germline segments, one of skill in the art can identify corresponding residues, using conserved and identical amino acids as guides. One of skill in the art can manually align a sequence or can use any of the numerous alignment programs available (for example, BLAST). Hence, an amino acid residues or positions that correspond to each other are those residues that are determined to correspond to one another based on sequence and/or structural alignments with a specified reference polypeptide.

As used herein, a consensus sequence is a sequence containing residues that are the most frequently occurring residues at each position when a plurality of related sequences (e.g. allelic variants, genes of the same family, species variants) are aligned. Hence a consensus sequence represents the residues that are the most abundant in the alignment at each position. For purposes herein, for example, germline sequences, or portions thereof, can be aligned to generate a consensus germline sequence.

As used herein, a locus in a library refers to a location or position, that can contain a member or members of library. The position does not have to be a physical position. For example, if the collection is provided as an array on a solid support, the support contains loci that can or do present members of the array.

As used herein, an address refers to a unique identifier for each locus in a collection whereby an addressed member (e.g. an antibody) can be identified. An addressed moiety is one that can be identified by virtue of its locus or location. Addressing can be effected by position on a surface, such as a well of a microplate. For example, an address for a protein in a microwell plate that is F9 means that the protein is located in row F, column 9 of the microwell plate. Addressing also can be effected by other identifiers, such as a tag encoded with a bar code or other symbology, a chemical tag, an electronic, such RF tag, a color-coded tag or other such identifier.

As used herein, an array refers to a collection of elements, such as antibodies, containing three or more members.

As used herein, a "spatial array" is an array where members are separated or occupy a distinct space in an array. Hence, spatial arrays are a type of addressable array. Examples of spatial arrays include microtiter plates where each well of a plate is an address in the array. Spacial arrays include any arrangement wherein a plurality of different molecules, e.g, polypeptides, are held, presented, positioned, situated, or supported. Arrays can include microtiter plates, such as 48-well, 96-well, 144-well, 192-well, 240-well, 288-well, 336-well, 384-well, 432-well, 480-well, 576-well, 672-well, 768-well, 864-well, 960-well, 1056-well, 1152-well, 1248-well, 1344-well, 1440-well, or 1536-well plates, tubes, slides, chips, flasks, or any other suitable laboratory apparatus. Furthermore, arrays can also include a plurality of sub-arrays. A plurality of sub-arrays encompasses an array where more than one arrangement is used to position the polypeptides. For example, multiple 96-well plates can constitute a plurality of sub-arrays and a single array.

As used herein, an addressable library is a collection of molecules such as nucleic acid molecules or protein agents, such as antibodies, in which each member of the collection is identifiable by virtue of its address.

As used herein, an addressable array is one in which the members of the array are identifiable by their address, the position in a spatial array, such as a well of a microtiter plate, or on a solid phase support, or by virtue of an identifiable or detectable label, such as by color, fluorescence, electronic signal (i.e. RF, microwave or other frequency that does not substantially alter the interaction of the molecules of interest), bar code or other symbology, chemical or other such label. Hence, in general the members of the array are located at identifiable loci on the surface of a solid phase or directly or indirectly linked to or otherwise associated with the identifiable label, such as affixed to a microsphere or other particulate support (herein referred to as beads) and suspended in solution or spread out on a surface.

As used herein, "an addressable combinatorial antibody library" refers to a collection of antibodies in which member antibodies are identifiable and all antibodies with the same identifier, such as position in a spatial array or on a solid support, or a chemical or RF tag, bind to the same antigen, and generally are substantially the same in amino acid sequence. For purposes herein, reference to an "addressable arrayed combinatorial antibody library" means that the antibody members are addressed in an array.

As used herein, a support (also referred to as a matrix support, a matrix, an insoluble support or solid support) refers to any solid or semisolid or insoluble support to which a molecule of interest, typically a biological molecule, organic molecule or biospecific ligand is linked or contacted. Such materials include any materials that are used as affinity matrices or supports for chemical and biological molecule syntheses and analyses, such as, but are not limited to: polystyrene, polycarbonate, polypropylene, nylon, glass, dextran, chitin, sand, pumice, agarose, polysaccharides, dendrimers, buckyballs, polyacrylamide, silicon, rubber, and other materials used as supports for solid phase syntheses, affinity separations and purifications, hybridization reactions, immunoassays and other such applications. The matrix herein can be particulate or can be in the form of a continuous surface, such as a microtiter dish or well, a glass slide, a silicon chip, a nitrocellulose sheet, nylon mesh, or other such materials. When particulate, typically the particles have at least one dimension in the 5-10 mm range or smaller. Such particles, referred collectively herein as "beads", are often, but not necessarily, spherical. Such reference, however, does not constrain the geometry of the matrix, which can be any shape, including random shapes, needles, fibers, and elongated. Roughly spherical "beads", particularly microspheres that can be used in the liquid phase, also are contemplated. The "beads" can include additional components, such as magnetic or paramagnetic particles (see, e.g., Dynabeads® (Dynal, Oslo, Norway)) for separation using magnets, as long as the additional components do not interfere with the methods and analyses herein.

As used herein, matrix or support particles refers to matrix materials that are in the form of discrete particles. The particles have any shape and dimensions, but typically have at least one dimension that is 100 mm or less, 50 mm or less, 10 mm or less, 1 mm or less, 100 μm or less, 50 μm or less and typically have a size that is 100 mm^3 or less, 50 mm^3 or less, 10 mm^3 or less, and 1 mm^3 or less, 100 μm^3 or less and can be on the order of cubic microns. Such particles are collectively called "beads."

As used herein, *in silico* refers to research and experiments performed using a computer. *In silico* methods include, but are not limited to, molecular modeling studies,

biomolecular docking experiments, and virtual representations of molecular structures and/or processes, such as molecular interactions. For purposes herein, the antibody members of a library can be designed using a computer program that selects component V, D and J germline segments from among those input into the computer and joins them in-frame to output a list of nucleic acid molecules for synthesis. Thus, the recombination of the components of the antibodies in the collections or libraries provided herein, can be performed *in silico* by combining the nucleotide sequences of each building block in accord with software that contains rules for doing so. The process can be performed manually without a computer, but the computer provides the convenience of speed.

As used herein, a database refers to a collection of data items. For purposes herein, reference to a database is typically with reference to antibody databases, which provide a collection of sequence and structure information for antibody genes and sequences. Exemplary antibody databases include, but are not limited to, IMGT®, the international ImMunoGeneTics information system (imgt.cines.fr; see e.g., Lefranc *et al.* (2008) Briefings in Bioinformatics, 9:263-275), National Center for Biotechnology Information (NCBI), the Kabat database and the Tomlinson's VBase database (Lefranc (2003) *Nucleic Acids Res.*, 31:307-310; Martin *et al.*, Bioinformatics Tools for Antibody Engineering in Handbook of Therapeutic Antibodies, Wiley-VCH (2007), pp. 104-107). A database also can be created by a user to include any desired sequences. The database can be created such that the sequences are inputted in a desired format (e.g., in a particular reading frame; lacking stop codons; lacking signal sequences). The database also can be created to include sequences in addition to antibody sequences.

As used herein, "a computer-based system" refers to the hardware, software, and data storage media and methods used to recombine germline segments. The minimum hardware of the computer-based systems provided herein include a central processing unit (CPU), input mean, output means and data storage means. A skilled artisan can select a suitable computer-based systems for use in the methods and systems provided herein.

As used herein, "recorded" refers to a process for storing information on computer readable medium. A skilled artisan can readily adopt any of the presently known methods for recording information on computer readable medium to array image data. The choice of the data storage structure can generally be based on the media and platforms chosen to access the stored information. In addition, a variety of data processor programs and formats can be used to store the array image information on computer readable medium. The image information can be represented in a word processing text file, formatted in commercially-available

software such as MICROSOFT Word®, graphics files or represented in the form of an ASCII file, stored in a database application, such as DB2®, Sybase® and Oracle®. A skilled artisan can adapt any number of data processor structuring formats (*e.g.*, text file or database) in order to obtain computer readable medium having recorded thereon the information or instructions as described herein.

As used herein, "screening" refers to identification or selection of an antibody or portion thereof from a collection or libriary of antibodies and/or portions thereof, based on determination of the activity or property of an antibody or portion thereof. Screening can be performed in any of a variety of ways, including, for example, by assays assessing direct binding (e.g. binding affinity) of the antibody to a target protein or by functional assays assessing modulation of an activity of a target protein.

As used herein, activity towards a target protein refers to binding specificity and/or modulation of a functional activity of a target protein, or other measurements that reflects the activity of an antibody or portion thereof towards a target protein.

As used herein the term assessing is intended to include quantitative and qualitative determination in the sense of obtaining an absolute value for the binding of an antibody or portion thereof with a target protein and/or modulation of an activity of a target protein by an antibody or portion thereof, and also of obtaining an index, ratio, percentage, visual or other value indicative of the level of the binding or activity. Assessment can be direct or indirect. For example, binding can be determined by directly labeling of an antibody or portion thereof with a detectable label and/or by using a secondary antibody that itself is labeled. In addition, functional activities can be determined using any of a variety of assays known to one of skill in the art, for example, proliferation, cytotoxicity and others as described herein, and comparing the activity of the target protein in the presence versus the absence of an antibody or portion thereof.

As used herein, a "target protein" refers to candidate proteins or peptides that are specifically recognized by an antibody or portion thereof and/or whose activity is modulated by an antibody or protion thereof. A target protein includes any peptide or protein that contains an epitope for antibody recognition. Target proteins include proteins involved in the etiology of a disease or disorder by virtue of expression or activity. Exemplary target proteins are described herein.

As used herein, "Hit" refers to an antibody or portion thereof identified, recognized or selected as having an activity in a screening assay.

As used herein, "iterative" with respect to screening means that the screening is repeated a plurality of times, such as 2, 3, 4, 5 or more times, until a "Hit" is identified whose activity is optimized or improved compared to prior iterations.

As used herein, "high-throughput" refers to a large-scale method or process that permits manipulation of large numbers of molecules or compounds, generally tens to hundred to thousands of compounds. For example, methods of purification and screening can be rendered high-throughput. High-throughput methods can be performed manually. Generally, however, high-throughput methods involve automation, robotics or software.

As used herein, "structure/activity relationship (SAR)" refers to the relationship between structure and function of a molecule. For purposes herein, structure is with reference to sequence, for example, a sequence of nucleotides encoding an antibody. By virtue of addressing library members, the identify of each antibody by its sequence is known based on its address. Hence, structure is known and can be correlated to a particular activity. Hence, SAR can be used to assess the affects of changes in structure on an activity.

As used herein, "functional activity" refer to activities of a polypeptide (e.g. target protein) or portion thereof associated with a full-length (complete) protein. Functional activities include, but are not limited to, biological activity, catalytic or enzymatic activity, antigenicity (ability to bind to or compete with a polypeptide for binding to an anti-polypeptide antibody), immunogenicity, ability to form multimers, the ability to specifically bind to a receptor or ligand for the polypeptide and signaling and downstream effector functions. For purposes herein, modulation (i.e. activation or inhibition) of a functional activity of a polypeptide by an antibody or portion thereof in the libraries herein means that a functional activity of the polypeptide is changed or altered in the presence of the antibody compared to the absence of the antibody or portion thereof.

As used herein, "modulate" or "modulation" and other various grammatical forms thereof with reference to the effect of an antibody or portion thereof on the functional activity of a target protein refers to increased activity such as induction or potentiation of activity, as well as inhibition of one or more activities of the target protein. Hence, modulation can include an increase in the activity (i.e., up-regulation or agonist activity) a decrease in activity (i.e., down-regulation or inhibition) or any other alteration in an activity (such as a change in periodicity, frequency, duration, kinetics or other parameter) . Modulation can be context dependent and typically modulation is compared to a designated state, for example, the wildtype protein, the protein in a constitutive state, or the protein as expressed in a designated cell type or condition. The functional activity of a target protein by an antibody or

portion thereof can be modulated by 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or more compared to the activity of the target protein in the abasence of the antibody or portion thereof.

As used herein, "agonist" refers to an antibody or portion thereof that modulates signal transduction or other functional activity of a receptor by potentiating, inducing or otherwise enhancing the signal transduction activity or other functional activity of a receptor. Agonists can modulate signal transduction or other functional activity when used alone or can alter signal transduction or other functional activity in the presence of the natural ligand of the receptor or other receptor stimulator to enhance signaling by the receptor compared to the ligand alone.

As used herein, "antagonist" refers to an antibody or portion thereof that modulates signal transduction or other functional activity of a receptor by blocking or decreasing the signal transduction activity or other functional activity of a receptor

As used herein, a label is a detectable marker that can be attached or linked directly or indirectly to a molecule or associated therewith. The detection method can be any method known in the art.

As used herein, binding activity refer to characteristics of a molecule, e.g. a polypeptide, relating to whether or not, and how, it binds one or more binding partners. Binding activities include ability to bind the binding partner(s), the affinity with which it binds to the binding partner (e.g. high affinity), the avidity with which it binds to the binding partner, the strength of the bond with the binding partner and specificity for binding with the binding partner.

As used herein, "affinity" or "binding affinity" refers to the strength with which an antibody molecule or portion thereof binds to an epitope on a target protein or antigen. Affinity is often measured by equilibrium association constant (K_A) or equilibrium dissociation constant (K_D). Low-affinity antibody-antigen interaction is weak, and the molecules tend to dissociate rapidly, while high affinity antibody-antigen binding is strong and the molecules remain bound for a longer amount of time. A high antibody affinity means that the antibody specifically binds to a target protein with an equilibrium association constant (K_A) of greater than or equal to about $10^6\,M^{-1}$, greater than or equal to about $10^7\,M^{-1}$, greater than or equal to about $10^8\,M^{-1}$, or greater than or equal to about $10^9\,M^{-1}$, $10^{10}\,M^{-1}$, $10^{11}\,M^{-1}$ or $10^{12}\,M^{-1}$. Antibodies also can be characterized by an equilibrium dissociation constant (K_D), for example, 10^{-4} M, 10^{-5} M, 10^{-6} M, 10^{-7} M, 10^{-8} M, 10^{-10} M, 10^{-11} M or 10^{-12} M or lower. Generally, antibodies having a nanomolar or sub-nanomolar dissociaton constant are deemed

to be high affinity antibodies. Such affinities can be readily determined using conventional techniques, such as by equilibrium dialysis; by using the BIAcore 2000 instrument, using general procedures outlined by the manufacturer; by radioimmunoassay using radiolabeled target antigen; or by another method known to the skilled artisan. The affinity data can be analyzed, for example, by the method of Scatchard *et al.*, *Ann N.Y. Acad. ScL*, 51:660 (1949).

As used herein, "epitope" refers to the localized region on the surface of an antigen or protein that is recognized by an antibody. Peptide epitopes include those that are continuous epitopes or discontinuous epitopes. An epitope is generally determined by the three dimensional structure of a protein as opposed to the linear amino acid sequence.

As used herein, "epitope mapping" is the process of identification of the molecular determinants for antibody-antigen recognition.

As used herein, Basic Local Alignment Search Tool (BLAST) is a search algorithm developed by Altschul *et al.* (1990) to separately search protein or DNA databases, for example, based on sequence identity. For example, blastn is a program that compares a nucleotide query sequence against a nucleotide sequence database (e.g. GenBank). BlastP is a program that compares an amino acid query sequence against a protein sequence database.

As used herein, a BLAST bit score is a value calculated from the number of gaps and substitutions associated with each aligned sequence. The higher the score, the more significant the alignment.

As used herein, a human protein is one encoded by a nucleic acid molecule, such as DNA, present in the genome of a human, including all allelic variants and conservative variations thereof. A variant or modification of a protein is a human protein if the modification is based on the wildtype or prominent sequence of a human protein.

As used herein, "naturally occurring amino acids" refer to the 20 L-amino acids that occur in polypeptides. The residues are those 20 α-amino acids found in nature which are incorporated into protein by the specific recognition of the charged tRNA molecule with its cognate mRNA codon in humans.

As used herein, non-naturally occurring amino acids refer to amino acids that are not genetically encoded. For example, a non-natural amino acid is an organic compound that has a structure similar to a natural amino acid but has been modified structurally to mimic the structure and reactivity of a natural amino acid. Non-naturally occurring amino acids thus include, for example, amino acids or analogs of amino acids other than the 20 naturally-occurring amino acids and include, but are not limited to, the D-isostereomers of amino acids. Exemplary non-natural amino acids are known to those of skill in the art.

As used herein, nucleic acids include DNA, RNA and analogs thereof, including peptide nucleic acids (PNA) and mixtures thereof. Nucleic acids can be single or double-stranded. When referring to probes or primers, which are optionally labeled, such as with a detectable label, such as a fluorescent or radiolabel, single-stranded molecules are contemplated. Such molecules are typically of a length such that their target is statistically unique or of low copy number (typically less than 5, generally less than 3) for probing or priming a library. Generally a probe or primer contains at least 14, 16 or 30 contiguous nucleotides of sequence complementary to or identical to a gene of interest. Probes and primers can be 10, 20, 30, 50, 100 or more nucleic acids long.

As used herein, a peptide refers to a polypeptide that is from 2 to 40 amino acids in length.

As used herein, the amino acids which occur in the various sequences of amino acids provided herein are identified according to their known, three-letter or one-letter abbreviations (Table 1). The nucleotides which occur in the various nucleic acid fragments are designated with the standard single-letter designations used routinely in the art.

As used herein, an "amino acid" is an organic compound containing an amino group and a carboxylic acid group. A polypeptide contains two or more amino acids. For purposes herein, amino acids include the twenty naturally-occurring amino acids, non-natural amino acids and amino acid analogs (i.e., amino acids wherein the α-carbon has a side chain).

As used herein, "amino acid residue" refers to an amino acid formed upon chemical digestion (hydrolysis) of a polypeptide at its peptide linkages. The amino acid residues described herein are presumed to be in the "L" isomeric form. Residues in the "D" isomeric form, which are so designated, can be substituted for any L-amino acid residue as long as the desired functional property is retained by the polypeptide. NH_2 refers to the free amino group present at the amino terminus of a polypeptide. COOH refers to the free carboxy group present at the carboxyl terminus of a polypeptide. In keeping with standard polypeptide nomenclature described in *J. Biol. Chem.*, 243: 3557-3559 (1968), and adopted 37 C.F.R. §§ 1.821-1.822, abbreviations for amino acid residues are shown in Table 1:

Table 1 – Table of Correspondence

SYMBOL		
1-Letter	**3-Letter**	**AMINO ACID**
Y	Tyr	Tyrosine
G	Gly	Glycine
F	Phe	Phenylalanine
M	Met	Methionine

SYMBOL		
1-Letter	**3-Letter**	**AMINO ACID**
A	Ala	Alanine
S	Ser	Serine
I	Ile	Isoleucine
L	Leu	Leucine
T	Thr	Threonine
V	Val	Valine
P	Pro	Proline
K	Lys	Lysine
H	His	Histidine
Q	Gln	Glutamine
E	Glu	Glutamic acid
Z	Glx	Glu and/or Gln
W	Trp	Tryptophan
R	Arg	Arginine
D	Asp	Aspartic acid
N	Asn	Asparagine
B	Asx	Asn and/or Asp
C	Cys	Cysteine
X	Xaa	Unknown or other

It should be noted that all amino acid residue sequences represented herein by formulae have a left to right orientation in the conventional direction of amino-terminus to carboxyl-terminus. In addition, the phrase "amino acid residue" is broadly defined to include the amino acids listed in the Table of Correspondence (Table 1) and modified and unusual amino acids, such as those referred to in 37 C.F.R. §§ 1.821-1.822, and incorporated herein by reference. Furthermore, it should be noted that a dash at the beginning or end of an amino acid residue sequence indicates a peptide bond to a further sequence of one or more amino acid residues, to an amino-terminal group such as NH_2 or to a carboxyl-terminal group such as COOH. The abbreviations for any protective groups, amino acids and other compounds, are, unless indicated otherwise, in accord with their common usage, recognized abbreviations, or the IUPAC-IUB Commission on Biochemical Nomenclature (see, (1972) *Biochem.* 11:1726). Each naturally occurring L-amino acid is identified by the standard three letter code (or single letter code) or the standard three letter code (or single letter code) with the prefix "L-"; the prefix "D-" indicates that the stereoisomeric form of the amino acid is D.

As used herein, an isokinetic mixture is one in which the molar ratios of amino acids has been adjusted based on their reported reaction rates (see, e.g., Ostresh *et al.*, (1994) *Biopolymers* 34:1681).

As used herein, modification is in reference to modification of a sequence of amino acids of a polypeptide or a sequence of nucleotides in a nucleic acid molecule and includes deletions, insertions, and replacements of amino acids and nucleotides, respectively. Methods of modifying a polypeptide are routine to those of skill in the art, such as by using recombinant DNA methodologies.

As used herein, suitable conservative substitutions of amino acids are known to those of skill in this art and can be made generally without altering the biological activity of the resulting molecule. Those of skill in this art recognize that, in general, single amino acid substitutions in non-essential regions of a polypeptide do not substantially alter biological activity (see, e.g., Watson *et al.* Molecular Biology of the Gene, 4th Edition, 1987, The Benjamin/Cummings Pub. co., p.224). Such substitutions can be made in accordance with those set forth in TABLE 2 as follows:

TABLE 2

Original residue	Exemplary conservative substitution
Ala (A)	Gly; Ser
Arg (R)	Lys
Asn (N)	Gln; His
Cys (C)	Ser
Gln (Q)	Asn
Glu (E)	Asp
Gly (G)	Ala; Pro
His (H)	Asn; Gln
Ile (I)	Leu; Val
Leu (L)	Ile; Val
Lys (K)	Arg; Gln; Glu
Met (M)	Leu; Tyr; Ile
Phe (F)	Met; Leu; Tyr
Ser (S)	Thr
Thr (T)	Ser
Trp (W)	Tyr
Tyr (Y)	Trp; Phe
Val (V)	Ile; Leu

Other substitutions also are permissible and can be determined empirically or in accord with known conservative substitutions.

As used herein, a DNA construct is a single or double stranded, linear or circular DNA molecule that contains segments of DNA combined and juxtaposed in a manner not found in nature. DNA constructs exist as a result of human manipulation, and include clones and other copies of manipulated molecules.

As used herein, a DNA segment is a portion of a larger DNA molecule having specified attributes. For example, a DNA segment encoding a specified polypeptide is a

portion of a longer DNA molecule, such as a plasmid or plasmid fragment, which, when read from the 5' to 3' direction , encodes the sequence of amino acids of the specified polypeptide.

As used herein, the term "nucleic acid" refers to single-stranded and/or double-stranded polynucleotides such as deoxyribonucleic acid (DNA), and ribonucleic acid (RNA) as well as analogs or derivatives of either RNA or DNA. Also included in the term "nucleic acid" are analogs of nucleic acids such as peptide nucleic acid (PNA), phosphorothioate DNA, and other such analogs and derivatives or combinations thereof. Nucleic acid can refer to polynucleotides such as deoxyribonucleic acid (DNA) and ribonucleic acid (RNA). The term also includes, as equivalents, derivatives, variants and analogs of either RNA or DNA made from nucleotide analogs, single (sense or antisense) and double-stranded polynucleotides. Deoxyribonucleotides include deoxyadenosine, deoxycytidine, deoxyguanosine and deoxythymidine. For RNA, the uracil base is uridine.

As used herein, "nucleic acid molecule encoding" refers to a nucleic acid molecule which directs the expression of a specific protein or peptide. The nucleic acid sequences include both the DNA strand sequence that is transcribed into RNA and the RNA sequence that is translated into protein or peptide. The nucleic acid molecule includes both the full length nucleic acid sequences as well as non-full length sequences derived from the full length mature polypeptide, such as for example a full length polypeptide lacking a precursor sequence. For purposes herein, a nucleic acid sequence also includes the degenerate codons of the native sequence or sequences which can be introduced to provide codon preference in a specific host.

As used herein, the term "polynucleotide" refers to an oligomer or polymer containing at least two linked nucleotides or nucleotide derivatives, including a deoxyribonucleic acid (DNA), a ribonucleic acid (RNA), and a DNA or RNA derivative containing, for example, a nucleotide analog or a "backbone" bond other than a phosphodiester bond, for example, a phosphotriester bond, a phosphoramidate bond, a phophorothioate bond, a thioester bond, or a peptide bond (peptide nucleic acid). The term "oligonucleotide" also is used herein essentially synonymously with "polynucleotide," although those in the art recognize that oligonucleotides, for example, PCR primers, generally are less than about fifty to one hundred nucleotides in length.

Polynucleotides can include nucleotide analogs, including, for example, mass modified nucleotides, which allow for mass differentiation of polynucleotides; nucleotides containing a detectable label such as a fluorescent, radioactive, luminescent or chemiluminescent label, which allow for detection of a polynucleotide; or nucleotides

containing a reactive group such as biotin or a thiol group, which facilitates immobilization of a polynucleotide to a solid support. A polynucleotide also can contain one or more backbone bonds that are selectively cleavable, for example, chemically, enzymatically or photolytically. For example, a polynucleotide can include one or more deoxyribonucleotides, followed by one or more ribonucleotides, which can be followed by one or more deoxyribonucleotides, such a sequence being cleavable at the ribonucleotide sequence by base hydrolysis. A polynucleotide also can contain one or more bonds that are relatively resistant to cleavage, for example, a chimeric oligonucleotide primer, which can include nucleotides linked by peptide nucleic acid bonds and at least one nucleotide at the 3' end, which is linked by a phosphodiester bond or other suitable bond, and is capable of being extended by a polymerase. Peptide nucleic acid sequences can be prepared using well-known methods (see, for example, Weiler *et al.* Nucleic acids Res. 25: 2792-2799 (1997)).

As used herein, "similarity" between two proteins or nucleic acids refers to the relatedness between the sequence of amino acids of the proteins or the nucleotide sequences of the nucleic acids. Similarity can be based on the degree of identity and/or homology of sequences of residues and the residues contained therein. Methods for assessing the degree of similarity between proteins or nucleic acids are known to those of skill in the art. For example, in one method of assessing sequence similarity, two amino acid or nucleotide sequences are aligned in a manner that yields a maximal level of identity between the sequences. "Identity" refers to the extent to which the amino acid or nucleotide sequences are invariant. Alignment of amino acid sequences, and to some extent nucleotide sequences, also can take into account conservative differences and/or frequent substitutions in amino acids (or nucleotides). Conservative differences are those that preserve the physico-chemical properties of the residues involved. Alignments can be global (alignment of the compared sequences over the entire length of the sequences and including all residues) or local (the alignment of a portion of the sequences that includes only the most similar region or regions).

"Identity" per se has an art-recognized meaning and can be calculated using published techniques. (See, e.g.: *Computational Molecular Biology*, Lesk, A.M., ed., Oxford University Press, New York, 1988; *Biocomputing: Informatics and Genome Projects*, Smith, D.W., ed., Academic Press, New York, 1993; *Computer Analysis of Sequence Data*, Part I, Griffin, A.M., and Griffin, H.G., eds., Humana Press, New Jersey, 1994; *Sequence Analysis in Molecular Biology*, von Heinje, G., Academic Press, 1987; and Sequence Analysis Primer, Gribskov, M. and Devereux, J., eds., M Stockton Press, New York, 1991). While there exists a number of methods to measure identity between two polynucleotide or polypeptides, the

term "identity" is well known to skilled artisans (Carillo, H. & Lipton, D., *SIAM J Applied Math 48*:1073 (1988)).

As used herein, homologous (with respect to nucleic acid and/or amino acid sequences) means about greater than or equal to 25% sequence homology, typically greater than or equal to 25%, 40%, 50%, 60%, 70%, 80%, 85%, 90% or 95% sequence homology; the precise percentage can be specified if necessary. For purposes herein the terms "homology" and "identity" are often used interchangeably, unless otherwise indicated. In general, for determination of the percentage homology or identity, sequences are aligned so that the highest order match is obtained (see, e.g.: *Computational Molecular Biology*, Lesk, A.M., ed., Oxford University Press, New York, 1988; *Biocomputing: Informatics and Genome Projects*, Smith, D.W., ed., Academic Press, New York, 1993; *Computer Analysis of Sequence Data, Part I*, Griffin, A.M., and Griffin, H.G., eds., Humana Press, New Jersey, 1994; *Sequence Analysis in Molecular Biology*, von Heinje, G., Academic Press, 1987; and *Sequence Analysis Primer*, Gribskov, M. and Devereux, J., eds., M Stockton Press, New York, 1991; Carillo *et al.* (1988) *SIAM J Applied Math 48*:1073). By sequence homology, the number of conserved amino acids is determined by standard alignment algorithms programs, and can be used with default gap penalties established by each supplier. Substantially homologous nucleic acid molecules hybridize typically at moderate stringency or at high stringency all along the length of the nucleic acid of interest. Also contemplated are nucleic acid molecules that contain degenerate codons in place of codons in the hybridizing nucleic acid molecule.

Whether any two molecules have nucleotide sequences or amino acid sequences that are at least 60%, 70%, 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% "identical" or "homologous" can be determined using known computer algorithms such as the "FASTA" program, using for example, the default parameters as in Pearson *et al.* (1988) *Proc. Natl. Acad. Sci. USA 85*:2444 (other programs include the GCG program package (Devereux, J., *et al., Nucleic Acids Research 12(I)*:387 (1984)), BLASTP, BLASTN, FASTA (Atschul, S.F., *et al., J Molec Biol 215*:403 (1990)); Guide to Huge Computers, Martin J. Bishop, ed., Academic Press, San Diego, 1994, and Carillo *et al.* (1988) *SIAM J Applied Math 48*:1073). For example, the BLAST function of the National Center for Biotechnology Information database can be used to determine identity. Other commercially or publicly available programs include, DNAStar "MegAlign" program (Madison, WI) and the University of Wisconsin Genetics Computer Group (UWG) "Gap" program (Madison WI). Percent homology or identity of proteins and/or nucleic acid molecules can be determined, for

example, by comparing sequence information using a GAP computer program (e.g., Needleman *et al.* (1970) *J. Mol. Biol.* 48:443, as revised by Smith and Waterman ((1981) *Adv. Appl. Math.* 2:482). Briefly, the GAP program defines similarity as the number of aligned symbols (i.e., nucleotides or amino acids), which are similar, divided by the total number of symbols in the shorter of the two sequences. Default parameters for the GAP program can include: (1) a unary comparison matrix (containing a value of 1 for identities and 0 for non-identities) and the weighted comparison matrix of Gribskov *et al.* (1986) *Nucl. Acids Res.* 14:6745, as described by Schwartz and Dayhoff, eds., *ATLAS OF PROTEIN SEQUENCE AND STRUCTURE*, National Biomedical Research Foundation, pp. 353-358 (1979); (2) a penalty of 3.0 for each gap and an additional 0.10 penalty for each symbol in each gap; and (3) no penalty for end gaps.

Therefore, as used herein, the term "identity" or "homology" represents a comparison between a test and a reference polypeptide or polynucleotide. As used herein, the term at least "90% identical to" refers to percent identities from 90 to 99.99 relative to the reference nucleic acid or amino acid sequence of the polypeptide. Identity at a level of 90% or more is indicative of the fact that, assuming for exemplification purposes a test and reference polypeptide length of 100 amino acids are compared. No more than 10% (i.e., 10 out of 100) of the amino acids in the test polypeptide differs from that of the reference polypeptide. Similar comparisons can be made between test and reference polynucleotides. Such differences can be represented as point mutations randomly distributed over the entire length of a polypeptide or they can be clustered in one or more locations of varying length up to the maximum allowable, e.g. 10/100 amino acid difference (approximately 90% identity). Differences are defined as nucleic acid or amino acid substitutions, insertions or deletions. At the level of homologies or identities above about 85-90%, the result should be independent of the program and gap parameters set; such high levels of identity can be assessed readily, often by manual alignment without relying on software.

As used herein, a polypeptide containing a specified percentage of amino acids set forth in a reference polypeptide refers to the proportion of contiguous identical amino acids shared between a polypeptide and a reference polypeptide. For example, an isoform that contains 70% of the amino acids set forth in a reference polypeptide having a sequence of amino acids set forth in SEQ ID NO:XX, which recites 147 amino acids, means that the reference polypeptide contains at least 103 contiguous amino acids set forth in the amino acid sequence of SEQ ID NO:XX.

As used herein, an aligned sequence refers to the use of homology (similarity and/or identity) to align corresponding positions in a sequence of nucleotides or amino acids. Typically, two or more sequences that are related by 50% or more identity are aligned. An aligned set of sequences refers to 2 or more sequences that are aligned at corresponding positions and can include aligning sequences derived from RNAs, such as ESTs and other cDNAs, aligned with genomic DNA sequence.

As used herein, "primer" refers to a nucleic acid molecule that can act as a point of initiation of template-directed DNA synthesis under appropriate conditions (e.g., in the presence of four different nucleoside triphosphates and a polymerization agent , such as DNA polymerase, RNA polymerase or reverse transcriptase) in an appropriate buffer and at a suitable temperature. It will be appreciated that a certain nucleic acid molecules can serve as a "probe" and as a "primer." A primer, however, has a 3' hydroxyl group for extension. A primer can be used in a variety of methods, including, for example, polymerase chain reaction (PCR), reverse-transcriptase (RT)-PCR, RNA PCR, LCR, multiplex PCR, panhandle PCR, capture PCR, expression PCR, 3' and 5' RACE, in situ PCR, ligation-mediated PCR and other amplification protocols.

As used herein, "primer pair" refers to a set of primers that includes a 5' (upstream) primer that hybridizes with the 5' end of a sequence to be amplified (e.g. by PCR) and a 3' (downstream) primer that hybridizes with the complement of the 3' end of the sequence to be amplified.

As used herein, "specifically hybridizes" refers to annealing, by complementary base-pairing, of a nucleic acid molecule (e.g. an oligonucleotide) to a target nucleic acid molecule. Those of skill in the art are familiar with *in vitro* and *in vivo* parameters that affect specific hybridization, such as length and composition of the particular molecule. Parameters particularly relevant to *in vitro* hybridization further include annealing and washing temperature, buffer composition and salt concentration. Exemplary washing conditions for removing non-specifically bound nucleic acid molecules at high stringency are 0.1 x SSPE, 0.1% SDS, 65°C, and at medium stringency are 0.2 x SSPE, 0.1% SDS, 50°C. Equivalent stringency conditions are known in the art. The skilled person can readily adjust these parameters to achieve specific hybridization of a nucleic acid molecule to a target nucleic acid molecule appropriate for a particular application.

As used herein, substantially identical to a product means sufficiently similar so that the property of interest is sufficiently unchanged so that the substantially identical product can be used in place of the product.

As used herein, it also is understood that the terms "substantially identical" or "similar" varies with the context as understood by those skilled in the relevant art.

As used herein, an allelic variant or allelic variation references any of two or more alternative forms of a gene occupying the same chromosomal locus. Allelic variation arises naturally through mutation, and can result in phenotypic polymorphism within populations. Gene mutations can be silent (no change in the encoded polypeptide) or can encode polypeptides having altered amino acid sequence. The term "allelic variant" also is used herein to denote a protein encoded by an allelic variant of a gene. Typically the reference form of the gene encodes a wildtype form and/or predominant form of a polypeptide from a population or single reference member of a species. Typically, allelic variants, which include variants between and among species typically have at least 80%, 90% or greater amino acid identity with a wildtype and/or predominant form from the same species; the degree of identity depends upon the gene and whether comparison is interspecies or intraspecies. Generally, intraspecies allelic variants have at least about 80%, 85%, 90% or 95% identity or greater with a wildtype and/or predominant form, including 96%, 97%, 98%, 99% or greater identity with a wildtype and/or predominant form of a polypeptide. Reference to an allelic variant herein generally refers to variations n proteins among members of the same species.

As used herein, "allele," which is used interchangeably herein with "allelic variant" refers to alternative forms of a gene or portions thereof. Alleles occupy the same locus or position on homologous chromosomes. When a subject has two identical alleles of a gene, the subject is said to be homozygous for that gene or allele. When a subject has two different alleles of a gene, the subject is said to be heterozygous for the gene. Alleles of a specific gene can differ from each other in a single nucleotide or several nucleotides, and can include substitutions, deletions and insertions of nucleotides. An allele of a gene also can be a form of a gene containing a mutation.

As used herein, species variants refer to variants in polypeptides among different species, including different mammalian species, such as mouse and human.

As used herein, a splice variant refers to a variant produced by differential processing of a primary transcript of genomic DNA that results in more than one type of mRNA.

As used herein, the term promoter means a portion of a gene containing DNA sequences that provide for the binding of RNA polymerase and initiation of transcription. Promoter sequences are commonly, but not always, found in the 5' non-coding region of genes.

As used herein, isolated or purified polypeptide or protein or biologically-active portion thereof is substantially free of cellular material or other contaminating proteins from the cell or tissue from which the protein is derived, or substantially free from chemical precursors or other chemicals when chemically synthesized. Preparations can be determined to be substantially free if they appear free of readily detectable impurities as determined by standard methods of analysis, such as thin layer chromatography (TLC), gel electrophoresis and high performance liquid chromatography (HPLC), used by those of skill in the art to assess such purity, or sufficiently pure such that further purification does not detectably alter the physical and chemical properties, such as enzymatic and biological activities, of the substance. Methods for purification of the compounds to produce substantially chemically pure compounds are known to those of skill in the art. A substantially chemically pure compound, however, can be a mixture of stereoisomers. In such instances, further purification might increase the specific activity of the compound.

The term substantially free of cellular material includes preparations of proteins in which the protein is separated from cellular components of the cells from which it is isolated or recombinantly-produced. In one embodiment, the term substantially free of cellular material includes preparations of protease proteins having less that about 30% (by dry weight) of non-protease proteins (also referred to herein as a contaminating protein), generally less than about 20% of non-protease proteins or 10% of non-protease proteins or less that about 5% of non-protease proteins. When the protease protein or active portion thereof is recombinantly produced, it also is substantially free of culture medium, i.e., culture medium represents less than about or at 20%, 10% or 5% of the volume of the protease protein preparation.

As used herein, the term substantially free of chemical precursors or other chemicals includes preparations of protease proteins in which the protein is separated from chemical precursors or other chemicals that are involved in the synthesis of the protein. The term includes preparations of protease proteins having less than about 30% (by dry weight) 20%, 10%, 5% or less of chemical precursors or non-protease chemicals or components.

As used herein, synthetic, with reference to, for example, a synthetic nucleic acid molecule or a synthetic gene or a synthetic peptide refers to a nucleic acid molecule or polypeptide molecule that is produced by recombinant methods and/or by chemical synthesis methods.

As used herein, production by recombinant means by using recombinant DNA methods means the use of the well known methods of molecular biology for expressing proteins encoded by cloned DNA.

As used herein, vector (or plasmid) refers to discrete elements that are used to introduce a heterologous nucleic acid into cells for either expression or replication thereof. The vectors typically remain episomal, but can be designed to effect integration of a gene or portion thereof into a chromosome of the genome. Also contemplated are vectors that are artificial chromosomes, such as yeast artificial chromosomes and mammalian artificial chromosomes. Selection and use of such vehicles are well known to those of skill in the art.

As used herein, an expression vector includes vectors capable of expressing DNA that is operatively linked with regulatory sequences, such as promoter regions, that are capable of effecting expression of such DNA fragments. Such additional segments can include promoter and terminator sequences, and optionally can include one or more origins of replication, one or more selectable markers, an enhancer, a polyadenylation signal, and the like. Expression vectors are generally derived from plasmid or viral DNA, or can contain elements of both. Thus, an expression vector refers to a recombinant DNA or RNA construct, such as a plasmid, a phage, recombinant virus or other vector that, upon introduction into an appropriate host cell, results in expression of the cloned DNA. Appropriate expression vectors are well known to those of skill in the art and include those that are replicable in eukaryotic cells and/or prokaryotic cells and those that remain episomal or those which integrate into the host cell genome.

As used herein, vector also includes "virus vectors" or "viral vectors." Viral vectors are engineered viruses that are operatively linked to exogenous genes to transfer (as vehicles or shuttles) the exogenous genes into cells.

As used herein, operably or operatively linked when referring to DNA segments means that the segments are arranged so that they function in concert for their intended purposes, e.g., transcription initiates in the promoter and proceeds through the coding segment to the terminator.

As used herein, biological sample refers to any sample obtained from a living or viral source and includes any cell type or tissue of a subject from which nucleic acid or protein or other macromolecule can be obtained. Biological samples include, but are not limited to, body fluids, such as blood, plasma, serum, cerebrospinal fluid, synovial fluid, urine and sweat, tissue and organ samples from animals and plants. Also included are soil and water samples and other environmental samples, viruses, bacteria, fungi, algae, protozoa and

components thereof. Hence bacterial and viral and other contamination of food products and environments can be assessed. The methods herein are practiced using biological samples and in some embodiments, such as for profiling, also can be used for testing any sample.

As used herein, macromolecule refers to any molecule having a molecular weight from the hundreds up to the millions. Macromolecules include peptides, proteins, nucleotides, nucleic acids, and other such molecules that are generally synthesized by biological organisms, but can be prepared synthetically or using recombinant molecular biology methods.

As used herein, the term "biopolymer" is a biological molecule, including macromolecules, composed of two or more monomeric subunits, or derivatives thereof, which are linked by a bond or a macromolecule. A biopolymer can be, for example, a polynucleotide, a polypeptide, a carbohydrate, or a lipid, or derivatives or combinations thereof, for example, a nucleic acid molecule containing a peptide nucleic acid portion or a glycoprotein, respectively. Biopolymers include, but are not limited to, nucleic acids, proteins, polysaccharides, lipids and other macromolecules. Nucleic acids include DNA, RNA, and fragments thereof. Nucleic acids can be derived from genomic DNA, RNA, mitochondrial nucleic acid, chloroplast nucleic acid and other organelles with separate genetic material.

As used herein, a biomolecule is any compound found in nature, or derivatives thereof. Biomolecules include, but are not limited to: oligonucleotides, oligonucleosides, proteins, peptides, amino acids, peptide nucleic acids (PNAs), oligosaccharides and monosaccharides.

As used herein, a biological particle refers to a virus, such as a viral vector or viral capsid with or without packaged nucleic acid, phage, including a phage vector or phage capsid, with or without encapsulated nucleic acid, a single cell, including eukaryotic and prokaryotic cells or fragments thereof, a liposome or micellar agent or other packaging particle, and other such biological materials.

As used herein, a composition refers to any mixture. It can be a solution, a suspension, liquid, powder, a paste, aqueous, non-aqueous or any combination thereof.

As used herein, a combination refers to any association between or among two or more items. The combination can be two or more separate items, such as two compositions or two collections, can be a mixture thereof, such as a single mixture of the two or more items, or any variation thereof.

As used herein, kit refers to a packaged combination, optionally including instructions and/or reagents for their use.

As used herein, fluid refers to any composition that can flow. Fluids thus encompass compositions that are in the form of semi-solids, pastes, solutions, aqueous mixtures, gels, lotions, creams and other such compositions.

As used herein, antigenic means that a polypeptide induce an immune response. Highly antigenic polypeptides are those that reproducibly and predictably induce an immune response.

As used herein, a pharmaceutical effect or therapeutic effect refers to an effect observed upon administration of an agent intended for treatment of a disease or disorder or for amelioration of the symptoms thereof.

As used herein, "disease or disorder" refers to a pathological condition in an organism resulting from cause or condition including, but not limited to, infections, acquired conditions, genetic conditions, and characterized by identifiable symptoms. Diseases and disorders of interest herein are those involving a specific target protein including those mediated by a target protein and those in which a target protein plays a role in the etiology or pathology. Exemplary target proteins and associated diseases and disorders are described elsewhere herein.

As used herein, "treating" a subject with a disease or condition means that the subject's symptoms are partially or totally alleviated, or remain static following treatment. Hence treatment encompasses prophylaxis, therapy and/or cure. Prophylaxis refers to prevention of a potential disease and/or a prevention of worsening of symptoms or progression of a disease. Treatment also encompasses any pharmaceutical use of a modified interferon and compositions provided herein.

As used herein, a therapeutic agent, therapeutic regimen, radioprotectant, or chemotherapeutic mean conventional drugs and drug therapies, including vaccines, which are known to those skilled in the art. Radiotherapeutic agents are well known in the art.

As used herein, treatment means any manner in which the symptoms of a condition, disorder or disease or other indication, are ameliorated or otherwise beneficially altered.

As used herein therapeutic effect means an effect resulting from treatment of a subject that alters, typically improves or ameliorates the symptoms of a disease or condition or that cures a disease or condition. A therapeutically effective amount refers to the amount of a composition, molecule or compound which results in a therapeutic effect following administration to a subject.

As used herein, the term "subject" refers to an animal, including a mammal, such as a human being.

As used herein, a patient refers to a human subject.

As used herein, amelioration of the symptoms of a particular disease or disorder by a treatment, such as by administration of a pharmaceutical composition or other therapeutic, refers to any lessening, whether permanent or temporary, lasting or transient, of the symptoms that can be attributed to or associated with administration of the composition or therapeutic.

As used herein, prevention or prophylaxis refers to methods in which the risk of developing disease or condition is reduced.

As used herein, an effective amount is the quantity of a therapeutic agent necessary for preventing, curing, ameliorating, arresting or partially arresting a symptom of a disease or disorder.

As used herein, administration refers to any method in which an antibody or protion thereof is contacted with its target protein. Adminstration can be effected *in vivo* or *ex vivo* or *in vitro*. For example, for *ex vivo* administration a body fluid, such as blood, is removed from a subject and contacted outside the body with the antibody or portion thereof. For *in vivo* administration, the antibody or portion thereof can be introduced into the body, such as by local, topical, systemic and/or other route of introduction. *In vitro* administration encompasses methods, such as cell culture methods.

As used herein, unit dose form refers to physically discrete units suitable for human and animal subjects and packaged individually as is known in the art.

As used herein, a single dosage formulation refers to a formulation for direct administration.

As used herein, an "article of manufacture" is a product that is made and sold. As used throughout this application, the term is intended to encompass compiled germline antibodies or antibodies obtained therefrom contained in articles of packaging.

As used herein, fluid refers to any composition that can flow. Fluids thus encompass compositions that are in the form of semi-solids, pastes, solutions, aqueous mixtures, gels, lotions, creams and other such compositions.

As used herein, animal includes any animal, such as, but are not limited to primates including humans, gorillas and monkeys; rodents, such as mice and rats; fowl, such as chickens; ruminants, such as goats, cows, deer, sheep; ovine, such as pigs and other animals. Non-human animals exclude humans as the contemplated animal. The germline segments, and resulting antibodies, provided herein are from any source, animal, plant, prokaryotic and

fungal. Most germline segments, and resulting antibodies, are of animal origin, including mammalian origin.

As used herein, a control refers to a sample that is substantially identical to the test sample, except that it is not treated with a test parameter, or, if it is a sample plasma sample, it can be from a normal volunteer not affected with the condition of interest. A control also can be an internal control.

As used herein, the singular forms "a," "an" and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to a compound, comprising "an extracellular domain" includes compounds with one or a plurality of extracellular domains.

As used herein, ranges and amounts can be expressed as "about" a particular value or range. About also includes the exact amount. Hence "about 5 bases" means "about 5 bases" and also "5 bases."

As used herein, "optional" or "optionally" means that the subsequently described event or circumstance does or does not occur, and that the description includes instances where said event or circumstance occurs and instances where it does not. For example, an optionally substituted group means that the group is unsubstituted or is substituted.

As used herein, the abbreviations for any protective groups, amino acids and other compounds, are, unless indicated otherwise, in accord with their common usage, recognized abbreviations, or the IUPAC-IUB Commission on Biochemical Nomenclature (see, (1972) Biochem. 11:1726).

B. OVERVIEW

Provided are methods for generating combinatorial libraries (i.e. collections) of functional antibodies, and the resulting libraries. The collections or libraries provided are addressable, where antibodies within each address have the same sequence, are known *a priori*, and are different from the antibodies at each other address in the collection. The collections can be provided as physical arrays or the members can be otherwise identified so that they can be sorted. The arrayed collections of antibodies can represent the complete repertoire of combined germline portions, a selected portion thereof, or collections of modified forms thereof. The members of the libraries are individually designed and addressed. Because of this, the libraries are highly diverse, permitting creation of libraries with far fewer members than other libraries, but having higher diversity. The libraries provided herein contain as few as 10^2 members and typically contain about or 10^3, 10^4, 2 x

10^4, 3 x 10^4, 4 x 10^4, 5 x 10^4, 6 x 10^4, 7 x 10^4, 8 x 10^4, 9 x 10^4, 10^5 and more unique members, including about or 10^6, 10^7, 10^8 , 10^9 and more unique members.

The collections of antibodies are addressable, such as in arrays or other addressable format, such that each member is identifiable and each locus has antibodies that are the same or that have the same binding specificity at each locus. The locus can be a physical locus or can be otherwise identifiable and sortable, such as an RF tag, attachment to label with a bar code , attachment to a chemical tag, in manners described for chemical libraries.

In contrast, other antibody libraries are produced such that they contain mixtures of antibodies at a locus, or contain unidentified members of libraries. Exemplary of such libraries are those described in any of the following: European Patent Application Nos. EP0368684 and EP89311731; International Published Patent Application Nos. WO92/001047, WO 02/38756, WO 97/08320, WO 2005/023993, WO 07/137616 and WO 2007/054816; United States Patent Nos. US 6,593,081 and US 6,989,250; United States Published Patent Application No. US 2002/0102613, US 2003/153038, US 2003/0022240, US 2005/0119455, US 2005/0079574 and US 2006/0234302; and Orlandi *et al.* (1989) *Proc Natl. Acad. Sci. U.S.A.,* 86:3833-3837; Ward *et al.* (1989) *Nature*, 341:544-546; Huse *et al.* (1989) *Science,* 246:1275-1281; Burton *et al.* (1991) *Proc. Natl. Acad. Sci., U.S.A.*, 88:10134-10137; Marks *et al.* (1991) *J Mol Biol*, 222:581-591; Hoogenboom *et al.* (1991) *J Mol Biol*, 227:381-388; Nissim *et al.* (1994) *EMBO J*, 13:692-698; Barbas *et al.* (1992) *Proc. Natl. Acad. Sci., U.S.A.*, 89:4457-4461; Akamatsu *et al.* (1993) *J. Immunol.*, 151:4651-1659; Griffiths *et al.* (1994) *EMBO J,* 13:3245-3260; Fellouse (2004) PNAS, 101:12467-12472; Persson *et al.* (2006) J. Mol. Biol. 357:607-620; Knappik *et al.* (2000) J. Mol. Biol. 296:57-86; Rothe *et al.* (2008) J. Mol. Biol. 376:1182-1200; Mondon *et al.* (2008) *Frontiers in Bioscience*, 13:1117-1129; and Behar, I (2007) *Expert Opin. Biol. Ther.*, 7:763-779.

Although many of these libraries contain large numbers of members (e.g. 10^8 -10^{10} members), there is no mechanism to ensure that all members are functional, nor to maximize diversity nor to represent the complete repertoire of germline sequences or a selected portion thereof. Thus, the composition and diversity of the library is not optimal. For example, many existing libraries are developed by PCR amplification of germline sequences. PCR amplification introduces errors into the resulting amplified products. In addition, in some methods hybrid primers are used to facilitate recombination of individual V(D)J segments. This can result in recombination events that are "out-of-frame" resulting in non-functional members. Also, in practicing such methods, members either are pooled (such as in a tube or via phage display) and screened together for binding to a target substrate or are introduced

into host cells as mixtures and then colonies are individually picked and grown. Upon identification of a positive interaction or other selected events, any "Hits" must be further characterized in order to be identified.

The combinatorial addressable libraries of antibodies provided herein do not share these problems. Each member of the collection is addressed, such that each member occupies a unique locus, for example, a spatial array or other array or other identifiable address (e.g., presentation in well-plates; being bound to a support or chip, bar-coded, color-coded, RF-tag labeled support or other such addressable format). Displaying members on an address is facilitated because each member is individually generated, and thus the sequence of each member is known. Display of the members can be achieved on any desired format, which permits screening the members not only for binding but also for function. The "Hits" can be quickly identified coincident with the screening results. Hence, structure/activity relationships (SAR) between members of the collections can be performed to identify similarities in characteristics or sequences between and among identified "Hits". Pharmacokinetics and dose-responses also are available on screening or immediately following "Hit" identification. Further optimization of "Hits" can be performed such as by mutagenesis and iterative screening. Accordingly, the methods provided herein for generating addressable combinatorial antibody collections and the resulting collections offer a robust alternative to identification of antibodies with desired specificities and/or activities, for example, for use as therapeutic antibodies.

1. Methods of Generating Addressable Combinatorial Antibody Collections

In one example of the methods provided herein, variable heavy (VH) and variable light (VL) chain members of the libraries are generated, recombinantly or synthetically by DNA synthesis, from known germline antibody sequences or modified sequences thereof. Thus, the members can represent the entire repertoire of the naïve germline, and are not restricted based on selection against "self" proteins. Combinatorial diversity in the collection exists from recombination (e.g. such as performed *in silico* by computer software as described herein) of individual V, D and J segments that make up the variable heavy chain and of individual V (V_κ or V_λ) and J (J_κ, or J_λ) segments that make up the variable light chains (see Figure 1). The sequences can be joined together by random recombination of all combinations of V(D)J segments generating maximal combinatorial diversity. Alternatively, the V(D)J segments can be recombined using rational or semi-rational approaches such that a specific sequence or subset of sequences are used in generating the members of the library. For example, germline segments can be selected based on sequence similarities or differences

or based on shared characteristics (e.g., a V region family, CDR3 length or composition or other biochemical attribute).

In the methods herein, the combinatorial diversity of the resulting members is optimized for functioning sequences that encode a full length polypeptide. Although all combinations of V(D)J segments can be recombined, the joints in the compiled sequences between the different V(D)J sequences are selected so that the resulting sequences are in-frame. Each functioning member occupies an address (e.g. a position in a well or chip) of a collection. *In vivo*, however, junctional diversity exists upon V(D)J recombination such that nucleotides are often inserted at junction regions, which can result in new amino acids at the junctions. Hence, in some example of the methods herein, the resulting in-frame members can be subjected to mutagenesis, for example, to introduce diversity at the junction regions (e.g., junctional diversity). In such examples, each locus can contain a pool of antibodies with the same V(D)J segments, but differing from each other by one or more mutations (e.g. insertions, deletions or replacements of amino acids).

In addition to generating naïve antibody libraries, the methods provided herein can be used to generate directed antibody libraries, whereby the resulting members are optimized against known targets. For example, the starting sequences of individual V(D)J segments of heavy and light chains can be generated to contain a known binding peptide against a target. The goal of such a library format is to generate a platform that allows the discovery of agonist or antagonist antibodies that mimic therapeutic targets, for example, growth factors, cytokines, hormones or other cellular activators.

Generally, the members of the collections provided herein contain all or a portion of a variable light (VL) and variable heavy (VH) chain, so long as the resulting antibody is sufficient to form an antigen binding site. Hence, in addition to combinatorial diversity, diversity in the collections provided herein is achieved by pairing diversity by combining heavy and light chains (Figure 1). Thus, the individually recombined VL and VH chains as discussed above can themselves be paired in varying combinations to generate a scalable collection of all possible combinations of VL and VH chains, or a subset thereof. For example, a library can be generated where all members have the same VH chains, but are paired with all or a subset of the individually recombined VL members. The heavy and light chain members can be paired by direct or indirect linkage. The resulting pairs of heavy and light chains can be presented in any desired library format, such as a complete antibody, Fab forms, single chain (sc) Fv forms, or any multimeric form thereof.

2. The Resulting Libraries

Provided herein are libraries of nucleic acid molecules encoding VL chains and libraries of nucleic acid molecules encoding VH chains. Also provided herein are combinatorial antibody libraries that are paired antibody libraries containing at a minimum all or a portion of a VL and VH chains, such that each resulting member in the library is sufficient to form an antigen binding site. The libraries can be naïve libraries representing all or a portion of all possible germline antibodies, or can be modified forms thereof. The resulting members of the paired antibody collections include, but are not limited to, Fab, single chain (sc) Fv, disulfide-stabilized Fv and multimeric formats such as minibodies, bis-scFv, diabodies, triabodies and tetrabodies. The libraries provided herein differ from existing antibody collections because each individual member of the collection is known and, in the case of the antibody libraries, each member is "productive" or "functional" because the encoding nucleic acid molecules lack stop codons that can otherwise truncate the resulting protein before a full length polypeptide can be produced. Typically, all libraries provided herein are in an addressable format, such that the identity of each member of the library is known based on its locus or "address". Exemplary of antibody collections provided herein are combinatorial Fab libraries, such as addressable combinatorial Fab libraries. Any of the above libraries can include 10^2, 10^3, 10^4 or 10^5, or more different members.

3. Applications of the Libraries

The resulting libraries can be used for any application or purpose as desired. Because of their diversity, specificity and effector functions, antibodies are attractive candidates for protein-based therapeutics. Thus, the libraries can be used in methods of screening for various activities to identify antibodies with unique functions, such as for use as therapeutic antibodies. For example, the antibody libraries provided herein can be used in screening assays based on function or binding against unknown or known targets. In particular, it is contemplated herein that the resulting libraries can be used in functional assays, such as cell based assays, to discover new MAbs (e.g., Fabs) against selected targets. Hence, the libraries provided herein offer advantages over existing libraries because they permit identification of antibodies that perhaps are low affinity binders, but functionally are ideal therapeutic antibody candidates. Accordingly, both agonist and antagonist antibodies can be easily discovered.

The resulting identified "Hits" can be further optimized against a desired target by iterative screening methods of antibody discovery (Figure 2). For example, antibody "Hits" identified from binding or activity-based screening assays, can be used to generate further libraries containing V(D)J germline segments related (e.g., by sequence identity or similarity)

to the V(D)J germline segments in the identified Hit(s). By virtue of the fact that the collections are arrayed, such that the identity of each individual member in the collection is known, iterative approaches can be used for the rapid expansion of "Hits" to identify antibody "Hits" with improved therapeutic applications. In addition, antibody "Hits" can be used as a scaffold for mutagenesis to generate modified heavy and light chains, and for successive generations of libraries of nucleic acid molecules encoding modified VL chains, libraries of nucleic acid molecules encoding modified VH chains and antibody libraries minimally containing modified VL and VH chains.

Finally, antibody "Hits" identified from the libraries herein and/or further optimized by iterative screening and/or other mutagenesis methods, can be used in a variety of *in vitro* and *in vivo* applications by virtue of the specificity for one or more target proteins. For example, the antibodies can be used in diagnostic methods. In another example, the antibodies can be used in methods of treatment and other uses for treating a disease or disorder which is associated with expression or activation of a particular target protein, and for which the antibody can modulate.

The following sections describe exemplary components of the methods and libraries, the methods of generating combinatorial antibody libraries, including arrayed libraries, the resulting libraries and applications of the libraries.

C. ANTIBODIES

Provided herein are methods of generating libraries of addressable combinatorial antibodies, and the resulting libraries and antibodies. The antibodies in the libraries minimally include all or a portion of a variable heavy chain (VH) and/or a variable light (VL) chain so long as the antibody contains a sufficient antibody binding site. For example, the VH and VL chains of the antibodies provided herein typically include one or more, generally two or more, and up to all of the three CDRs making up the antigen binding site. In some examples, the antibodies can be generated to contain a synthetic CDR, whereby a peptide against a known target is grafted into the CDR regions of the variable region to effect directed binding and activation of the target (see e.g., Frederickson *et al.* (2006) *PNAS* 103: 14307-14312).

Optionally, the antibodies can include all or a portion of the constant heavy chain (e.g. one or more CH domains such as CH1, CH2, CH3 and CH4 and/or a constant heavy chain (CL)). Hence, the antibodies included in the libraries herein include those that are full-length antibodies, and also include fragments or portions thereof including, for example, Fab, Fab', $F(ab')_2$, single-chain Fvs (scFv), Fv, dsFv, diabody, Fd and Fd' fragments Fab

fragments, Fd fragments, scFv fragments, and scFab fragments. For example, antibodies in the libraries provided herein include Fabs.

A description of the structure, sequence and function of antibodies are known to one of skill in the art and one of skill in the art is familiar with the mechanisms that give rise to diversity in the germline. It is contemplated herein that libraries of combinatorial antibodies can be made by recombination of germline DNA sequences that mimic the process of germline recombination during B cell differentiation. Such recombination can be performed *in silico* (e.g., by a computer) as described herein or can be performed manually using molecular biology techniques. Recombined sequences can be individually generated, such as by DNA synthesis or by recombinant DNA techniques, to generate all permutations of variable heavy and light chain sequences. The antibodies can be expressed in any desired form , and in some instances, pairing of variable and constant regions can be achieved. The result is that the libraries of combinatorial antibodies provided herein can represent the entire naïve antibody repertoire or a subset thereof.

1. Antibody Polypeptides

Antibodies are produced naturally by B cells in membrane-bound and secreted forms. Antibodies specifically recognize and bind antigen epitopes through cognate interactions. Antibody binding to cognate antigens can initiate multiple effector functions, which cause neutralization and clearance of toxins, pathogens and other infectious agents. Diversity in antibody specificity arises naturally due to recombination events during B cell development. Through these events, various combinations of multiple antibody V, D and J gene segments, which encode variable regions of antibody molecules, are joined with constant region genes to generate a natural antibody repertoire with large numbers of diverse antibodies. A human antibody repertoire contains more than 10^{10} different antigen specificities and thus theoretically can specifically recognize any foreign antigen. Antibodies include such naturally produced antibodies, as well as synthetically, i.e. recombinantly, produced antibodies, such as antibody fragments.

In folded antibody polypeptides, binding specificity is conferred by antigen binding site domains, which contain portions of heavy and/or light chain variable region domains. Other domains on the antibody molecule serve effector functions by participating in events such as signal transduction and interaction with other cells, polypeptides and biomolecules. These effector functions cause neutralization and/or clearance of the infecting agent recognized by the antibody.

2. Antibody structural and functional domains

A full-length antibody contains four polypeptide chains, two identical heavy (H) chains (each usually containing about 440 amino acids) and two identical light (L) chains (each containing about 220 amino acids). The light chains exist in two distinct forms called kappa (κ) and lambda (λ). Each chain is organized into a series of domains organized as immunoglobulin (Ig) domains, including variable (V) and constant (C) region domains. Light chains have two domains, corresponding to the C region (CL) and the V region (VL). Heavy chains have four domains, the V region (VH) and three or four domains in the C region (CH1, CH2 , CH3 and CH4), and, in some cases, hinge region. The four chains (two heavy and two light) are held together by a combination of covalent and non-covalent (disulfide) bonds.

Antibodies include those that are full-lengths and those that are fragments thereof, namely Fab, Fab', $F(ab')_2$, single-chain Fvs (scFv), Fv, dsFv, diabody, Fd and Fd' fragments. The fragments include those that are in single-chain or dimeric form. The Fv fragment, which contains only the VH and VL domain, is the smallest immunoglobulin fragment that retains the whole antigen-binding site (see, for example, *Methods in Molecular Biology*, Vol 207: *Recombinant Antibodies for Cancer Therapy Methods and Protocols* (2003); Chapter 1; p 3-25, Kipriyanov). Stabilization of Fv are achieved by direct linkage of the VH and VL chains, such as for example, by linkage with peptides (to generate single-chain Fvs (scFv)), disulfide bridges or knob-into-hole mutations. Fab fragments, in contrast, are stable because of the presence of the CH1 and CL domains that hold together the variable chains. Fd antibodies, which contain only the VH domain, lack a complete antigen-binding site and can be insoluble.

3. Antibody Sequence and Specificity

The variable region of the heavy and light chains are encoded by multiple germline gene segments separated by non-coding regions, or introns, and often are present on different chromosomes. For example, the genes for the immunoglobulin heavy chain region contains approximately 65 variable (V_H) genes, 27 Diversity (D_H) genes, and 6 Joining (J_H) genes. The kappa (κ) and lambda (λ) light chains are also each encoded by a similar number of V_L and J_L gene segments, but do not include any D gene segments. Exemplary V_H, D_H, J_H and V_L (V_κ or V_λ) and J_L (J_κ or J_λ) germline gene segments are set forth in Tables 3-5.

During B cell differentiation germline DNA is rearranged whereby one D_H and one J_H gene segment of the heavy chain locus are recombined, which is followed by the joining of one V_H gene segment forming a rearranged VDJ gene that encodes a VH chain. The rearrangement occurs only on a single heavy chain allele by the process of allelic exclusion. Allelic exclusion is regulated by in-frame or "productive" recombination of the VDJ

segments, which occurs in only about one-third of VDJ recombinations of the variable heavy chain. When such productive recombination events first occur in a cell, this results in production of a μ heavy chain that gets expressed on the surface of a pre- B cell and transmits a signal to shut off further heavy chain recombination, thereby preventing expression of the allelic heavy chain locus. The surface-expressed μ heavy chain also acts to activate the kappa (κ) locus for rearrangement. The lambda (λ) locus is only activated for rearrangement if the κ recombination is unproductive on both loci. The light chain rearrangement events are similar to heavy chain, except that only the V_L and J_L segments are recombined. Before primary transcription of each, the corresponding constant chain gene is added. Subsequent transcription and RNA splicing leads to mRNA that is translated into an intact light chain or heavy chain.

The variable regions of antibodies confer antigen binding and specificity due to recombination events of individual germline V, D and J segments, whereby the resulting recombined nucleic acid sequences encoding the variable region domains differ among antibodies and confer antigen-specificity to a particular antibody. The variation, however, is limited to three complementarity determining regions (CDR1, CDR2, and CDR3) found within the N-terminal domain of the heavy (H) and (L) chain variable regions. The CDRs are interspersed with regions that are more conserved, termed "framework regions" (FR). The extent of the framework region and CDRs has been precisely defined (see e.g., Kabat, E.A. *et al.* (1991) *Sequences of Proteins of Immunological Interest*, Fifth Edition, U.S. Department of Health and Human Services, NIH Publication No. 91-3242, and Chothia, C. *et al.* (1987) *J. Mol. Biol.* 196:901-917). Each VH and VL is typically composed of three CDRs and four FRs arranged from the amino terminus to carboxy terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3 and FR4. Sequence variability among VL and VH domains is generally limited to the CDRs, which are the regions that form the antigen binding site. For example, for the heavy chain, generally, V_H genes encode the N-terminal three framework regions, the first two complete CDRs and the first part of the third CDR; the D_H gene encodes the central portion of the third CDR, and the J_H gene encodes the last part of the third CDR and the fourth framework region. For the light chain, the V_L genes encode the first CDR and second CDR. The third CDR (CDRL3) is formed by the joining of the V_L and J_L gene segments. Hence, CDRs 1 and 2 are exclusively encoded by germline V gene segment sequences. The VH and VL chain CDR3s form the center of the Ag-binding site, with CDRs 1 and 2 form the outside boundaries; the FRs support the scaffold by orienting the H and L CDRs. On average, an antigen binding site typically requires that at least four of the CDRs

make contact with the antigen's epitope, with CDR3 of both the heavy and light chain being the most variable and contributing the most specificity to antigen binding (see e.g., Janis Kuby, Immunology, Third Edition, New York, W.H. Freeman and Company, 1998, pp. 115-118). CDRH3, which includes all of the D gene segment, is the most diverse component of the Ab-binding site, and typically plays a critical role in defining the specificity of the Ab. In addition to sequence variation, there is variation in the length of the CDRs between the heavy and light chains (see Table 26 in Example 12).

The constant regions, on the other hand, are encoded by sequences that are more conserved among antibodies. These domains confer functional properties to antibodies, for example, the ability to interact with cells of the immune system and serum proteins in order to cause clearance of infectious agents. Different classes of antibodies, for example IgM, IgD, IgG, IgE and IgA, have different constant regions, allowing them to serve distinct effector functions.

These natural recombination events of V, D, and J, can provide nearly $2x10^7$ different antibodies with both high affinity and specificity. Additional diversity is introduced by nucleotide insertions and deletions in the joining segments and also by somatic hypermutation of V regions. The result is that there are approximately 10^{10} antibodies present in an individual with differing antigen specificities.

The methods provided herein take advantage of the mechanisms responsible for generating diversity between and among germline antibodies, thereby permitting generation of collections of antibodies that can be tested for varied functional or other properties.

D. METHODS OF GENERATING MEMBERS OF THE COMBINATORIAL ANTIBODY LIBRARY

Provided herein are methods of producing combinatorial antibody libraries and the resulting libraries. Typically, each member in the library contains a variable heavy chain and a variable light chain, or portions thereof sufficient to form an antigen binding site. In the methods provided herein, each antibody member of the library is generated by mimicking natural recombination events by combining known V(D)J gene segment sequences (e.g. from publicly available databases of germline sequences), or modified forms thereof, in various permutations, in-frame, to generate a plurality of nucleic acid sequences encoding functional VH and VL chains. For example, in the steps of the methods nucleic acid molecules encoding the variable heavy (VH) chain are generated by recombining individual V, D and J segments. Nucleic acid molecules encoding the variable light (VL) chain are generated by recombining individual V (V_κ or V_λ) and J (J_κ, or J_λ) segments that make up the variable light chains. The segments can be germline segments, or degenerate sequences thereof. In such

examples, the resulting antibodies produced by the method are naïve antibodies. It is contemplated herein, however, that the method can be performed using any modified form of a known germline segment, for example, to introduce further diversity into the library. For example, the method can be performed using reverse complement (i.e. inverted) sequences of D_H germline segments. The process of recombining germline segments in-frame can be performed manually using molecular biology techniques or in silico (e.g. using a computer programmed to perform an algorithm).

In the methods, the recombination is effected so that each gene segment is in-frame, such that resulting recombined nucleic acid molecules encodes a functional VH or VL polypeptide. Also, in the methods, each nucleic acid molecule is individually generated and synthesized. In the methods, resulting members of the library are produced by co-expression of nucleic acid molecules encoding the recombined variable region genes together, such that when expressed, a combinatorial antibody member is generated minimally containing a VH and VL chain, or portions thereof. In some examples of the methods, the nucleic acid molecule encoding the VH and VL chain can be expressed as a single nucleic acid molecule, whereby the genes encoding the heavy and light chain are joined by a linker. In another example of the methods, the nucleic acid molecules encoding the VH and VL chain can be separately provided for expression together. Thus, upon expression from the recombined nucleic acid molecules, each different member of the library represents a germline encoded antibody, whereby diversity is achieved by combinatorial diversity of V(D)J segments and pairing diversity of heavy and light chains. In the method, additional diversity can be introduced into the library using any of a number of approaches known in the art, including but not limited to, random mutagenesis, semi-rational or rational mutagenesis.

One or more or all steps of the method can be performed in an addressable format, such that the identity of each member in the process is known by its location at an addressed locus. Hence, provided herein are addressable libraries of germline recombined nucleic acid sequences encoding VH chains, addressable libraries of germline recombined nucleic acid sequences encoding VL chains, and addressable libraries formed by combinations of nucleic acids molecules encoding VL chains and nucleic acid molecules encoding VH chains at each locus. Also provided are addressable cells, each cell at a locus containing different combinations of a recombined nucleic acid molecule encoding a VL and a recombined nucleic acid encoding a VH. Resulting antibody libraries also can be addressable. Such addressable antibody libraries permit rapid identification of "Hits" and assessment of structure/activity relationships between and among "Hits." The resulting libraries of

antibodies can be screened for a variety of activities, such as but not limited to binding, proliferation, cytotoxicity and low affinity leads against difficult antigens, such as self antigens, ion channels, G-protein coupled receptors, novel epitopes, non-protein antigens and the discovery of agonist antibodies.

1. Methods for Producing Functional Recombined Germline Variable Region Genes

Provided herein is a method for generating nucleic acid molecules generated by recombination of germline segments or modified forms thereof, each nucleic acid molecule encoding a different and functional variable region of the heavy or light chains. Variable gene segments include V_H, D_H, J_H, V_κ, J_κ, V_λ and J_λ. Germline segments can be selected from but not limited to human, mouse, rat, sheep, pig, goat horse, rabbit or dog germline segments. Exemplary germline segments are of human origin.

a. Variable Gene Segments

i. Germline Segments

In practicing the methods herein, germline segment sequences are obtained from any source that provides antibody germlines gene segments. These include any databases or published literature that sets forth sequences of germline gene segments. Exemplary antibody germline sources include but are not limited to databases at the National Center for Biotechnology Information (NCBI), the international ImMunoGeneTics information system® (IMGT), the Kabat database and the Tomlinson's VBase database (Lefranc (2003) *Nucleic Acids Res.*, 31:307-310; Martin *et al.*, Bioinformatics Tools for Antibody Engineering in Handbook of Therapeutic Antibodies, Wiley-VCH (2007), pp. 104-107). If desired, nucleic acid sequences for non-human germline segments also can be obtained from published literature or publicly available databases. For example, an exemplary mouse germline databases is ABG database available at ibt.unam.mx/vir/v_mice.html. The Sequence Listing provided herein provides sequences of exemplary human germline segment sequences collected from the IMGT database and other public database (see e.g., SEQ ID NOS:10-451 and 868).

For example, exemplary human Heavy Chain Germline Segments (SEQ ID NO. 10-285) are listed in Table 3. Exemplary human Light Chain Kappa Germline Segments (SEQ ID NO. 286-364 and SEQ ID NO. 868) are listed in Table 4. Exemplary human Light Chain Lambda Germline Segments (SEQ ID NO. 365-451) are listed in Table 5. Germline segments are listed using IMGT gene names and definitions previously approved by the Human Genome Organization (HUGO) nomenclature committee. The segments are named

using IMGT nomenclature, whereby the first three letters indicate the locus (IGH, IGK or IGL), the fourth letter represents the gene (e.g., V for V-gene, D for D-gene, J for J-gene), the fifth position indicates the number of the subgroup, followed by a hyphen indicating the gene number classification. For alleles, the IMGT name is followed by an asterisk and a two figure number.

Tables 6-8 list alternative nomenclature for Human Heavy Chain V Genes, Human Light Chain Kappa V Genes, and Human Light Chain Lambda V Genes, respectively (see e.g. Lefranc, M.-P. *Exp Clin Immunogenet*, 18:100-116 (**2001**), Zachau, H.G. *Immunologist*, 4:49-54 (**1996**), Lefranc, M.-P. *Exp Clin Immunogenet*, 18:161-174 (**2000**), Kawasaki et al, *Genome Res*, 7:250-261 (**1997**), Lefranc, M.-P. *Exp Clin Immunogenet*, 18:242-254 (**2001**). Any desired naming convention can be used to identify antibody germline segments. One of skill in the art can identify a nucleic acid sequence using any desired naming convention. For purposes herein when describing recombined nucleic acid sequences (see e.g., Table 22), VH germline segments are named using IMGT nomenclature without any allele identified. Table 6 lists the IMGT nomenclature and corresponding IMGT nomenclature with the respective allele. VK germline segments are named using Zachau nomenclature. Table 7 lists the Zachau nomenclature and the corresponding IMGT nomenclature. VL germline segments are identified using Kawasaki nomenclature. Table 8 lists the Kawasaki nomenclature and the corresponding IMGT nomenclature. DH, JH, JK and JL germline segments are named using IMGT nomenclature.

Table 3: Human Heavy Chain Germline Segments

SEQ ID NO.	V Segments	SEQ ID NO.	D Segments	SEQ ID NO.	J Segments
10	IGHV1-18*01	239	IGHD1-1*01	273	IGHJ1*01
11	IGHV1-18*02	240	IGHD1-14*01	274	IGHJ2*01
12	IGHV1-2*01	241	IGHD1-20*01	275	IGHJ3*01
13	IGHV1-2*02	242	IGHD1-26*01	276	IGHJ3*02
14	IGHV1-2*03	243	IGHD1-7*01	277	IGHJ4*01
15	IGHV1-2*04	244	IGHD2-15*01	278	IGHJ4*02
16	IGHV1-24*01	245	IGHD2-2*01	279	IGHJ4*03
17	IGHV1-3*01	246	IGHD2-2*02	280	IGHJ5*01
18	IGHV1-3*02	247	IGHD2-2*03	281	IGHJ5*02
19	IGHV1-45*01	248	IGHD2-21*01	282	IGHJ6*01
20	IGHV1-45*02	249	IGHD2-21*02	283	IGHJ6*02
21	IGHV1-45*03	250	IGHD2-8*01	284	IGHJ6*03
22	IGHV1-46*01	251	IGHD2-8*02	285	IGHJ6*04
23	IGHV1-46*02	252	IGHD3-10*01		
24	IGHV1-46*03	253	IGHD3-10*02		

25	IGHV1-58*01	254	IGHD3-16*01		
26	IGHV1-58*02	255	IGHD3-16*02		
27	IGHV1-69*01	256	IGHD3-22*01		
28	IGHV1-69*02	257	IGHD3-3*01		
29	IGHV1-69*03	258	IGHD3-3*02		
30	IGHV1-69*04	259	IGHD3-9*01		
31	IGHV1-69*05	260	IGHD4-11*01		
32	IGHV1-69*06	261	IGHD4-17*01		
33	IGHV1-69*07	262	IGHD4-23*01		
34	IGHV1-69*08	263	IGHD4-4*01		
35	IGHV1-69*09	264	IGHD5-12*01		
36	IGHV1-69*10	265	IGHD5-18*01		
37	IGHV1-69*11	266	IGHD5-24*01		
38	IGHV1-69*12	267	IGHD5-5*01		
39	IGHV1-69*13	268	IGHD6-13*01		
40	IGHV1-8*01	269	IGHD6-19*01		
41	IGHV1-c*01	270	IGHD6-25*01		
42	IGHV1-f*01	271	IGHD6-6*01		
43	IGHV1-f*02	272	IGHD7-27*01		
44	IGHV2-26*01				
45	IGHV2-5*01				
46	IGHV2-5*02				
47	IGHV2-5*03				
48	IGHV2-5*04				
49	IGHV2-5*05				
50	IGHV2-5*06				
51	IGHV2-5*07				
52	IGHV2-5*08				
53	IGHV2-5*09				
54	IGHV2-5*10				
55	IGHV2-70*01				
56	IGHV2-70*02				
57	IGHV2-70*03				
58	IGHV2-70*04				
59	IGHV2-70*05				
60	IGHV2-70*06				
61	IGHV2-70*07				
62	IGHV2-70*08				
63	IGHV2-70*09				
64	IGHV2-70*10				
65	IGHV2-70*11				
66	IGHV2-70*12				
67	IGHV2-70*13				
68	IGHV3-11*01				
69	IGHV3-11*03				
70	IGHV3-13*01				
71	IGHV3-13*02				
72	IGHV3-13*02				
73	IGHV3-15*01				

74	IGHV3-15*02				
75	IGHV3-15*03				
76	IGHV3-15*04				
77	IGHV3-15*05				
78	IGHV3-15*06				
79	IGHV3-15*07				
80	IGHV3-15*08				
81	IGHV3-16*01				
82	IGHV3-16*02				
83	IGHV3-20*01				
84	IGHV3-21*01				
85	IGHV3-21*02				
86	IGHV3-23*01				
87	IGHV3-23*02				
88	IGHV3-23*03				
89	IGHV3-23*04				
90	IGHV3-23*05				
91	IGHV3-30*01				
92	IGHV3-30*02				
93	IGHV3-30*03				
94	IGHV3-30*04				
95	IGHV3-30*05				
96	IGHV3-30*06				
97	IGHV3-30*07				
98	IGHV3-30*08				
99	IGHV3-30*09				
100	IGHV3-30*10				
101	IGHV3-30*11				
102	IGHV3-30*12				
103	IGHV3-30*13				
104	IGHV3-30*14				
105	IGHV3-30*15				
106	IGHV3-30*16				
107	IGHV3-30*17				
108	IGHV3-30*18				
109	IGHV3-30*19				
110	IGHV3-30-3*01				
111	IGHV3-30-3*02				
112	IGHV3-33*01				
113	IGHV3-33*02				
114	IGHV3-33*03				
115	IGHV3-33*04				
116	IGHV3-33*05				
117	IGHV3-35*01				
118	IGHV3-38*01				
119	IGHV3-38*02				
120	IGHV3-43*01				
121	IGHV3-43*02				
122	IGHV3-48*01				

123	IGHV3-48*02				
124	IGHV3-48*03				
125	IGHV3-49*01				
126	IGHV3-49*02				
127	IGHV3-49*03				
128	IGHV3-49*04				
129	IGHV3-49*05				
130	IGHV3-53*01				
131	IGHV3-53*02				
132	IGHV3-53*03				
133	IGHV3-64*01				
134	IGHV3-64*02				
135	IGHV3-64*03				
136	IGHV3-64*04				
137	IGHV3-64*05				
138	IGHV3-66*01				
139	IGHV3-66*02				
140	IGHV3-66*03				
141	IGHV3-66*04				
142	IGHV3-7*01				
143	IGHV3-7*02				
144	IGHV3-72*01				
145	IGHV3-72*02				
146	IGHV3-73*01				
147	IGHV3-73*02				
148	IGHV3-74*01				
149	IGHV3-74*02				
150	IGHV3-74*03				
151	IGHV3-9*01				
152	IGHV3-d*0153				
153	IGHV4-28*01				
154	IGHV4-28*02				
155	IGHV4-28*03				
156	IGHV4-28*04				
157	IGHV4-28*05				
158	IGHV4-30-2*01				
159	IGHV4-30-2*02				
160	IGHV4-30-2*03				
161	IGHV4-30-2*04				
162	IGHV4-30-4*01				
163	IGHV4-30-4*02				
164	IGHV4-30-4*03				
165	IGHV4-30-4*04				
166	IGHV4-30-4*05				
167	IGHV4-30-4*06				
168	IGHV4-31*01				
169	IGHV4-31*02				
170	IGHV4-31*03				
171	IGHV4-31*04				

172	IGHV4-31*05				
173	IGHV4-31*06				
174	IGHV4-31*07				
175	IGHV4-31*08				
176	IGHV4-31*09				
177	IGHV4-31*10				
178	IGHV4-34*01				
179	IGHV4-34*02				
180	IGHV4-34*03				
181	IGHV4-34*04				
182	IGHV4-34*05				
183	IGHV4-34*06				
184	IGHV4-34*07				
185	IGHV4-34*08				
186	IGHV4-34*09				
187	IGHV4-34*10				
188	IGHV4-34*11				
189	IGHV4-34*12				
190	IGHV4-34*13				
191	IGHV4-39*01				
192	IGHV4-39*02				
193	IGHV4-39*03				
194	IGHV4-39*04				
195	IGHV4-39*05				
196	IGHV4-39*06				
197	IGHV4-39*07				
198	IGHV4-4*01				
199	IGHV4-4*02				
200	IGHV4-4*03				
201	IGHV4-4*04				
202	IGHV4-4*05				
203	IGHV4-4*06				
204	IGHV4-4*07				
205	IGHV4-59*01				
206	IGHV4-59*02				
207	IGHV4-59*03				
208	IGHV4-59*04				
209	IGHV4-59*05				
210	IGHV4-59*06				
211	IGHV4-59*07				
212	IGHV4-59*08				
213	IGHV4-59*09				
214	IGHV4-59*10				
215	IGHV4-61*01				
216	IGHV4-61*02				
217	IGHV4-61*03				
218	IGHV4-61*04				
219	IGHV4-61*05				
220	IGHV4-61*06				

221	IGHV4-61*07				
222	IGHV4-61*08				
223	IGHV4-b*01				
224	IGHV4-b*02				
225	IGHV5-51*01				
226	IGHV5-51*02				
227	IGHV5-51*03				
228	IGHV5-51*04				
229	IGHV5-51*05				
230	IGHV5-a*01				
231	IGHV5-a*03				
232	IGHV5-a*04				
233	IGHV6-1*01				
234	IGHV6-1*02				
235	IGHV7-4-1*01				
236	IGHV7-4-1*02				
237	IGHV7-4-1*03				
238	IGHV7-81*01				

Table 4: Human Light Chain Kappa Germline Segments

SEQ ID NO.	V Segments	SEQ ID NO.	J SEGMENTS
286	IGKV1-12*01	356	IGKJ1*01
287	IGKV1-12*02	357	IGKJ2*01
288	IGKV1-13*02	358	IGKJ2*02
289	IGKV1-16*01	359	IGKJ2*03
290	IGKV1-17*01	360	IGKJ2*04
291	IGKV1-17*02	361	IGKJ3*01
292	IGKV1-27*01	362	IGKJ4*01
293	IGKV1-33*01	363	IGKJ4*02
294	IGKV1-37*01	364	IGKJ5*01
295	IGKV1-39*01		
296	IGKV1-5*01		
297	IGKV1-5*02		
298	IGKV1-5*03		
299	IGKV1-6*01		
300	IGKV1-8*01		
301	IGKV1-9*01		
302	IGKV1-NL1*01		
303	IGKV1/OR2-0*01		
304	IGKV1/OR2-108*01		
305	IGKV1D-12*01		
306	IGKV1D-12*02		
307	IGKV1D-13*01		
308	IGKV1D-16*01		
309	IGKV1D-16*02		
310	IGKV1D-17*01		

311	IGKV1D-33*01		
312	IGKV1D-37*01		
313	IGKV1D-39*01		
314	IGKV1D-42*01		
315	IGKV1D-43*01		
316	IGKV1D-8*01		
317	IGKV2-24*01		
318	IGKV2-28*01		
319	IGKV2-29*02		
320	IGKV2-29*03		
321	IGKV2-30*01		
322	IGKV2-40*01		
323	IGKV2-40*02		
324	IGKV2D-24*01		
325	IGKV2D-26*01		
326	IGKV2D-26*02		
327	IGKV2D-28*01		
328	IGKV2D-29*01		
329	IGKV2D-29*02		
330	IGKV2D-30*01		
331	IGKV2D-40*01		
332	IGKV3-11*01		
333	IGKV3-11*02		
334	IGKV3-15*01		
335	IGKV3-20*01		
336	IGKV3-20*02		
337	IGKV3-7*01		
338	IGKV3-7*02		
339	IGKV3-7*03		
340	IGKV3-NL1*01		
341	IGKV3-NL2*01		
342	IGKV3-NL3*01		
343	IGKV3-NL4*01		
344	IGKV3-NL5*01		
345	IGKV3/OR2-268*01		
346	IGKV3/OR2-268*02		
347	IGKV3D-11*01		
348	IGKV3D-15*01		
349	IGKV3D-20*01		
350	IGKV3D-7*01		
351	IGKV4-1*01		
352	IGKV5-2*01		
353	IGKV6-21*01		
354	IGKV6D-21*01		
355	IGKV6D-41*01		
868	IGKV1-39*02		

Table 5: Human Light Chain Lambda Germline Segments

SEQ ID NO.	V Segments	SEQ ID NO.	J SEGMENTS
365	IGLV1-36*01	442	IGLJ1*01
366	IGLV1-40*01	443	IGLJ2*01
367	IGLV1-40*02	444	IGLJ3*01
368	IGLV1-40*03	445	IGLJ3*02
369	IGLV1-41*01	446	IGLJ4*01
370	IGLV1-44*01	447	IGLJ5*01
371	IGLV1-47*01	448	IGLJ5*02
372	IGLV1-47*02	449	IGLJ6*01
373	IGLV1-50*01	450	IGLJ7*01
374	IGLV1-51*01	451	IGLJ7*02
375	IGLV1-51*02		
376	IGLV10-54*01		
377	IGLV10-54*02		
378	IGLV10-54*03		
379	IGLV11-55*01		
380	IGLV2-11*01		
381	IGLV2-11*02		
382	IGLV2-11*03		
383	IGLV2-14*01		
384	IGLV2-14*02		
385	IGLV2-14*03		
386	IGLV2-14*04		
387	IGLV2-18*01		
388	IGLV2-18*02		
389	IGLV2-18*03		
390	IGLV2-18*04		
391	IGLV2-23*01		
392	IGLV2-23*02		
393	IGLV2-23*03		
394	IGLV2-33*01		
395	IGLV2-33*02		
396	IGLV2-33*03		
397	IGLV2-8*01		
398	IGLV2-8*02		
399	IGLV2-8*03		
400	IGLV3-1*01		
401	IGLV3-10*01		
402	IGLV3-10*02		
403	IGLV3-12*01		
404	IGLV3-12*02		
405	IGLV3-16*01		
406	IGLV3-19*01		
407	IGLV3-21*01		
408	IGLV3-21*02		
409	IGLV3-21*03		
410	IGLV3-22*01		

411	IGLV3-25*01		
412	IGLV3-25*02		
413	IGLV3-25*03		
414	IGLV3-27*01		
415	IGLV3-32*01		
416	IGLV3-9*01		
417	IGLV3-9*02		
418	IGLV4-3*01		
419	IGLV4-60*01		
420	IGLV4-60*02		
421	IGLV4-60*03		
422	IGLV4-69*01		
423	IGLV4-69*02		
424	IGLV5-37*01		
425	IGLV5-39*01		
426	IGLV5-39*02		
427	IGLV5-45*01		
428	IGLV5-45*02		
429	IGLV5-45*03		
430	IGLV5-48*01		
431	IGLV5-52*01		
432	IGLV6-57*01		
433	IGLV7-43*01		
434	IGLV7-46*01		
435	IGLV7-46*02		
436	IGLV8-61*01		
437	IGLV8-61*02		
438	IGLV8-61*03		
439	IGLV9-49*01		
440	IGLV9-49*02		
441	IGLV9-49*03		

Table 6: Human Heavy Chain V Genes		
IMGT Nomenclature	**IMGT Nomenclature with alleles**	**SEQ ID No.**
VH1-18	IGHV1-18*01	10
VH1-2	IGHV1-2*02	13
VH1-24	IGHV1-24*01	16
VH1-3	IGHV1-3*02	18
VH1-45	IGHV1-45*02	20
VH1-46	IGHV1-46*01	22
VH1-58	IGHV1-58*02	26
VH1-69	IGHV1-69*06	32
VH1-8	IGHV1-8*01	40
VH2-26	IGHV2-26*01	44
VH2-5	IGHV2-5*01	45
VH2-70	IGHV2-70*13	67

VH3-11	IGHV3-11*01	68
VH3-13	IGHV3-13*01	70
VH3-15	IGHV3-15*01	73
VH3-16	IGHV3-16*02	82
VH3-20	IGHV3-20*01	83
VH3-21	IGHV3-21*01	84
VH3-23	IGHV3-23*01	86
VH3-30	IGHV3-30*03	93
VH3-33	IGHV3-33*01	112
VH3-35	IGHV3-35*01	117
VH3-38	IGHV3-38*02	119
VH3-43	IGHV3-43*01	120
VH3-48	IGHV3-48*02	123
VH3-49	IGHV3-49*03	127
VH3-53	IGHV3-53*01	130
VH3-64	IGHV3-64*02	134
VH3-66	IGHV3-66*03	140
VH3-7	IGHV3-7*01	142
VH3-72	IGHV3-72*01	144
VH3-73	IGHV3-73*02	147
VH3-74	IGHV3-74*01	148
VH3-9	IGHV3-9*01	151
VH4-28	IGHV4-28*01	153
VH4-31	IGHV4-31*02	169
VH4-34	IGHV4-34*01	178
VH4-39	IGHV4-39*01	191
VH4-4	IGHV4-4*07	204
VH4-59	IGHV4-59*01	205
VH4-61	IGHV4-61*08	222
VH5-51	IGHV5-51*03	227
VH6-1	IGHV6-1*01	233
VH7-81	IGHV7-81*01	238

Table 7: Human Light Chain Kappa V Genes		
Zachau Nomencalture	**IMGT Nomenclature**	**SEQ ID No.**
A1	IGKV2D-30*01	330
A10	IGKV6D-21*01	354
A11	IGKV3D-20*01	349
A14	IGKV6D-41*01	355
A17	IGKV2-30*01	321
A18b	IGKV2-29*02	319
A19	IGKV2-28*01	318
A2	IGKV2D-29*01	328
A20	IGKV1-27*01	292
A23	IGKV2-24*01	317
A26	IGKV6D-21*01	354
A27	IGKV3-20*01	335
A3	IGKV2D-28*01	327
A30	IGKV1-17*01	290

A5	IGKV2D-26*01	325
A7	IGKV2D-24*01	324
B2	IGKV5-2*01	352
B3	IGKV4-1*01	351
L1	IGKV1-16*01	289
L10	IGKV3-7*01	337
L10a	IGKV3-7*02	338
L11	IGKV1-6*01	299
L12	IGKV1-5*01	296
L12a	IGKV1-5*03	298
L14	IGKV1D-17*01	310
L15	IGKV1D-16*01	308
L15a	IGKV1D-16*02	309
L16	IGKV3D-15*01	348
L18	IGKV1D-13*01	307
L19	IGKV1D-12*01	305
L2	IGKV3-15*01	334
L20	IGKV3D-11*01	347
L22	IGKV1D-42*01	314
L23	IGKV1D-43*01	315
L24	IGKV1D-8*01	316
L25	IGKV3D-7*01	350
L4/18a	IGKV1-13*02	288
L5	IGKV1-12*01	286
L6	IGKV3-11*01	332
L8	IGKV1-9*01	301
L9	IGKV1-8*01	300
O1	IGKV2D-40*01	331
O11	IGKV2-40*01	322
O11a	IGKV2-40*02	323
O12	IGKV1-39*01	295
O12a	IGKV1-39*02	868
O14	IGKV1-37*01	294
O18	IGKV1-33*01	293
O2	IGKV1D-39*01	313
O4	IGKV1D-37*01	312
O8	IGKV1D-33*01	311
Z0	IGKV1/OR2-0*01	303

Table 8: Human Light Chain Lambda V Genes		
Kawasaki Nomenclature	**IMGT Nomenclature**	**SEQ ID No.**
V1-11	IGLV1-36*01	365
V1-13	IGLV1-40*01	366
V1-16	IGLV1-44*01	369
V1-17	IGLV1-47*02	372
V1-18	IGLV1-50*01	373
V1-19	IGLV1-51*01	374
V1-2	IGLV2-8*01	397
V1-20	IGLV10-54*02	377

V1-22	IGLV6-57*01	432
V1-3	IGLV2-11*01	380
V1-4	IGLV2-14*01	383
V1-5	IGLV2-18*01	387
V1-7	IGLV2-23*03	393
V1-9	IGLV2-33*01	394
V2-1	IGLV3-1*01	400
V2-11	IGLV3-16*01	405
V2-13	IGLV3-19*01	406
V2-14	IGLV3-21*02	408
V2-15	IGLV3-22*01	410
V2-17	IGLV3-25*02	412
V2-19	IGLV3-27*01	414
V2-6	IGLV3-9*01	416
V2-7	IGLV3-10*01	401
V2-8	IGLV3-12*02	404
V3-2	IGLV7-43*01	433
V3-3	IGLV7-46*02	435
V3-4	IGLV8-61*01	436
V4-1	IGLV5-37*01	424
V4-2	IGLV5-45*03	429
V4-3	IGLV5-48*01	430
V4-4	IGLV5-52*01	431
V4-6	IGLV11-55*01	379
V5-1	IGLV4-3*01	418
V5-2	IGLV9-49*2	440
V5-4	IGLV4-60*02	420
V5-6	IGLV4-69*01	422

ii. Modified Germline Segments

It is contemplated herein that the practice of the method is not limited to germline segment sequences. Hence, any modified V_H, D_H, J_H, V_κ, J_κ, V_λ and or J_λ segment sequences, or any sequence analogous thereto, can be used in the practice of the method. By virtue of adding to the repertoire of segment sequences by modification thereto, the diversity of the library and the permutations of compiled segments can be further increased. The germline segments can be modified randomly or empirically. The germline segments can be modified to generate further diversity in the library. Alternatively or in addition, the germline segments can be modified to facilitate generation of the recombined full-length nucleic acid molecules by the introduction of linkers, restriction enzyme sites or other sequences of nucleotides required for practice of the method described herein.

Generally, the modified germline segments include those that are derived from germline sequences. The germline segments can be modified by introducing mutations into the germline sequence, randomly or empirically, or can be modified to generate germline

consensus sequences. For example, modified J_H germline segments are set forth in SEQ ID NOS: 3450-3455.

In another example, additional modifications of the germline segments include the addition of flanking sequences at one or both of the 5' and 3' termini of individual germline segments that provide restriction sites. Such modifications can be incorporated into the germline sequences using DNA synthesis, or by PCR, for example using primers that incorporate the restriction enzyme sites. In one example, as discussed below, the addition of such restriction sites facilitate joining of germline segments. In some cases, however, modifications of germline segments include the removal of restrictions sites. Restriction sites include any restriction site known in the art. Exemplary restriction site sequences are set forth in Table 15. Generally, the restriction site chosen is compatible with the subsequent compilation of germline segment sequences and can be chosen to facilitate blunt-ended ligation or sticky-ended ligation. The choice of restriction enzyme is routine and is well within the level of one of skill in the art.

In some examples, sequences of known antibodies, including monoclonal antibodies, particularly therapeutic antibodies, that are derived from germline sequences can be used in the methods herein. Since monoclonal antibodies already have a recognized antigen specificity, it is contemplated herein that incorporation of such derived sequences into the methods will permit the identification of antibodies with improved specificity and functionality against a target antigen. The nucleotide sequences derived from germline sequences, for example corresponding to any one or more of a V_H, D_H, J_H, V_κ, J_κ, V_λ and or J_λ, can themselves be combined with germline segment sequences. One of skill in the art can identify the corresponding sequences in a nucleic acid molecule encoding a particular antibody that are derived from germline sequences. Table 9 below identifies V, D and J regions that correlate with the derived germline sequences.

Table 9. Exemplary Monoclonal Antibody Sequences
(V regions, normal font; D regions, underlined; J regions, boldface)

TARGET	ANTIBODY	HEAVY CHAIN SEQUENCE	Protein SEQ ID NO:	Nucleotide SEQ ID NO:
CD20	Rituxan (rituximab)	QVQLQQPGAELVKPGASVKMSCKASGYTF TSYNMHWVKQTPGRGLEWIGAIYPGNGDT SYNQKFKGKATLTADKSSSTAYMQLSSLT SEDSAVYYCARSTYYGGDWY**FNVWGAGTT VTVSA**	1027	1043
EGFR	Erbitux (cetuximab	QVQLKQSGPGLVQPSQSLSITCTVSGFSL TNYGVHWVRQSPGKGLEWLGVIWSGGNTD YNTPFTSRLSINKDNSKSQVFFKMNSLQS NDTAIYYCARALTYYDYE**FAYWGQGTLVT VSA**	1028	1044

Her2/Neu	Herceptin (trastuzumab)	EVQLVESGGGLVQPGGSLRLSCAASGFNI KDTYIHWVRQAPGKGLEWVARIYPTNGYT RYADSVKGRFTISADTSKNTAYLQMNSLR AEDTAVYYCSRWGGDG**FYAMDYWGQGTLV TVSS**	1029	452
VEGFA	Avastin (bevacizumab)	EVQLVESGGGLVQPGGSLRLSCAASGYTF TNYGMNWVRQAPGKGLEWVGWINTYTGEP TYAADFKRRFTFSLDTSKSTAYLQMNSLR AEDTAVYYCAKYPHYYGSS**HWYFDVWGQG TLVTVSS**	1030	1045
VEGFA	Lucentis (ranibizumab)	EVQLVESGGGLVQPGGSLRLSCAASGYDF THYGMNWVRQAPGKGLEWVGWINTYTGEP TYAADFKRRFTFSLDTSKSTAYLQMNSLR AEDTAVYYCAKYPYYYGTS**HWYFDVWGQG TLVTVSS**	1031	1046
CD52	Campath (alemtuzumab)	QVQLQESGPGLVRPSQTLSLTCTVSGFTF TDFYMNWVRQPPGRGLEWIGFIRDKAKGY TTEYNPSVKGRVTMLVDTSKNQFSLRLSS VTAADTAVYYCAREGHTAAP**FDYWGQGSL VTVSS**	1032	1047
TNFα	Humira (adalimumab)	EVQLVESGGGLVQPGRSLRLSCAASGFTF DDYAMHWVRQAPGKGLEWVSAITWNSGHI DYADSVEGRFTISRDNAKNSLYLQMNSLR AEDTAVYYCAKVSYLSTAS**SLDYWGQGTL VTVSS**	1033	1048
EGFR	Vectibix (panitumumab)	QVQLQESGPGLVKPSETLSLTCTVSGGSV SSGDYYWTWIRQSPGKGLEWIGHIYYSGN TNYNPSLKSRLTISIDTSKTQFSLKLSSV TAADTAIYYCVRDRVTGA**FDIWGQGTMVT SS**	1034	1049
TARGET	ANTIBODY	LIGHT CHAIN SEQUENCE	Protein SEQ ID NO:	Nucleotide SEQ ID NO:
CD20	Rituxan (rituximab)	QIVLSQSPAILSASPGEKVTMTCRASSSV SYIHWFQQKPGSSPKPWIYATSNLASGVP VRFSGSGSGTSYSLTISRVEAEDAATYYC QQWTSNPP**TFGGGTKLEIK**	1035	1050
EGFR	Erbitux (cetuximab	DILLTQSPVILSVSPGERVSFSCRASQSI GTNIHWYQQRTNGSPRLLIKYASESISGI PSRFSGSGSGTDFTLSINSVESEDIADYY CQQNNNWPT**TFGAGTKLELK**	1036	1051
Her2/Neu	Herceptin (trastuzumab)	DIQMTQSPSSLSASVGDRVTITCRASQDV NTAVAWYQQKPGKAPKLLIYSASFLYSGV PSRFSGSRSGTDFTLTISSLQPEDFATYY CQQHYTTPP**TFGQGTKVEIK**	1037	818
VEGFA	Avastin (bevacizumab)	DIQMTQSPSSLSASVGDRVTITCSASQDI SNYLNWYQQKPGKAPKVLIYFTSSLHSGV PSRFSGSGSGTDFTLTISSLQPEDFATYY CQQYSTVP**WTFGQGTKVEIK**	1038	1052
VEGFA	Lucentis (ranibizumab)	DIQLTQSPSSLSASVGDRVTITCSASQDI SNYLNWYQQKPGKAPKVLIYFTSSLHSGV PSRFSGSGSGTDFTLTISSLQPEDFATYY CQQYSTVP**WTFGQGTKVEIK**	1039	1053
CD52	Campath (alemtuzumab)	DIQMTQSPSSLSASVGDRVTITCKASQNI DKYLNWYQQKPGKAPKLLIYNTNNLQTGV PSRFSGSGSGTDFTFTISSLQPEDIATYY CLQHISRPR**TFGQGTKVEIK**	1040	1054

TNFα	Humira (adalimumab)	DIQMTQSPSSLSASVGDRVTITCRASQGI RNYLAWYQQKPGKAPKLLIYAASTLQSGV PSRFSGSGSGTDFTLTISSLQPEDVATYY CQRYNRAP**YTFGQGTKVEIK**	1041	1055
EGFR	Vectibix (panitumumab)	DIQMTQSPSSLSASVGDRVTITCQASQDI SNYLNWYQQKPGKAPKLLIYDASNLETGV PSRFSGSGSGTDFTFTISSLQPEDIATYF CQHFDHLP**LAFGGGTKVEIK**	1042	1056

In some examples, the modified germline sequence can include a sequence of nucleotides that replaces all or some of the nucleotides of a germline segment. For example, it is further contemplated herein, that the modified germline sequences designated D_H can be any sequence of nucleotides. The D_H segment of a nucleic acid molecule encodes the central portion of the CDRH3 and is largely responsible for the antigen specificity and variability among antibodies. Since this region is the most variable among antibodies, it can tolerate more modification. Also, it is the region most responsible for antigen specificity. Generally, a segment designated D_H includes 5, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100 or more nucleotides. The sequence of nucleotides is chosen such that once compiled, in-frame, with a V_H and J_H as discussed below, an antibody molecule or fragment or portion thereof is produced that contains a sufficient antigen-binding site. The nucleotides are chosen randomly or empirically. In some examples, a segment of nucleotides designated D_H can include a random sequence of nucleotides. In other examples, the segment of nucleotides can be selected to be targeted against a specific antigen. For example, the segment of nucleotides can encode a peptide mimetic (see e.g. Table 16 below). In additional examples, a segment of nucleotides designated D_H can include nucleotides that are the reverse complement (i.e. inverted) compared to a known D_H germline segment. This is exemplified in Example 14.

In other examples, germline segment sequences can be modified to provide a consensus sequence between and among germline segments. Generally, due to the variability between and among the CDR regions, consensus sequences are generated in framework regions. Such modifications aid in the practice of the method by facilitating manipulation of a common sequence, for example, where the method of generating a combinatorial antibody library is performed manually. This is exemplified in Example 1 where each of the J_H contain a common F4 framework region.

b. Choosing Germline Segments or Modified Segments Thereof

As described herein above, each VH and VL chain is encoded by a nucleic acid molecule combinatorially generated from gene segments, generally germline segments or

modified forms thereof. The members of the resulting library can be chosen by selecting, randomly or empirically, the gene segments that can be recombined. One of skill in the art can select any desired V(D)J gene segment or subsets thereof for recombination to generate in-frame nucleic acid molecules encoding VH or VL.

In one example, the germline V(D)J segment sequences can be recombined randomly, whereby all known germline sequences (e.g. any described in the Sequence Listing herein or any available in public databases or known to those of skill in the art, and any modified forms thereof) are recombined together in all possible permutations. In such an example, every V_H gene segment is recombined with every D_H which is recombined with every J_H. Similarly, every V_L(κ or λ) is recombined with every J_L(κ or λ). In such an example, the resulting recombined germline nucleic acid molecules represent the complete repertoire of naïve VH and VL. For example, if germline segments are recombined based on known germline segment sequences set forth in Tables 3-5, greater then or about 100,000 different recombined nucleic acid molecules encoding VH can be generated, greater then or about 600 different recombined nucleic acids encoding VL_κ can be generated, and greater then or about 700 different recombined nucleic acid molecules encoding VL_λ can be generated. Thus, libraries of nucleic acids encoding variable heavy and light chains provided herein can encode for every possible recombined antibody variable region. In addition, further diversity can be introduced by modification, such as by mutagenesis, by introducing directed peptides, or by using inverted D_H sequences, as described herein above.

Alternatively, the V(D)J segments can be recombined using rational or semi-rational approaches such that a specific germline segment sequence or subset of sequences used are restricted in generating the members of the library. For example, as described in Example 14 herein, all members of the library contain a V_H germline segment that is an IGHV3-23*01. In other examples, germline segment sequences can be selected that contain modifications, for example, those that contain mutations to a specific region or region generated randomly (e.g. by site-directed mutagenesis to a particular CDR) or empirically (e.g. modified to contain directed peptide mimetics). By permitting selection of germline segment sequences, the libraries provided herein are versatile and can be rationally designed based on the application of the library.

For example, antibody germline segments can be selected wherein the resulting nucleic acid sequences are restricted based on sequence similarities or differences or other shared characteristics. For example, germline segment sequences can be selected based on sequence similarities or differences or based on shared characteristics (e.g., a V region family,

length, CDR3 length or composition, species, functionality, specificity, group, subgroup, pattern within the CDR, specific amino acids or other biochemical attribute). Antibody structure databases (e.g. CATH database: available at cathwww.biochem.ucl.ac.uk/; SACS database: available at bioinf.org.uk/abs/sacs/; IMGT 3D structure database: available at imgt3d.igh.cnrs.fr/) or other databases are available to sort germline segments based on a selected criteria. Alternatively, such selection can be done manually, for example, using sequence alignments or other manual sorting.

In one example, germline segments can be selected based on their sequence similarity or differences. One of skill in the art knows or can determine the sequence identity between and among germline segments, and identify germline segments that have a particular sequence identity. In one example, germline segment sequences from one or more of a V_H, D_H, J_H, V_κ, J_κ, V_λ and or J_λ, group can be selected based on sequence similarity. Sequence similarity between selected segments can include, but is not limited to, 60%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more. For example, subsets of germline segment belonging to the same subgroup or gene family can be selected, which generally share a high degree (e.g. greater then 70%, typically 75% or more) sequence identity. Tables 3-5 above identify germline segments belonging to the same subgroup or gene family. For example, in Table 3, IGHV1, IGHV2, IGHV3, IGHV4, IGHV5, IGHV6 and IGHV7 each represent a subgroup of a V_H segment, and germline segments within a subgroup share at least 75% sequence identity. Thus, all germline segments in the IGHV1 can be selected, or all germline segments in IGHV2 can be selected, or all germline segments in IGHV3 can be selected, etc. In another example, in Table 3 IGHV1-18*01 and IGHV1-18*02 represent a gene family having germline segments that are alleles. Thus, all germline segments that are related by virtue of being in the same family can be selected as a subset of germline sequences.

In another example, germline segments can be selected based on sequence differences so that the resulting subset represents a diverse repertoire of sequences. One of skill in the art knows or can identify germline segments that have a particular sequence identity. Sequence differences between selected segments can include those that exhibit 60%, 50%, 40%, 30%, 25%, 20%, 15%, 10%, or less sequence similarity. For example, subsets of germline segments, each from a different subgroup can be selected. Thus, in one example, V_H segments can be selected from each of the IGHV1, IGHV2, IGHV3, IGHV4, IGHV5, IGHV6 and IGHV7 subgroups; for example, a subset can include IGHV1-18*01, IGHV1-26*01, IGHV3-11*01, IGHV4-28*01, IGHV6-1*01, IGHV7-4-1*03. In another example, a V_H

segment can be selected from each gene family; for example, a subset can include IGHV1-18*01, IGHV1-2*01, IGHV1-3*01, IGHV1-45*01, IGHV1-46*01, IGHV1-58*01, IGHV1-69*01, IGHV1-8*01, IGHV1-c*01, IGHV1-f*01, IGHV2-26*01, IGHV2-5*01, IGHV2-70*01, IGHV3-11*01, IGHV3-13*01, IGHV3-15*01, IGHV3-16*01, IGHV3-20*01, IGHV3-21*01, IGHV3-23*01, IGHV3-30*01, IGHV3-33*01, IGHV3-38*01, IGHV3-43*01, IGHV3-48*01, IGHV3-49*01, IGHV3-53*01, IGHV3-64*01, IGHV3-66*01, IGHV3-7*01, IGHV3-72*01, IGHV3-73*01, IGHV3-74*01, IGHV3-9*01; IGHV4-28*01, IGHV4-30-2*01, IGHV4-31*01, IGHV4-34*01, IGHV4-39*01, IGHV4-59*01, IGHV4-61*01, IGHV5-51*01, IGHV6-1*01 and IGHV7-4-1*01. One of skill of the art is able to select any subset of germline sequences as desired based on sequence differences. Subsets for other germline segments sequences also can be selected based on sequence differences. Tables 10-12 sets forth exemplary selected V_H, D_H, J_H, V_κ, J_κ, V_λ and or J_λ, germline segments representing selection of at least one germline segment from each gene family.

Table 10: Selected Human Heavy Chain Germline Segments

V Segments	SEQ ID NO.	D Segments	SEQ ID NO.	J Segments	SEQ ID NO.
IGHV1-18*01	10	IGHD1-1*01	239	IGHJ1*01	273
IGHV1-2*02	13	IGHD1-14*01	240	IGHJ2*01	274
IGHV1-24*01	16	IGHD1-20*01	241	IGHJ3*01	275
IGHV1-3*02	18	IGHD1-26*01	242	IGHJ4*01	277
IGHV1-45*02	20	IGHD1-7*01	243	IGHJ5*01	280
IGHV1-46*01	22	IGHD2-15*01	244	IGHJ6*01	282
IGHV1-58*02	26	IGHD2-2*01	245		
IGHV1-69*06	32	IGHD2-21*01	248		
IGHV1-8*01	40	IGHD2-8*01	250		
IGHV2-26*01	44	IGHD3-10*01	252		
IGHV2-5*01	45	IGHD3-16*01	254		
IGHV2-70*13	67	IGHD3-22*01	256		
IGHV3-11*01	68	IGHD3-3*01	257		
IGHV3-13*01	70	IGHD3-9*01	259		
IGHV3-15*01	73	IGHD4-11*01	260		
IGHV3-16*02	82	IGHD4-17*01	261		
IGHV3-20*01	83	IGHD4-23*01	262		
IGHV3-21*01	84	IGHD4-4*01	263		
IGHV3-23*01	86	IGHD5-12*01	264		
IGHV3-30*03	93	IGHD5-18*01	265		
IGHV3-35*01	117	IGHD5-24*01	266		
IGHV3-38*02	119	IGHD5-5*01	267		
IGHV3-43*01	120	IGHD6-13*01	268		
IGHV3-48*02	123	IGHD6-19*01	269		
IGHV3-49*03	127	IGHD6-25*01	270		
IGHV3-53*01	130	IGHD6-6*01	271		

IGHV3-64*02	134	IGHD7-27*01	272		
IGHV3-66*03	140				
IGHV3-7*01	142				
IGHV3-72*01	144				
IGHV3-73*02	147				
IGHV3-74*01	148				
IGHV3-9*01	151				
IGHV4-28*01	153				
IGHV4-31*02	169				
IGHV4-34*01	178				
IGHV4-39*01	191				
IGHV4-4*07	204				
IGHV4-59*01	205				
IGHV5-51*03	227				
IGHV6-1*01	233				
IGHV7-81*01	238				

Table 11: Human Light Chain Kappa Germline Segments Selected for Manual Compilation

V Segments	SEQ ID NO.	J Segments	SEQ ID NO.
IGKV2D-30*01	330	IGKJ1*01	356
IGKV2-30*01	321	IGKJ2*01	357
IGKV2D-29*01	328	IGKJ3*01	361
IGKV1-27*01	292		
IGKV2-24*01	317		
IGKV6D-21*01	354		
IGKV3-20*01	335		
IGKV1-17*01	290		
IGKV5-2*01	352		
IGKV4-1*01	351		
IGKV1-6*01	299		
IGKV1-5*01	296		
IGKV1D-17*01	310		
IGKV3-15*01	334		
IGKV1D-42*01	314		
IGKV1D-43*01	315		
IGKV3D-7*01	350		
IGKV1-13*02	288		
IGKV1-12*01	286		
IGKV3-11*01	332		
IGKV1-9*01	301		
IGKV1-8*01	300		
IGKV2D-40*01	331		
IGKV1-39*01	295		
IGKV1-33*01	293		

Table 12: Human Light Chain Lambda Germline Segments Selected for Manual Compilation			
V Segments	**SEQ ID NO.**	**J Segments**	**SEQ ID NO.**
IGLV1-36*01	365	IGLJ1*01	442
IGLV1-40*01	366	IGLJ2*01	443
IGLV1-44*01	369	IGLJ4*01	446
IGLV1-50*01	373	IGLJ5*01	447
IGLV2-8*01	397	IGLJ6*01	449
IGLV10-54*02	377	IGLJ7*01	450
IGLV6-57*01	432		
IGLV2-11*01	380		
IGLV2-14*01	383		
IGLV2-18*01	387		
IGLV2-23*03	393		
IGLV2-33*01	394		
IGLV3-1*01	400		
IGLV3-16*01	405		
IGLV3-19*01	406		
IGLV3-21*02	408		
IGLV3-22*01	410		
IGLV3-25*02	412		
IGLV3-27*01	414		
IGLV3-9*01	416		
IGLV3-10*01	401		
IGLV3-12*02	404		
IGLV7-43*01	433		
IGLV7-46*02	435		
IGLV8-61*01	436		
IGLV5-37*01	424		
IGLV5-45*03	429		
IGLV5-48*01	430		
IGLV5-52*01	431		
IGLV11-55*01	379		
IGLV4-60*02	420		
IGLV4-69*01	422		

In all of the examples above, selection of germline segments based on sequence similarity or differences or other characteristics can be restricted for only one group of germline segments (from among any of V_H, D_H, J_H, V_κ, J_κ, V_λ and or J_λ), 2 groups, 3 groups, 4 groups, 5 groups, 6 groups or all 7 groups. Thus, for example, in recombining the gene segments to encode for a plurality of VH chains, only the V_H germline segment sequences can be restricted based on sequence similarity or differences or other characteristic, and the D_H and J_H segment sequences can represent all known D_H and J_H germline segment sequences. In another example, each of the V_H, D_H and J_H segment sequences can be selected based on

sequence similarity or differences or other characteristic, thereby resulting in a restricted subset of germline segment sequences for compilation herein. In yet another example, in recombining the gene segments to encode for a plurality of VH chains, the D_H segment is restricted based on its modification to include nucleotides encoding a particular peptide mimetic or mimetics against a target. In such an example, the V_H and J_H segment sequences can represent all known germline segment sequences to be recombined with the restricted subset of D_H (e.g. modified) segment. The choice of germline segments selected for use in the compilation method provided herein depends on a variety of factors including, but not limited to, the diversity of the resulting library, knowledge regarding preference for a particular germline segment sequence for a target from an initial screen of a library (as described herein below under Section G.4 entitled iterative screening), and the size of the library.

c. Sequence Compilation

In the methods provided herein, the variable gene segment sequences are recombined to generate heavy chain variable regions (5'-$V_HD_HJ_H$-3'), kappa light chain variable regions (5'-$V_\kappa J_\kappa$-3'), and lambda light chain variable regions (5'-$V_\lambda J_\lambda$-3') as described below. The gene segments can be recombined to generate full-length variable regions, or variable regions that are less then full length (i.e. portion thereof of full length), so long as the portion is sufficient to form an antigen binding site when expressed. The nucleic acid sequences are combined so that the resulting nucleic acid molecule is in-frame and encodes a functional VH or VL polypeptide, i.e. a full-length polypeptide or a portion thereof that is sufficient to form an antigen binding site.

The compilation method provided herein can be implemented by any procedures known to one of skill in the art. For example, it can be implemented manually, *in silico* (e.g. through computer software) or combinations thereof. In some examples, as described elsewhere herein below, the method can be implemented using sequence compilation software. In addition, public databases, such as those providing germline segment sequences or other public bioinformatics tools can be use to aid practice of the method.

Generally, full length heavy chain variable regions (5'-$V_HD_HJ_H$-3'), or portions thereof, are recombined such that a V_H segment is combined with a D_H segment which is combined with a J_H segment. Heavy chain segments are always combined such that the V_H segment is 5' to the D_H segment which is 5' to the J_H segment. The exact $V_HD_HJ_H$ can be chosen randomly or empirically and can represent germline segments, or modified forms thereof as discussed above. It is understood that when the method is performed manually

using molecular biology techniques, restriction enzymes can be added to the ends of germline segments to facilitate joining of segments. Hence, in some examples, the resulting VH chain can contain additional amino acids between germline segments. For example, as described in the examples herein, nucleic acid molecule library members encoding a VH chain can encode sequences that contain amino acids SY at 5'end of the J_H region between the joined D_H region.

In one example of the methods herein, all permutations of $V_HD_HJ_H$ gene segments can be recombined to generate a nucleic acid molecule encoding a variable heavy chain. Thus, every V_H segment (e.g., set forth in any of SEQ ID NOS:10-238), is combined with every D_H segment (e.g., any set forth in SEQ ID NOS: 239-272), which is combined with every J_H segment (e.g. any set forth in SEQ ID NOS: 273-285). In such an example, based on the exemplary heavy chain germline segments set forth in Table 3, greater then or about 100,000 nucleic acid molecules encoding a variable heavy (VH) chain can be generated. In other examples, the $V_HD_HJ_H$ gene segments can be recombined empirically (e.g. using rational or semi-rational approaches as discussed below). For example, as discussed below any subset of V_H, D_H and/or J_H gene segment can be chosen to generate a recombined nucleic acid molecule. In some examples, individual gene segments are selected because of a shared characteristic including, but not limited to, diversity, same V region family, CDR3 length, composition or other biochemical attribute.

Full length kappa light chain variable regions (5'-$V_\kappa J_\kappa$-3'), or portions thereof, are recombined such that a V_κ segment is combined with a J_κ segment. Full length lambda light chain variable regions (5'-$V_\lambda J_\lambda$-3') are recombined such that a V_λ segment is combined with a J_λ segment. Light chain segments are always combined such that the V_L segment is 5' to the J_L segment. The exact $V_\kappa J_\kappa$ or $V_\lambda J_\lambda$ can be chosen randomly or empirically and can represent germline segments, or modified forms thereof as discussed above. It is understood that when the method is performed manually using molecular biology techniques, restriction enzymes can be added to the ends of germline segments to facilitate joining of segments. Hence, in some examples, the resulting VL chain can contain additional amino acids between germline segments.

In one example of the methods herein, all permutations of $V_\kappa J_\kappa$ can be recombined to generate a nucleic acid molecule encoding a variable kappa light chain. Thus, every V_κ (e.g. any set forth in SEQ ID NOS:286-355, 868) is combined with every J_κ (e.g. any set forth in SEQ ID NOS: 356-364). In such an example, based on the exemplary kappa light chain germ line segments set forth in Table 4, greater then or about 600 nucleic acid molecules encoding

a variable kappa light chain can be generated. In another example, all permutations of $V_\lambda J_\lambda$ can be recombined to generate a nucleic acid molecule encoding a variable lambda light chain. Thus, every V_λ (e.g. any set forth in any of SEQ ID NOS:365-441) is combined with every J_λ (e.g. any set forth in any of SEQ ID NOS: 442-451). In such an example, based on the exemplary lambda light chain germline segment set forth in Table 5, greater then or about 700 nucleic acid molecules encoding a variable lambda light chain can be generated. In another example, the $V_\kappa J_\kappa$ or $V_\lambda J_\lambda$ gene segments can be recombined empirically as described herein below.

In all of the examples above, recombined segments are joined such that the recombined full length nucleic acid is in frame with the 5' start codon (ATG), thereby allowing expression of a full length polypeptide. Any combination of a V(D)J can be made, and junctions modified accordingly in order to generate a compiled V(D)J sequence that is in-frame, while preserving reading frames of each segment. The choice of junction modification is a function of the combination of V(D)J that will be joined, and the proper reading frame of each gene segment. For example, any of the variable gene segments can exist in reading frame 1, 2 or 3 when compiled. Generally, however, for the practice of the method herein, the V sequence (V_H, V_κ or V_λ) is always reading frame 1. Also, the reading frame of the J sequence is set to be either reading frame 1, 2 or 3 such that the resulting gene segment encodes the correct amino acids. Table 13 below sets forth the reading frames of the exemplary J germline sequences.

Table 13. J Germline Segment Sequences in Coding Frames

Heavy	SEQUENCE	SEQ ID NO
IGHJ1*01	GCT GAA TAC TTC CAG CAC TGG GGC CAG GGC ACC CTG GTC ACC GTC TCC TCA G	273
IGHJ2*01	C TAC TGG TAC TTC GAT CTC TGG GGC CGT GGC ACC CTG GTC ACT GTC TCC TCA G	274
IGHJ3*01	T GAT GCT TTT GAT GTC TGG GGC CAA GGG ACA ATG GTC ACC GTC TCT TCA G	275
IGHJ3*02	T GAT GCT TTT GAT ATC TGG GGC CAA GGG ACA ATG GTC ACC GTC TCT TCA G	276
IGHJ4*01	AC TAC TTT GAC TAC TGG GGC CAA GGA ACC CTG GTC ACC GTC TCC TCA G	277
IGHJ4*02	AC TAC TTT GAC TAC TGG GGC CAG GGA ACC CTG GTC ACC GTC TCC TCA G	278
IGHJ4*03	GC TAC TTT GAC TAC TGG GGC CAA GGG ACC CTG GTC ACC GTC TCC TCA G	279
IGHJ5*01	AC AAC TGG TTC GAC TCC TGG GGC CAA GGA ACC CTG GTC ACC GTC TCC TCA G	280
IGHJ5*02	AC AAC TGG TTC GAC CCC TGG GGC CAG GGA ACC CTG GTC ACC GTC TCC TCA G	281

IGHJ6*01	AT TAC TAC TAC TAC TAC GGT ATG GAC GTC TGG GGG CAA GGG ACC ACG GTC ACC GTC TCC TCA G	282
IGHJ6*02	AT TAC TAC TAC TAC TAC GGT ATG GAC GTC TGG GGC CAA GGG ACC ACG GTC ACC GTC TCC TCA	283
IGHJ6*03	AT TAC TAC TAC TAC TAC TAC ATG GAC GTC TGG GGC AAA GGG ACC ACG GTC ACC GTC TCC TCA	284
IGHJ6*04	AT TAC TAC TAC TAC TAC GGT ATG GAC GTC TGG GGC AAA GGG ACC ACG GTC ACC GTC TCC TCA G	285
Light Kappa	**SEQUENCE**	**SEQ ID NO**
IGKJ1*01	G TGG ACG TTC GGC CAA GGG ACC AAG GTG GAA ATC AAA C	356
IGKJ2*01	TG TAC ACT TTT GGC CAG GGG ACC AAG CTG GAG ATC AAA C	357
IGKJ2*02	G TGC ACT TTT GGC CAG GGG ACC AAG CTG GAG ATC AAA C	358
IGKJ2*03	TG TAC AGT TTT GGC CAG GGG ACC AAG CTG GAG ATC AAA C	359
IGKJ2*04	TG TGC AGT TTT GGC CAG GGG ACC AAG CTG GAG ATC AAA C	360
IGKJ3*01	A TTC ACT TTC GGC CCT GGG ACC AAA GTG GAT ATC AAA C	361
IGKJ4*01	G CTC ACT TTC GGC GGA GGG ACC AAG GTG GAG ATC AAA C	362
IGKJ4*02	G CTC ACG TTC GGC GGA GGG ACC AAG GTG GAG ATC AAA C	363
IGKJ5*01	G ATC ACC TTC GGC CAA GGG ACA CGA CTG GAG ATT AAA C	364
Light Lambda	**SEQUENCE**	**SEQ ID NO**
IGLJ1*01	T TAT GTC TTC GGA ACT GGG ACC AAG GTC ACC GTC CTA G	442
IGLJ2*01	T GTG GTA TTC GGC GGA GGG ACC AAG CTG ACC GTC CTA G	443
IGLJ3*01	T GTG GTA TTC GGC GGA GGG ACC AAG CTG ACC GTC CTA G	444
IGLJ3*02	T TGG GTG TTC GGC GGA GGG ACC AAG CTG ACC GTC CTA G	445
IGLJ4*01	T TTT GTA TTT GGT GGA GGA ACC CAG CTG ATC ATT TTA G	446
IGLJ5*01	C TGG GTG TTT GGT GAG GGG ACC GAG CTG ACC GTC CTA G	447
IGLJ5*02	C TGG GTG TTT GGT GAG GGG ACG GAG CTG ACC GTC CTA G	448
IGLJ6*01	T AAT GTG TTC GGC AGT GGC ACC AAG GTG ACC GTC CTC G	449
IGLJ7*01	T GCT GTG TTC GGA GGA GGC ACC CAG CTG ACC GTC CTC G	450
IGLJ7*02	T GCT GTG TTC GGA GGA GGC ACC CAG CTG ACC GCC CTC G	451

For the heavy chain, the reading frame of the D variable gene segment sequence chosen is less rigid then for the V or J germline segments. This is because the D gene sequence is responsible for encoding the central portion of the CDRH3, which plays a prominent role in antigen specificity. Hence, variation of amino acids is expected in the D gene segment sequence. Thus, for example, the D_H gene segment can be any D_H gene segment in any reading frame, an inverted or reverse complement thereof, or a modified form thereof, or any sequence of nucleotides designated as the D_H. In some examples, however, the reading frame of the D germline sequence is chosen so that the resulting encoded amino acids are predominately hydrophilic. CDR3 is an antigen-binding site, and thereby is rich in hydrophilic residues that are surface exposed (see e.g., Zanetti and Billetta, Antigenized Antibodies from Concepts to Applications (1996), In The *Antibodies, Volume 2* (pp. 75-122),

Harwood Academic Publishers; Pommie *et al.* (2004) J Mol. Recognition, 17:17-32). One of skill in the art is familiar with techniques to assess the hydrophobicity/hydrophilicity of sequences. For example, hydrophilicity can be measured using protein grand average of hydropathy (GRAVY), which gives hydropathy value for a sequence by adding the hydropathy value for each residue and dividing by the length of the sequence (see e.g., Kyte and Doolittle (1982 and bioinformatics.org/sms2/protein_gravy.html). The lower the GRAVY value, the more hydrophilic a sequence is.

In some instances, compilation of variable gene segments in-frame, while preserving reading frames, requires no manipulation, i.e. no modification of joint regions. In other instances, however, simply compiling V(D)J sequences does not conserve reading frames. Thus, where the junctions between gene segments are not in the desired frame, modifications are made to nucleotides within the junctions between the segments so that each gene segment is in its desired reading frame, and the full length sequence is in-frame. Nucleic acid modifications include replacements or substitutions, insertions, or deletions of nucleotides, or any combination thereof. For example, at the V-D junction, one or more nucleotide can be deleted from the 5' end of the D, one or more nucleotide can be deleted from the 3' end of the V or one or more nucleotides can be inserted between the V and D (e.g. a nucleotide can be added to the 3' end of the V). In another example, at the D-J junction, one or more nucleotides can be deleted from the 5' end of the J, one or more nucleotides can be deleted from the 3' end of the D, or one or more nucleotides can be inserted between the D and J (e.g., a nucleotide can be added to the 3' end of the D). In a further example, at the V-J junction, as occurs in generation of a light chain, one or more nucleotides can be deleted from the 5' end of the J, one or more nucleotides can be deleted from the 3' end of the V or one or more nucleotides can be inserted between the V and J (e.g. a nucleotide can be added to the 3' end of the V). In such examples where nucleotides are inserted, any nucleotide insertion from among one or more of a guanine (G), adenine (A), cytosine (C) and thymine (T) is contemplated. In some examples, guanine (G) is chosen as the inserted nucleotide because of the slight preference of terminal deoxynucleotidyl transferase (TdT) for guanine residues (Alt *et al.* 1982).

In the methods, heavy chain segments are recombined separately from light chain gene segment sequences. Thus, an individual nucleic acid molecule encodes for either a heavy chain (VH) or a light chain (VL) variable region. In the methods, a plurality of VH nucleic acid molecules encoding a VH chain and a plurality of nucleic acid molecules encoding a VL chain are generated. The number of such sequences can be up to all possible

permutations depending on the number of V, D or J gene segments available for combination. For example, where all known germline segment sequences are used for practice of the method, a fully naïve antibody library is generated. In other examples, modified gene segments can also be used for practice of the method. Alternatively, the number of permutations is a function of the selected V, D and J, which can be a subset of all germline segments or modified forms thereof.

Once a nucleic acid sequence is compiled, it is further modified to remove stop codons so that the resulting molecule is functional, i.e. encodes a polypeptide that is not truncated early. For example, modifications to remove stop codons include substitutions of nucleotides. Exemplary of such modifications, include, but are not limited to, stop codon TAA replaced by codons TAT; stop codon TAG replaced by codons TAT, and stop codon TGA replaced by codons TCA.

d. Further Sequence Modification of Recombined Nucleic Acid Sequences

As discussed above, germline segment sequences can be modified before performing compilation as described herein. In addition or alternatively, modification can be made directly to the recombined nucleic acid sequence. Hence, it is understood that any of the modifications described below also can be made to individual germline segment sequences before compilation so long as the reading frames are maintained and the rules governing compilation as described herein are observed to generate in-frame recombined nucleic acid sequences.

Thus, any of the plurality of recombined nucleic acids encoding a VH chain or a VL chain can be further modified. Modifications of the nucleic acid sequences include replacements or substitutions, insertions, or deletions of nucleotides, or any combination thereof. Any modification contemplated by one of skill in the art can be made to the nucleic acid molecule, so long as the modification(s) do not interfere with or alter the junction joints made to maintain reading frames of the V(D)J segments achieved by virtue of practice of the method (as discussed in the Section entitled "Sequence Compilation" above). Any modification should be checked to confirm that all reading frames are intact to ensure that the resulting full length nucleic acid is in frame with the 5' start codon (ATG) thereby allowing expression of a full length VH or VL polypeptide, or a portion thereof that is sufficient to form an antigen binding site.

The resulting recombined germline variable heavy and light chain nucleic acid sequences can be further modified through DNA synthesis (i.e. modifications introduced upon

synthesis of the nucleic acid molecule) or by using standard molecular biology techniques. Thus, in one example, any desired modification contemplated can be made to a nucleic acid molecule encoding a recombined variable heavy or variable light chain and the resulting nucleic acid molecule including any modifications synthesized as described in sub-section e.iii below. Due to the degeneracy of the genetic code nucleic acid sequences can be designed to avoid unwanted nucleotide sequences, including unwanted restriction sites, splicing donor or acceptor sites, or other nucleotide sequences potentially detrimental to efficient translation. Additionally, organisms sometimes favor particular codon usage and/or a defined ratio of GC to AT nucleotides. Thus, degeneracy of the genetic code permits design of nucleic acid sequences tailored for expression in particular organisms or groups of organisms. Additionally, nucleic acid molecules can be designed for different levels of expression based on optimizing (or non-optimizing) of the sequences. In another example, generated recombined germline VH and VL nucleic acid molecules as described in sub-section e.iii below, can be further modified using using standard molecular biology techniques, such as PCR, site-directed mutagenesis, restriction enzyme digestion, ligation, cloning and any combination thereof. The choice of whether to generate such modifications during DNA synthesis or using molecular biology techniques is dependent on the end user and can be influenced by factors such as the purpose of the modification, the extent of the modification and timing considerations.

Modifications of recombined germline nucleic acid molecules encoding VH or VL can be generated randomly or empirically. For example, random mutation of one or more regions can increase diversity of the library, particularly where modifications are made to any of the CDR-loop regions, which contribute to the specificity and affinity of the antibody. This library with increased diversity permits the generation of antibodies, derivatives thereof or portions or fragments thereof, which potentially can bind to any desired antigen with a high affinity. In another example, modifications can be empirically generated using rational or semi-rational approaches. Among such empirical modifications of nucleic acid molecules encoding VH and VL chains contemplated herein include, but are not limited to, modifications of the CDR regions, for example for the generation of directed libraries, modifications to optimize codon usage, and/or modifications to introduce restriction sites or detectable moieties. Modifications also can include a combinations of random and empirical modifications.

i. Codon Usage

For example, nucleic acid sequences can be modified to adapt the codon usage for expression such as, for example, bacterial expression. Codon usage is degenerate in that multiple codons encode for the same amino acid. Thus a single amino acid is therefore encoded by multiple codons, however within any organism, codon usage varies for any given amino acid. The full length nucleic acids provided herein are modified to replace rare codons with more abundant codons utilized in the particular expression system. Typically, modifications include silent mutations, such that the substitutions do not alter the specificity of the codon. Codon usage tables are known to those of skill in the art, particularly for common expression systems. For example, for expression in bacteria *E. coli* K12, codon usage Tables are known (see, e.g., Grantham, R. *et al.*, *Nuc. Acids Res.*, 8:1892-1912 **(1980)**; Grantham, R. *et al.*, *Nuc. Acids Res.*, 9:r43-r74 **(1981)** and also Table 14). The codon usage table lists all of the sixty four possible three nucleotide codons for DNA or RNA with their frequency of usage in the bacteria *E. coli* K12. The Table shows that while a single amino acid is encoded by multiple codons (redundancy), these codons are not used at the same rate for any given amino acid. For example, the amino acid arginine is coded for by six different codons: CGT, CGC, CGA, CGG, AGA and AGG. The codon AGA has a frequency of 2.0 % while the codon CGC has a frequency of 22 %.

TABLE 14: Codon Usage in *E. coli* K12

fields: [triplet] [frequency: per thousand] ([number])

TTT 22.2 (30361)	TCT 8.4 (11498)	TAT 16.1 (22071)	TGT 5.1 (7020)
TTC 16.6 (22649)	TCC 8.6 (11804)	TAC 12.2 (16734)	TGC 6.4 (8787)
TTA 13.8 (18915)	TCA 7.1 (9706)	TAA 2.0 (2752)	TGA 0.9 (1261)
TTG 13.6 (18601)	TCG 8.9 (12156)	TAG 0.2 (321)	TGG 15.2 (20835)
CTT 11.0 (15043)	CCT 7.0 (9554)	CAT 12.9 (17656)	CGT 21.0 (28700)
CTC 11.1 (15183)	CCC 5.4 (7448)	CAC 9.7 (13329)	CGC 22.0 (30159)
CTA 3.9 (5303)	CCA 8.4 (11518)	CAA 15.3 (20970)	CGA 3.5 (4787)
CTG 52.9 (72403)	CCG 23.3 (31869)	CAG 28.9 (39560)	CGG 5.4 (7320)
ATT 30.4 (41551)	ACT 8.9 (12197)	AAT 17.7 (24192)	AGT 8.7 (11917)
ATC 25.2 (34426)	ACC 23.5 (32101)	AAC 21.7 (29656)	AGC 16.1 (21961)
ATA 4.3 (5827)	ACA 7.0 (9564)	AAA 33.7 (46044)	AGA 2.0 (2783)
ATG 27.8 (38012)	AGC 14.4 (19743)	AAG 10.3 (14043)	AGG 1.1 (1533)
GTT 18.3 (25079)	GCT 15.3 (20863)	GAT 32.2 (44103)	GGT 24.9 (34009)
GTC 15.3 (20913)	GCC 25.6 (35018)	GAC 19.2 (26201)	GGC 29.8 (40725)
GTA 10.9 (14885)	GCA 20.2 (27638)	GAA 39.7 (54267)	GGA 7.9 (10817)
GTG 26.3 (35960)	GCG 33.8 (46222)	GAG 17.8 (24414)	GGG 11.0 (15116)

ii. Adding or Removing Restriction Enzyme sites

In another example, additional modifications of the nucleic acids include the addition of flanking sequences at one or both of the 5' and 3' termini of recombined VH or VL nucleic acid sequences that provide restriction sites. Such modifications can be incorporated into the germline recombined nucleic acid molecules during DNA synthesis, or by PCR, for example using primers that incorporate the restriction enzyme sites. In some examples, addition of such restriction sites facilitate cloning of the nucleic acids into a selected vector. For example, restriction sites include any restriction site known in the art. Exemplary restriction site sequences are set forth in Table 15. Generally, the restriction site chosen is compatible with the expression vector and can be chosen to facilitate blunt-ended ligation or sticky-ended ligation. The choice of restriction enzyme is routine and is well within the level of one of skill in the art.

Table 15. Common Restriction Enzyme Cleavage Recognition Sites

Restriction Enzyme	Cleavage Sequence	SEQ ID NO
NcoI	CCATGG	977
NheI	GCTAGC	978
AvrII	CCTAGG	979
BsiWI	CGTACG	980
SfiI	GGCCNNNNNGGCC	1889
NotI	GCGGCCGC	1890
HindIII	AAGCTT	1891
EcoRI	GAATTC	1892
BamHI	GGATCC	1893
EcoRV	GATATC	1894
PstI	CTGCAG	1895
SalI	GTCGAC	1896
SmaI	CCCGGG	1897
XmaI	CCCGGG	1898
BglI	GCCNNNNNGGC	1899
MfeI	CAATTG	1900
BsaI	GGTCTCN	3719

In some examples, nucleic acids can be modified to remove any restriction sites that occur within the nucleic acid sequence. In particular, removal of restriction sites is desired so that such sites do not interfere with subsequent digestion, ligation and cloning procedures. For example, as discussed above, recombined nucleic acid molecules can be modified to contain terminal flanking restriction sites to facilitate cloning into expression vectors. Generally, such restriction sites are chosen to be unique so that the presence of the site exists only at the terminal flanking end(s). If the site is not unique, modifications can be made to the sequence of the nucleic acid molecule to remove any conflicting restriction sites. One of

skill in the art is familiar with restriction sites and can identify such sites within a nucleic acid sequence. Table 15 lists exemplary restriction sites that can be removed.

In some instances, a single nucleotide change is possible to effect change of the restriction site. In other instances, two or three nucleotide changes are necessary to remove a restriction site. Typically, modification of restriction sites existing internally in a recombined nucleic acid molecule are made in view of the codon usage as discussed above. For example, if a Sal I restriction sites (GTCGAC; SEQ ID NO:1896) exists internally in a nucleic acid molecule, the GTC codon that codes for valine (V) can be modified to GTA, GTG, GTT or GTC codons. Simply changing the last C to G correlates to changing the GTC codon (15.3% frequency of usage) to GTG (26.3% frequency of usage), which is an 11% increase in frequency of codon usage. Alternatively, the GAC codon (19.2% frequency of usage) that codes for asparagine (D) can be modified to GAT (32.2% frequency of usage) by changing the last C to T, which is a 13% increase in codon usage. In this example, either of the above modifications can be made. Typically, modifications are made to convey the highest absolute beneficial increase in frequency of codon usage.

iii. Linkers

In additional examples, nucleic acid molecules can be modified with a linker sequence. For example, where a single-chain antibody is desired (e.g. an scFv antibody) the variable heavy and light chains can first be joined by a linker. The linkage can be direct or via a linker. For example, nucleic acids encoding peptide linkers can be added during DNA synthesis or using molecular biology techniques to the 5' end of a first sequence (e.g. variable heavy chain) and the 3' terminus of a second nucleic acid sequence (e.g. variable light chain). Typically, the linker is of sufficient length so that the resulting polypeptide is soluble. Nucleic acid sequences for use as linkers can encode peptide linkers from about 2 or 2 to about 60 or 60 amino acid residues, for example from about 5 to 40, or from about 10 to 30, 2 to 6, 7, or 8 amino acid residues. Examples of known linker moieties include, but are not limited to, peptides, such as $(Gly_mSer)n$ and $(Ser_mGly)n$, in which n is 1 to 6, including 1 to 4 and 2 to 4, and m is 1 to 6, including 1 to 4, and 2 to 4. Exemplary of such linkers include any that encode peptide linkers such as glycine serine polypeptides, such as —Gly-Gly—, GGGGG (SEQ ID NO:981), GGGGS (SEQ ID NO:982) or (GGGGS)n (SEQ ID NO:985), SSSSG (SEQ ID NO:983) or (SSSSG)n (SEQ ID NO:1996). Linking moieties are described, for example, in Huston *et al.* (1988) *PNAS* 85:5879-5883, Whitlow *et al.* (1993) *Protein Engineering* 6:989-995, and Newton *et al.*, (1996) *Biochemistry* 35:545-553. Other suitable linkers include any encoding a peptide linker, such as any of those described in U.S. Patent

No. 4,751,180 or 4,935,233, which are hereby incorporated by reference. A polynucleotide encoding a desired peptide linker can be inserted anywhere in variable heavy or light chain sequence or at the 5'- or 3'- terminus, in frame, using any suitable conventional technique. For example, restriction sites can be added to the 5' terminus of the heavy chain sequence and to the 3' terminus of the light chain sequence while a nucleic acid encoding a linker segment (e.g. $(Gly_4Ser)_3$; SEQ ID NO:984) can be added to the 3' terminus of the heavy chain sequence connecting it to the 5' terminus of the light chain sequence. Upon expression, such a nucleic acid molecule encodes an scFv antibody where the heavy chain variable region is operably linked to the light chain variable region.

iv. Tags or detectable moieties

Additionally, a small epitope tag, such as a myc tag, His tag, Flag tag or other small epitope tag, and/or any other additional DNA sequence can be added for incorporation into a nucleic acid sequence encoding a variable heavy chain or variable light chain (Arnau *et al.* (2006) *Protein Expression and Purification*, 48:1-13). In some instances, for example, a tag that permit attachment, for example, an LPETG tag, can be added that allows for site specific modification using the protein ligase, sortase (Chan *et al.* (2007) PLoS ONE, 2:e1164). Hence, inclusion of such a tag permits immobilization (e.g. on a BIAcore chip) and/or selective sorting in the presence of a sortase. Generally, the additional DNA sequence is added to the 3' or 5' terminus of the nucleic acid molecule encoding the recombined variable sequence directly or indirectly using a linker. Alternatively, the additional DNA sequence can be included in the expression vector of choice, such that, upon expression, the resulting antibody contains the additional sequence. For example, plasmid A set forth in SEQ ID NO:1 contains a His-Flag Tag corresponding to nucleotides 3265-3306 (Flag corresponds to nucleotides 3265-3288; His corresponds to nucleotides 3289-3306). In another example, Plasmid D set forth in SEQ ID NO: 2 contains a Flag tag corresponding to nucleotides 3265-3288, an LPETG tag corresponding to nucleotides 3289-3303. Thus, upon expression of the heavy chains, alone or together with a variable light chain, resulting antibodies can be detected using anti-Flag or anti-His tag reagents. This is described in Example 10. One of skill in the art can add any desired detectable sequence or other identifiable moiety to a nucleic acid molecule encoding a recombined variable heavy or light chain sequence to facilitate identification and/or purification of the resulting antibodies.

v. Mutational Diversity

In other examples, modifications can be made to introduce mutational diversity into the resulting nucleic acid molecules. Any modification can be made, such as by replacement,

substitution, deletion or addition of amino acids, either randomly or empirically (i.e. into any region or segment of the recombined nucleic acid molecule). The modifications can be made during DNA synthesis or using routine molecular biology techniques such as site-directed mutagenesis, digestion with restriction enzymes and/or cloning.

For example, modification(s) can be introduced into a nucleic acid molecule encoding the VH chain, a nucleic acid molecule encoding the VL chain, or both. The modification(s) can be introduced in the region of one or more of CDR1, CDR2, CDR3, FR1, FR2, FR3 or FR4. For example, modifications can be introduced into one, two or all three of the three CDRs of a given variable domain (VH, VL or both). In one example, modifications are introduced into CDR1 and CDR2, e.g. of a heavy chain variable domain. Typically, modification(s) are introduced into the CDR3 of the heavy chain (CDRH3). Any combination is contemplated. One of skill in the art knows and can identify CDR1, CDR2, CDR3, FR1, FR2, FR3 and FR4 regions in a nucleic acid molecule encoding a VH or VL (see e.g., Chothia *et al.* (1989) Nature 342:877-883; Al-Lazikani *et al.* (1997) J Mol. Biol., 273:927-948); WO/2007/137616; bioinf.org.uk/abs/; bioc.unizh.ch/antibody/Numbering/NumFrame.html; Martin *et al.*, Bioinformatics Tools for Antibody Engineering in Handbook of Therapeutic Antibodies, Wiley-VCH (2007), pp. 96-103). For example, CDRs can be identified in VH and VL chains using Kabat numbering based on sequence alignment or the Chothia numbering scheme based on structural topology. Since the Kabat numbering scheme was developed from sequence alignment, insertions in the sequence relative to the numbering scheme by alignment are indicated by letters (e.g. 27, 27A, 27B, 27C, etc...) and deletions have the corresponding number skipped. The residues corresponding to the six CDRs of the light and heavy chains based on Kabat numbering are CDR-L1: L24-L34; CDR-L2: L50-L56; CDR-L3: L89-L97; CDR-H1: H31-H35B; CDR-H2: H50-H65; CDR-H3: H95-H102. One of skill in the art knows that CDR lengths can vary and can identify corresponding residues, for example, by alignment and use of kabat numbering.

vi. Directed Peptides

In some cases, modifications include rationally generated modifications to generate antibodies and portions or fragments thereof that mimic the activity of biologically active peptides against known targets (see e.g., International published PCT Application No. WO 2004/050017). Important biological functions, such as receptor binding, activation and enzymatic activity, are often attributable to discrete regions of larger protein molecules, containing a limited number of amino acid residues termed peptide epitopes and mimitopes. These peptide epitopes and mimitopes can be used as therapeutics, but due to their small size,

are typically unstable in vivo due to rapid degradation. The peptide epitopes, however, can be introduced into variable regions of antibodies, which can act to mimic the activity of the biologically active peptide. Such antibodies are more stable, and exhibit increased half-life. Thus, antibodies or portions thereof can be directed toward a known target or function by incorporating sequences into the variable regions of an antibody that correspond to a polynucleotide target of interest. Often, structure and or function information of the known targets is available. These libraries are useful in providing lead antibodies for future antibody libraries.

Hence, included in the modifications herein are nucleic acid sequences encoding germline recombined VH and VL, wherein nucleotides corresponding to one or more CDR is replaced with nucleotides encoding one or more amino acid residues for a peptide of choice. In one example, the modifications in a nucleic acid molecule encoding a germline recombined VH and/or VL can be generated during DNA synthesis. Alternatively, the modification can be introduced into a nucleic acid molecule encoding a germline recombined VH and/or VL by restriction digestion followed by ligation with a peptide of choice. If necessary, restriction sites can be created in a CDR, such as by site-directed mutagenesis or PCR, to facilitate ligation of the peptide. This latter method is described in Example 12 herein.

The nucleotides can encode for peptides of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 16, 20, 25 or more amino acids. Any peptide that exhibits a useful property is suitable for insertion into an antibody scaffold. Generally, the peptide is one that specifically binds a target molecule. The peptides also include those that exhibit a specific activity, for example, an agonist or antagonist activity upon binding to the target. Peptide activities and uses include, but are not limited to, binding a receptor, binding a membrane bound surface molecule, binding a ligand, binding an enzyme or structural protein, activating or inhibiting a receptor, target drug delivery or any enzymatic activity. Exemplary of peptides are those that bind to a cell surface receptor such as a receptor for a cytokine, growth factor or growth inhibitor. Peptide mimetics for incorporation into a recombined germline VH or VL include any set forth in US Patent No. 7169905; US Patent No. 7396917, US Patent No. 7272508, US Patent No. 7019017; U.S. published Patent Appl. No. US200701344; published International Appl. No. WO2005060642; Johnson *et al.* (2000) Nephrol Dial. Transplant, 15:1274-1277. Exemplary of such peptides are set forth in Table 16. Other peptides for incorporation into the VH and VL encoded by the recombined germline nucleic acids provided herein are known in the art (see e.g., any of the references cited above) and/or can be identified depending on the desired target.

Table 16. Exemplary Peptide Mimetics		
Peptide	**Sequence**	**SEQ ID NO:**
TPO	IEGPTLRQWLAARA	987
	GGCADGPTLREWISFCGGK	988
	GGCADGPTLREWISFCGG	989
	LAI EGPTLRQWLHGNGRDT	990
	GNADGPTLRQWLEGRRPKN	991
	TIKGPTLRQWLKSREHTS	992
EPO	TYSCHFGPLTWVCKPQ	891
	DYHCRMGPLTWVCKPLGG	993
	GGTYSCHFGPLTWVCKPQGG	994
	DREGCRRGWVGQCKAWFN	995
	QRVEILEGRTECVLSNLRGRTRY	996
G-CSF	EEDCK	997
IL-5	TGGGDGYVCVEWARCPTCK	998
	EGYVCVEWAACPTCR	999
human brain natriuretic peptide (hBNP-32)	CFGRKMDRISSSSGLGC	1000
	FGRKMDRISSSSGLG	1001
Exendin 4	HGEGRFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPS	1002
GLP-1	HAEGTFTSDVSSYLEGQMKEFIAWLVKGR	1003
GLP-2	HADGSFSDEMNTILDNLAARDFINWLIQTKITDR	1004
Glucagon	HSQGTFTSDYSKYLDSRRAQDRVQWLMNT	1005
PACAP-38	HSDGIFTDSYSRYRKQMAVKKYLAAVLGKRYKQRVKNK	1006
CD209L	RYWNSGEPNNSGNEDCAEFSGSGWNCNRCDVDN	1007
TNF	YCFTASENHCY	1008
	YCFTNSENHCY	1009
VEGF	VEPNCDIHVMWEWECFERL	1010
	GERWCFDGPLTWVCGEES	1011
MMP inhibitor	CTTHWGFTLC	1012
CTLA-4	CSLHWGFWWC	1013
	GFVCSGIFAVGVGRC	1014

Nucleic acid molecules encoding for recombined germline VH or VL can be modified by replacement or introduction of nucleotides encoding a peptide into one or more of CDR1, CDR2, CDR3, FR1, FR2, FR3 or FR4. For example, nucleic acid molecules encoding for recombined germline VH or VL can be modified by replacement of an entire CDR with nucleotides encoding a peptide. The CDR replaced by a peptide can be CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and/or CDRL3. For example, in the resulting VH or VL chain one or more CDRs is replaced by a peptide. The peptides can be the same or different. In another example, nucleic acid molecules encoding for recombined human germline VH and VL are modified by replacement of a portion of a CDR with nucleotides encoding a peptide. The portion of the CDR replaced by the nucleotides is a portion of CDRH1,

CDRH2, CDRH3, CDRL1, CDRL2, and/or CDRL3. The portion of the CDR replaced by the nucleotides can encode for a peptide that is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 16, 20 or 25 or more amino acids. In an additional example, one or more portions of two or more CDRs are replaced by nucleotides encoding a peptide. The resulting peptides can be the same or different. In a further example, nucleic acid molecules encoding for recombined human germline VH or VL can be modified by insertion of nucleotides encoding a peptide between two nucleotides of a CDR of the antibody. The CDR with a peptide inserted is CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and/or CDRL3. In some instances, the resulting VH or VL chain includes one or more peptides inserted in one or more CDRs. The peptides inserted into the CDRs can be the same or different.

The addition of flanking sequences at the carboxy or N-terminal ends of a peptide have been shown to increase biological activity, by altering the presentation of the peptide within the antibody scaffold. Hence, nucleic acid molecules can be modified to encode peptides having adding flanking sequences at the carboxy or N-terminal ends of the peptides. Flanking sequences can encode for 1, 2, 3, 4, 5 or more amino acids. Flanking sequences can encode for any amino acid or any combinations of amino acids. Glycine is the smallest and simplest of the amino acids, containing only a single hydrogen atom in its side chain. Due to its small size, glycine can fit into small spaces and can adopt particular conformations that other amino acids can not. Proline is a sterically constrained amino acid that has been shown to increase activity of a peptide when flanking the peptide sequence (REF). Generally, flanking sequences encode for glycine or proline. Typically, flanking sequences encode for proline. For example, a nucleic acid molecule can encode a peptide containing proline and/or glycine added to the N- or C- terminus of the EPO peptide set forth in SEQ ID NO:891. Exemplary of nucleic acid molecules containing flanking sequences encode any of the EPO peptides set forth in SEQ ID NOS: 874-895.

e. Generating Variable Heavy and Light Chain Sequences and Nucleic Acid Molecules

The sequences for recombined nucleic acid molecules encoding VH and VL chain compiled by practice of the method herein are collected and stored. The collected sequences can be analyzed for any particular characteristic, such as for example, sequence similarity between and among other recombined sequences. The sequences then can be ranked based on sequence diversity. All recombined sequences, or a subset thereof, can be generated into recombined nucleic acid molecules using DNA synthesis and/or recombinant DNA

technology. For example, a subset of sequences can be selected based on their sequence similarity or difference for generation of an antibody library.

i. Storage and Collection

Sequences recombined by the method herein are collected and stored. Typically, collection and storage is in an addressable format, such that the identity of each sequence is known by its locus. For example, the sequences can be stored in a database or in a list. Further, the individual gene segment components of each nucleic acid sequence are known, and the recombined nucleic acid sequence identified by the component segments. For example, a nucleic acid sequence named VH1-18_IGHD1-26*01_IGHJ2*01 identifies a nucleic acid sequence encoding a variable heavy chain containing the VH germline segment VH1-18 (also called VH1-18*01 by some nomenclature standards), the DH germline segment IGHD1-26*01, and the JH germline segment IGHJ2*01. One of skill in the art can identify a nucleic acid sequence using any desired naming convention, so long as the component segments are easily identified.

Generally sequences encoding VH chains are recombined, collected and stored separately from VL chains. Further, among VL chains, sequences encoding V-kappa light chains are recombined, collected and stored separate from sequences encoding V-lambda chains. The identity of the nucleic acid sequence at each locus is known and can be mapped to an output file that contains the sequences for all the nucleic acid molecules within the addressable format.

For purposes herein, the sequences are addressably stored such that each sequence can be easily identified, including by its component parts (e.g. the individual compiled segments). By practice of the methods above, a plurality of different recombined nucleic acid sequences encoding a VH chain can be generated, which can represent all possible permutations of recombined segments or subsets thereof. For example, 10, 100, 500, 1000 (10^3), $2x10^3$, $4x10^3$, $6x10^3$, $8x10^3$, 10^4, $2x10^4$, $3x10^4$, $4x10^4$, $5x10^4$, $6x10^4$, $7x10^4$, $8x10^4$, $9x10^4$, 10^5, $2x10^5$, $3x10^5$, $4x10^5$, $5x10^5$, $6x10^5$, $7x10^5$, $8x10^5$, $9x10^5$, 10^6, 10^7 or more VH nucleic acid sequences can be generated. By practice of the methods above, a plurality of different recombined nucleic acid sequences encoding a VL chain can be generated, which can represent all possible permutations of recombined segments or subsets thereof. For example, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000 (10^3), $2x10^3$, $3x10^3$, $4x10^3$, $5x10^3$, $6x10^3$, $7x10^3$, $8x10^3$, $9x10^3$, 10^4, $5x10^4$, 10^5 or more VL nucleic acid sequences can be generated.

The examples exemplify collection and storage of sequences compiled by practice of the method in a SequenceHistory.txt file. Such a file represents sequences generated in the Examples by the exemplified software and ordered for DNA synthesis. Sequences also can be stored manually, for example, in spreadsheets or lists.

ii. Determining Sequence Diversity of Collected Nucleic Acid Sequences

In some examples, recombined nucleic acid molecules can be collected and stored based on their sequence diversity. It is contemplated herein that knowledge of the sequence diversity of library members can be employed to select a restricted subset of nucleic acid sequences encoding VH chain and VL chain for synthesis and expression as described herein below. Hence, resulting antibody libraries can be made to maximize sequence diversity among members due to sequence differences. Alternatively, resulting antibody libraries can be made to minimize sequence diversity among members due to sequence similarities. Thus, for example, the sequence of a selected recombined nucleic acid can be compared to all other sequences in the libraries, and those sequences that are different (e.g. having sequence similarity that is less then 70%, e.g., 10%, 20%, 30%, 40%, 50%, 60%, 65%) can be selected. In another example, if a "Hit" is identified in an initial screen, a further library can be created where all members have a high sequence similarity (e.g. 70%, 75%, 80%, 85%, 90%, 95% or more) to the identified "Hit." The percentages given are for exemplification only. One of skill in the art can choose any desired limit of sequence similarity by which to select sequences for inclusion in a particular library.

To determine the sequence similarity or difference between and among recombined nucleic acid sequences sequence diversity based on sequence similarity of all collected nucleic acid sequences is assessed. Typically, due to the degeneracy of the genetic code, recombined nucleic acid sequences are first translated to give an amino acid sequence, and then sequence similarity between and among the resulting amino acid sequences is determined. Translation is performed based on the genetic code, whereby 64 codons encode the 20 amino acids plus three stop codons (see Table 20). Translation of each sequence can be performed manually or by other computer-based or automated methods. One of skill in the art is familiar with methods of translating proteins. The sequences can be grouped or stored based on their sequence diversity.

Typically, sequence diversity is assessed based on sequence similarity of two or more sequences, such as for example, as determined by alignment. One of skill in the art is familiar with various techniques to determine the sequence similarity (e.g. identity) between and

among sequences. For example, sequence similarity can be determined manually by determining nucleotide differences between and among sequences. Sequence similarity or sequence identity of nucleotide or amino acid sequences also can be determined using conventional software or computer programs. Such algorithms are well known to one of skill in the art. For example, to find the best segment of identity or similarity of sequences, BLAST (Altschul et al (1990) J. Mol. Biol. 215:403-410 and Lipman et al (1990) J. Mol. Biol. 215:403-410), FASTA (Lipman et al (1985) Science 227:1435-1441), or Smith and Waterman (Smith and Waterman (1981) J. Mol. Biol. 147:195-197) homology search programs can be used. To perform global alignments, sequence alignment programs such as the CLUSTAL W (Thompson et al (1994) Nucleic Acids Research 22:4673-4680) can be used.

For example, nucleic acid or amino acid sequences can be assessed for sequence similarity using BLAST. Parameters for sufficient similarity to determine relatedness are computed based on well known methods for calculating statistical similarity. Exemplary parameters for determining relatedness of two or more sequences using the BLAST algorithm, for example, can be as set forth below. Briefly, amino acid sequence alignments can be performed using BLASTP version 2.0.8 (Jan. 05, 1999) and the following parameters: Matrix: 0 BLOSUM62; gap open: 11; gap extension: 1; x_dropoff: 50; expect: 10.0; wordsize: 3; filter: on. Nucleic acid sequence alignments can be performed using BLASTN version 2.0.6 (Sep. 16, 1998) and the following parameters: Match: 1; mismatch:-2; gap open: 5; gap extension: 2; x_dropoff: 50; expect: 10.0; wordsize: I 1; filter: off. Those skilled in the art will know what modifications can be made to the above parameters to either increase or decrease the stringency of the comparison, for example, and determine the relatedness of two or more sequences. The BLAST program provides an output indicator, the BLAST bit score, which is a value calculated from the number of gaps and substitutions associated with each aligned sequence. The higher the score, the more significant the alignment. The bit score can be used to select sequences that have either the most sequence diversity or alternatively, the least sequence diversity to every other selected sequence.

In another example, sequence diversity also can be assessed by comparison of two or more amino acid or nucleic acid sequences by alignment methods, e.g., the CLUSTAL method. (See, e.g., Higgins, D. G. and P. M. Sharp (1988) Gene 73:237-244.) The CLUSTAL algorithm groups sequences into clusters by examining the distances between all pairs. The clusters are aligned pairwise and then in groups. The percentage similarity between two amino acid sequences, e.g., sequence A and sequence B, is calculated by dividing the length

of sequence A, minus the number of gap residues in sequence A, minus the number of gap residues in sequence B, into the sum of the residue matches between sequence A and sequence B, times one hundred. Gaps of low or of no similarity between the two amino acid sequences are not included in determining percentage similarity. Sequence similarity (e.g. sequence identity) between nucleic acid sequences can also be counted or calculated by other methods known in the art, e.g., the Jotun Hein method. (See, e.g., Hein, J. (1990) Methods Enzymol. 183:626-645.) Identity between sequences can also be determined by other methods known in the art, e.g., by varying hybridization conditions. BLASTclust is another program that can be used for cluster analysis. BLASTclust is used in the software compilation program described in the Examples.

Diversity and cluster information as well as BLAST bit score information provide the user with several options when selecting sequences. For example, the user can create an antibody library where the selected sequences are as diverse as possible. To do this, the user can use the diversity score and cluster information, and select sequences from different clusters that have the highest diversity. Alternatively, for example, the user can create a an antibody library where one sequence is initially selected and all subsequent sequences are as similar as possible to the first sequence. This can be accomplished by using the BLAST function. The user can BLAST the selected first sequence, and then select all the other sequences for the library using the BLAST bit score, choosing sequences with the highest score and therefore the highest sequence similarity. For example, Example 5 describes implementation of assessing sequence sequence diversity between and among recombined sequences using Software Compilation software. The Example illustrates that BLAST can be performed on all sequences and Blast bit scores calculated to identify the sequence similarity or differences between sequences.

iii. Generating Nucleic Acid Molecules From Recombined Sequences

a) Synthesis

Where desired, the sequences can be individually synthesized into nucleic acid molecules. All collected sequences can be synthesized, or a subset of sequences synthesized. Nucleic acid molecules encoding VH or VL chain can be synthesized by methods known to one of skill in the art using synthetic gene synthesis (see e.g., U.S. Patent Nos. 4,652,639; 5,132,215; 5,093,251; 6,110,668; 6,472,184; published U.S. application Nos. US20060281113; US20070004041; US20070122817; and International PCT Published Application Nos. WO98/15567; WO99/47536; WO00/75364; WO2004035781;

WO2005071077). These include standard solid phase polypeptide synthesis methods involving synthesis of single stranded oligos that are ligated together. Methods also include methods using standard triplets that act as universal building blocks that represent all possible sequence combinations, and can be combined in a series of reaction steps (Slonomics®).

Nucleic acids can be synthesized that are 20, 50, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000 or more base pairs in length. Gene synthesis can be performed by automated methods. Any of the known synthesis methods can be used to produce the nucleic acid molecules. For example, companies exist for the purpose of synthesizing oligonucleotides and genes, for example, Integrated DNA Technologies (IDT) (Coralville, IA), TriLink Biotechnologies (San Diego, CA), Blue Heron Gene Synthesis (Bothell, WA), and Sloning Biotechnology (Puchheim, Germany).

The nucleotide monomers used in the synthesis can be purine and pyrimidine deoxyribonucleotides (adenosine (A), cytidine (C), guanosine (G) and thymidine (T)) or ribonucleotides (A, G, C and U (uridine)), or they can analogs or derivatives of these nucleotides, such as peptide nucleic acid (PNA), phosphorothioate DNA, and other such analogs and derivatives or combinations thereof. Other nucleotide analogs are well known in the art and can be used in synthesizing the oligonucleotides provided herein.

The nucleic acid molecules can be synthesized with nucleotide modifications. In one example, each oligonucleotide contains a terminal phosphate group, for example, a 5' phosphate group. For example, when it is desired to seal nicks between two adjacent oligonucleotides, e.g. following hybridization of the two oligonucleotides to a common opposite strand polynucleotide according to the methods herein, a 5' phosphate group is added to the end of the oligonucleotide whose 5' terminus will be joined with the 3' terminus of another oligonucleotide to seal the nick. In one example, a 5' phosphate (PO_4) group is added during oligonucleotide synthesis. In another example, a kinase, such as T4 polynucleotide kinase (T4 PK) is added to the oligonucleotide for addition of the 5' phosphate group. Other oligonucleotide modifications are well-known and can be used with the provided methods.

The synthetic oligonucleotides can be chemically synthesized. Methods for chemical synthesis of oligonucleotides are well-known and involve the addition of nucleotide monomers or trimers to a growing oligonucleotide chain. Typically, synthetic oligonucleotides are made by chemically joining single nucleotide monomers or nucleotide trimers containing protective groups. For example, phosphoramidites, single nucleotides containing protective groups, can be added one at a time. Synthesis typically begins with the

3' end of the oligonucleotide. The 3' most phosphoramidite is attached to a solid support and synthesis proceeds by adding each phosphoramidite to the 5' end of the last. After each addition, the protective group is removed from the 5' phosphate group on the most recently added base, allowing addition of another phosphoramidite. See, for example, Behlke *et al.* "Chemical Synthesis of Oligonucleotides" Integrated DNA Technologies (2005), 1-12; Allen *et al.* "UltramersTM- The Longest Oligonucleotides Available with Mass Spectrometry" Integrated DNA Technologies, Technical Report (2007); and McBride and Caruthers *Tetrahedron Lett.* 24:245-248, which describe synthesizing oligonucleotides using standard cyanoethyl chemistry (using phosphoramidite monomers and tetrazole catalysis). Such methods typically result in generation of oligonucleotides of 100-200 bases.

Thus, to synthesize larger genes, methods include annealing of a series of smaller oligonucleotides. In such a method, individually designed oligonucleotides are made, such as by using an automated DNA synthesizer, purified and connected by specific annealing using standard ligation or polymerase reactions. Generally, the oligos are designed with overlapping stretches of common sequence to permit annealing. Several methods of gene synthesis have been described, including, but not limited to the ligation of phosphorylated overlapping oligonucleotides (Gupta,N.K. *et al.* (1968) Studies on polynucleotides, 88. Enzymatic joining of chemically synthesized segments corresponding to the gene for alanine-tRNA. Proc. Natl Acad. Sci. USA, 60, 1338–1344; Fuhrmann M *et al.*, A synthetic gene coding for the green fluorescent protein (GFP) is a versatile reporter in Chlamydomonas reinhardtii. Plant J. 1999 Aug;19(3):353-61); de novo gene construction using Ultramers (Allen *et al.* "UltramersTM- The Longest Oligonucleotides Avialable with Mass Spectrometry" Integrated DNA Technologies, Technical Report (2007); the Fok I method (Mandecki,W. and Bolling,T.J. (1988) FokI method of gene synthesis. Gene, 68, 101–107); a modified form of ligase chain reaction for gene synthesis; PCR assembly whereby the full-length molecule is generated progressively by overlap extension (Stemmer,W.P., Crameri,A., Ha,K.D., Brennan,T.M. and Heyneker,H.L. (1995) Single-step assembly of a gene and entire plasmid from large numbers of oligodeoxyribonucleotides. Gene, 164, 49–53), thermodynamically balanced inside-out (Gao X, Yo P, Keith A, Ragan TJ, Harris TK. Thermodynamically balanced inside-out (TBIO) PCR-based gene synthesis: a novel method of primer design for high-fidelity assembly of longer gene sequences. Nucleic Acids Res. 2003 Nov 15;31(22):e143) or combined approaches (Young L, Dong Q. Two-step total gene synthesis method. Nucleic Acids Res. 2004 Apr 15;32(7):e59). Since the error frequency

increases with longer oligonucleotides, methods typically include using shorter oligonucleotides (200 base pairs or less) assembled together.

The synthesized molecules can be purified by a number of well-known methods, for example, high-performance liquid chromatography (HPLC), thin layer chromatography (TLC), Polyacrylamide Gel Electrophoresis (PAGE) and desalting.

In one embodiment, the synthesized nucleic acids are arrayed in multiwell plates, with each individual well of a plate corresponding to one individual nucleic acid. More specifically, each individual locus of a plate contains an nucleic acid encoding an antibody variable region, either heavy or light. The identity of the nucleic acid contained within each well of the multiwell plate is known and mapped to an output file that contains the nucleic acid sequences for all of the nucleic acids within the plate. Multiwell plates can include but are not limited to 96-well plates, 384-well plates, and 1536-well plates. In an exemplary embodiment, the nucleic acids are spatially arrayed in a 96-well plate.

Upon synthesis, the resulting nucleic acid molecules are individually addressed into a locus (e.g. a well, chip, tag, and other addressable formats). Each individual locus of a plate can contain a different recombined and synthesized nucleic acid molecule encoding for either a heavy chain variable region or a light chain variable region or portion thereof compared to all other addresses. The identity of the nucleic acid molecule at each locus is known and can be mapped to an output file that contains the sequences for all the nucleic acid molecules within the addressable format. For example, nucleic acid molecules can be addressed by spatial array into multiwell plates, with each individual locus of a plate containing one individual nucleic acid molecule. Multiwell plates can include but are not limited to 12-well plates, 24-well plates, 96-well plates, 384-well plates, and 1536-well plates.

b) Recombinant Generation

In some examples, recombined VH and/or VL sequences, or a subset thereof, can be generated into recombined nucleic acid molecules using recombinant DNA technology. One of skill in the art is familiar with general recombinant DNA techniques, including but not limited to, PCR, cloning and restriction enzyme digestion. Such techniques can be used to combine germline segments as discussed herein above to generate recombined nucleic acid molecules that are in-frame. Generally, each vector is generated individually, such that the identity of the sequence of each vector is known through the cloning process. Thus, the recombinant generation of a combinatorial antibody library is addressable.

In the methods of generating combinatorial antibody libraries using recombinant DNA techniques, germline segments can be linked directly or indirectly by a linker so long as

the resulting nucleic acid molecule is in-frame, resulting in a functional and productive antibody. The linker can be a peptide, polypeptide or an amino acid. For example, it is understood that by virtue of using recombinant DNA technologies, including the use of restriction enzymes, that amino acids can be inserted between V-D, D-J and V-J junctions in order to facilitate joining of germline segments. Exemplary of a linker as described herein in Example 14 is a sequence of nucleotides encoding an SY between the 3'end of the D_H germline segment and the 5'end of the J_H germline segment.

In methods of generating a combinatorial antibody library by recombinant DNA techniques, a parent vector or vectors can be generated that contain common nucleic acid sequences between and among members of the library. For example, a vector can be generated that contains nucleic acid sequence for a V_H, D_H and/or J_H germline segment, modified forms thereof, or portions thereof and/or a V_L and/or J_L that are common between all members of the library. It is understood that introduction of segments is with reference to the reading frames as described herein above, such that the resulting compiled nucleic acid molecule is in-frame. The description below provides a general summary of a method of generating a combinatorial antibody library using recombinant DNA techniques. It is understood that the reference to the examples is for exemplification only. Using the description provided herein one of skill in the art can generate similar vectors containing nucleic acid compiled from germline segments or modified forms thereof to generate recombined VH or VL chains that are in-frame. For example, it is understood that the order of addition of $V_H/D_H/J_H$ or V_L/J_L segments or portions thereof to the recombinant vectors can occur in any order, so long as the resulting cloned nucleotide sequence encodes a recombined VH or VL chain that is in-frame.

Thus, a parent vector is typically generated containing a sequence common to all members of the library. For example, if all vectors share a common V_H germline sequence, a vector can be generated carrying the V_H germline sequence in its correct reading frame, which can be manipulated for subsequent inclusion of other germline segments. For example, the V_H germline sequence can be modified to include restriction enzyme sites on the 3'end for subsequent joining with a D_H germline sequence. In another example, vectors can be generated containing a portion of a V_H, D_H or J_H germline sequence. For example, a vector can be generated containing a common framework consensus sequence as described elsewhere herein. This is exemplified in Example 14 where a modified Plasmid A vector was generated to contain a common framework 4 region of a J_H germline segment. An exemplary parent vector for use in generating a combinatorial antibody library using the methods herein

is set forth in SEQ ID NO:2051, which contains a common V_H germline segment (VH3-23 (IGHV3-23*01) that is modified to remove an internal restriction site and add additional restriction sites at the 3'end) and a common framework 4 region of a JH germline segment.

The parent vector can then be used to further introduce remaining germline segments, modified forms thereof, or portions thereof such that a plurality of final vectors are generated each containing a nucleic acid sequence encoding a recombined VH and/or VL chain. The generation from a parent vector to a final vector can occur in steps, thereby resulting in intermediate vectors, generally at least one intermediate vector. Generally, nucleic acid sequences for subsequent germline segments, modified forms thereof or portions thereof are generated as oligonucleotides for subsequent cloning into the parent vector or an intermediate vector. It is understood that if a stop codon is inserted at any step, the stop codon is either removed as described herein above, or the particular segment containing the stop codon is not cloned. To facilitate joining with adjacent nucleic acid sequences, the oligonucleotides are generated to contain complementary restriction enzyme sites at the 3'and/or 5'ends.

For example, depending on the components contained in the parent vector, an intermediate vector can be generated to contain remaining germline segments, modified forms thereof or portions thereof. For example, intermediate vectors can be generated from the parent vector above (set forth in SEQ ID NO:2051), whereby each intermediate vector contains a different J_H segment in its correct reading frame (see e.g. Table 13). The J_H segment can be a germline segment or a modified form thereof. Exemplary of modified J_H segments are any set forth in SEQ ID NOS: 3450-3455 and encoding J_H regions set forth in any of SEQ ID NOS: 3456-3461. The entire J_H segment or a portion of a J_H segment can be added to an existing parent or intermediate vector. For example, if a parent vector is made to contain a consensus framework 4 region as described above, a portion of a J_H segment containing nucleotides corresponding to the last portion of a CDR3 in the J_H segment can be introduced. By virtue of the addition of different segments, for example different J_H segments, in the intermediate vectors, the diversity of the library can be increased. Thus, generally, a plurality of intermediate vectors are generated. For example, Example 14 describes the generation of six intermediate vectors (having a sequence set forth in any of SEQ ID NOS: 2064-2069).

A plurality of final vectors are generated that contain the all components of a compiled germline sequence. As above, the remaining nucleotide to be inserted into the vector are generated as oligonucleotides, and typically contain complementary restriction enzyme sites at the 3'and/or 5'ends. As noted, the oligonucleotides are generated to provide

the correct reading frame for the inserted segment and do not contain stop codons. In addition, the oligonucleotides are generated to preserve existing reading frames for the segments contained in the parent or intermediate vectors. For example, as described elsewhere herein, it is understood that the reading frame of the D_H region is not critical. Thus, D_H segments, including D_H germline segments, can be inserted in any reading frame, or can be a random sequence of nucleotides. Example 14 exemplifies generation of a plurality of final vectors by introduction of D_H germline segments (e.g., any set forth in any of SEQ ID NOS: 239-245, 248, 250, 252, 254, 256, 258-272), or inverted segments thereof (e.g., any set forth in any of SEQ ID NOS: 3462-3488), in all three reading frames. In generating the oligonucleotides, however, one or more nucleotides are removed or added from the 3'or 5'ends in order to preserve reading frames of the adjacent J_H segments. This is exemplified in Example 14, which sets forth conditions for removing or adding nucleotides in order to preserve reading frames.

The resulting final vectors contain compiled $V_H/D_H/J_H$ or V_L/J_L germline segments, or modified forms thereof, that encode a recombined VH chain or VL chain. Each final vector is different and contains a different nucleic acid sequence encoding a different recombined VH chain or VL chain. Since the nucleic acid molecules are already cloned into an expression vector, they can be directly transformed into an expression system as discussed in Section f below.

f. Expressing and Producing Antibodies or Portions or Fragments Thereof

In the methods provided herein, recombined nucleic acid molecules, such as synthetic recombined nucleic acid molecules or recombined nucleic acid molecules generated recombinantly, are cloned into an expression vector. The polynucleotides typically are inserted into the vectors using restriction digest and ligation. Any conventional vector known to one of skill in the art can be used for expression in eukaryotic or prokaryotic cells. Exemplary vectors include plasmid A, C and D described herein below. The vector can be used to transform any expression system compatible therewith for amplification of the nucleic acid and/or expression of the encoded variable heavy or variable light chain polypeptide.

Typically, ligation into a vector is in an addressable format such that the identity of the recombined polypeptide expressed therefrom is known. For example, the vectors containing nucleic acids are spatially arrayed in multiwell plates, with each individual locus of a plate containing a vector with one individual nucleic acid inserted. More specifically, each individual locus of a plate contains a vector encoding for either a heavy chain or a light

chain. The identity of the nucleic acid contained within each well of the multiwell plate is known, for example, by mapping to stored sequences collected from the compilation or synthesis above. For example, ligation into vectors can be performed directly into multiwall plates already containing synthesized nucleic acid molecules from above. Multiwell plates can include but are not limited to 96-well plates, 384-well plates, and 1536-well plates. In an exemplary embodiment, the nucleic acids are spatially arrayed in a 96-well plate.

Generally in practicing the methods, a nucleic acid molecules encoding a variable heavy chain is ligated into a first vector. A nucleic acid molecule encoding a variable light chain is ligated into a second vector. The first vector and second vector can be co-transformed into the same expression host for co-expression of a variable heavy chain and a variable light chain. The polypeptides, upon expression, will become operably joined by virtue of interactions between the heavy and light chain polypeptides. In some examples, it is possible to operably join the nucleic acid molecules directly prior to expression, such as by including a linker. In such examples, a single nucleic acid molecule encodes a variable heavy chain and a variable light chain, and can be ligated into a single vector for expression thereof.

In all methods herein, the expressed antibodies minimally include a VH chain and a VL chain, or portions thereof sufficient to form an antigen-binding site. In addition, if desired, a constant chain can be included for expression in operative linkage with the variable chains. In all examples of the methods, the recombined nucleic acid molecules, upon expression and ligation, encode for antibodies or fragments thereof, including, but not limited to an IgG, a Fab fragment, a $F(ab')_2$ fragment or a Fv fragment, such as a disulfide-linked Fv or a single chain Fv. An exemplary antibody is a Fab fragment. Such antibodies or fragments thereof can be purified by any methods known to one of skill in the art.

Section F describes methods of expressing and purifying antibodies or fragments thereof.

2. Automation

Any of the steps of the method described above can be automated and/or made high-throughput and/or otherwise rendered more efficient or fast. One of skill in the art is familiar with methods of automation of systems and processes, including the implementation of *in silico* databases, application of computer programs, robotics and/or other high-throughput methods that can be used in practice of the method. It is contemplated that the entire process of the method can be automated or only a few steps can be automated. The choice of automation is up to the user. The description below and examples exemplify automation of various processes of the method.

a. User-Created Database

To practice the methods herein, sequences of germline segments or modified forms thereof must be obtained. Such sequences are known to one of skill in the art and can be obtained from commercially available databases, such as described above. Such germline segment sequences are set forth in the sequence listing as set forth in Tables 3-5 above. Exemplary of modified J_H germline segments are set forth in SEQ ID NOS: 3450-3455. The sequences can be compiled into a user-created database for ease of access. Generation of a file or database containing all of the sequence information provides immediate access to these sequences. In addition the sequence file can be linked to other systems and processes to facilitate performance of the method. For example, as exemplified in Figure 9, in Example 4, a database file is linked to the Sequence Compilation Alogrithm as an input file for identification of V(D)J heavy and light chain sequences for sequence compilation.

The database file contains sequences for germline V_H, D_H, J_H, V_κ, J_κ, V_λ and J_λ segments. In particular, the database file can contain sequences of nucleic acids set forth in any of SEQ ID NOS:10-451, 868, or a subset thereof. It is helpful if the sequences are specified using FASTA format and all sequences contain a blank line between them. For purposes of practice of the method, the J_H, J_κ and J_λ segment sequences are set forth in the database file in coding frame triplets corresponding to their optimal reading frame, which is set forth in Table 13 above. The sequences in the database file are named for identification. For example, germline segments are identified by section title headings [VH], [DH], [JH], [VK], [JK], [VL], and [JL]. Such a databased file is described in the Examples (e.g. Example 3) as a SequenceDatabase.txt.file. Figure 11 provides a schematic illustration of a Sequence Database file format.

In addition, the database can contain other sequences used in practicing the method. For example, the database can contain nucleic acid sequences for restriction sites, and can be identified in the database under the section title heading [Restriction Sites]. These sequences can be accessed by particular program processes as described below to identify nucleic acid sequences corresponding to restriction sites within a recombined nucleic acid molecule. Restriction site sequences contained in the database include any of SEQ ID NOS:977-980, 1889-1900. Any restriction site sequence known to one of skill in the art can be contained in the database file. For example, the schematic illustration of a database file in Figure 11 includes a sequence for the restriction enzyme Mfe I.

It is contemplated that the database file can be periodically updated to contain additional sequences. The database file also can be updated to include any sequence

contemplated for practice of the method. For example, nucleic acid sequences that encode for proteins other than antibody germline segments can be entered into the database, using FASTA format, under an appropriate heading . These sequences are then available to be recombined into the germline antibody sequences. For example, one can insert peptide sequences into an antibody at D_H by including nucleic acid sequences encoding for the peptide under the section title [DH].

b. Sequence Compilation

The method of compilation of sequence can be performed *in silico*, for example, using software. Any software programmed to perform an algorithm or process allowing for compiling germline segments in accordance with the method herein or any suitable method, can be used. One of skill in the art familiar with software programming can generate a computer program capable of performing such an algorithm or process. Generally, the software is programmed to perform any one or more of the following processes:

(a) accessing a user-created *in silico* database of all available antibody germline segments (V_H, D_H, J_H, V_κ, J_κ, V_λ and J_λ);

(b) applying an algorithm to generate every possible recombined full length nucleic acid sequence for heavy chains (5'-V_H-D_H-J_H-3' combinations), every possible recombined full length nucleic acid sequence for kappa light chains (5'-V_κ-J_κ-3' combinations) and every possible recombined full length nucleic acid sequence for lambda light chains (5'-V_λ-J_λ-3' combinations);

(c) applying an algorithm to modify the nucleic acid sequences of the joints so that the resulting nucleic acids sequences are in frame;

(d) modifying the resulting nucleic acid sequences of the joints to remove any inadvertently generated stop codons;

(e) modifying the resulting full length nucleic acid to optimize codon usage for bacterial expression;

(f) modifying the resulting nucleic acid to remove any undesired restriction sites;

(g) inserting flanking nucleic acids containing restriction sites for cloning at the 5' and 3' termini of the optimized full length nucleic acid sequences;

(h) ranking recombined nucleic acid sequences based on their sequence diversity;

(g) selecting recombined nucleic acid sequence(s) (encoding either a heavy chain variable region or a light chain variable region) from the library of recombined nucleic acid sequences;

(h) assigning the selected nucleic acid sequence to a unique locus of an addressable format;

(i) generating an output file that contains all recombined nucleic acid sequences in the form of the addressed format that lists the distinct heavy chain or light chain sequences such that each locus is addressed and corresponds to a locus of the addressed format (e.g. 96-well plate).

Provided herein are software, computer-readable media, and computer systems for performing the method as described herein. The Examples describe an exemplary software, computer-readable media, computer system and systems. It is understood that those of skill in the art can modify such software, computer-readable meadia, computer systems and systems based upon this disclosure and that such modifications are included herein.

For example, each of these processes of the method described herein is performed by an exemplary computer software exemplified in the Examples herein. For example, Example 2 and Figures 8 and 9 describe an exemplary process for sequence compilation of germline segments. The flow chart in Figure 9 describes processes for each of steps (a)- (d) and (f) above. In addition, Example 2 and Figure 10 describes an exemplary process for ranking sequences based on sequence diversity. The flow chart in Figure 10 describes the process used to rank sequences after determination of diversity scores and an example of the ranking is set forth in Figure 17.

c. Automation of protein expression and purification

Methods of automating protein expression and purification are known to one of skill in the art (see, e.g., Lesley *et al.* (2001) Protein Expression and Purification, 22:159-164; Acton TB *et al.* (2005) Methods Enzymol., 394:210-43; Nguyen *et al.* (2004) Journal of Structural and Functional Genomics, 5:23-27). Such processes typically include robotic methods.

Exemplary of a high-throughput automated method of protein expression and purification is Piccolo™ (Wollerton *et al.* (2006) JALA, 11:291-303). The Piccolo™ system automates protein expression and purification of proteins from both *E.coli* and baculovirus mediated insect cell expression systems. Piccolo is able to perform multiple different protein expression and purifications in parallel. The Piccolo system utilizes a 24-position culture vessel block (CVB) in an aeration assembly that supports the expression and purification of multiple samples at once. The Piccolo system contains four modules that perform these functions: a liquid handling module, CVB incubators, a centrifuge and storage carousels. A rail mounted 6-axis RX60L Spinal Transfer Robot (ST Robot; Staubli, Horgen, Switzerland) moves the lab ware between the liquid handling module, incubators, centrifuge and storage carousels. The system is controlled by software that permits the user to control expression and purification conditions.

Expression can be initated by inoculation of CVB plates containing appropriate growth medium with an an input inoculum, such as a bacterial culture. A total of 576 individual cultures can be grown at any one time, corresponding to 24 culture vessel blocks. The plates can be incubated under user-specified periods and conditions. Typical growth and induction temperatures range from 16 °C to 37 °C. Selection of optimal temperatures for growth and induction is well within the level of skill of the skilled artisan. Bacterial growth can be monitored. If desired, protein expression can be induced by adding an appropriate amount of inducer into the CVB plate assembly and further grown under appropriate conditons. Protein expression can be induced by addition of any inducer compatible with the expression vector, including isopropyl β-D-1-thiogalactopyranoside (IPTG) and arabinose. Expression times range from 2 hours to 48 hours. Selection of optimal expression times is well within the level of skill of the skilled artisan. Following expression, plates can be stored under cooling conditions. For example, as set forth in Example 9, spatially arrayed transformed cells are mapped to a 24-well culture vessel block for cell growth and protein expression. For each 96-well plate of transformed cells, four culture vessel blocks are generated, thereby allowing the growth of Fabs corresponding to every well of the 96-well plate.

Following expression of the desired protein, the Piccolo™ system also can be used to purify the resulting proteins. The Piccolo machine is programmed to perform lysis and purification steps. The cells are harvested and lysed using an appropriate lysis buffer that is compatible with the purification technique. Selection of a lysis buffer is well within the level of skill of the skilled artisan. The resulting supernatant is then purified by column chromatography with an appropriately modified resin, such as an anti-flag resin or Ni-charged resin. One of skill in the art can identify an appropriate resin for protein purification as described elsewhere herein. The resin should be manually equilibrated in an appropriate wash buffer before starting the run. The bound protein can be eluted with an appropriate elution buffer and the eluate collected in an output plate. The output plate can be stored at cool temperatures (e.g. 6°C) until collected by the operator.

Purity can be assessed by any method known in the art including gel electrophoresis and staining and spectrophotometric techniques. Additional purification methods can be combined with Piccolo such as are described elsewhere herein. For example, proteins can be further purified using an orthogonal secondary high throughput method of protein purification (*see* e.g. Example 10). Additional column chromatography can be performed using a

compatible resin, an Aktapurifier (GE Healthcare) and an autosampler. Exemplary of purifying antibodies, a protein G resin can be utilized.

E. Libraries

Provided herein are libraries. The libraries include nucleic acid libraries encoding VH or VL chains, vector libraries transformed with recombined nucleic acid molecules, and antibody libraries. In some examples, the members of each of the libraries are addressed in an addressable format, such as any discussed in Section E.2. The members of the libraries and the resulting libraries can be produced by the methods described herein above.

1. VH Nucleic Acid Libraries and Vector Libraries Thereof

Provided herein are recombined nucleic acid libraries encoding VH chains. The libraries provided herein include recombined nucleic acid molecules made up entirely of V_H, D_H and J_H germline segments or modified forms thereof. The V_H, D_H and J_H germline segments include any set forth in Table 3 above, modified forms thereof, or a subset thereof. Any permutation is possible. The resulting nucleic acid molecule in the library have a sequence such that the V_H segment is 5' to the D_H segment which is 5' to the J_H segment. The segments can be linked directly or indirectly by a peptide linker.

Because the nucleic acid molecules in the library are derived from germline segments, members of such a nucleic acid library are capable of encoding a naïve antibody when co-expressed with a nucleic acid encoding a VL chain. It is understood that the library is considered to be naïve and derived from germline even though, in practicing the method herein, the joint regions of the segments are altered to render the resulting encoding nucleic acid molecules in frame. Such alterations, however, are minor and variously include insertion or deletion generally of only a single nucleotide of a germline segment. In addition, other modification made to the recombined nucleic acid sequence by virtue of practice of the method herein, such as removal of stop codons and restriction enzyme site sequences, also result in naïve antibodies.

It is understood that libraries can be generated that are compiled from sequences that include modified germline segments. In some examples of the libraries, the libraries include recombined nucleic acid molecules made up entirely of a V_H and a J_H germline segment, and also any sequence of nucleotides between the V_H and J_H germline segment. This is the region that includes the central portion of the CDRH3, which is largely responsible for the antigen specificity of the resulting antibody. The sequence of nucleotides can be any random sequence of nucleotides. In some instances, the sequence of nucleotides is a sequence that encodes a peptide mimetic against any desired target, for example, a cell surface receptor.

Exemplary peptide mimetics are set forth in Table 16. Generally, the sequence of nucleotides is or is about 5, 10, 15, 20, 25, 30, 40, 50, 60, 70, 80, 90 or more nucleotides in length. The resulting nucleic acid molecule in the library have a sequence such that the V_H segment is 5' to the random sequence of nucleotides which is 5' to the J_H segment. In some examples, the random sequence of nucleotides is a D_H germline segment.

In other examples, the libraries provided herein include recombined nucleic acid molecules where at least one, two or all three of a V_H, D_H and J_H germline segment contained therein are modified, for example, due to modification by insertion, deletion or addition of amino acids. For example, the libraries include nucleic acid molecules containing sequences encoding a directed peptide. The libraries also include recombined nucleic acid molecules containing nucleotide mutations encoding amino acid replacements, for example, of one or more amino acids of a CDR. In an additional example, the libraries provided herein include recombined nucleic acid molecules where at least a portion of the nucleic acid molecule, such as the entire nucleic acid molecule encoding the VH chain, or at least one or more of a V_H, D_H and J_H are derived from an existing monoclonal antibody, including, but not limited to, any monoclonal antibody set forth in Table 9. For example, exemplary libraries provided herein can include a nucleic acid molecule encoding the VH chain of an anti-CD20 antibody such as is set forth in SEQ ID NO:1043 or SEQ ID NO:1058 (SEQ ID NO:453 including terminal restriction site sequences) or Herceptin such as is set forth in SEQ ID NO:1057 (SEQ ID NO:452 including terminal restriction site sequences)

Libraries of recombined nucleic acid molecules provided herein can include members that represent one, some or all of the above examples. Any of the libraries provided herein also can include members whose sequences include heterologous sequence, for example, restriction site sequences, linker sequences, sequences encoding tags or other detectable moieties or other sequences.

In the VH nucleic acid libraries provided herein, each recombined nucleic acid molecule member of the library is productive and, when co-expressed with a nucleic acid molecule encoding a VH chain, generates a functional antibody or portion thereof that is sufficient to form an antigen-binding site. In addition, in the VH nucleic acid libraries provided herein, each nucleic acid member of the library is different. The VH nucleic acid libraries provided herein can contain 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, 2000, 3000, 4000, 5000, 6000, 7000, 8000, 9000, 10,000 (10^4), $2x10^4$, $3x10^4$, $4x10^4$, $5x10^4$, $6x10^4$, $7x10^4$, $8x10^4$, $9x10^4$, 10^5, $2x10^5$, $3x10^5$, $4x10^5$, $5x10^5$, $6x10^5$, $7x10^5$, $8x10^5$, $9x10^5$, 10^6 or more different members. The nucleic acid members are

provided in addressed formats, such that when addressed the identity of each nucleic acid is known by its location in the array.

For example, an exemplary VH nucleic acid library includes members set forth in SEQ ID NOS: 454-805, each representing a different recombined nucleic acid molecule of V_H, D_H and J_H germline segments. Such a library includes members containing heterologous sequence for restriction sites at the 3' and 5 ' ends. It is understood that members of the library also can include those having sequences not including the heterologous sequence, such as is set forth in any of SEQ ID NOS: 1059-1410.

In an additional example, an exemplary VH nucleic acid library includes members set forth in SEQ ID NOS: 2070-2759, each representing a different recombined nucleic acid molecule of V_H, D_H and J_H germline segments or modified forms thereof. Such a library includes members containing heterologous sequence for restriction sites at the 3'end corresponding to CTAGC (set forth in SEQ ID NO:1903) and at the 5'end corresponding to CCATGGCA (set forth in SEQ ID NO:1901). It is understood that members of the library also can include those having sequences set forth in any of SEQ ID NOS: 2070-2759 that do no include the heterologous sequences at one or both of the 3'and 5'ends.

A VH nucleic acid library can include members from any of the libraries provided herein, or a subset thereof. For example, a VH nucleic acid library includes members set forth in any of SEQ ID NOS:454-805 and 2070-2759, or a subset thereof. The library members can include those containing heterologous sequences at the 3' or 5'ends, and/or members that do not include heterologous sequences.

In some examples, any of the nucleic acid sequences in the libraries provided herein can be included in a vector to generate vector libraries. Exemplary of vector libraries are libraries of recombined nucleic acid molecules encoding VH chain included in backbone Plasmid A or Plasmid D.

2. VL nucleic acid libraries and Vector Libraries Thereof

Provided herein are recombined nucleic acid libraries encoding VL chains. The libraries include those encoding for lambda or gamma light chains, or combinations thereof. Thus, the libraries provided herein include recombined nucleic acid molecules made up entirely of V_κ and J_κ germline segments and/or V_λ and J_λ germline segments. The V_κ and J_κ germline segments and/or V_λ and J_λ germline segments include any set forth in Tables 4-5 above, or a subset thereof. Any permutation is possible. The resulting nucleic acid molecules in the library have a sequence such that the V_L segment (V_κ or V_λ) is 5' to the J_L segment (J_κ or J_λ).

Because the nucleic acid molecules in the library are derived from germline segments, members of such a nucleic acid library are capable of encoding a naïve antibody when co-expressed with a nucleic acid encoding a VH chain. It is understood that the library is considered to be naïve and derived from germline even though, in practicing the method herein, the joint regions of the segments are altered to render the resulting encoding nucleic acid molecules in frame. Such alterations, however, are minor and variously include insertion or deletion generally of only a single nucleotide of a germline segment. In addition, other modification made to the recombined nucleic acid sequence by virtue of practice of the method herein, such as removal of stop codons and restriction enzyme site sequences, also result in naïve antibodies.

In some examples, the libraries provided herein include recombined nucleic acid molecules where at least one or both a V_κ, and J_κ germline segment or a V_λ and J_λ germline segment contained therein are modified, for example, due to modification by insertion, deletion or addition of amino acids. For example, the libraries include nucleic acid molecules containing sequences encoding a directed peptide. The libraries also include recombined nucleic acid molecules containing nucleotide mutations encoding amino acid replacements, for example, of one or more amino acids of a CDR. In an additional example, the libraries provided herein include recombined nucleic acid molecules where at least a portion of the nucleic acid molecule, such as the entire nucleic acid molecule encoding the VH chain, or at least one or more of a V_κ, and J_κ or V_λ and J_λ are derived from an existing monoclonal antibody including, but not limited to, any monoclonal antibody set forth in Table 9. For example, exemplary libraries provided herein can include a nucleic acid molecule encoding the VL chain of Herceptin such as is set forth in SEQ ID NO: 1423 (SEQ ID NO:818 including terminal restriction site sequences) or the VL chain of an anti-CD20 antibody such as is set forth in SEQ ID NO: 1050 or SEQ ID NO:1440 (SEQ ID NO:835 including terminal restriction site sequences).

Libraries of recombined nucleic acid molecules provided herein can include members that represent one, some or all of the above examples. Any of the libraries provided herein also can include members whose sequences include heterologous sequence, for example, restriction site sequences, linker sequences, sequences encoding tags or other detectable moieties or other sequences.

In the VL nucleic acid libraries provided herein, each recombined nucleic acid molecule member of the library is productive and, when co-expressed with a nucleic acid molecule encoding a VH chain, generates a functional antibody or portion thereof that

contains a sufficient antigen-binding site. In addition, in the VL nucleic acid libraries provided herein, each nucleic acid member of the library is different. The VL nucleic acid libraries provided herein can contain 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, 2000, 3000, 4000, 5000, 6000, 7000, 8000, 9000, 10,000 (10^4), 2x 10^4, 3x10^4, 4x10^4, 5x10^4, 6x10^4, 7x10^4, 8x10^4, 9x10^4, 10^5, 2x10^5, 3x10^5, 4x10^5, 5x10^5, 6x10^5, 7x10^5, 8x10^5, 9x10^5, 10^6 or more different members. The nucleic acid members are provided in addressed formats, such that when addressed the identity of each nucleic acid is known by its location in the array.

For example, an exemplary VL nucleic acid library includes members set forth in SEQ ID NOS: 806-815, 817, 819-834, 836-867 each representing a different recombined nucleic acid molecule of V_K, and J_K germline segments. Such a library includes members containing heterologous sequence for restriction sites at the 3' and 5 ' ends. It is understood that members of the library also can include those having sequences not including the heterologous sequence, such as is set forth in any of SEQ ID NOS: 1411-1422, 1424-1439, 1441-1472.

In some examples, any of the nucleic acid sequences in the libraries provided herein can be included in a vector to generate vector libraries. Exemplary of vector libraries are libraries of recombined nucleic acid molecules encoding VL chain included in backbone Plasmid C or Plasmid E.

3. Paired Nucleic Acid Libraries or Vector Libraries Thereof

Also provided herein are libraries containing both recombined nucleic acid molecules encoding a VH chain and nucleic acid molecules encoding a VL chain, i.e. paired nucleic acid libraries. The paired libraries provided herein can contain a first nucleic acid molecule that is any of the nucleic acid members of the VH nucleic acid library in Section E.1 above and a second nucleic acid molecule that is any of the nucleic acid members of the VL nucleic acid library in Section E.2 above. The nucleic acid members in the paired libraries include those having heterologous sequence and those not having heterologous sequence. In some examples, one of the nucleic acid molecules in the pair can contain a heterologous sequence (e.g. a tag or other detectable moiety), while the other paired molecule at the locus in the library does not contain any heterologous sequence.

The paired nucleic acid libraries can be provided as addressed libraries. In such libraries, each locus of an addressed format contains one nucleic acid molecule encoding a VH chain and one nucleic acid molecule encoding a VL chain. Each nucleic acid pair (i.e. the combination of the nucleic acid molecule encoding the VH chain and the nucleic acid

molecule encoding the VL chain) is different compared to all other pairs at all other addressed loci.

In some examples, the nucleic acid molecules can be contained in vectors to generate paired vector libraries. In such libraries, each locus of the addressed library includes a vector containing a nucleic acid molecule encoding a VL chain and a vector containing a nucleic acid molecule encoding a VH chain.

In some examples, the paired nucleic acid libraries can contain a common nucleic acid molecule encoding a VL chain such that each locus in the library contains the same nucleic acid molecule. In other examples, the paired nucleic acid libraries can contain a common nucleic acid molecule encoding a VH chain such that each locus in the library contains the same nucleic acid molecule. Generally, a library contains 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, 5,000, 10,000 or more nucleic acid molecules encoding a VL chain and 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, 5,000, 10,000 or more nucleic acid molecules encoding a VH chain. The resulting paired library contains 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, 2000, 3000, 4000, 5000, 6000, 7000, 8000, 9000, 10,000 (10^4), 2x 10^4, $3x10^4$, $4x10^4$, $5x10^4$, $6x10^4$, $7x10^4$, $8x10^4$, $9x10^4$, 10^5, $2x10^5$, $3x10^5$, $4x10^5$, $5x10^5$, $6x10^5$, $7x10^5$, $8x10^5$, $9x10^5$, 10^6, 10^7, 10^8, 10^9, 10^{10} or more different paired members.

As described herein below, upon co-expression of a first and second nucleic acid molecule (e.g a nucleic acid molecule encoding a VH chain and a nucleic acid encoding a light chain), a library of antibodies can be generated. If the nucleic acid molecule further contains a sequence encoding a CH, a Fab library can be generated, whereby each member in the library contains a VH chain and a VL chain linked by a CH.

For example, an exemplary nucleic acid paired library includes those where a first nucleic acid is any one or more nucleic acids molecules set forth in any of SEQ ID NOS: 454-805 or 2070-2759 (each encoding a VH chain), and a second nucleic acid molecule set forth in any of SEQ ID NOS: 806-815, 817, 819-834, and 836-867 (each encoding a VL chain). The sequences set forth above contain heterologous sequence for restriction sites at the 3' and 5 ' ends. It is understood that nucleic acid libraries can be generated without the heterologus sequences. Thus, in some examples, members of the library also can include those having sequences not including a heterologous sequence. For example, an exemplary nucleic acid paired library includes nucleic acid sequences not containing heterologous sequence for restriction sites at the 3' and 5' ends from a first nucleic acid set forth in any of

SEQ ID NOS: 1059-1410 or 2070-2759 (not including the 3'and 5'restriction sites) (each encoding a VH chain) and a second nucleic acid molecule set forth in SEQ ID NOS: 1411-1422, 1424-1439 and 1441-1471. Such a library can include all permutations of any of the above paired nucleic acid sequences. Thus, the paired library can contain at or about 1.5 x10^5, 2.1 x 10^5, 2.5 x 10^5, 3.5 x 10^5, 4 x 10^5, 4.2 x 10^5, 4.4 x 10^5, 4.6 x 10^5, 4.8 x 10^5, 5 x 10^5, 5.2 x 10^5, 5.4 x 10^5, 5.6 x 105, 5.8 x 10^5, 6 x 10^5, or more members, or a subset thereof such as 500, 600, 700, 800, 900, 10^3, 5x10^3, 10^4, 5x10^4, 10^5 or more members.

Exemplary of a paired library is set forth in Table 17, where each row sets forth a different loci of the library. In the Table, SEQ ID NOS for the nucleic acid molecules are set forth as "RS" (containing a heterologous restriction site sequence) and "NO RS" (not containing a heterologous restriction site sequence).

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
1	gnl|Fabrus|VH3-23_IGHD1-1*01_IGHJ4*01	595	1200	gnl|Fabrus|O12_IGKJ1*01	833	1438
2	gnl|Fabrus|VH3-23_IGHD2-15*01_IGHJ4*01	598	1203	gnl|Fabrus|O12_IGKJ1*01	833	1438
3	gnl|Fabrus|VH3-23_IGHD3-22*01_IGHJ4*01	602	1207	gnl|Fabrus|O12_IGKJ1*01	833	1438
4	gnl|Fabrus|VH3-23_IGHD4-11*01_IGHJ4*01	604	1209	gnl|Fabrus|O12_IGKJ1*01	833	1438
5	gnl|Fabrus|VH3-23_IGHD5-12*01_IGHJ4*01	606	1211	gnl|Fabrus|O12_IGKJ1*01	833	1438
6	gnl|Fabrus|VH3-23_IGHD5-5*01_IGHJ4*01	608	1213	gnl|Fabrus|O12_IGKJ1*01	833	1438
7	gnl|Fabrus|VH3-23_IGHD6-13*01_IGHJ4*01	609	1214	gnl|Fabrus|O12_IGKJ1*01	833	1438
8	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ4*01	612	1217	gnl|Fabrus|O12_IGKJ1*01	833	1438
9	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ6*01	613	1218	gnl|Fabrus|O12_IGKJ1*01	833	1438
10	gnl|Fabrus|VH1-69_IGHD1-14*01_IGHJ4*01	502	1107	gnl|Fabrus|O12_IGKJ1*01	833	1438
11	gnl|Fabrus|VH1-69_IGHD2-2*01_IGHJ4*01	503	1108	gnl|Fabrus|O12_IGKJ1*01	833	1438
12	gnl|Fabrus|VH1-69_IGHD2-8*01_IGHJ6*01	504	1109	gnl|Fabrus|O12_IGKJ1*01	833	1438
13	gnl|Fabrus|VH1-69_IGHD3-16*01_IGHJ4*01	505	1110	gnl|Fabrus|O12_IGKJ1*01	833	1438
14	gnl|Fabrus|VH1-69_IGHD3-3*01_IGHJ4*01	506	1111	gnl|Fabrus|O12_IGKJ1*01	833	1438

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
15	gnl|Fabrus|VH1-69_IGHD4-17*01_IGHJ4*01	508	1113	gnl|Fabrus|O12_IGKJ1*01	833	1438
16	gnl|Fabrus|VH1-69_IGHD5-12*01_IGHJ4*01	509	1114	gnl|Fabrus|O12_IGKJ1*01	833	1438
17	gnl|Fabrus|VH1-69_IGHD6-19*01_IGHJ4*01	511	1116	gnl|Fabrus|O12_IGKJ1*01	833	1438
18	gnl|Fabrus|VH1-69_IGHD7-27*01_IGHJ4*01	513	1118	gnl|Fabrus|O12_IGKJ1*01	833	1438
19	gnl|Fabrus|VH4-34_IGHD1-7*01_IGHJ4*01	749	1354	gnl|Fabrus|O12_IGKJ1*01	833	1438
20	gnl|Fabrus|VH4-34_IGHD2-2*01_IGHJ4*01	750	1355	gnl|Fabrus|O12_IGKJ1*01	833	1438
21	gnl|Fabrus|VH4-34_IGHD3-16*01_IGHJ4*01	751	1356	gnl|Fabrus|O12_IGKJ1*01	833	1438
22	gnl|Fabrus|VH4-34_IGHD4-17*01_IGHJ4*01	753	1358	gnl|Fabrus|O12_IGKJ1*01	833	1438
23	gnl|Fabrus|VH4-34_IGHD5-12*01_IGHJ4*01	754	1359	gnl|Fabrus|O12_IGKJ1*01	833	1438
24	gnl|Fabrus|VH4-34_IGHD6-13*01_IGHJ4*01	755	1360	gnl|Fabrus|O12_IGKJ1*01	833	1438
25	gnl|Fabrus|VH4-34_IGHD6-25*01_IGHJ6*01	756	1361	gnl|Fabrus|O12_IGKJ1*01	833	1438
26	gnl|Fabrus|VH4-34_IGHD7-27*01_IGHJ4*01	758	1363	gnl|Fabrus|O12_IGKJ1*01	833	1438
27	gnl|Fabrus|VH2-26_IGHD1-20*01_IGHJ4*01	521	1126	gnl|Fabrus|O12_IGKJ1*01	833	1438
28	gnl|Fabrus|VH2-26_IGHD2-2*01_IGHJ4*01	523	1128	gnl|Fabrus|O12_IGKJ1*01	833	1438
29	gnl|Fabrus|VH2-26_IGHD3-10*01_IGHJ4*01	524	1129	gnl|Fabrus|O12_IGKJ1*01	833	1438
30	gnl|Fabrus|VH2-26_IGHD4-11*01_IGHJ4*01	526	1131	gnl|Fabrus|O12_IGKJ1*01	833	1438
31	gnl|Fabrus|VH2-26_IGHD5-18*01_IGHJ4*01	528	1133	gnl|Fabrus|O12_IGKJ1*01	833	1438
32	gnl|Fabrus|VH2-26_IGHD6-13*01_IGHJ4*01	529	1134	gnl|Fabrus|O12_IGKJ1*01	833	1438
33	gnl|Fabrus|VH2-26_IGHD7-27*01_IGHJ4*01	530	1135	gnl|Fabrus|O12_IGKJ1*01	833	1438
34	gnl|Fabrus|VH5-51_IGHD1-14*01_IGHJ4*01	776	1381	gnl|Fabrus|O12_IGKJ1*01	833	1438
35	gnl|Fabrus|VH5-51_IGHD2-8*01_IGHJ4*01	778	1383	gnl|Fabrus|O12_IGKJ1*01	833	1438
36	gnl|Fabrus|VH5-51_IGHD3-3*01_IGHJ4*01	780	1385	gnl|Fabrus|O12_IGKJ1*01	833	1438
37	gnl|Fabrus|VH5-51_IGHD4-17*01_IGHJ4*01	781	1386	gnl|Fabrus|O12_IGKJ1*01	833	1438

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
38	gnl|Fabrus|VH5-51_IGHD5-18*01>3_IGHJ4*01	782	1387	gnl|Fabrus|O12_IGKJ1*01	833	1438
39	gnl|Fabrus|VH5-51_IGHD5-18*01>1_IGHJ4*01	783	1388	gnl|Fabrus|O12_IGKJ1*01	833	1438
40	gnl|Fabrus|VH5-51_IGHD6-25*01_IGHJ4*01	784	1389	gnl|Fabrus|O12_IGKJ1*01	833	1438
41	gnl|Fabrus|VH5-51_IGHD7-27*01_IGHJ4*01	785	1390	gnl|Fabrus|O12_IGKJ1*01	833	1438
42	gnl|Fabrus|VH6-1_IGHD1-1*01_IGHJ4*01	786	1391	gnl|Fabrus|O12_IGKJ1*01	833	1438
43	gnl|Fabrus|VH6-1_IGHD2-15*01_IGHJ4*01	788	1393	gnl|Fabrus|O12_IGKJ1*01	833	1438
44	gnl|Fabrus|VH6-1_IGHD3-3*01_IGHJ4*01	791	1396	gnl|Fabrus|O12_IGKJ1*01	833	1438
45	gnl|Fabrus|VH6-1_IGHD4-23*01_IGHJ4*01	793	1398	gnl|Fabrus|O12_IGKJ1*01	833	1438
46	gnl|Fabrus|VH6-1_IGHD4-11*01_IGHJ6*01	792	1397	gnl|Fabrus|O12_IGKJ1*01	833	1438
47	gnl|Fabrus|VH6-1_IGHD5-5*01_IGHJ4*01	794	1399	gnl|Fabrus|O12_IGKJ1*01	833	1438
48	gnl|Fabrus|VH6-1_IGHD6-13*01_IGHJ4*01	795	1400	gnl|Fabrus|O12_IGKJ1*01	833	1438
49	gnl|Fabrus|VH6-1_IGHD6-25*01_IGHJ6*01	796	1401	gnl|Fabrus|O12_IGKJ1*01	833	1438
50	gnl|Fabrus|VH6-1_IGHD7-27*01_IGHJ4*01	797	1402	gnl|Fabrus|O12_IGKJ1*01	833	1438
51	gnl|Fabrus|VH4-59_IGHD6-25*01_IGHJ3*01	775	1380	gnl|Fabrus|O12_IGKJ1*01	833	1438
52	gnl|Fabrus|VH3-48_IGHD6-6*01_IGHJ1*01	655	1260	gnl|Fabrus|O12_IGKJ1*01	833	1438
53	gnl|Fabrus|VH3-30_IGHD6-6*01_IGHJ1*01	625	1230	gnl|Fabrus|O12_IGKJ1*01	833	1438
54	gnl|Fabrus|VH3-66_IGHD6-6*01_IGHJ1*01	681	1286	gnl|Fabrus|O12_IGKJ1*01	833	1438
55	gnl|Fabrus|VH3-53_IGHD5-5*01_IGHJ4*01	670	1275	gnl|Fabrus|O12_IGKJ1*01	833	1438
56	gnl|Fabrus|VH2-5_IGHD5-12*01_IGHJ4*01	536	1141	gnl|Fabrus|O12_IGKJ1*01	833	1438
57	gnl|Fabrus|VH2-70_IGHD5-12*01_IGHJ4*01	543	1148	gnl|Fabrus|O12_IGKJ1*01	833	1438
58	gnl|Fabrus|VH3-15_IGHD5-12*01_IGHJ4*01	567	1172	gnl|Fabrus|O12_IGKJ1*01	833	1438
59	gnl|Fabrus|VH3-15_IGHD3-10*01_IGHJ4*01	565	1170	gnl|Fabrus|O12_IGKJ1*01	833	1438
60	gnl|Fabrus|VH3-49_IGHD5-18*01_IGHJ4*01	662	1267	gnl|Fabrus|O12_IGKJ1*01	833	1438

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
61	gnl|Fabrus|VH3-49_IGHD6-13*01_IGHJ4*01	663	1268	gnl|Fabrus|O12_IGKJ1*01	833	1438
62	gnl|Fabrus|VH3-72_IGHD5-18*01_IGHJ4*01	699	1304	gnl|Fabrus|O12_IGKJ1*01	833	1438
63	gnl|Fabrus|VH3-72_IGHD6-6*01_IGHJ1*01	701	1306	gnl|Fabrus|O12_IGKJ1*01	833	1438
64	gnl|Fabrus|VH3-73_IGHD5-12*01_IGHJ4*01	709	1314	gnl|Fabrus|O12_IGKJ1*01	833	1438
65	gnl|Fabrus|VH3-73_IGHD4-23*01_IGHJ5*01	708	1313	gnl|Fabrus|O12_IGKJ1*01	833	1438
66	gnl|Fabrus|VH3-43_IGHD3-22*01_IGHJ4*01	650	1255	gnl|Fabrus|O12_IGKJ1*01	833	1438
67	gnl|Fabrus|VH3-43_IGHD6-13*01_IGHJ4*01	653	1258	gnl|Fabrus|O12_IGKJ1*01	833	1438
68	gnl|Fabrus|VH3-9_IGHD3-22*01_IGHJ4*01	724	1329	gnl|Fabrus|O12_IGKJ1*01	833	1438
69	gnl|Fabrus|VH3-9_IGHD1-7*01_IGHJ5*01	721	1326	gnl|Fabrus|O12_IGKJ1*01	833	1438
70	gnl|Fabrus|VH3-9_IGHD6-13*01_IGHJ4*01	727	1332	gnl|Fabrus|O12_IGKJ1*01	833	1438
71	gnl|Fabrus|VH4-39_IGHD3-10*01_IGHJ4*01	762	1367	gnl|Fabrus|O12_IGKJ1*01	833	1438
72	gnl|Fabrus|VH4-39_IGHD5-12*01_IGHJ4*01	766	1371	gnl|Fabrus|O12_IGKJ1*01	833	1438
73	gnl|Fabrus|VH1-18_IGHD6-6*01_IGHJ1*01	460	1065	gnl|Fabrus|O12_IGKJ1*01	833	1438
74	gnl|Fabrus|VH1-24_IGHD5-12*01_IGHJ4*01	467	1072	gnl|Fabrus|O12_IGKJ1*01	833	1438
75	gnl|Fabrus|VH1-2_IGHD1-1*01_IGHJ3*01	461	1066	gnl|Fabrus|O12_IGKJ1*01	833	1438
76	gnl|Fabrus|VH1-3_IGHD6-6*01_IGHJ1*01	475	1080	gnl|Fabrus|O12_IGKJ1*01	833	1438
77	gnl|Fabrus|VH1-45_IGHD3-10*01_IGHJ4*01	480	1085	gnl|Fabrus|O12_IGKJ1*01	833	1438
78	gnl|Fabrus|VH1-46_IGHD1-26*01_IGHJ4*01	486	1091	gnl|Fabrus|O12_IGKJ1*01	833	1438
79	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ6*01	800	1405	gnl|Fabrus|O12_IGKJ1*01	833	1438
80	gnl|Fabrus|VH2-70_IGHD3-9*01_IGHJ6*01	542	1147	gnl|Fabrus|O12_IGKJ1*01	833	1438
81	gnl|Fabrus|VH1-58_IGHD3-10*01_IGHJ6*01	496	1101	gnl|Fabrus|O12_IGKJ1*01	833	1438
82	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ2*01	799	1404	gnl|Fabrus|O12_IGKJ1*01	833	1438
83	gnl|Fabrus|VH4-28_IGHD3-9*01_IGHJ6*01	734	1339	gnl|Fabrus|O12_IGKJ1*01	833	1438

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
84	gnl|Fabrus|VH4-31_IGHD2-15*01_IGHJ2*01	740	1345	gnl|Fabrus|O12_IGKJ1*01	833	1438
85	gnl|Fabrus|VH2-5_IGHD3-9*01_IGHJ6*01	535	1140	gnl|Fabrus|O12_IGKJ1*01	833	1438
86	gnl|Fabrus|VH1-8_IGHD2-15*01_IGHJ6*01	515	1120	gnl|Fabrus|O12_IGKJ1*01	833	1438
87	gnl|Fabrus|VH2-70_IGHD2-15*01_IGHJ2*01	540	1145	gnl|Fabrus|O12_IGKJ1*01	833	1438
88	gnl|Fabrus|VH3-38_IGHD3-10*01_IGHJ4*01	639	1244	gnl|Fabrus|O12_IGKJ1*01	833	1438
89	gnl|Fabrus|VH3-16_IGHD1-7*01_IGHJ6*01	570	1175	gnl|Fabrus|O12_IGKJ1*01	833	1438
90	gnl|Fabrus|VH3-73_IGHD3-9*01_IGHJ6*01	706	1311	gnl|Fabrus|O12_IGKJ1*01	833	1438
91	gnl|Fabrus|VH3-11_IGHD3-9*01_IGHJ6*01	548	1153	gnl|Fabrus|O12_IGKJ1*01	833	1438
92	gnl|Fabrus|VH3-11_IGHD6-6*01_IGHJ1*01	552	1157	gnl|Fabrus|O12_IGKJ1*01	833	1438
93	gnl|Fabrus|VH3-20_IGHD5-12*01_IGHJ4*01	584	1189	gnl|Fabrus|O12_IGKJ1*01	833	1438
94	gnl|Fabrus|VH3-16_IGHD2-15*01_IGHJ2*01	571	1176	gnl|Fabrus|O12_IGKJ1*01	833	1438
95	gnl|Fabrus|VH3-7_IGHD6-6*01_IGHJ1*01	692	1297	gnl|Fabrus|O12_IGKJ1*01	833	1438
96	gnl|Fabrus|VH3-16_IGHD6-13*01_IGHJ4*01	576	1181	gnl|Fabrus|O12_IGKJ1*01	833	1438
97	gnl|Fabrus|VH3-23_IGHD1-1*01_IGHJ4*01	595	1200	gnl|Fabrus|O18_IGKJ1*01	834	1439
98	gnl|Fabrus|VH3-23_IGHD2-15*01_IGHJ4*01	598	1203	gnl|Fabrus|O18_IGKJ1*01	834	1439
99	gnl|Fabrus|VH3-23_IGHD3-22*01_IGHJ4*01	602	1207	gnl|Fabrus|O18_IGKJ1*01	834	1439
100	gnl|Fabrus|VH3-23_IGHD4-11*01_IGHJ4*01	604	1209	gnl|Fabrus|O18_IGKJ1*01	834	1439
101	gnl|Fabrus|VH3-23_IGHD5-12*01_IGHJ4*01	606	1211	gnl|Fabrus|O18_IGKJ1*01	834	1439
102	gnl|Fabrus|VH3-23_IGHD5-5*01_IGHJ4*01	608	1213	gnl|Fabrus|O18_IGKJ1*01	834	1439
103	gnl|Fabrus|VH3-23_IGHD6-13*01_IGHJ4*01	609	1214	gnl|Fabrus|O18_IGKJ1*01	834	1439
104	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ4*01	612	1217	gnl|Fabrus|O18_IGKJ1*01	834	1439
105	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ6*01	613	1218	gnl|Fabrus|O18_IGKJ1*01	834	1439
106	gnl|Fabrus|VH1-69_IGHD1-14*01_IGHJ4*01	502	1107	gnl|Fabrus|O18_IGKJ1*01	834	1439

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
107	gnl|Fabrus|VH1-69_IGHD2-2*01_IGHJ4*01	503	1108	gnl|Fabrus|O18_IGKJ1*01	834	1439
108	gnl|Fabrus|VH1-69_IGHD2-8*01_IGHJ6*01	504	1109	gnl|Fabrus|O18_IGKJ1*01	834	1439
109	gnl|Fabrus|VH1-69_IGHD3-16*01_IGHJ4*01	505	1110	gnl|Fabrus|O18_IGKJ1*01	834	1439
110	gnl|Fabrus|VH1-69_IGHD3-3*01_IGHJ4*01	506	1111	gnl|Fabrus|O18_IGKJ1*01	834	1439
111	gnl|Fabrus|VH1-69_IGHD4-17*01_IGHJ4*01	508	1113	gnl|Fabrus|O18_IGKJ1*01	834	1439
112	gnl|Fabrus|VH1-69_IGHD5-12*01_IGHJ4*01	509	1114	gnl|Fabrus|O18_IGKJ1*01	834	1439
113	gnl|Fabrus|VH1-69_IGHD6-19*01_IGHJ4*01	511	1116	gnl|Fabrus|O18_IGKJ1*01	834	1439
114	gnl|Fabrus|VH1-69_IGHD7-27*01_IGHJ4*01	513	1118	gnl|Fabrus|O18_IGKJ1*01	834	1439
115	gnl|Fabrus|VH4-34_IGHD1-7*01_IGHJ4*01	749	1354	gnl|Fabrus|O18_IGKJ1*01	834	1439
116	gnl|Fabrus|VH4-34_IGHD2-2*01_IGHJ4*01	750	1355	gnl|Fabrus|O18_IGKJ1*01	834	1439
117	gnl|Fabrus|VH4-34_IGHD3-16*01_IGHJ4*01	751	1356	gnl|Fabrus|O18_IGKJ1*01	834	1439
118	gnl|Fabrus|VH4-34_IGHD4-17*01_IGHJ4*01	753	1358	gnl|Fabrus|O18_IGKJ1*01	834	1439
119	gnl|Fabrus|VH4-34_IGHD5-12*01_IGHJ4*01	754	1359	gnl|Fabrus|O18_IGKJ1*01	834	1439
120	gnl|Fabrus|VH4-34_IGHD6-13*01_IGHJ4*01	755	1360	gnl|Fabrus|O18_IGKJ1*01	834	1439
121	gnl|Fabrus|VH4-34_IGHD6-25*01_IGHJ6*01	756	1361	gnl|Fabrus|O18_IGKJ1*01	834	1439
122	gnl|Fabrus|VH4-34_IGHD7-27*01_IGHJ4*01	758	1363	gnl|Fabrus|O18_IGKJ1*01	834	1439
123	gnl|Fabrus|VH2-26_IGHD1-20*01_IGHJ4*01	521	1126	gnl|Fabrus|O18_IGKJ1*01	834	1439
124	gnl|Fabrus|VH2-26_IGHD2-2*01_IGHJ4*01	523	1128	gnl|Fabrus|O18_IGKJ1*01	834	1439
125	gnl|Fabrus|VH2-26_IGHD3-10*01_IGHJ4*01	524	1129	gnl|Fabrus|O18_IGKJ1*01	834	1439
126	gnl|Fabrus|VH2-26_IGHD4-11*01_IGHJ4*01	526	1131	gnl|Fabrus|O18_IGKJ1*01	834	1439
127	gnl|Fabrus|VH2-26_IGHD5-18*01_IGHJ4*01	528	1133	gnl|Fabrus|O18_IGKJ1*01	834	1439
128	gnl|Fabrus|VH2-26_IGHD6-13*01_IGHJ4*01	529	1134	gnl|Fabrus|O18_IGKJ1*01	834	1439
129	gnl|Fabrus|VH2-26_IGHD7-27*01_IGHJ4*01	530	1135	gnl|Fabrus|O18_IGKJ1*01	834	1439

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
130	gnl|Fabrus|VH5-51_IGHD1-14*01_IGHJ4*01	776	1381	gnl|Fabrus|O18_IGKJ1*01	834	1439
131	gnl|Fabrus|VH5-51_IGHD2-8*01_IGHJ4*01	778	1383	gnl|Fabrus|O18_IGKJ1*01	834	1439
132	gnl|Fabrus|VH5-51_IGHD3-3*01_IGHJ4*01	780	1385	gnl|Fabrus|O18_IGKJ1*01	834	1439
133	gnl|Fabrus|VH5-51_IGHD4-17*01_IGHJ4*01	781	1386	gnl|Fabrus|O18_IGKJ1*01	834	1439
134	gnl|Fabrus|VH5-51_IGHD5-18*01>3_IGHJ4*01	782	1387	gnl|Fabrus|O18_IGKJ1*01	834	1439
135	gnl|Fabrus|VH5-51_IGHD5-18*01>1_IGHJ4*01	783	1388	gnl|Fabrus|O18_IGKJ1*01	834	1439
136	gnl|Fabrus|VH5-51_IGHD6-25*01_IGHJ4*01	784	1389	gnl|Fabrus|O18_IGKJ1*01	834	1439
137	gnl|Fabrus|VH5-51_IGHD7-27*01_IGHJ4*01	785	1390	gnl|Fabrus|O18_IGKJ1*01	834	1439
138	gnl|Fabrus|VH6-1_IGHD1-1*01_IGHJ4*01	786	1391	gnl|Fabrus|O18_IGKJ1*01	834	1439
139	gnl|Fabrus|VH6-1_IGHD2-15*01_IGHJ4*01	788	1393	gnl|Fabrus|O18_IGKJ1*01	834	1439
140	gnl|Fabrus|VH6-1_IGHD3-3*01_IGHJ4*01	791	1396	gnl|Fabrus|O18_IGKJ1*01	834	1439
141	gnl|Fabrus|VH6-1_IGHD4-23*01_IGHJ4*01	793	1398	gnl|Fabrus|O18_IGKJ1*01	834	1439
142	gnl|Fabrus|VH6-1_IGHD4-11*01_IGHJ6*01	792	1397	gnl|Fabrus|O18_IGKJ1*01	834	1439
143	gnl|Fabrus|VH6-1_IGHD5-5*01_IGHJ4*01	794	1399	gnl|Fabrus|O18_IGKJ1*01	834	1439
144	gnl|Fabrus|VH6-1_IGHD6-13*01_IGHJ4*01	795	1400	gnl|Fabrus|O18_IGKJ1*01	834	1439
145	gnl|Fabrus|VH6-1_IGHD6-25*01_IGHJ6*01	796	1401	gnl|Fabrus|O18_IGKJ1*01	834	1439
146	gnl|Fabrus|VH6-1_IGHD7-27*01_IGHJ4*01	797	1402	gnl|Fabrus|O18_IGKJ1*01	834	1439
147	gnl|Fabrus|VH4-59_IGHD6-25*01_IGHJ3*01	775	1380	gnl|Fabrus|O18_IGKJ1*01	834	1439
148	gnl|Fabrus|VH3-48_IGHD6-6*01_IGHJ1*01	655	1260	gnl|Fabrus|O18_IGKJ1*01	834	1439
149	gnl|Fabrus|VH3-30_IGHD6-6*01_IGHJ1*01	625	1230	gnl|Fabrus|O18_IGKJ1*01	834	1439
150	gnl|Fabrus|VH3-66_IGHD6-6*01_IGHJ1*01	681	1286	gnl|Fabrus|O18_IGKJ1*01	834	1439
151	gnl|Fabrus|VH3-53_IGHD5-5*01_IGHJ4*01	670	1275	gnl|Fabrus|O18_IGKJ1*01	834	1439
152	gnl|Fabrus|VH2-5_IGHD5-12*01_IGHJ4*01	536	1141	gnl|Fabrus|O18_IGKJ1*01	834	1439

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
153	gnl|Fabrus|VH2-70_IGHD5-12*01_IGHJ4*01	543	1148	gnl|Fabrus|O18_IGKJ1*01	834	1439
154	gnl|Fabrus|VH3-15_IGHD5-12*01_IGHJ4*01	567	1172	gnl|Fabrus|O18_IGKJ1*01	834	1439
155	gnl|Fabrus|VH3-15_IGHD3-10*01_IGHJ4*01	565	1170	gnl|Fabrus|O18_IGKJ1*01	834	1439
156	gnl|Fabrus|VH3-49_IGHD5-18*01_IGHJ4*01	662	1267	gnl|Fabrus|O18_IGKJ1*01	834	1439
157	gnl|Fabrus|VH3-49_IGHD6-13*01_IGHJ4*01	663	1268	gnl|Fabrus|O18_IGKJ1*01	834	1439
158	gnl|Fabrus|VH3-72_IGHD5-18*01_IGHJ4*01	699	1304	gnl|Fabrus|O18_IGKJ1*01	834	1439
159	gnl|Fabrus|VH3-72_IGHD6-6*01_IGHJ1*01	701	1306	gnl|Fabrus|O18_IGKJ1*01	834	1439
160	gnl|Fabrus|VH3-73_IGHD5-12*01_IGHJ4*01	709	1314	gnl|Fabrus|O18_IGKJ1*01	834	1439
161	gnl|Fabrus|VH3-73_IGHD4-23*01_IGHJ5*01	708	1313	gnl|Fabrus|O18_IGKJ1*01	834	1439
162	gnl|Fabrus|VH3-43_IGHD3-22*01_IGHJ4*01	650	1255	gnl|Fabrus|O18_IGKJ1*01	834	1439
163	gnl|Fabrus|VH3-43_IGHD6-13*01_IGHJ4*01	653	1258	gnl|Fabrus|O18_IGKJ1*01	834	1439
164	gnl|Fabrus|VH3-9_IGHD3-22*01_IGHJ4*01	724	1329	gnl|Fabrus|O18_IGKJ1*01	834	1439
165	gnl|Fabrus|VH3-9_IGHD1-7*01_IGHJ5*01	721	1326	gnl|Fabrus|O18_IGKJ1*01	834	1439
166	gnl|Fabrus|VH3-9_IGHD6-13*01_IGHJ4*01	727	1332	gnl|Fabrus|O18_IGKJ1*01	834	1439
167	gnl|Fabrus|VH4-39_IGHD3-10*01_IGHJ4*01	762	1367	gnl|Fabrus|O18_IGKJ1*01	834	1439
168	gnl|Fabrus|VH4-39_IGHD5-12*01_IGHJ4*01	766	1371	gnl|Fabrus|O18_IGKJ1*01	834	1439
169	gnl|Fabrus|VH1-18_IGHD6-6*01_IGHJ1*01	460	1065	gnl|Fabrus|O18_IGKJ1*01	834	1439
170	gnl|Fabrus|VH1-24_IGHD5-12*01_IGHJ4*01	467	1072	gnl|Fabrus|O18_IGKJ1*01	834	1439
171	gnl|Fabrus|VH1-2_IGHD1-1*01_IGHJ3*01	461	1066	gnl|Fabrus|O18_IGKJ1*01	834	1439
172	gnl|Fabrus|VH1-3_IGHD6-6*01_IGHJ1*01	475	1080	gnl|Fabrus|O18_IGKJ1*01	834	1439
173	gnl|Fabrus|VH1-45_IGHD3-10*01_IGHJ4*01	480	1085	gnl|Fabrus|O18_IGKJ1*01	834	1439
174	gnl|Fabrus|VH1-46_IGHD1-26*01_IGHJ4*01	486	1091	gnl|Fabrus|O18_IGKJ1*01	834	1439
175	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ6*01	800	1405	gnl|Fabrus|O18_IGKJ1*01	834	1439

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
176	gnl|Fabrus|VH2-70_IGHD3-9*01_IGHJ6*01	542	1147	gnl|Fabrus|O18_IGKJ1*01	834	1439
177	gnl|Fabrus|VH1-58_IGHD3-10*01_IGHJ6*01	496	1101	gnl|Fabrus|O18_IGKJ1*01	834	1439
178	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ2*01	799	1404	gnl|Fabrus|O18_IGKJ1*01	834	1439
179	gnl|Fabrus|VH4-28_IGHD3-9*01_IGHJ6*01	734	1339	gnl|Fabrus|O18_IGKJ1*01	834	1439
180	gnl|Fabrus|VH4-31_IGHD2-15*01_IGHJ2*01	740	1345	gnl|Fabrus|O18_IGKJ1*01	834	1439
181	gnl|Fabrus|VH2-5_IGHD3-9*01_IGHJ6*01	535	1140	gnl|Fabrus|O18_IGKJ1*01	834	1439
182	gnl|Fabrus|VH1-8_IGHD2-15*01_IGHJ6*01	515	1120	gnl|Fabrus|O18_IGKJ1*01	834	1439
183	gnl|Fabrus|VH2-70_IGHD2-15*01_IGHJ2*01	540	1145	gnl|Fabrus|O18_IGKJ1*01	834	1439
184	gnl|Fabrus|VH3-38_IGHD3-10*01_IGHJ4*01	639	1244	gnl|Fabrus|O18_IGKJ1*01	834	1439
185	gnl|Fabrus|VH3-16_IGHD1-7*01_IGHJ6*01	570	1175	gnl|Fabrus|O18_IGKJ1*01	834	1439
186	gnl|Fabrus|VH3-73_IGHD3-9*01_IGHJ6*01	706	1311	gnl|Fabrus|O18_IGKJ1*01	834	1439
187	gnl|Fabrus|VH3-11_IGHD3-9*01_IGHJ6*01	548	1153	gnl|Fabrus|O18_IGKJ1*01	834	1439
188	gnl|Fabrus|VH3-11_IGHD6-6*01_IGHJ1*01	552	1157	gnl|Fabrus|O18_IGKJ1*01	834	1439
189	gnl|Fabrus|VH3-20_IGHD5-12*01_IGHJ4*01	584	1189	gnl|Fabrus|O18_IGKJ1*01	834	1439
190	gnl|Fabrus|VH3-16_IGHD2-15*01_IGHJ2*01	571	1176	gnl|Fabrus|O18_IGKJ1*01	834	1439
191	gnl|Fabrus|VH3-7_IGHD6-6*01_IGHJ1*01	692	1297	gnl|Fabrus|O18_IGKJ1*01	834	1439
192	gnl|Fabrus|VH3-16_IGHD6-13*01_IGHJ4*01	576	1181	gnl|Fabrus|O18_IGKJ1*01	834	1439
193	gnl|Fabrus|VH3-23_IGHD1-1*01_IGHJ4*01	595	1200	gnl|Fabrus|A20_IGKJ1*01	809	1414
194	gnl|Fabrus|VH3-23_IGHD2-15*01_IGHJ4*01	598	1203	gnl|Fabrus|A20_IGKJ1*01	809	1414
195	gnl|Fabrus|VH3-23_IGHD3-22*01_IGHJ4*01	602	1207	gnl|Fabrus|A20_IGKJ1*01	809	1414
196	gnl|Fabrus|VH3-23_IGHD4-11*01_IGHJ4*01	604	1209	gnl|Fabrus|A20_IGKJ1*01	809	1414
197	gnl|Fabrus|VH3-23_IGHD5-12*01_IGHJ4*01	606	1211	gnl|Fabrus|A20_IGKJ1*01	809	1414
198	gnl|Fabrus|VH3-23_IGHD5-5*01_IGHJ4*01	608	1213	gnl|Fabrus|A20_IGKJ1*01	809	1414

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
199	gnl|Fabrus|VH3-23_IGHD6-13*01_IGHJ4*01	609	1214	gnl|Fabrus|A20_IGKJ1*01	809	1414
200	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ4*01	612	1217	gnl|Fabrus|A20_IGKJ1*01	809	1414
201	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ6*01	613	1218	gnl|Fabrus|A20_IGKJ1*01	809	1414
202	gnl|Fabrus|VH1-69_IGHD1-14*01_IGHJ4*01	502	1107	gnl|Fabrus|A20_IGKJ1*01	809	1414
203	gnl|Fabrus|VH1-69_IGHD2-2*01_IGHJ4*01	503	1108	gnl|Fabrus|A20_IGKJ1*01	809	1414
204	gnl|Fabrus|VH1-69_IGHD2-8*01_IGHJ6*01	504	1109	gnl|Fabrus|A20_IGKJ1*01	809	1414
205	gnl|Fabrus|VH1-69_IGHD3-16*01_IGHJ4*01	505	1110	gnl|Fabrus|A20_IGKJ1*01	809	1414
206	gnl|Fabrus|VH1-69_IGHD3-3*01_IGHJ4*01	506	1111	gnl|Fabrus|A20_IGKJ1*01	809	1414
207	gnl|Fabrus|VH1-69_IGHD4-17*01_IGHJ4*01	508	1113	gnl|Fabrus|A20_IGKJ1*01	809	1414
208	gnl|Fabrus|VH1-69_IGHD5-12*01_IGHJ4*01	509	1114	gnl|Fabrus|A20_IGKJ1*01	809	1414
209	gnl|Fabrus|VH1-69_IGHD6-19*01_IGHJ4*01	511	1116	gnl|Fabrus|A20_IGKJ1*01	809	1414
210	gnl|Fabrus|VH1-69_IGHD7-27*01_IGHJ4*01	513	1118	gnl|Fabrus|A20_IGKJ1*01	809	1414
211	gnl|Fabrus|VH4-34_IGHD1-7*01_IGHJ4*01	749	1354	gnl|Fabrus|A20_IGKJ1*01	809	1414
212	gnl|Fabrus|VH4-34_IGHD2-2*01_IGHJ4*01	750	1355	gnl|Fabrus|A20_IGKJ1*01	809	1414
213	gnl|Fabrus|VH4-34_IGHD3-16*01_IGHJ4*01	751	1356	gnl|Fabrus|A20_IGKJ1*01	809	1414
214	gnl|Fabrus|VH4-34_IGHD4-17*01_IGHJ4*01	753	1358	gnl|Fabrus|A20_IGKJ1*01	809	1414
215	gnl|Fabrus|VH4-34_IGHD5-12*01_IGHJ4*01	754	1359	gnl|Fabrus|A20_IGKJ1*01	809	1414
216	gnl|Fabrus|VH4-34_IGHD6-13*01_IGHJ4*01	755	1360	gnl|Fabrus|A20_IGKJ1*01	809	1414
217	gnl|Fabrus|VH4-34_IGHD6-25*01_IGHJ6*01	756	1361	gnl|Fabrus|A20_IGKJ1*01	809	1414
218	gnl|Fabrus|VH4-34_IGHD7-27*01_IGHJ4*01	758	1363	gnl|Fabrus|A20_IGKJ1*01	809	1414
219	gnl|Fabrus|VH2-26_IGHD1-20*01_IGHJ4*01	521	1126	gnl|Fabrus|A20_IGKJ1*01	809	1414
220	gnl|Fabrus|VH2-26_IGHD2-2*01_IGHJ4*01	523	1128	gnl|Fabrus|A20_IGKJ1*01	809	1414
221	gnl|Fabrus|VH2-26_IGHD3-10*01_IGHJ4*01	524	1129	gnl|Fabrus|A20_IGKJ1*01	809	1414

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
222	gnl|Fabrus|VH2-26_IGHD4-11*01_IGHJ4*01	526	1131	gnl|Fabrus|A20_IGKJ1*01	809	1414
223	gnl|Fabrus|VH2-26_IGHD5-18*01_IGHJ4*01	528	1133	gnl|Fabrus|A20_IGKJ1*01	809	1414
224	gnl|Fabrus|VH2-26_IGHD6-13*01_IGHJ4*01	529	1134	gnl|Fabrus|A20_IGKJ1*01	809	1414
225	gnl|Fabrus|VH2-26_IGHD7-27*01_IGHJ4*01	530	1135	gnl|Fabrus|A20_IGKJ1*01	809	1414
226	gnl|Fabrus|VH5-51_IGHD1-14*01_IGHJ4*01	776	1381	gnl|Fabrus|A20_IGKJ1*01	809	1414
227	gnl|Fabrus|VH5-51_IGHD2-8*01_IGHJ4*01	778	1383	gnl|Fabrus|A20_IGKJ1*01	809	1414
228	gnl|Fabrus|VH5-51_IGHD3-3*01_IGHJ4*01	780	1385	gnl|Fabrus|A20_IGKJ1*01	809	1414
229	gnl|Fabrus|VH5-51_IGHD4-17*01_IGHJ4*01	781	1386	gnl|Fabrus|A20_IGKJ1*01	809	1414
230	gnl|Fabrus|VH5-51_IGHD5-18*01>3_IGHJ4*01	782	1387	gnl|Fabrus|A20_IGKJ1*01	809	1414
231	gnl|Fabrus|VH5-51_IGHD5-18*01>1_IGHJ4*01	783	1388	gnl|Fabrus|A20_IGKJ1*01	809	1414
232	gnl|Fabrus|VH5-51_IGHD6-25*01_IGHJ4*01	784	1389	gnl|Fabrus|A20_IGKJ1*01	809	1414
233	gnl|Fabrus|VH5-51_IGHD7-27*01_IGHJ4*01	785	1390	gnl|Fabrus|A20_IGKJ1*01	809	1414
234	gnl|Fabrus|VH6-1_IGHD1-1*01_IGHJ4*01	786	1391	gnl|Fabrus|A20_IGKJ1*01	809	1414
235	gnl|Fabrus|VH6-1_IGHD2-15*01_IGHJ4*01	788	1393	gnl|Fabrus|A20_IGKJ1*01	809	1414
236	gnl|Fabrus|VH6-1_IGHD3-3*01_IGHJ4*01	791	1396	gnl|Fabrus|A20_IGKJ1*01	809	1414
237	gnl|Fabrus|VH6-1_IGHD4-23*01_IGHJ4*01	793	1398	gnl|Fabrus|A20_IGKJ1*01	809	1414
238	gnl|Fabrus|VH6-1_IGHD4-11*01_IGHJ6*01	792	1397	gnl|Fabrus|A20_IGKJ1*01	809	1414
239	gnl|Fabrus|VH6-1_IGHD5-5*01_IGHJ4*01	794	1399	gnl|Fabrus|A20_IGKJ1*01	809	1414
240	gnl|Fabrus|VH6-1_IGHD6-13*01_IGHJ4*01	795	1400	gnl|Fabrus|A20_IGKJ1*01	809	1414
241	gnl|Fabrus|VH6-1_IGHD6-25*01_IGHJ6*01	796	1401	gnl|Fabrus|A20_IGKJ1*01	809	1414
242	gnl|Fabrus|VH6-1_IGHD7-27*01_IGHJ4*01	797	1402	gnl|Fabrus|A20_IGKJ1*01	809	1414
243	gnl|Fabrus|VH4-59_IGHD6-25*01_IGHJ3*01	775	1380	gnl|Fabrus|A20_IGKJ1*01	809	1414
244	gnl|Fabrus|VH3-48_IGHD6-6*01_IGHJ1*01	655	1260	gnl|Fabrus|A20_IGKJ1*01	809	1414

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
245	gnl|Fabrus|VH3-30_IGHD6-6*01_IGHJ1*01	625	1230	gnl|Fabrus|A20_IGKJ1*01	809	1414
246	gnl|Fabrus|VH3-66_IGHD6-6*01_IGHJ1*01	681	1286	gnl|Fabrus|A20_IGKJ1*01	809	1414
247	gnl|Fabrus|VH3-53_IGHD5-5*01_IGHJ4*01	670	1275	gnl|Fabrus|A20_IGKJ1*01	809	1414
248	gnl|Fabrus|VH2-5_IGHD5-12*01_IGHJ4*01	536	1141	gnl|Fabrus|A20_IGKJ1*01	809	1414
249	gnl|Fabrus|VH2-70_IGHD5-12*01_IGHJ4*01	543	1148	gnl|Fabrus|A20_IGKJ1*01	809	1414
250	gnl|Fabrus|VH3-15_IGHD5-12*01_IGHJ4*01	567	1172	gnl|Fabrus|A20_IGKJ1*01	809	1414
251	gnl|Fabrus|VH3-15_IGHD3-10*01_IGHJ4*01	565	1170	gnl|Fabrus|A20_IGKJ1*01	809	1414
252	gnl|Fabrus|VH3-49_IGHD5-18*01_IGHJ4*01	662	1267	gnl|Fabrus|A20_IGKJ1*01	809	1414
253	gnl|Fabrus|VH3-49_IGHD6-13*01_IGHJ4*01	663	1268	gnl|Fabrus|A20_IGKJ1*01	809	1414
254	gnl|Fabrus|VH3-72_IGHD5-18*01_IGHJ4*01	699	1304	gnl|Fabrus|A20_IGKJ1*01	809	1414
255	gnl|Fabrus|VH3-72_IGHD6-6*01_IGHJ1*01	701	1306	gnl|Fabrus|A20_IGKJ1*01	809	1414
256	gnl|Fabrus|VH3-73_IGHD5-12*01_IGHJ4*01	709	1314	gnl|Fabrus|A20_IGKJ1*01	809	1414
257	gnl|Fabrus|VH3-73_IGHD4-23*01_IGHJ5*01	708	1313	gnl|Fabrus|A20_IGKJ1*01	809	1414
258	gnl|Fabrus|VH3-43_IGHD3-22*01_IGHJ4*01	650	1255	gnl|Fabrus|A20_IGKJ1*01	809	1414
259	gnl|Fabrus|VH3-43_IGHD6-13*01_IGHJ4*01	653	1258	gnl|Fabrus|A20_IGKJ1*01	809	1414
260	gnl|Fabrus|VH3-9_IGHD3-22*01_IGHJ4*01	724	1329	gnl|Fabrus|A20_IGKJ1*01	809	1414
261	gnl|Fabrus|VH3-9_IGHD1-7*01_IGHJ5*01	721	1326	gnl|Fabrus|A20_IGKJ1*01	809	1414
262	gnl|Fabrus|VH3-9_IGHD6-13*01_IGHJ4*01	727	1332	gnl|Fabrus|A20_IGKJ1*01	809	1414
263	gnl|Fabrus|VH4-39_IGHD3-10*01_IGHJ4*01	762	1367	gnl|Fabrus|A20_IGKJ1*01	809	1414
264	gnl|Fabrus|VH4-39_IGHD5-12*01_IGHJ4*01	766	1371	gnl|Fabrus|A20_IGKJ1*01	809	1414
265	gnl|Fabrus|VH1-18_IGHD6-6*01_IGHJ1*01	460	1065	gnl|Fabrus|A20_IGKJ1*01	809	1414
266	gnl|Fabrus|VH1-24_IGHD5-12*01_IGHJ4*01	467	1072	gnl|Fabrus|A20_IGKJ1*01	809	1414
267	gnl|Fabrus|VH1-2_IGHD1-1*01_IGHJ3*01	461	1066	gnl|Fabrus|A20_IGKJ1*01	809	1414

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
268	gnl|Fabrus|VH1-3_IGHD6-6*01_IGHJ1*01	475	1080	gnl|Fabrus|A20_IGKJ1*01	809	1414
269	gnl|Fabrus|VH1-45_IGHD3-10*01_IGHJ4*01	480	1085	gnl|Fabrus|A20_IGKJ1*01	809	1414
270	gnl|Fabrus|VH1-46_IGHD1-26*01_IGHJ4*01	486	1091	gnl|Fabrus|A20_IGKJ1*01	809	1414
271	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ6*01	800	1405	gnl|Fabrus|A20_IGKJ1*01	809	1414
272	gnl|Fabrus|VH2-70_IGHD3-9*01_IGHJ6*01	542	1147	gnl|Fabrus|A20_IGKJ1*01	809	1414
273	gnl|Fabrus|VH1-58_IGHD3-10*01_IGHJ6*01	496	1101	gnl|Fabrus|A20_IGKJ1*01	809	1414
274	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ2*01	799	1404	gnl|Fabrus|A20_IGKJ1*01	809	1414
275	gnl|Fabrus|VH4-28_IGHD3-9*01_IGHJ6*01	734	1339	gnl|Fabrus|A20_IGKJ1*01	809	1414
276	gnl|Fabrus|VH4-31_IGHD2-15*01_IGHJ2*01	740	1345	gnl|Fabrus|A20_IGKJ1*01	809	1414
277	gnl|Fabrus|VH2-5_IGHD3-9*01_IGHJ6*01	535	1140	gnl|Fabrus|A20_IGKJ1*01	809	1414
278	gnl|Fabrus|VH1-8_IGHD2-15*01_IGHJ6*01	515	1120	gnl|Fabrus|A20_IGKJ1*01	809	1414
279	gnl|Fabrus|VH2-70_IGHD2-15*01_IGHJ2*01	540	1145	gnl|Fabrus|A20_IGKJ1*01	809	1414
280	gnl|Fabrus|VH3-38_IGHD3-10*01_IGHJ4*01	639	1244	gnl|Fabrus|A20_IGKJ1*01	809	1414
281	gnl|Fabrus|VH3-16_IGHD1-7*01_IGHJ6*01	570	1175	gnl|Fabrus|A20_IGKJ1*01	809	1414
282	gnl|Fabrus|VH3-73_IGHD3-9*01_IGHJ6*01	706	1311	gnl|Fabrus|A20_IGKJ1*01	809	1414
283	gnl|Fabrus|VH3-11_IGHD3-9*01_IGHJ6*01	548	1153	gnl|Fabrus|A20_IGKJ1*01	809	1414
284	gnl|Fabrus|VH3-11_IGHD6-6*01_IGHJ1*01	552	1157	gnl|Fabrus|A20_IGKJ1*01	809	1414
285	gnl|Fabrus|VH3-20_IGHD5-12*01_IGHJ4*01	584	1189	gnl|Fabrus|A20_IGKJ1*01	809	1414
286	gnl|Fabrus|VH3-16_IGHD2-15*01_IGHJ2*01	571	1176	gnl|Fabrus|A20_IGKJ1*01	809	1414
287	gnl|Fabrus|VH3-7_IGHD6-6*01_IGHJ1*01	692	1297	gnl|Fabrus|A20_IGKJ1*01	809	1414
288	gnl|Fabrus|VH3-16_IGHD6-13*01_IGHJ4*01	576	1181	gnl|Fabrus|A20_IGKJ1*01	809	1414
289	gnl|Fabrus|VH3-23_IGHD1-1*01_IGHJ4*01	595	1200	gnl|Fabrus|A30_IGKJ1*01	814	1419
290	gnl|Fabrus|VH3-23_IGHD2-15*01_IGHJ4*01	598	1203	gnl|Fabrus|A30_IGKJ1*01	814	1419

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
291	gnl|Fabrus|VH3-23_IGHD3-22*01_IGHJ4*01	602	1207	gnl|Fabrus|A30_IGKJ1*01	814	1419
292	gnl|Fabrus|VH3-23_IGHD4-11*01_IGHJ4*01	604	1209	gnl|Fabrus|A30_IGKJ1*01	814	1419
293	gnl|Fabrus|VH3-23_IGHD5-12*01_IGHJ4*01	606	1211	gnl|Fabrus|A30_IGKJ1*01	814	1419
294	gnl|Fabrus|VH3-23_IGHD5-5*01_IGHJ4*01	608	1213	gnl|Fabrus|A30_IGKJ1*01	814	1419
295	gnl|Fabrus|VH3-23_IGHD6-13*01_IGHJ4*01	609	1214	gnl|Fabrus|A30_IGKJ1*01	814	1419
296	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ4*01	612	1217	gnl|Fabrus|A30_IGKJ1*01	814	1419
297	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ6*01	613	1218	gnl|Fabrus|A30_IGKJ1*01	814	1419
298	gnl|Fabrus|VH1-69_IGHD1-14*01_IGHJ4*01	502	1107	gnl|Fabrus|A30_IGKJ1*01	814	1419
299	gnl|Fabrus|VH1-69_IGHD2-2*01_IGHJ4*01	503	1108	gnl|Fabrus|A30_IGKJ1*01	814	1419
300	gnl|Fabrus|VH1-69_IGHD2-8*01_IGHJ6*01	504	1109	gnl|Fabrus|A30_IGKJ1*01	814	1419
301	gnl|Fabrus|VH1-69_IGHD3-16*01_IGHJ4*01	505	1110	gnl|Fabrus|A30_IGKJ1*01	814	1419
302	gnl|Fabrus|VH1-69_IGHD3-3*01_IGHJ4*01	506	1111	gnl|Fabrus|A30_IGKJ1*01	814	1419
303	gnl|Fabrus|VH1-69_IGHD4-17*01_IGHJ4*01	508	1113	gnl|Fabrus|A30_IGKJ1*01	814	1419
304	gnl|Fabrus|VH1-69_IGHD5-12*01_IGHJ4*01	509	1114	gnl|Fabrus|A30_IGKJ1*01	814	1419
305	gnl|Fabrus|VH1-69_IGHD6-19*01_IGHJ4*01	511	1116	gnl|Fabrus|A30_IGKJ1*01	814	1419
306	gnl|Fabrus|VH1-69_IGHD7-27*01_IGHJ4*01	513	1118	gnl|Fabrus|A30_IGKJ1*01	814	1419
307	gnl|Fabrus|VH4-34_IGHD1-7*01_IGHJ4*01	749	1354	gnl|Fabrus|A30_IGKJ1*01	814	1419
308	gnl|Fabrus|VH4-34_IGHD2-2*01_IGHJ4*01	750	1355	gnl|Fabrus|A30_IGKJ1*01	814	1419
309	gnl|Fabrus|VH4-34_IGHD3-16*01_IGHJ4*01	751	1356	gnl|Fabrus|A30_IGKJ1*01	814	1419
310	gnl|Fabrus|VH4-34_IGHD4-17*01_IGHJ4*01	753	1358	gnl|Fabrus|A30_IGKJ1*01	814	1419
311	gnl|Fabrus|VH4-34_IGHD5-12*01_IGHJ4*01	754	1359	gnl|Fabrus|A30_IGKJ1*01	814	1419
312	gnl|Fabrus|VH4-34_IGHD6-13*01_IGHJ4*01	755	1360	gnl|Fabrus|A30_IGKJ1*01	814	1419
313	gnl|Fabrus|VH4-34_IGHD6-25*01_IGHJ6*01	756	1361	gnl|Fabrus|A30_IGKJ1*01	814	1419

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
314	gnl|Fabrus|VH4-34_IGHD7-27*01_IGHJ4*01	758	1363	gnl|Fabrus|A30_IGKJ1*01	814	1419
315	gnl|Fabrus|VH2-26_IGHD1-20*01_IGHJ4*01	521	1126	gnl|Fabrus|A30_IGKJ1*01	814	1419
316	gnl|Fabrus|VH2-26_IGHD2-2*01_IGHJ4*01	523	1128	gnl|Fabrus|A30_IGKJ1*01	814	1419
317	gnl|Fabrus|VH2-26_IGHD3-10*01_IGHJ4*01	524	1129	gnl|Fabrus|A30_IGKJ1*01	814	1419
318	gnl|Fabrus|VH2-26_IGHD4-11*01_IGHJ4*01	526	1131	gnl|Fabrus|A30_IGKJ1*01	814	1419
319	gnl|Fabrus|VH2-26_IGHD5-18*01_IGHJ4*01	528	1133	gnl|Fabrus|A30_IGKJ1*01	814	1419
320	gnl|Fabrus|VH2-26_IGHD6-13*01_IGHJ4*01	529	1134	gnl|Fabrus|A30_IGKJ1*01	814	1419
321	gnl|Fabrus|VH2-26_IGHD7-27*01_IGHJ4*01	530	1135	gnl|Fabrus|A30_IGKJ1*01	814	1419
322	gnl|Fabrus|VH5-51_IGHD1-14*01_IGHJ4*01	776	1381	gnl|Fabrus|A30_IGKJ1*01	814	1419
323	gnl|Fabrus|VH5-51_IGHD2-8*01_IGHJ4*01	778	1383	gnl|Fabrus|A30_IGKJ1*01	814	1419
324	gnl|Fabrus|VH5-51_IGHD3-3*01_IGHJ4*01	780	1385	gnl|Fabrus|A30_IGKJ1*01	814	1419
325	gnl|Fabrus|VH5-51_IGHD4-17*01_IGHJ4*01	781	1386	gnl|Fabrus|A30_IGKJ1*01	814	1419
326	gnl|Fabrus|VH5-51_IGHD5-18*01>3_IGHJ4*01	782	1387	gnl|Fabrus|A30_IGKJ1*01	814	1419
327	gnl|Fabrus|VH5-51_IGHD5-18*01>1_IGHJ4*01	783	1388	gnl|Fabrus|A30_IGKJ1*01	814	1419
328	gnl|Fabrus|VH5-51_IGHD6-25*01_IGHJ4*01	784	1389	gnl|Fabrus|A30_IGKJ1*01	814	1419
329	gnl|Fabrus|VH5-51_IGHD7-27*01_IGHJ4*01	785	1390	gnl|Fabrus|A30_IGKJ1*01	814	1419
330	gnl|Fabrus|VH6-1_IGHD1-1*01_IGHJ4*01	786	1391	gnl|Fabrus|A30_IGKJ1*01	814	1419
331	gnl|Fabrus|VH6-1_IGHD2-15*01_IGHJ4*01	788	1393	gnl|Fabrus|A30_IGKJ1*01	814	1419
332	gnl|Fabrus|VH6-1_IGHD3-3*01_IGHJ4*01	791	1396	gnl|Fabrus|A30_IGKJ1*01	814	1419
333	gnl|Fabrus|VH6-1_IGHD4-23*01_IGHJ4*01	793	1398	gnl|Fabrus|A30_IGKJ1*01	814	1419
334	gnl|Fabrus|VH6-1_IGHD4-11*01_IGHJ6*01	792	1397	gnl|Fabrus|A30_IGKJ1*01	814	1419
335	gnl|Fabrus|VH6-1_IGHD5-5*01_IGHJ4*01	794	1399	gnl|Fabrus|A30_IGKJ1*01	814	1419
336	gnl|Fabrus|VH6-1_IGHD6-13*01_IGHJ4*01	795	1400	gnl|Fabrus|A30_IGKJ1*01	814	1419

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
337	gnl|Fabrus|VH6-1_IGHD6-25*01_IGHJ6*01	796	1401	gnl|Fabrus|A30_IGKJ1*01	814	1419
338	gnl|Fabrus|VH6-1_IGHD7-27*01_IGHJ4*01	797	1402	gnl|Fabrus|A30_IGKJ1*01	814	1419
339	gnl|Fabrus|VH4-59_IGHD6-25*01_IGHJ3*01	775	1380	gnl|Fabrus|A30_IGKJ1*01	814	1419
340	gnl|Fabrus|VH3-48_IGHD6-6*01_IGHJ1*01	655	1260	gnl|Fabrus|A30_IGKJ1*01	814	1419
341	gnl|Fabrus|VH3-30_IGHD6-6*01_IGHJ1*01	625	1230	gnl|Fabrus|A30_IGKJ1*01	814	1419
342	gnl|Fabrus|VH3-66_IGHD6-6*01_IGHJ1*01	681	1286	gnl|Fabrus|A30_IGKJ1*01	814	1419
343	gnl|Fabrus|VH3-53_IGHD5-5*01_IGHJ4*01	670	1275	gnl|Fabrus|A30_IGKJ1*01	814	1419
344	gnl|Fabrus|VH2-5_IGHD5-12*01_IGHJ4*01	536	1141	gnl|Fabrus|A30_IGKJ1*01	814	1419
345	gnl|Fabrus|VH2-70_IGHD5-12*01_IGHJ4*01	543	1148	gnl|Fabrus|A30_IGKJ1*01	814	1419
346	gnl|Fabrus|VH3-15_IGHD5-12*01_IGHJ4*01	567	1172	gnl|Fabrus|A30_IGKJ1*01	814	1419
347	gnl|Fabrus|VH3-15_IGHD3-10*01_IGHJ4*01	565	1170	gnl|Fabrus|A30_IGKJ1*01	814	1419
348	gnl|Fabrus|VH3-49_IGHD5-18*01_IGHJ4*01	662	1267	gnl|Fabrus|A30_IGKJ1*01	814	1419
349	gnl|Fabrus|VH3-49_IGHD6-13*01_IGHJ4*01	663	1268	gnl|Fabrus|A30_IGKJ1*01	814	1419
350	gnl|Fabrus|VH3-72_IGHD5-18*01_IGHJ4*01	699	1304	gnl|Fabrus|A30_IGKJ1*01	814	1419
351	gnl|Fabrus|VH3-72_IGHD6-6*01_IGHJ1*01	701	1306	gnl|Fabrus|A30_IGKJ1*01	814	1419
352	gnl|Fabrus|VH3-73_IGHD5-12*01_IGHJ4*01	709	1314	gnl|Fabrus|A30_IGKJ1*01	814	1419
353	gnl|Fabrus|VH3-73_IGHD4-23*01_IGHJ5*01	708	1313	gnl|Fabrus|A30_IGKJ1*01	814	1419
354	gnl|Fabrus|VH3-43_IGHD3-22*01_IGHJ4*01	650	1255	gnl|Fabrus|A30_IGKJ1*01	814	1419
355	gnl|Fabrus|VH3-43_IGHD6-13*01_IGHJ4*01	653	1258	gnl|Fabrus|A30_IGKJ1*01	814	1419
356	gnl|Fabrus|VH3-9_IGHD3-22*01_IGHJ4*01	724	1329	gnl|Fabrus|A30_IGKJ1*01	814	1419
357	gnl|Fabrus|VH3-9_IGHD1-7*01_IGHJ5*01	721	1326	gnl|Fabrus|A30_IGKJ1*01	814	1419
358	gnl|Fabrus|VH3-9_IGHD6-13*01_IGHJ4*01	727	1332	gnl|Fabrus|A30_IGKJ1*01	814	1419
359	gnl|Fabrus|VH4-39_IGHD3-10*01_IGHJ4*01	762	1367	gnl|Fabrus|A30_IGKJ1*01	814	1419

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
360	gnl|Fabrus|VH4-39_IGHD5-12*01_IGHJ4*01	766	1371	gnl|Fabrus|A30_IGKJ1*01	814	1419
361	gnl|Fabrus|VH1-18_IGHD6-6*01_IGHJ1*01	460	1065	gnl|Fabrus|A30_IGKJ1*01	814	1419
362	gnl|Fabrus|VH1-24_IGHD5-12*01_IGHJ4*01	467	1072	gnl|Fabrus|A30_IGKJ1*01	814	1419
363	gnl|Fabrus|VH1-2_IGHD1-1*01_IGHJ3*01	461	1066	gnl|Fabrus|A30_IGKJ1*01	814	1419
364	gnl|Fabrus|VH1-3_IGHD6-6*01_IGHJ1*01	475	1080	gnl|Fabrus|A30_IGKJ1*01	814	1419
365	gnl|Fabrus|VH1-45_IGHD3-10*01_IGHJ4*01	480	1085	gnl|Fabrus|A30_IGKJ1*01	814	1419
366	gnl|Fabrus|VH1-46_IGHD1-26*01_IGHJ4*01	486	1091	gnl|Fabrus|A30_IGKJ1*01	814	1419
367	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ6*01	800	1405	gnl|Fabrus|A30_IGKJ1*01	814	1419
368	gnl|Fabrus|VH2-70_IGHD3-9*01_IGHJ6*01	542	1147	gnl|Fabrus|A30_IGKJ1*01	814	1419
369	gnl|Fabrus|VH1-58_IGHD3-10*01_IGHJ6*01	496	1101	gnl|Fabrus|A30_IGKJ1*01	814	1419
370	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ2*01	799	1404	gnl|Fabrus|A30_IGKJ1*01	814	1419
371	gnl|Fabrus|VH4-28_IGHD3-9*01_IGHJ6*01	734	1339	gnl|Fabrus|A30_IGKJ1*01	814	1419
372	gnl|Fabrus|VH4-31_IGHD2-15*01_IGHJ2*01	740	1345	gnl|Fabrus|A30_IGKJ1*01	814	1419
373	gnl|Fabrus|VH2-5_IGHD3-9*01_IGHJ6*01	535	1140	gnl|Fabrus|A30_IGKJ1*01	814	1419
374	gnl|Fabrus|VH1-8_IGHD2-15*01_IGHJ6*01	515	1120	gnl|Fabrus|A30_IGKJ1*01	814	1419
375	gnl|Fabrus|VH2-70_IGHD2-15*01_IGHJ2*01	540	1145	gnl|Fabrus|A30_IGKJ1*01	814	1419
376	gnl|Fabrus|VH3-38_IGHD3-10*01_IGHJ4*01	639	1244	gnl|Fabrus|A30_IGKJ1*01	814	1419
377	gnl|Fabrus|VH3-16_IGHD1-7*01_IGHJ6*01	570	1175	gnl|Fabrus|A30_IGKJ1*01	814	1419
378	gnl|Fabrus|VH3-73_IGHD3-9*01_IGHJ6*01	706	1311	gnl|Fabrus|A30_IGKJ1*01	814	1419
379	gnl|Fabrus|VH3-11_IGHD3-9*01_IGHJ6*01	548	1153	gnl|Fabrus|A30_IGKJ1*01	814	1419
380	gnl|Fabrus|VH3-11_IGHD6-6*01_IGHJ1*01	552	1157	gnl|Fabrus|A30_IGKJ1*01	814	1419
381	gnl|Fabrus|VH3-20_IGHD5-12*01_IGHJ4*01	584	1189	gnl|Fabrus|A30_IGKJ1*01	814	1419
382	gnl|Fabrus|VH3-16_IGHD2-15*01_IGHJ2*01	571	1176	gnl|Fabrus|A30_IGKJ1*01	814	1419

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
383	gnl|Fabrus|VH3-7_IGHD6-6*01_IGHJ1*01	692	1297	gnl|Fabrus|A30_IGKJ1*01	814	1419
384	gnl|Fabrus|VH3-16_IGHD6-13*01_IGHJ4*01	576	1181	gnl|Fabrus|A30_IGKJ1*01	814	1419
385	gnl|Fabrus|VH3-23_IGHD1-1*01_IGHJ4*01	595	1200	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
386	gnl|Fabrus|VH3-23_IGHD2-15*01_IGHJ4*01	598	1203	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
387	gnl|Fabrus|VH3-23_IGHD3-22*01_IGHJ4*01	602	1207	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
388	gnl|Fabrus|VH3-23_IGHD4-11*01_IGHJ4*01	604	1209	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
389	gnl|Fabrus|VH3-23_IGHD5-12*01_IGHJ4*01	606	1211	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
390	gnl|Fabrus|VH3-23_IGHD5-5*01_IGHJ4*01	608	1213	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
391	gnl|Fabrus|VH3-23_IGHD6-13*01_IGHJ4*01	609	1214	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
392	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ4*01	612	1217	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
393	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ6*01	613	1218	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
394	gnl|Fabrus|VH1-69_IGHD1-14*01_IGHJ4*01	502	1107	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
395	gnl|Fabrus|VH1-69_IGHD2-2*01_IGHJ4*01	503	1108	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
396	gnl|Fabrus|VH1-69_IGHD2-8*01_IGHJ6*01	504	1109	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
397	gnl|Fabrus|VH1-69_IGHD3-16*01_IGHJ4*01	505	1110	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
398	gnl|Fabrus|VH1-69_IGHD3-3*01_IGHJ4*01	506	1111	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
399	gnl|Fabrus|VH1-69_IGHD4-17*01_IGHJ4*01	508	1113	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
400	gnl|Fabrus|VH1-69_IGHD5-12*01_IGHJ4*01	509	1114	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
401	gnl|Fabrus|VH1-69_IGHD6-19*01_IGHJ4*01	511	1116	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
402	gnl|Fabrus|VH1-69_IGHD7-27*01_IGHJ4*01	513	1118	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
403	gnl|Fabrus|VH4-34_IGHD1-7*01_IGHJ4*01	749	1354	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
404	gnl|Fabrus|VH4-34_IGHD2-2*01_IGHJ4*01	750	1355	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
405	gnl|Fabrus|VH4-34_IGHD3-16*01_IGHJ4*01	751	1356	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
406	gnl|Fabrus|VH4-34_IGHD4-17*01_IGHJ4*01	753	1358	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
407	gnl|Fabrus|VH4-34_IGHD5-12*01_IGHJ4*01	754	1359	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
408	gnl|Fabrus|VH4-34_IGHD6-13*01_IGHJ4*01	755	1360	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
409	gnl|Fabrus|VH4-34_IGHD6-25*01_IGHJ6*01	756	1361	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
410	gnl|Fabrus|VH4-34_IGHD7-27*01_IGHJ4*01	758	1363	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
411	gnl|Fabrus|VH2-26_IGHD1-20*01_IGHJ4*01	521	1126	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
412	gnl|Fabrus|VH2-26_IGHD2-2*01_IGHJ4*01	523	1128	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
413	gnl|Fabrus|VH2-26_IGHD3-10*01_IGHJ4*01	524	1129	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
414	gnl|Fabrus|VH2-26_IGHD4-11*01_IGHJ4*01	526	1131	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
415	gnl|Fabrus|VH2-26_IGHD5-18*01_IGHJ4*01	528	1133	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
416	gnl|Fabrus|VH2-26_IGHD6-13*01_IGHJ4*01	529	1134	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
417	gnl|Fabrus|VH2-26_IGHD7-27*01_IGHJ4*01	530	1135	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
418	gnl|Fabrus|VH5-51_IGHD1-14*01_IGHJ4*01	776	1381	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
419	gnl|Fabrus|VH5-51_IGHD2-8*01_IGHJ4*01	778	1383	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
420	gnl|Fabrus|VH5-51_IGHD3-3*01_IGHJ4*01	780	1385	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
421	gnl|Fabrus|VH5-51_IGHD4-17*01_IGHJ4*01	781	1386	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
422	gnl|Fabrus|VH5-51_IGHD5-18*01>3_IGHJ4*01	782	1387	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
423	gnl|Fabrus|VH5-51_IGHD5-18*01>1_IGHJ4*01	783	1388	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
424	gnl|Fabrus|VH5-51_IGHD6-25*01_IGHJ4*01	784	1389	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
425	gnl|Fabrus|VH5-51_IGHD7-27*01_IGHJ4*01	785	1390	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
426	gnl|Fabrus|VH6-1_IGHD1-1*01_IGHJ4*01	786	1391	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
427	gnl|Fabrus|VH6-1_IGHD2-15*01_IGHJ4*01	788	1393	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
428	gnl|Fabrus|VH6-1_IGHD3-3*01_IGHJ4*01	791	1396	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
429	gnl|Fabrus|VH6-1_IGHD4-23*01_IGHJ4*01	793	1398	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
430	gnl|Fabrus|VH6-1_IGHD4-11*01_IGHJ6*01	792	1397	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
431	gnl|Fabrus|VH6-1_IGHD5-5*01_IGHJ4*01	794	1399	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
432	gnl|Fabrus|VH6-1_IGHD6-13*01_IGHJ4*01	795	1400	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
433	gnl|Fabrus|VH6-1_IGHD6-25*01_IGHJ6*01	796	1401	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
434	gnl|Fabrus|VH6-1_IGHD7-27*01_IGHJ4*01	797	1402	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
435	gnl|Fabrus|VH4-59_IGHD6-25*01_IGHJ3*01	775	1380	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
436	gnl|Fabrus|VH3-48_IGHD6-6*01_IGHJ1*01	655	1260	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
437	gnl|Fabrus|VH3-30_IGHD6-6*01_IGHJ1*01	625	1230	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
438	gnl|Fabrus|VH3-66_IGHD6-6*01_IGHJ1*01	681	1286	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
439	gnl|Fabrus|VH3-53_IGHD5-5*01_IGHJ4*01	670	1275	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
440	gnl|Fabrus|VH2-5_IGHD5-12*01_IGHJ4*01	536	1141	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
441	gnl|Fabrus|VH2-70_IGHD5-12*01_IGHJ4*01	543	1148	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
442	gnl|Fabrus|VH3-15_IGHD5-12*01_IGHJ4*01	567	1172	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
443	gnl|Fabrus|VH3-15_IGHD3-10*01_IGHJ4*01	565	1170	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
444	gnl|Fabrus|VH3-49_IGHD5-18*01_IGHJ4*01	662	1267	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
445	gnl|Fabrus|VH3-49_IGHD6-13*01_IGHJ4*01	663	1268	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
446	gnl|Fabrus|VH3-72_IGHD5-18*01_IGHJ4*01	699	1304	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
447	gnl|Fabrus|VH3-72_IGHD6-6*01_IGHJ1*01	701	1306	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
448	gnl|Fabrus|VH3-73_IGHD5-12*01_IGHJ4*01	709	1314	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
449	gnl|Fabrus|VH3-73_IGHD4-23*01_IGHJ5*01	708	1313	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
450	gnl|Fabrus|VH3-43_IGHD3-22*01_IGHJ4*01	650	1255	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
451	gnl|Fabrus|VH3-43_IGHD6-13*01_IGHJ4*01	653	1258	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
452	gnl|Fabrus|VH3-9_IGHD3-22*01_IGHJ4*01	724	1329	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
453	gnl|Fabrus|VH3-9_IGHD1-7*01_IGHJ5*01	721	1326	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
454	gnl|Fabrus|VH3-9_IGHD6-13*01_IGHJ4*01	727	1332	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
455	gnl|Fabrus|VH4-39_IGHD3-10*01_IGHJ4*01	762	1367	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
456	gnl|Fabrus|VH4-39_IGHD5-12*01_IGHJ4*01	766	1371	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
457	gnl|Fabrus|VH1-18_IGHD6-6*01_IGHJ1*01	460	1065	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
458	gnl|Fabrus|VH1-24_IGHD5-12*01_IGHJ4*01	467	1072	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
459	gnl|Fabrus|VH1-2_IGHD1-1*01_IGHJ3*01	461	1066	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
460	gnl|Fabrus|VH1-3_IGHD6-6*01_IGHJ1*01	475	1080	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
461	gnl|Fabrus|VH1-45_IGHD3-10*01_IGHJ4*01	480	1085	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
462	gnl|Fabrus|VH1-46_IGHD1-26*01_IGHJ4*01	486	1091	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
463	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ6*01	800	1405	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
464	gnl|Fabrus|VH2-70_IGHD3-9*01_IGHJ6*01	542	1147	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
465	gnl|Fabrus|VH1-58_IGHD3-10*01_IGHJ6*01	496	1101	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
466	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ2*01	799	1404	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
467	gnl|Fabrus|VH4-28_IGHD3-9*01_IGHJ6*01	734	1339	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
468	gnl|Fabrus|VH4-31_IGHD2-15*01_IGHJ2*01	740	1345	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
469	gnl|Fabrus|VH2-5_IGHD3-9*01_IGHJ6*01	535	1140	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
470	gnl|Fabrus|VH1-8_IGHD2-15*01_IGHJ6*01	515	1120	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
471	gnl|Fabrus|VH2-70_IGHD2-15*01_IGHJ2*01	540	1145	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
472	gnl|Fabrus|VH3-38_IGHD3-10*01_IGHJ4*01	639	1244	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
473	gnl|Fabrus|VH3-16_IGHD1-7*01_IGHJ6*01	570	1175	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
474	gnl|Fabrus|VH3-73_IGHD3-9*01_IGHJ6*01	706	1311	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
475	gnl|Fabrus|VH3-11_IGHD3-9*01_IGHJ6*01	548	1153	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
476	gnl|Fabrus|VH3-11_IGHD6-6*01_IGHJ1*01	552	1157	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
477	gnl|Fabrus|VH3-20_IGHD5-12*01_IGHJ4*01	584	1189	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
478	gnl|Fabrus|VH3-16_IGHD2-15*01_IGHJ2*01	571	1176	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
479	gnl|Fabrus|VH3-7_IGHD6-6*01_IGHJ1*01	692	1297	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
480	gnl|Fabrus|VH3-16_IGHD6-13*01_IGHJ4*01	576	1181	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
481	gnl|Fabrus|VH3-23_IGHD1-1*01_IGHJ4*01	595	1200	gnl|Fabrus|L5_IGKJ1*01	828	1433
482	gnl|Fabrus|VH3-23_IGHD2-15*01_IGHJ4*01	598	1203	gnl|Fabrus|L5_IGKJ1*01	828	1433
483	gnl|Fabrus|VH3-23_IGHD3-22*01_IGHJ4*01	602	1207	gnl|Fabrus|L5_IGKJ1*01	828	1433
484	gnl|Fabrus|VH3-23_IGHD4-11*01_IGHJ4*01	604	1209	gnl|Fabrus|L5_IGKJ1*01	828	1433
485	gnl|Fabrus|VH3-23_IGHD5-12*01_IGHJ4*01	606	1211	gnl|Fabrus|L5_IGKJ1*01	828	1433
486	gnl|Fabrus|VH3-23_IGHD5-5*01_IGHJ4*01	608	1213	gnl|Fabrus|L5_IGKJ1*01	828	1433
487	gnl|Fabrus|VH3-23_IGHD6-13*01_IGHJ4*01	609	1214	gnl|Fabrus|L5_IGKJ1*01	828	1433
488	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ4*01	612	1217	gnl|Fabrus|L5_IGKJ1*01	828	1433
489	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ6*01	613	1218	gnl|Fabrus|L5_IGKJ1*01	828	1433
490	gnl|Fabrus|VH1-69_IGHD1-14*01_IGHJ4*01	502	1107	gnl|Fabrus|L5_IGKJ1*01	828	1433
491	gnl|Fabrus|VH1-69_IGHD2-2*01_IGHJ4*01	503	1108	gnl|Fabrus|L5_IGKJ1*01	828	1433
492	gnl|Fabrus|VH1-69_IGHD2-8*01_IGHJ6*01	504	1109	gnl|Fabrus|L5_IGKJ1*01	828	1433
493	gnl|Fabrus|VH1-69_IGHD3-16*01_IGHJ4*01	505	1110	gnl|Fabrus|L5_IGKJ1*01	828	1433
494	gnl|Fabrus|VH1-69_IGHD3-3*01_IGHJ4*01	506	1111	gnl|Fabrus|L5_IGKJ1*01	828	1433
495	gnl|Fabrus|VH1-69_IGHD4-17*01_IGHJ4*01	508	1113	gnl|Fabrus|L5_IGKJ1*01	828	1433
496	gnl|Fabrus|VH1-69_IGHD5-12*01_IGHJ4*01	509	1114	gnl|Fabrus|L5_IGKJ1*01	828	1433
497	gnl|Fabrus|VH1-69_IGHD6-19*01_IGHJ4*01	511	1116	gnl|Fabrus|L5_IGKJ1*01	828	1433

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
498	gnl|Fabrus|VH1-69_IGHD7-27*01_IGHJ4*01	513	1118	gnl|Fabrus|L5_IGKJ1*01	828	1433
499	gnl|Fabrus|VH4-34_IGHD1-7*01_IGHJ4*01	749	1354	gnl|Fabrus|L5_IGKJ1*01	828	1433
500	gnl|Fabrus|VH4-34_IGHD2-2*01_IGHJ4*01	750	1355	gnl|Fabrus|L5_IGKJ1*01	828	1433
501	gnl|Fabrus|VH4-34_IGHD3-16*01_IGHJ4*01	751	1356	gnl|Fabrus|L5_IGKJ1*01	828	1433
502	gnl|Fabrus|VH4-34_IGHD4-17*01_IGHJ4*01	753	1358	gnl|Fabrus|L5_IGKJ1*01	828	1433
503	gnl|Fabrus|VH4-34_IGHD5-12*01_IGHJ4*01	754	1359	gnl|Fabrus|L5_IGKJ1*01	828	1433
504	gnl|Fabrus|VH4-34_IGHD6-13*01_IGHJ4*01	755	1360	gnl|Fabrus|L5_IGKJ1*01	828	1433
505	gnl|Fabrus|VH4-34_IGHD6-25*01_IGHJ6*01	756	1361	gnl|Fabrus|L5_IGKJ1*01	828	1433
506	gnl|Fabrus|VH4-34_IGHD7-27*01_IGHJ4*01	758	1363	gnl|Fabrus|L5_IGKJ1*01	828	1433
507	gnl|Fabrus|VH2-26_IGHD1-20*01_IGHJ4*01	521	1126	gnl|Fabrus|L5_IGKJ1*01	828	1433
508	gnl|Fabrus|VH2-26_IGHD2-2*01_IGHJ4*01	523	1128	gnl|Fabrus|L5_IGKJ1*01	828	1433
509	gnl|Fabrus|VH2-26_IGHD3-10*01_IGHJ4*01	524	1129	gnl|Fabrus|L5_IGKJ1*01	828	1433
510	gnl|Fabrus|VH2-26_IGHD4-11*01_IGHJ4*01	526	1131	gnl|Fabrus|L5_IGKJ1*01	828	1433
511	gnl|Fabrus|VH2-26_IGHD5-18*01_IGHJ4*01	528	1133	gnl|Fabrus|L5_IGKJ1*01	828	1433
512	gnl|Fabrus|VH2-26_IGHD6-13*01_IGHJ4*01	529	1134	gnl|Fabrus|L5_IGKJ1*01	828	1433
513	gnl|Fabrus|VH2-26_IGHD7-27*01_IGHJ4*01	530	1135	gnl|Fabrus|L5_IGKJ1*01	828	1433
514	gnl|Fabrus|VH5-51_IGHD1-14*01_IGHJ4*01	776	1381	gnl|Fabrus|L5_IGKJ1*01	828	1433
515	gnl|Fabrus|VH5-51_IGHD2-8*01_IGHJ4*01	778	1383	gnl|Fabrus|L5_IGKJ1*01	828	1433
516	gnl|Fabrus|VH5-51_IGHD3-3*01_IGHJ4*01	780	1385	gnl|Fabrus|L5_IGKJ1*01	828	1433
517	gnl|Fabrus|VH5-51_IGHD4-17*01_IGHJ4*01	781	1386	gnl|Fabrus|L5_IGKJ1*01	828	1433
518	gnl|Fabrus|VH5-51_IGHD5-18*01>3_IGHJ4*01	782	1387	gnl|Fabrus|L5_IGKJ1*01	828	1433
519	gnl|Fabrus|VH5-51_IGHD5-18*01>1_IGHJ4*01	783	1388	gnl|Fabrus|L5_IGKJ1*01	828	1433
520	gnl|Fabrus|VH5-51_IGHD6-25*01_IGHJ4*01	784	1389	gnl|Fabrus|L5_IGKJ1*01	828	1433

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
521	gnl|Fabrus|VH5-51_IGHD7-27*01_IGHJ4*01	785	1390	gnl|Fabrus|L5_IGKJ1*01	828	1433
522	gnl|Fabrus|VH6-1_IGHD1-1*01_IGHJ4*01	786	1391	gnl|Fabrus|L5_IGKJ1*01	828	1433
523	gnl|Fabrus|VH6-1_IGHD2-15*01_IGHJ4*01	788	1393	gnl|Fabrus|L5_IGKJ1*01	828	1433
524	gnl|Fabrus|VH6-1_IGHD3-3*01_IGHJ4*01	791	1396	gnl|Fabrus|L5_IGKJ1*01	828	1433
525	gnl|Fabrus|VH6-1_IGHD4-23*01_IGHJ4*01	793	1398	gnl|Fabrus|L5_IGKJ1*01	828	1433
526	gnl|Fabrus|VH6-1_IGHD4-11*01_IGHJ6*01	792	1397	gnl|Fabrus|L5_IGKJ1*01	828	1433
527	gnl|Fabrus|VH6-1_IGHD5-5*01_IGHJ4*01	794	1399	gnl|Fabrus|L5_IGKJ1*01	828	1433
528	gnl|Fabrus|VH6-1_IGHD6-13*01_IGHJ4*01	795	1400	gnl|Fabrus|L5_IGKJ1*01	828	1433
529	gnl|Fabrus|VH6-1_IGHD6-25*01_IGHJ6*01	796	1401	gnl|Fabrus|L5_IGKJ1*01	828	1433
530	gnl|Fabrus|VH6-1_IGHD7-27*01_IGHJ4*01	797	1402	gnl|Fabrus|L5_IGKJ1*01	828	1433
531	gnl|Fabrus|VH4-59_IGHD6-25*01_IGHJ3*01	775	1380	gnl|Fabrus|L5_IGKJ1*01	828	1433
532	gnl|Fabrus|VH3-48_IGHD6-6*01_IGHJ1*01	655	1260	gnl|Fabrus|L5_IGKJ1*01	828	1433
533	gnl|Fabrus|VH3-30_IGHD6-6*01_IGHJ1*01	625	1230	gnl|Fabrus|L5_IGKJ1*01	828	1433
534	gnl|Fabrus|VH3-66_IGHD6-6*01_IGHJ1*01	681	1286	gnl|Fabrus|L5_IGKJ1*01	828	1433
535	gnl|Fabrus|VH3-53_IGHD5-5*01_IGHJ4*01	670	1275	gnl|Fabrus|L5_IGKJ1*01	828	1433
536	gnl|Fabrus|VH2-5_IGHD5-12*01_IGHJ4*01	536	1141	gnl|Fabrus|L5_IGKJ1*01	828	1433
537	gnl|Fabrus|VH2-70_IGHD5-12*01_IGHJ4*01	543	1148	gnl|Fabrus|L5_IGKJ1*01	828	1433
538	gnl|Fabrus|VH3-15_IGHD5-12*01_IGHJ4*01	567	1172	gnl|Fabrus|L5_IGKJ1*01	828	1433
539	gnl|Fabrus|VH3-15_IGHD3-10*01_IGHJ4*01	565	1170	gnl|Fabrus|L5_IGKJ1*01	828	1433
540	gnl|Fabrus|VH3-49_IGHD5-18*01_IGHJ4*01	662	1267	gnl|Fabrus|L5_IGKJ1*01	828	1433
541	gnl|Fabrus|VH3-49_IGHD6-13*01_IGHJ4*01	663	1268	gnl|Fabrus|L5_IGKJ1*01	828	1433
542	gnl|Fabrus|VH3-72_IGHD5-18*01_IGHJ4*01	699	1304	gnl|Fabrus|L5_IGKJ1*01	828	1433
543	gnl|Fabrus|VH3-72_IGHD6-6*01_IGHJ1*01	701	1306	gnl|Fabrus|L5_IGKJ1*01	828	1433

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
544	gnl|Fabrus|VH3-73_IGHD5-12*01_IGHJ4*01	709	1314	gnl|Fabrus|L5_IGKJ1*01	828	1433
545	gnl|Fabrus|VH3-73_IGHD4-23*01_IGHJ5*01	708	1313	gnl|Fabrus|L5_IGKJ1*01	828	1433
546	gnl|Fabrus|VH3-43_IGHD3-22*01_IGHJ4*01	650	1255	gnl|Fabrus|L5_IGKJ1*01	828	1433
547	gnl|Fabrus|VH3-43_IGHD6-13*01_IGHJ4*01	653	1258	gnl|Fabrus|L5_IGKJ1*01	828	1433
548	gnl|Fabrus|VH3-9_IGHD3-22*01_IGHJ4*01	724	1329	gnl|Fabrus|L5_IGKJ1*01	828	1433
549	gnl|Fabrus|VH3-9_IGHD1-7*01_IGHJ5*01	721	1326	gnl|Fabrus|L5_IGKJ1*01	828	1433
550	gnl|Fabrus|VH3-9_IGHD6-13*01_IGHJ4*01	727	1332	gnl|Fabrus|L5_IGKJ1*01	828	1433
551	gnl|Fabrus|VH4-39_IGHD3-10*01_IGHJ4*01	762	1367	gnl|Fabrus|L5_IGKJ1*01	828	1433
552	gnl|Fabrus|VH4-39_IGHD5-12*01_IGHJ4*01	766	1371	gnl|Fabrus|L5_IGKJ1*01	828	1433
553	gnl|Fabrus|VH1-18_IGHD6-6*01_IGHJ1*01	460	1065	gnl|Fabrus|L5_IGKJ1*01	828	1433
554	gnl|Fabrus|VH1-24_IGHD5-12*01_IGHJ4*01	467	1072	gnl|Fabrus|L5_IGKJ1*01	828	1433
555	gnl|Fabrus|VH1-2_IGHD1-1*01_IGHJ3*01	461	1066	gnl|Fabrus|L5_IGKJ1*01	828	1433
556	gnl|Fabrus|VH1-3_IGHD6-6*01_IGHJ1*01	475	1080	gnl|Fabrus|L5_IGKJ1*01	828	1433
557	gnl|Fabrus|VH1-45_IGHD3-10*01_IGHJ4*01	480	1085	gnl|Fabrus|L5_IGKJ1*01	828	1433
558	gnl|Fabrus|VH1-46_IGHD1-26*01_IGHJ4*01	486	1091	gnl|Fabrus|L5_IGKJ1*01	828	1433
559	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ6*01	800	1405	gnl|Fabrus|L5_IGKJ1*01	828	1433
560	gnl|Fabrus|VH2-70_IGHD3-9*01_IGHJ6*01	542	1147	gnl|Fabrus|L5_IGKJ1*01	828	1433
561	gnl|Fabrus|VH1-58_IGHD3-10*01_IGHJ6*01	496	1101	gnl|Fabrus|L5_IGKJ1*01	828	1433
562	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ2*01	799	1404	gnl|Fabrus|L5_IGKJ1*01	828	1433
563	gnl|Fabrus|VH4-28_IGHD3-9*01_IGHJ6*01	734	1339	gnl|Fabrus|L5_IGKJ1*01	828	1433
564	gnl|Fabrus|VH4-31_IGHD2-15*01_IGHJ2*01	740	1345	gnl|Fabrus|L5_IGKJ1*01	828	1433
565	gnl|Fabrus|VH2-5_IGHD3-9*01_IGHJ6*01	535	1140	gnl|Fabrus|L5_IGKJ1*01	828	1433
566	gnl|Fabrus|VH1-8_IGHD2-15*01_IGHJ6*01	515	1120	gnl|Fabrus|L5_IGKJ1*01	828	1433

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
567	gnl|Fabrus|VH2-70_IGHD2-15*01_IGHJ2*01	540	1145	gnl|Fabrus|L5_IGKJ1*01	828	1433
568	gnl|Fabrus|VH3-38_IGHD3-10*01_IGHJ4*01	639	1244	gnl|Fabrus|L5_IGKJ1*01	828	1433
569	gnl|Fabrus|VH3-16_IGHD1-7*01_IGHJ6*01	570	1175	gnl|Fabrus|L5_IGKJ1*01	828	1433
570	gnl|Fabrus|VH3-73_IGHD3-9*01_IGHJ6*01	706	1311	gnl|Fabrus|L5_IGKJ1*01	828	1433
571	gnl|Fabrus|VH3-11_IGHD3-9*01_IGHJ6*01	548	1153	gnl|Fabrus|L5_IGKJ1*01	828	1433
572	gnl|Fabrus|VH3-11_IGHD6-6*01_IGHJ1*01	552	1157	gnl|Fabrus|L5_IGKJ1*01	828	1433
573	gnl|Fabrus|VH3-20_IGHD5-12*01_IGHJ4*01	584	1189	gnl|Fabrus|L5_IGKJ1*01	828	1433
574	gnl|Fabrus|VH3-16_IGHD2-15*01_IGHJ2*01	571	1176	gnl|Fabrus|L5_IGKJ1*01	828	1433
575	gnl|Fabrus|VH3-7_IGHD6-6*01_IGHJ1*01	692	1297	gnl|Fabrus|L5_IGKJ1*01	828	1433
576	gnl|Fabrus|VH3-16_IGHD6-13*01_IGHJ4*01	576	1181	gnl|Fabrus|L5_IGKJ1*01	828	1433
577	gnl|Fabrus|VH3-23_IGHD1-1*01_IGHJ4*01	595	1200	gnl|Fabrus|L8_IGKJ1*01	830	1435
578	gnl|Fabrus|VH3-23_IGHD2-15*01_IGHJ4*01	598	1203	gnl|Fabrus|L8_IGKJ1*01	830	1435
579	gnl|Fabrus|VH3-23_IGHD3-22*01_IGHJ4*01	602	1207	gnl|Fabrus|L8_IGKJ1*01	830	1435
580	gnl|Fabrus|VH3-23_IGHD4-11*01_IGHJ4*01	604	1209	gnl|Fabrus|L8_IGKJ1*01	830	1435
581	gnl|Fabrus|VH3-23_IGHD5-12*01_IGHJ4*01	606	1211	gnl|Fabrus|L8_IGKJ1*01	830	1435
582	gnl|Fabrus|VH3-23_IGHD5-5*01_IGHJ4*01	608	1213	gnl|Fabrus|L8_IGKJ1*01	830	1435
583	gnl|Fabrus|VH3-23_IGHD6-13*01_IGHJ4*01	609	1214	gnl|Fabrus|L8_IGKJ1*01	830	1435
584	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ4*01	612	1217	gnl|Fabrus|L8_IGKJ1*01	830	1435
585	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ6*01	613	1218	gnl|Fabrus|L8_IGKJ1*01	830	1435
586	gnl|Fabrus|VH1-69_IGHD1-14*01_IGHJ4*01	502	1107	gnl|Fabrus|L8_IGKJ1*01	830	1435
587	gnl|Fabrus|VH1-69_IGHD2-2*01_IGHJ4*01	503	1108	gnl|Fabrus|L8_IGKJ1*01	830	1435
588	gnl|Fabrus|VH1-69_IGHD2-8*01_IGHJ6*01	504	1109	gnl|Fabrus|L8_IGKJ1*01	830	1435
589	gnl|Fabrus|VH1-69_IGHD3-16*01_IGHJ4*01	505	1110	gnl|Fabrus|L8_IGKJ1*01	830	1435

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
590	gnl|Fabrus|VH1-69_IGHD3-3*01_IGHJ4*01	506	1111	gnl|Fabrus|L8_IGKJ1*01	830	1435
591	gnl|Fabrus|VH1-69_IGHD4-17*01_IGHJ4*01	508	1113	gnl|Fabrus|L8_IGKJ1*01	830	1435
592	gnl|Fabrus|VH1-69_IGHD5-12*01_IGHJ4*01	509	1114	gnl|Fabrus|L8_IGKJ1*01	830	1435
593	gnl|Fabrus|VH1-69_IGHD6-19*01_IGHJ4*01	511	1116	gnl|Fabrus|L8_IGKJ1*01	830	1435
594	gnl|Fabrus|VH1-69_IGHD7-27*01_IGHJ4*01	513	1118	gnl|Fabrus|L8_IGKJ1*01	830	1435
595	gnl|Fabrus|VH4-34_IGHD1-7*01_IGHJ4*01	749	1354	gnl|Fabrus|L8_IGKJ1*01	830	1435
596	gnl|Fabrus|VH4-34_IGHD2-2*01_IGHJ4*01	750	1355	gnl|Fabrus|L8_IGKJ1*01	830	1435
597	gnl|Fabrus|VH4-34_IGHD3-16*01_IGHJ4*01	751	1356	gnl|Fabrus|L8_IGKJ1*01	830	1435
598	gnl|Fabrus|VH4-34_IGHD4-17*01_IGHJ4*01	753	1358	gnl|Fabrus|L8_IGKJ1*01	830	1435
599	gnl|Fabrus|VH4-34_IGHD5-12*01_IGHJ4*01	754	1359	gnl|Fabrus|L8_IGKJ1*01	830	1435
600	gnl|Fabrus|VH4-34_IGHD6-13*01_IGHJ4*01	755	1360	gnl|Fabrus|L8_IGKJ1*01	830	1435
601	gnl|Fabrus|VH4-34_IGHD6-25*01_IGHJ6*01	756	1361	gnl|Fabrus|L8_IGKJ1*01	830	1435
602	gnl|Fabrus|VH4-34_IGHD7-27*01_IGHJ4*01	758	1363	gnl|Fabrus|L8_IGKJ1*01	830	1435
603	gnl|Fabrus|VH2-26_IGHD1-20*01_IGHJ4*01	521	1126	gnl|Fabrus|L8_IGKJ1*01	830	1435
604	gnl|Fabrus|VH2-26_IGHD2-2*01_IGHJ4*01	523	1128	gnl|Fabrus|L8_IGKJ1*01	830	1435
605	gnl|Fabrus|VH2-26_IGHD3-10*01_IGHJ4*01	524	1129	gnl|Fabrus|L8_IGKJ1*01	830	1435
606	gnl|Fabrus|VH2-26_IGHD4-11*01_IGHJ4*01	526	1131	gnl|Fabrus|L8_IGKJ1*01	830	1435
607	gnl|Fabrus|VH2-26_IGHD5-18*01_IGHJ4*01	528	1133	gnl|Fabrus|L8_IGKJ1*01	830	1435
608	gnl|Fabrus|VH2-26_IGHD6-13*01_IGHJ4*01	529	1134	gnl|Fabrus|L8_IGKJ1*01	830	1435
609	gnl|Fabrus|VH2-26_IGHD7-27*01_IGHJ4*01	530	1135	gnl|Fabrus|L8_IGKJ1*01	830	1435
610	gnl|Fabrus|VH5-51_IGHD1-14*01_IGHJ4*01	776	1381	gnl|Fabrus|L8_IGKJ1*01	830	1435
611	gnl|Fabrus|VH5-51_IGHD2-8*01_IGHJ4*01	778	1383	gnl|Fabrus|L8_IGKJ1*01	830	1435
612	gnl|Fabrus|VH5-51_IGHD3-3*01_IGHJ4*01	780	1385	gnl|Fabrus|L8_IGKJ1*01	830	1435

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
613	gnl|Fabrus|VH5-51_IGHD4-17*01_IGHJ4*01	781	1386	gnl|Fabrus|L8_IGKJ1*01	830	1435
614	gnl|Fabrus|VH5-51_IGHD5-18*01>3_IGHJ4*01	782	1387	gnl|Fabrus|L8_IGKJ1*01	830	1435
615	gnl|Fabrus|VH5-51_IGHD5-18*01>1_IGHJ4*01	783	1388	gnl|Fabrus|L8_IGKJ1*01	830	1435
616	gnl|Fabrus|VH5-51_IGHD6-25*01_IGHJ4*01	784	1389	gnl|Fabrus|L8_IGKJ1*01	830	1435
617	gnl|Fabrus|VH5-51_IGHD7-27*01_IGHJ4*01	785	1390	gnl|Fabrus|L8_IGKJ1*01	830	1435
618	gnl|Fabrus|VH6-1_IGHD1-1*01_IGHJ4*01	786	1391	gnl|Fabrus|L8_IGKJ1*01	830	1435
619	gnl|Fabrus|VH6-1_IGHD2-15*01_IGHJ4*01	788	1393	gnl|Fabrus|L8_IGKJ1*01	830	1435
620	gnl|Fabrus|VH6-1_IGHD3-3*01_IGHJ4*01	791	1396	gnl|Fabrus|L8_IGKJ1*01	830	1435
621	gnl|Fabrus|VH6-1_IGHD4-23*01_IGHJ4*01	793	1398	gnl|Fabrus|L8_IGKJ1*01	830	1435
622	gnl|Fabrus|VH6-1_IGHD4-11*01_IGHJ6*01	792	1397	gnl|Fabrus|L8_IGKJ1*01	830	1435
623	gnl|Fabrus|VH6-1_IGHD5-5*01_IGHJ4*01	794	1399	gnl|Fabrus|L8_IGKJ1*01	830	1435
624	gnl|Fabrus|VH6-1_IGHD6-13*01_IGHJ4*01	795	1400	gnl|Fabrus|L8_IGKJ1*01	830	1435
625	gnl|Fabrus|VH6-1_IGHD6-25*01_IGHJ6*01	796	1401	gnl|Fabrus|L8_IGKJ1*01	830	1435
626	gnl|Fabrus|VH6-1_IGHD7-27*01_IGHJ4*01	797	1402	gnl|Fabrus|L8_IGKJ1*01	830	1435
627	gnl|Fabrus|VH4-59_IGHD6-25*01_IGHJ3*01	775	1380	gnl|Fabrus|L8_IGKJ1*01	830	1435
628	gnl|Fabrus|VH3-48_IGHD6-6*01_IGHJ1*01	655	1260	gnl|Fabrus|L8_IGKJ1*01	830	1435
629	gnl|Fabrus|VH3-30_IGHD6-6*01_IGHJ1*01	625	1230	gnl|Fabrus|L8_IGKJ1*01	830	1435
630	gnl|Fabrus|VH3-66_IGHD6-6*01_IGHJ1*01	681	1286	gnl|Fabrus|L8_IGKJ1*01	830	1435
631	gnl|Fabrus|VH3-53_IGHD5-5*01_IGHJ4*01	670	1275	gnl|Fabrus|L8_IGKJ1*01	830	1435
632	gnl|Fabrus|VH2-5_IGHD5-12*01_IGHJ4*01	536	1141	gnl|Fabrus|L8_IGKJ1*01	830	1435
633	gnl|Fabrus|VH2-70_IGHD5-12*01_IGHJ4*01	543	1148	gnl|Fabrus|L8_IGKJ1*01	830	1435
634	gnl|Fabrus|VH3-15_IGHD5-12*01_IGHJ4*01	567	1172	gnl|Fabrus|L8_IGKJ1*01	830	1435
635	gnl|Fabrus|VH3-15_IGHD3-10*01_IGHJ4*01	565	1170	gnl|Fabrus|L8_IGKJ1*01	830	1435

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
636	gnl|Fabrus|VH3-49_IGHD5-18*01_IGHJ4*01	662	1267	gnl|Fabrus|L8_IGKJ1*01	830	1435
637	gnl|Fabrus|VH3-49_IGHD6-13*01_IGHJ4*01	663	1268	gnl|Fabrus|L8_IGKJ1*01	830	1435
638	gnl|Fabrus|VH3-72_IGHD5-18*01_IGHJ4*01	699	1304	gnl|Fabrus|L8_IGKJ1*01	830	1435
639	gnl|Fabrus|VH3-72_IGHD6-6*01_IGHJ1*01	701	1306	gnl|Fabrus|L8_IGKJ1*01	830	1435
640	gnl|Fabrus|VH3-73_IGHD5-12*01_IGHJ4*01	709	1314	gnl|Fabrus|L8_IGKJ1*01	830	1435
641	gnl|Fabrus|VH3-73_IGHD4-23*01_IGHJ5*01	708	1313	gnl|Fabrus|L8_IGKJ1*01	830	1435
642	gnl|Fabrus|VH3-43_IGHD3-22*01_IGHJ4*01	650	1255	gnl|Fabrus|L8_IGKJ1*01	830	1435
643	gnl|Fabrus|VH3-43_IGHD6-13*01_IGHJ4*01	653	1258	gnl|Fabrus|L8_IGKJ1*01	830	1435
644	gnl|Fabrus|VH3-9_IGHD3-22*01_IGHJ4*01	724	1329	gnl|Fabrus|L8_IGKJ1*01	830	1435
645	gnl|Fabrus|VH3-9_IGHD1-7*01_IGHJ5*01	721	1326	gnl|Fabrus|L8_IGKJ1*01	830	1435
646	gnl|Fabrus|VH3-9_IGHD6-13*01_IGHJ4*01	727	1332	gnl|Fabrus|L8_IGKJ1*01	830	1435
647	gnl|Fabrus|VH4-39_IGHD3-10*01_IGHJ4*01	762	1367	gnl|Fabrus|L8_IGKJ1*01	830	1435
648	gnl|Fabrus|VH4-39_IGHD5-12*01_IGHJ4*01	766	1371	gnl|Fabrus|L8_IGKJ1*01	830	1435
649	gnl|Fabrus|VH1-18_IGHD6-6*01_IGHJ1*01	460	1065	gnl|Fabrus|L8_IGKJ1*01	830	1435
650	gnl|Fabrus|VH1-24_IGHD5-12*01_IGHJ4*01	467	1072	gnl|Fabrus|L8_IGKJ1*01	830	1435
651	gnl|Fabrus|VH1-2_IGHD1-1*01_IGHJ3*01	461	1066	gnl|Fabrus|L8_IGKJ1*01	830	1435
652	gnl|Fabrus|VH1-3_IGHD6-6*01_IGHJ1*01	475	1080	gnl|Fabrus|L8_IGKJ1*01	830	1435
653	gnl|Fabrus|VH1-45_IGHD3-10*01_IGHJ4*01	480	1085	gnl|Fabrus|L8_IGKJ1*01	830	1435
654	gnl|Fabrus|VH1-46_IGHD1-26*01_IGHJ4*01	486	1091	gnl|Fabrus|L8_IGKJ1*01	830	1435
655	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ6*01	800	1405	gnl|Fabrus|L8_IGKJ1*01	830	1435
656	gnl|Fabrus|VH2-70_IGHD3-9*01_IGHJ6*01	542	1147	gnl|Fabrus|L8_IGKJ1*01	830	1435
657	gnl|Fabrus|VH1-58_IGHD3-10*01_IGHJ6*01	496	1101	gnl|Fabrus|L8_IGKJ1*01	830	1435
658	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ2*01	799	1404	gnl|Fabrus|L8_IGKJ1*01	830	1435

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
659	gnl|Fabrus|VH4-28_IGHD3-9*01_IGHJ6*01	734	1339	gnl|Fabrus|L8_IGKJ1*01	830	1435
660	gnl|Fabrus|VH4-31_IGHD2-15*01_IGHJ2*01	740	1345	gnl|Fabrus|L8_IGKJ1*01	830	1435
661	gnl|Fabrus|VH2-5_IGHD3-9*01_IGHJ6*01	535	1140	gnl|Fabrus|L8_IGKJ1*01	830	1435
662	gnl|Fabrus|VH1-8_IGHD2-15*01_IGHJ6*01	515	1120	gnl|Fabrus|L8_IGKJ1*01	830	1435
663	gnl|Fabrus|VH2-70_IGHD2-15*01_IGHJ2*01	540	1145	gnl|Fabrus|L8_IGKJ1*01	830	1435
664	gnl|Fabrus|VH3-38_IGHD3-10*01_IGHJ4*01	639	1244	gnl|Fabrus|L8_IGKJ1*01	830	1435
665	gnl|Fabrus|VH3-16_IGHD1-7*01_IGHJ6*01	570	1175	gnl|Fabrus|L8_IGKJ1*01	830	1435
666	gnl|Fabrus|VH3-73_IGHD3-9*01_IGHJ6*01	706	1311	gnl|Fabrus|L8_IGKJ1*01	830	1435
667	gnl|Fabrus|VH3-11_IGHD3-9*01_IGHJ6*01	548	1153	gnl|Fabrus|L8_IGKJ1*01	830	1435
668	gnl|Fabrus|VH3-11_IGHD6-6*01_IGHJ1*01	552	1157	gnl|Fabrus|L8_IGKJ1*01	830	1435
669	gnl|Fabrus|VH3-20_IGHD5-12*01_IGHJ4*01	584	1189	gnl|Fabrus|L8_IGKJ1*01	830	1435
670	gnl|Fabrus|VH3-16_IGHD2-15*01_IGHJ2*01	571	1176	gnl|Fabrus|L8_IGKJ1*01	830	1435
671	gnl|Fabrus|VH3-7_IGHD6-6*01_IGHJ1*01	692	1297	gnl|Fabrus|L8_IGKJ1*01	830	1435
672	gnl|Fabrus|VH3-16_IGHD6-13*01_IGHJ4*01	576	1181	gnl|Fabrus|L8_IGKJ1*01	830	1435
673	gnl|Fabrus|VH3-23_IGHD1-1*01_IGHJ4*01	595	1200	gnl|Fabrus|L11_IGKJ1*01	819	1424
674	gnl|Fabrus|VH3-23_IGHD2-15*01_IGHJ4*01	598	1203	gnl|Fabrus|L11_IGKJ1*01	819	1424
675	gnl|Fabrus|VH3-23_IGHD3-22*01_IGHJ4*01	602	1207	gnl|Fabrus|L11_IGKJ1*01	819	1424
676	gnl|Fabrus|VH3-23_IGHD4-11*01_IGHJ4*01	604	1209	gnl|Fabrus|L11_IGKJ1*01	819	1424
677	gnl|Fabrus|VH3-23_IGHD5-12*01_IGHJ4*01	606	1211	gnl|Fabrus|L11_IGKJ1*01	819	1424
678	gnl|Fabrus|VH3-23_IGHD5-5*01_IGHJ4*01	608	1213	gnl|Fabrus|L11_IGKJ1*01	819	1424
679	gnl|Fabrus|VH3-23_IGHD6-13*01_IGHJ4*01	609	1214	gnl|Fabrus|L11_IGKJ1*01	819	1424
680	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ4*01	612	1217	gnl|Fabrus|L11_IGKJ1*01	819	1424
681	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ6*01	613	1218	gnl|Fabrus|L11_IGKJ1*01	819	1424

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
682	gnl|Fabrus|VH1-69_IGHD1-14*01_IGHJ4*01	502	1107	gnl|Fabrus|L11_IGKJ1*01	819	1424
683	gnl|Fabrus|VH1-69_IGHD2-2*01_IGHJ4*01	503	1108	gnl|Fabrus|L11_IGKJ1*01	819	1424
684	gnl|Fabrus|VH1-69_IGHD2-8*01_IGHJ6*01	504	1109	gnl|Fabrus|L11_IGKJ1*01	819	1424
685	gnl|Fabrus|VH1-69_IGHD3-16*01_IGHJ4*01	505	1110	gnl|Fabrus|L11_IGKJ1*01	819	1424
686	gnl|Fabrus|VH1-69_IGHD3-3*01_IGHJ4*01	506	1111	gnl|Fabrus|L11_IGKJ1*01	819	1424
687	gnl|Fabrus|VH1-69_IGHD4-17*01_IGHJ4*01	508	1113	gnl|Fabrus|L11_IGKJ1*01	819	1424
688	gnl|Fabrus|VH1-69_IGHD5-12*01_IGHJ4*01	509	1114	gnl|Fabrus|L11_IGKJ1*01	819	1424
689	gnl|Fabrus|VH1-69_IGHD6-19*01_IGHJ4*01	511	1116	gnl|Fabrus|L11_IGKJ1*01	819	1424
690	gnl|Fabrus|VH1-69_IGHD7-27*01_IGHJ4*01	513	1118	gnl|Fabrus|L11_IGKJ1*01	819	1424
691	gnl|Fabrus|VH4-34_IGHD1-7*01_IGHJ4*01	749	1354	gnl|Fabrus|L11_IGKJ1*01	819	1424
692	gnl|Fabrus|VH4-34_IGHD2-2*01_IGHJ4*01	750	1355	gnl|Fabrus|L11_IGKJ1*01	819	1424
693	gnl|Fabrus|VH4-34_IGHD3-16*01_IGHJ4*01	751	1356	gnl|Fabrus|L11_IGKJ1*01	819	1424
694	gnl|Fabrus|VH4-34_IGHD4-17*01_IGHJ4*01	753	1358	gnl|Fabrus|L11_IGKJ1*01	819	1424
695	gnl|Fabrus|VH4-34_IGHD5-12*01_IGHJ4*01	754	1359	gnl|Fabrus|L11_IGKJ1*01	819	1424
696	gnl|Fabrus|VH4-34_IGHD6-13*01_IGHJ4*01	755	1360	gnl|Fabrus|L11_IGKJ1*01	819	1424
697	gnl|Fabrus|VH4-34_IGHD6-25*01_IGHJ6*01	756	1361	gnl|Fabrus|L11_IGKJ1*01	819	1424
698	gnl|Fabrus|VH4-34_IGHD7-27*01_IGHJ4*01	758	1363	gnl|Fabrus|L11_IGKJ1*01	819	1424
699	gnl|Fabrus|VH2-26_IGHD1-20*01_IGHJ4*01	521	1126	gnl|Fabrus|L11_IGKJ1*01	819	1424
700	gnl|Fabrus|VH2-26_IGHD2-2*01_IGHJ4*01	523	1128	gnl|Fabrus|L11_IGKJ1*01	819	1424
701	gnl|Fabrus|VH2-26_IGHD3-10*01_IGHJ4*01	524	1129	gnl|Fabrus|L11_IGKJ1*01	819	1424
702	gnl|Fabrus|VH2-26_IGHD4-11*01_IGHJ4*01	526	1131	gnl|Fabrus|L11_IGKJ1*01	819	1424
703	gnl|Fabrus|VH2-26_IGHD5-18*01_IGHJ4*01	528	1133	gnl|Fabrus|L11_IGKJ1*01	819	1424
704	gnl|Fabrus|VH2-26_IGHD6-13*01_IGHJ4*01	529	1134	gnl|Fabrus|L11_IGKJ1*01	819	1424

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
705	gnl|Fabrus|VH2-26_IGHD7-27*01_IGHJ4*01	530	1135	gnl|Fabrus|L11_IGKJ1*01	819	1424
706	gnl|Fabrus|VH5-51_IGHD1-14*01_IGHJ4*01	776	1381	gnl|Fabrus|L11_IGKJ1*01	819	1424
707	gnl|Fabrus|VH5-51_IGHD2-8*01_IGHJ4*01	778	1383	gnl|Fabrus|L11_IGKJ1*01	819	1424
708	gnl|Fabrus|VH5-51_IGHD3-3*01_IGHJ4*01	780	1385	gnl|Fabrus|L11_IGKJ1*01	819	1424
709	gnl|Fabrus|VH5-51_IGHD4-17*01_IGHJ4*01	781	1386	gnl|Fabrus|L11_IGKJ1*01	819	1424
710	gnl|Fabrus|VH5-51_IGHD5-18*01>3_IGHJ4*01	782	1387	gnl|Fabrus|L11_IGKJ1*01	819	1424
711	gnl|Fabrus|VH5-51_IGHD5-18*01>1_IGHJ4*01	783	1388	gnl|Fabrus|L11_IGKJ1*01	819	1424
712	gnl|Fabrus|VH5-51_IGHD6-25*01_IGHJ4*01	784	1389	gnl|Fabrus|L11_IGKJ1*01	819	1424
713	gnl|Fabrus|VH5-51_IGHD7-27*01_IGHJ4*01	785	1390	gnl|Fabrus|L11_IGKJ1*01	819	1424
714	gnl|Fabrus|VH6-1_IGHD1-1*01_IGHJ4*01	786	1391	gnl|Fabrus|L11_IGKJ1*01	819	1424
715	gnl|Fabrus|VH6-1_IGHD2-15*01_IGHJ4*01	788	1393	gnl|Fabrus|L11_IGKJ1*01	819	1424
716	gnl|Fabrus|VH6-1_IGHD3-3*01_IGHJ4*01	791	1396	gnl|Fabrus|L11_IGKJ1*01	819	1424
717	gnl|Fabrus|VH6-1_IGHD4-23*01_IGHJ4*01	793	1398	gnl|Fabrus|L11_IGKJ1*01	819	1424
718	gnl|Fabrus|VH6-1_IGHD4-11*01_IGHJ6*01	792	1397	gnl|Fabrus|L11_IGKJ1*01	819	1424
719	gnl|Fabrus|VH6-1_IGHD5-5*01_IGHJ4*01	794	1399	gnl|Fabrus|L11_IGKJ1*01	819	1424
720	gnl|Fabrus|VH6-1_IGHD6-13*01_IGHJ4*01	795	1400	gnl|Fabrus|L11_IGKJ1*01	819	1424
721	gnl|Fabrus|VH6-1_IGHD6-25*01_IGHJ6*01	796	1401	gnl|Fabrus|L11_IGKJ1*01	819	1424
722	gnl|Fabrus|VH6-1_IGHD7-27*01_IGHJ4*01	797	1402	gnl|Fabrus|L11_IGKJ1*01	819	1424
723	gnl|Fabrus|VH4-59_IGHD6-25*01_IGHJ3*01	775	1380	gnl|Fabrus|L11_IGKJ1*01	819	1424
724	gnl|Fabrus|VH3-48_IGHD6-6*01_IGHJ1*01	655	1260	gnl|Fabrus|L11_IGKJ1*01	819	1424
725	gnl|Fabrus|VH3-30_IGHD6-6*01_IGHJ1*01	625	1230	gnl|Fabrus|L11_IGKJ1*01	819	1424
726	gnl|Fabrus|VH3-66_IGHD6-6*01_IGHJ1*01	681	1286	gnl|Fabrus|L11_IGKJ1*01	819	1424
727	gnl|Fabrus|VH3-53_IGHD5-5*01_IGHJ4*01	670	1275	gnl|Fabrus|L11_IGKJ1*01	819	1424

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
728	gnl|Fabrus|VH2-5_IGHD5-12*01_IGHJ4*01	536	1141	gnl|Fabrus|L11_IGKJ1*01	819	1424
729	gnl|Fabrus|VH2-70_IGHD5-12*01_IGHJ4*01	543	1148	gnl|Fabrus|L11_IGKJ1*01	819	1424
730	gnl|Fabrus|VH3-15_IGHD5-12*01_IGHJ4*01	567	1172	gnl|Fabrus|L11_IGKJ1*01	819	1424
731	gnl|Fabrus|VH3-15_IGHD3-10*01_IGHJ4*01	565	1170	gnl|Fabrus|L11_IGKJ1*01	819	1424
732	gnl|Fabrus|VH3-49_IGHD5-18*01_IGHJ4*01	662	1267	gnl|Fabrus|L11_IGKJ1*01	819	1424
733	gnl|Fabrus|VH3-49_IGHD6-13*01_IGHJ4*01	663	1268	gnl|Fabrus|L11_IGKJ1*01	819	1424
734	gnl|Fabrus|VH3-72_IGHD5-18*01_IGHJ4*01	699	1304	gnl|Fabrus|L11_IGKJ1*01	819	1424
735	gnl|Fabrus|VH3-72_IGHD6-6*01_IGHJ1*01	701	1306	gnl|Fabrus|L11_IGKJ1*01	819	1424
736	gnl|Fabrus|VH3-73_IGHD5-12*01_IGHJ4*01	709	1314	gnl|Fabrus|L11_IGKJ1*01	819	1424
737	gnl|Fabrus|VH3-73_IGHD4-23*01_IGHJ5*01	708	1313	gnl|Fabrus|L11_IGKJ1*01	819	1424
738	gnl|Fabrus|VH3-43_IGHD3-22*01_IGHJ4*01	650	1255	gnl|Fabrus|L11_IGKJ1*01	819	1424
739	gnl|Fabrus|VH3-43_IGHD6-13*01_IGHJ4*01	653	1258	gnl|Fabrus|L11_IGKJ1*01	819	1424
740	gnl|Fabrus|VH3-9_IGHD3-22*01_IGHJ4*01	724	1329	gnl|Fabrus|L11_IGKJ1*01	819	1424
741	gnl|Fabrus|VH3-9_IGHD1-7*01_IGHJ5*01	721	1326	gnl|Fabrus|L11_IGKJ1*01	819	1424
742	gnl|Fabrus|VH3-9_IGHD6-13*01_IGHJ4*01	727	1332	gnl|Fabrus|L11_IGKJ1*01	819	1424
743	gnl|Fabrus|VH4-39_IGHD3-10*01_IGHJ4*01	762	1367	gnl|Fabrus|L11_IGKJ1*01	819	1424
744	gnl|Fabrus|VH4-39_IGHD5-12*01_IGHJ4*01	766	1371	gnl|Fabrus|L11_IGKJ1*01	819	1424
745	gnl|Fabrus|VH1-18_IGHD6-6*01_IGHJ1*01	460	1065	gnl|Fabrus|L11_IGKJ1*01	819	1424
746	gnl|Fabrus|VH1-24_IGHD5-12*01_IGHJ4*01	467	1072	gnl|Fabrus|L11_IGKJ1*01	819	1424
747	gnl|Fabrus|VH1-2_IGHD1-1*01_IGHJ3*01	461	1066	gnl|Fabrus|L11_IGKJ1*01	819	1424
748	gnl|Fabrus|VH1-3_IGHD6-6*01_IGHJ1*01	475	1080	gnl|Fabrus|L11_IGKJ1*01	819	1424
749	gnl|Fabrus|VH1-45_IGHD3-10*01_IGHJ4*01	480	1085	gnl|Fabrus|L11_IGKJ1*01	819	1424
750	gnl|Fabrus|VH1-46_IGHD1-26*01_IGHJ4*01	486	1091	gnl|Fabrus|L11_IGKJ1*01	819	1424

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
751	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ6*01	800	1405	gnl|Fabrus|L11_IGKJ1*01	819	1424
752	gnl|Fabrus|VH2-70_IGHD3-9*01_IGHJ6*01	542	1147	gnl|Fabrus|L11_IGKJ1*01	819	1424
753	gnl|Fabrus|VH1-58_IGHD3-10*01_IGHJ6*01	496	1101	gnl|Fabrus|L11_IGKJ1*01	819	1424
754	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ2*01	799	1404	gnl|Fabrus|L11_IGKJ1*01	819	1424
755	gnl|Fabrus|VH4-28_IGHD3-9*01_IGHJ6*01	734	1339	gnl|Fabrus|L11_IGKJ1*01	819	1424
756	gnl|Fabrus|VH4-31_IGHD2-15*01_IGHJ2*01	740	1345	gnl|Fabrus|L11_IGKJ1*01	819	1424
757	gnl|Fabrus|VH2-5_IGHD3-9*01_IGHJ6*01	535	1140	gnl|Fabrus|L11_IGKJ1*01	819	1424
758	gnl|Fabrus|VH1-8_IGHD2-15*01_IGHJ6*01	515	1120	gnl|Fabrus|L11_IGKJ1*01	819	1424
759	gnl|Fabrus|VH2-70_IGHD2-15*01_IGHJ2*01	540	1145	gnl|Fabrus|L11_IGKJ1*01	819	1424
760	gnl|Fabrus|VH3-38_IGHD3-10*01_IGHJ4*01	639	1244	gnl|Fabrus|L11_IGKJ1*01	819	1424
761	gnl|Fabrus|VH3-16_IGHD1-7*01_IGHJ6*01	570	1175	gnl|Fabrus|L11_IGKJ1*01	819	1424
762	gnl|Fabrus|VH3-73_IGHD3-9*01_IGHJ6*01	706	1311	gnl|Fabrus|L11_IGKJ1*01	819	1424
763	gnl|Fabrus|VH3-11_IGHD3-9*01_IGHJ6*01	548	1153	gnl|Fabrus|L11_IGKJ1*01	819	1424
764	gnl|Fabrus|VH3-11_IGHD6-6*01_IGHJ1*01	552	1157	gnl|Fabrus|L11_IGKJ1*01	819	1424
765	gnl|Fabrus|VH3-20_IGHD5-12*01_IGHJ4*01	584	1189	gnl|Fabrus|L11_IGKJ1*01	819	1424
766	gnl|Fabrus|VH3-16_IGHD2-15*01_IGHJ2*01	571	1176	gnl|Fabrus|L11_IGKJ1*01	819	1424
767	gnl|Fabrus|VH3-7_IGHD6-6*01_IGHJ1*01	692	1297	gnl|Fabrus|L11_IGKJ1*01	819	1424
768	gnl|Fabrus|VH3-16_IGHD6-13*01_IGHJ4*01	576	1181	gnl|Fabrus|L11_IGKJ1*01	819	1424
769	gnl|Fabrus|VH3-23_IGHD1-1*01_IGHJ4*01	595	1200	gnl|Fabrus|L12_IGKJ1*01	820	1425
770	gnl|Fabrus|VH3-23_IGHD2-15*01_IGHJ4*01	598	1203	gnl|Fabrus|L12_IGKJ1*01	820	1425
771	gnl|Fabrus|VH3-23_IGHD3-22*01_IGHJ4*01	602	1207	gnl|Fabrus|L12_IGKJ1*01	820	1425
772	gnl|Fabrus|VH3-23_IGHD4-11*01_IGHJ4*01	604	1209	gnl|Fabrus|L12_IGKJ1*01	820	1425
773	gnl|Fabrus|VH3-23_IGHD5-12*01_IGHJ4*01	606	1211	gnl|Fabrus|L12_IGKJ1*01	820	1425

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
774	gnl|Fabrus|VH3-23_IGHD5-5*01_IGHJ4*01	608	1213	gnl|Fabrus|L12_IGKJ1*01	820	1425
775	gnl|Fabrus|VH3-23_IGHD6-13*01_IGHJ4*01	609	1214	gnl|Fabrus|L12_IGKJ1*01	820	1425
776	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ4*01	612	1217	gnl|Fabrus|L12_IGKJ1*01	820	1425
777	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ6*01	613	1218	gnl|Fabrus|L12_IGKJ1*01	820	1425
778	gnl|Fabrus|VH1-69_IGHD1-14*01_IGHJ4*01	502	1107	gnl|Fabrus|L12_IGKJ1*01	820	1425
779	gnl|Fabrus|VH1-69_IGHD2-2*01_IGHJ4*01	503	1108	gnl|Fabrus|L12_IGKJ1*01	820	1425
780	gnl|Fabrus|VH1-69_IGHD2-8*01_IGHJ6*01	504	1109	gnl|Fabrus|L12_IGKJ1*01	820	1425
781	gnl|Fabrus|VH1-69_IGHD3-16*01_IGHJ4*01	505	1110	gnl|Fabrus|L12_IGKJ1*01	820	1425
782	gnl|Fabrus|VH1-69_IGHD3-3*01_IGHJ4*01	506	1111	gnl|Fabrus|L12_IGKJ1*01	820	1425
783	gnl|Fabrus|VH1-69_IGHD4-17*01_IGHJ4*01	508	1113	gnl|Fabrus|L12_IGKJ1*01	820	1425
784	gnl|Fabrus|VH1-69_IGHD5-12*01_IGHJ4*01	509	1114	gnl|Fabrus|L12_IGKJ1*01	820	1425
785	gnl|Fabrus|VH1-69_IGHD6-19*01_IGHJ4*01	511	1116	gnl|Fabrus|L12_IGKJ1*01	820	1425
786	gnl|Fabrus|VH1-69_IGHD7-27*01_IGHJ4*01	513	1118	gnl|Fabrus|L12_IGKJ1*01	820	1425
787	gnl|Fabrus|VH4-34_IGHD1-7*01_IGHJ4*01	749	1354	gnl|Fabrus|L12_IGKJ1*01	820	1425
788	gnl|Fabrus|VH4-34_IGHD2-2*01_IGHJ4*01	750	1355	gnl|Fabrus|L12_IGKJ1*01	820	1425
789	gnl|Fabrus|VH4-34_IGHD3-16*01_IGHJ4*01	751	1356	gnl|Fabrus|L12_IGKJ1*01	820	1425
790	gnl|Fabrus|VH4-34_IGHD4-17*01_IGHJ4*01	753	1358	gnl|Fabrus|L12_IGKJ1*01	820	1425
791	gnl|Fabrus|VH4-34_IGHD5-12*01_IGHJ4*01	754	1359	gnl|Fabrus|L12_IGKJ1*01	820	1425
792	gnl|Fabrus|VH4-34_IGHD6-13*01_IGHJ4*01	755	1360	gnl|Fabrus|L12_IGKJ1*01	820	1425
793	gnl|Fabrus|VH4-34_IGHD6-25*01_IGHJ6*01	756	1361	gnl|Fabrus|L12_IGKJ1*01	820	1425
794	gnl|Fabrus|VH4-34_IGHD7-27*01_IGHJ4*01	758	1363	gnl|Fabrus|L12_IGKJ1*01	820	1425
795	gnl|Fabrus|VH2-26_IGHD1-20*01_IGHJ4*01	521	1126	gnl|Fabrus|L12_IGKJ1*01	820	1425
796	gnl|Fabrus|VH2-26_IGHD2-2*01_IGHJ4*01	523	1128	gnl|Fabrus|L12_IGKJ1*01	820	1425

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
797	gnl|Fabrus|VH2-26_IGHD3-10*01_IGHJ4*01	524	1129	gnl|Fabrus|L12_IGKJ1*01	820	1425
798	gnl|Fabrus|VH2-26_IGHD4-11*01_IGHJ4*01	526	1131	gnl|Fabrus|L12_IGKJ1*01	820	1425
799	gnl|Fabrus|VH2-26_IGHD5-18*01_IGHJ4*01	528	1133	gnl|Fabrus|L12_IGKJ1*01	820	1425
800	gnl|Fabrus|VH2-26_IGHD6-13*01_IGHJ4*01	529	1134	gnl|Fabrus|L12_IGKJ1*01	820	1425
801	gnl|Fabrus|VH2-26_IGHD7-27*01_IGHJ4*01	530	1135	gnl|Fabrus|L12_IGKJ1*01	820	1425
802	gnl|Fabrus|VH5-51_IGHD1-14*01_IGHJ4*01	776	1381	gnl|Fabrus|L12_IGKJ1*01	820	1425
803	gnl|Fabrus|VH5-51_IGHD2-8*01_IGHJ4*01	778	1383	gnl|Fabrus|L12_IGKJ1*01	820	1425
804	gnl|Fabrus|VH5-51_IGHD3-3*01_IGHJ4*01	780	1385	gnl|Fabrus|L12_IGKJ1*01	820	1425
805	gnl|Fabrus|VH5-51_IGHD4-17*01_IGHJ4*01	781	1386	gnl|Fabrus|L12_IGKJ1*01	820	1425
806	gnl|Fabrus|VH5-51_IGHD5-18*01>3_IGHJ4*01	782	1387	gnl|Fabrus|L12_IGKJ1*01	820	1425
807	gnl|Fabrus|VH5-51_IGHD5-18*01>1_IGHJ4*01	783	1388	gnl|Fabrus|L12_IGKJ1*01	820	1425
808	gnl|Fabrus|VH5-51_IGHD6-25*01_IGHJ4*01	784	1389	gnl|Fabrus|L12_IGKJ1*01	820	1425
809	gnl|Fabrus|VH5-51_IGHD7-27*01_IGHJ4*01	785	1390	gnl|Fabrus|L12_IGKJ1*01	820	1425
810	gnl|Fabrus|VH6-1_IGHD1-1*01_IGHJ4*01	786	1391	gnl|Fabrus|L12_IGKJ1*01	820	1425
811	gnl|Fabrus|VH6-1_IGHD2-15*01_IGHJ4*01	788	1393	gnl|Fabrus|L12_IGKJ1*01	820	1425
812	gnl|Fabrus|VH6-1_IGHD3-3*01_IGHJ4*01	791	1396	gnl|Fabrus|L12_IGKJ1*01	820	1425
813	gnl|Fabrus|VH6-1_IGHD4-23*01_IGHJ4*01	793	1398	gnl|Fabrus|L12_IGKJ1*01	820	1425
814	gnl|Fabrus|VH6-1_IGHD4-11*01_IGHJ6*01	792	1397	gnl|Fabrus|L12_IGKJ1*01	820	1425
815	gnl|Fabrus|VH6-1_IGHD5-5*01_IGHJ4*01	794	1399	gnl|Fabrus|L12_IGKJ1*01	820	1425
816	gnl|Fabrus|VH6-1_IGHD6-13*01_IGHJ4*01	795	1400	gnl|Fabrus|L12_IGKJ1*01	820	1425
817	gnl|Fabrus|VH6-1_IGHD6-25*01_IGHJ6*01	796	1401	gnl|Fabrus|L12_IGKJ1*01	820	1425
818	gnl|Fabrus|VH6-1_IGHD7-27*01_IGHJ4*01	797	1402	gnl|Fabrus|L12_IGKJ1*01	820	1425
819	gnl|Fabrus|VH4-59_IGHD6-25*01_IGHJ3*01	775	1380	gnl|Fabrus|L12_IGKJ1*01	820	1425

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
820	gnl|Fabrus|VH3-48_IGHD6-6*01_IGHJ1*01	655	1260	gnl|Fabrus|L12_IGKJ1*01	820	1425
821	gnl|Fabrus|VH3-30_IGHD6-6*01_IGHJ1*01	625	1230	gnl|Fabrus|L12_IGKJ1*01	820	1425
822	gnl|Fabrus|VH3-66_IGHD6-6*01_IGHJ1*01	681	1286	gnl|Fabrus|L12_IGKJ1*01	820	1425
823	gnl|Fabrus|VH3-53_IGHD5-5*01_IGHJ4*01	670	1275	gnl|Fabrus|L12_IGKJ1*01	820	1425
824	gnl|Fabrus|VH2-5_IGHD5-12*01_IGHJ4*01	536	1141	gnl|Fabrus|L12_IGKJ1*01	820	1425
825	gnl|Fabrus|VH2-70_IGHD5-12*01_IGHJ4*01	543	1148	gnl|Fabrus|L12_IGKJ1*01	820	1425
826	gnl|Fabrus|VH3-15_IGHD5-12*01_IGHJ4*01	567	1172	gnl|Fabrus|L12_IGKJ1*01	820	1425
827	gnl|Fabrus|VH3-15_IGHD3-10*01_IGHJ4*01	565	1170	gnl|Fabrus|L12_IGKJ1*01	820	1425
828	gnl|Fabrus|VH3-49_IGHD5-18*01_IGHJ4*01	662	1267	gnl|Fabrus|L12_IGKJ1*01	820	1425
829	gnl|Fabrus|VH3-49_IGHD6-13*01_IGHJ4*01	663	1268	gnl|Fabrus|L12_IGKJ1*01	820	1425
830	gnl|Fabrus|VH3-72_IGHD5-18*01_IGHJ4*01	699	1304	gnl|Fabrus|L12_IGKJ1*01	820	1425
831	gnl|Fabrus|VH3-72_IGHD6-6*01_IGHJ1*01	701	1306	gnl|Fabrus|L12_IGKJ1*01	820	1425
832	gnl|Fabrus|VH3-73_IGHD5-12*01_IGHJ4*01	709	1314	gnl|Fabrus|L12_IGKJ1*01	820	1425
833	gnl|Fabrus|VH3-73_IGHD4-23*01_IGHJ5*01	708	1313	gnl|Fabrus|L12_IGKJ1*01	820	1425
834	gnl|Fabrus|VH3-43_IGHD3-22*01_IGHJ4*01	650	1255	gnl|Fabrus|L12_IGKJ1*01	820	1425
835	gnl|Fabrus|VH3-43_IGHD6-13*01_IGHJ4*01	653	1258	gnl|Fabrus|L12_IGKJ1*01	820	1425
836	gnl|Fabrus|VH3-9_IGHD3-22*01_IGHJ4*01	724	1329	gnl|Fabrus|L12_IGKJ1*01	820	1425
837	gnl|Fabrus|VH3-9_IGHD1-7*01_IGHJ5*01	721	1326	gnl|Fabrus|L12_IGKJ1*01	820	1425
838	gnl|Fabrus|VH3-9_IGHD6-13*01_IGHJ4*01	727	1332	gnl|Fabrus|L12_IGKJ1*01	820	1425
839	gnl|Fabrus|VH4-39_IGHD3-10*01_IGHJ4*01	762	1367	gnl|Fabrus|L12_IGKJ1*01	820	1425
840	gnl|Fabrus|VH4-39_IGHD5-12*01_IGHJ4*01	766	1371	gnl|Fabrus|L12_IGKJ1*01	820	1425
841	gnl|Fabrus|VH1-18_IGHD6-6*01_IGHJ1*01	460	1065	gnl|Fabrus|L12_IGKJ1*01	820	1425
842	gnl|Fabrus|VH1-24_IGHD5-12*01_IGHJ4*01	467	1072	gnl|Fabrus|L12_IGKJ1*01	820	1425

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
843	gnl|Fabrus|VH1-2_IGHD1-1*01_IGHJ3*01	461	1066	gnl|Fabrus|L12_IGKJ1*01	820	1425
844	gnl|Fabrus|VH1-3_IGHD6-6*01_IGHJ1*01	475	1080	gnl|Fabrus|L12_IGKJ1*01	820	1425
845	gnl|Fabrus|VH1-45_IGHD3-10*01_IGHJ4*01	480	1085	gnl|Fabrus|L12_IGKJ1*01	820	1425
846	gnl|Fabrus|VH1-46_IGHD1-26*01_IGHJ4*01	486	1091	gnl|Fabrus|L12_IGKJ1*01	820	1425
847	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ6*01	800	1405	gnl|Fabrus|L12_IGKJ1*01	820	1425
848	gnl|Fabrus|VH2-70_IGHD3-9*01_IGHJ6*01	542	1147	gnl|Fabrus|L12_IGKJ1*01	820	1425
849	gnl|Fabrus|VH1-58_IGHD3-10*01_IGHJ6*01	496	1101	gnl|Fabrus|L12_IGKJ1*01	820	1425
850	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ2*01	799	1404	gnl|Fabrus|L12_IGKJ1*01	820	1425
851	gnl|Fabrus|VH4-28_IGHD3-9*01_IGHJ6*01	734	1339	gnl|Fabrus|L12_IGKJ1*01	820	1425
852	gnl|Fabrus|VH4-31_IGHD2-15*01_IGHJ2*01	740	1345	gnl|Fabrus|L12_IGKJ1*01	820	1425
853	gnl|Fabrus|VH2-5_IGHD3-9*01_IGHJ6*01	535	1140	gnl|Fabrus|L12_IGKJ1*01	820	1425
854	gnl|Fabrus|VH1-8_IGHD2-15*01_IGHJ6*01	515	1120	gnl|Fabrus|L12_IGKJ1*01	820	1425
855	gnl|Fabrus|VH2-70_IGHD2-15*01_IGHJ2*01	540	1145	gnl|Fabrus|L12_IGKJ1*01	820	1425
856	gnl|Fabrus|VH3-38_IGHD3-10*01_IGHJ4*01	639	1244	gnl|Fabrus|L12_IGKJ1*01	820	1425
857	gnl|Fabrus|VH3-16_IGHD1-7*01_IGHJ6*01	570	1175	gnl|Fabrus|L12_IGKJ1*01	820	1425
858	gnl|Fabrus|VH3-73_IGHD3-9*01_IGHJ6*01	706	1311	gnl|Fabrus|L12_IGKJ1*01	820	1425
859	gnl|Fabrus|VH3-11_IGHD3-9*01_IGHJ6*01	548	1153	gnl|Fabrus|L12_IGKJ1*01	820	1425
860	gnl|Fabrus|VH3-11_IGHD6-6*01_IGHJ1*01	552	1157	gnl|Fabrus|L12_IGKJ1*01	820	1425
861	gnl|Fabrus|VH3-20_IGHD5-12*01_IGHJ4*01	584	1189	gnl|Fabrus|L12_IGKJ1*01	820	1425
862	gnl|Fabrus|VH3-16_IGHD2-15*01_IGHJ2*01	571	1176	gnl|Fabrus|L12_IGKJ1*01	820	1425
863	gnl|Fabrus|VH3-7_IGHD6-6*01_IGHJ1*01	692	1297	gnl|Fabrus|L12_IGKJ1*01	820	1425
864	gnl|Fabrus|VH3-16_IGHD6-13*01_IGHJ4*01	576	1181	gnl|Fabrus|L12_IGKJ1*01	820	1425
865	gnl|Fabrus|VH3-23_IGHD1-1*01_IGHJ4*01	595	1200	gnl|Fabrus|O1_IGKJ1*01	832	1437

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
866	gnl|Fabrus|VH3-23_IGHD2-15*01_IGHJ4*01	598	1203	gnl|Fabrus|O1_IGKJ1*01	832	1437
867	gnl|Fabrus|VH3-23_IGHD3-22*01_IGHJ4*01	602	1207	gnl|Fabrus|O1_IGKJ1*01	832	1437
868	gnl|Fabrus|VH3-23_IGHD4-11*01_IGHJ4*01	604	1209	gnl|Fabrus|O1_IGKJ1*01	832	1437
869	gnl|Fabrus|VH3-23_IGHD5-12*01_IGHJ4*01	606	1211	gnl|Fabrus|O1_IGKJ1*01	832	1437
870	gnl|Fabrus|VH3-23_IGHD5-5*01_IGHJ4*01	608	1213	gnl|Fabrus|O1_IGKJ1*01	832	1437
871	gnl|Fabrus|VH3-23_IGHD6-13*01_IGHJ4*01	609	1214	gnl|Fabrus|O1_IGKJ1*01	832	1437
872	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ4*01	612	1217	gnl|Fabrus|O1_IGKJ1*01	832	1437
873	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ6*01	613	1218	gnl|Fabrus|O1_IGKJ1*01	832	1437
874	gnl|Fabrus|VH1-69_IGHD1-14*01_IGHJ4*01	502	1107	gnl|Fabrus|O1_IGKJ1*01	832	1437
875	gnl|Fabrus|VH1-69_IGHD2-2*01_IGHJ4*01	503	1108	gnl|Fabrus|O1_IGKJ1*01	832	1437
876	gnl|Fabrus|VH1-69_IGHD2-8*01_IGHJ6*01	504	1109	gnl|Fabrus|O1_IGKJ1*01	832	1437
877	gnl|Fabrus|VH1-69_IGHD3-16*01_IGHJ4*01	505	1110	gnl|Fabrus|O1_IGKJ1*01	832	1437
878	gnl|Fabrus|VH1-69_IGHD3-3*01_IGHJ4*01	506	1111	gnl|Fabrus|O1_IGKJ1*01	832	1437
879	gnl|Fabrus|VH1-69_IGHD4-17*01_IGHJ4*01	508	1113	gnl|Fabrus|O1_IGKJ1*01	832	1437
880	gnl|Fabrus|VH1-69_IGHD5-12*01_IGHJ4*01	509	1114	gnl|Fabrus|O1_IGKJ1*01	832	1437
881	gnl|Fabrus|VH1-69_IGHD6-19*01_IGHJ4*01	511	1116	gnl|Fabrus|O1_IGKJ1*01	832	1437
882	gnl|Fabrus|VH1-69_IGHD7-27*01_IGHJ4*01	513	1118	gnl|Fabrus|O1_IGKJ1*01	832	1437
883	gnl|Fabrus|VH4-34_IGHD1-7*01_IGHJ4*01	749	1354	gnl|Fabrus|O1_IGKJ1*01	832	1437
884	gnl|Fabrus|VH4-34_IGHD2-2*01_IGHJ4*01	750	1355	gnl|Fabrus|O1_IGKJ1*01	832	1437
885	gnl|Fabrus|VH4-34_IGHD3-16*01_IGHJ4*01	751	1356	gnl|Fabrus|O1_IGKJ1*01	832	1437
886	gnl|Fabrus|VH4-34_IGHD4-17*01_IGHJ4*01	753	1358	gnl|Fabrus|O1_IGKJ1*01	832	1437
887	gnl|Fabrus|VH4-34_IGHD5-12*01_IGHJ4*01	754	1359	gnl|Fabrus|O1_IGKJ1*01	832	1437
888	gnl|Fabrus|VH4-34_IGHD6-13*01_IGHJ4*01	755	1360	gnl|Fabrus|O1_IGKJ1*01	832	1437

Table 17. Exemplary Nucleic Acid Paired Library						
	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
889	gnl|Fabrus|VH4-34_IGHD6-25*01_IGHJ6*01	756	1361	gnl|Fabrus|O1_IGKJ1*01	832	1437
890	gnl|Fabrus|VH4-34_IGHD7-27*01_IGHJ4*01	758	1363	gnl|Fabrus|O1_IGKJ1*01	832	1437
891	gnl|Fabrus|VH2-26_IGHD1-20*01_IGHJ4*01	521	1126	gnl|Fabrus|O1_IGKJ1*01	832	1437
892	gnl|Fabrus|VH2-26_IGHD2-2*01_IGHJ4*01	523	1128	gnl|Fabrus|O1_IGKJ1*01	832	1437
893	gnl|Fabrus|VH2-26_IGHD3-10*01_IGHJ4*01	524	1129	gnl|Fabrus|O1_IGKJ1*01	832	1437
894	gnl|Fabrus|VH2-26_IGHD4-11*01_IGHJ4*01	526	1131	gnl|Fabrus|O1_IGKJ1*01	832	1437
895	gnl|Fabrus|VH2-26_IGHD5-18*01_IGHJ4*01	528	1133	gnl|Fabrus|O1_IGKJ1*01	832	1437
896	gnl|Fabrus|VH2-26_IGHD6-13*01_IGHJ4*01	529	1134	gnl|Fabrus|O1_IGKJ1*01	832	1437
897	gnl|Fabrus|VH2-26_IGHD7-27*01_IGHJ4*01	530	1135	gnl|Fabrus|O1_IGKJ1*01	832	1437
898	gnl|Fabrus|VH5-51_IGHD1-14*01_IGHJ4*01	776	1381	gnl|Fabrus|O1_IGKJ1*01	832	1437
899	gnl|Fabrus|VH5-51_IGHD2-8*01_IGHJ4*01	778	1383	gnl|Fabrus|O1_IGKJ1*01	832	1437
900	gnl|Fabrus|VH5-51_IGHD3-3*01_IGHJ4*01	780	1385	gnl|Fabrus|O1_IGKJ1*01	832	1437
901	gnl|Fabrus|VH5-51_IGHD4-17*01_IGHJ4*01	781	1386	gnl|Fabrus|O1_IGKJ1*01	832	1437
902	gnl|Fabrus|VH5-51_IGHD5-18*01>3_IGHJ4*01	782	1387	gnl|Fabrus|O1_IGKJ1*01	832	1437
903	gnl|Fabrus|VH5-51_IGHD5-18*01>1_IGHJ4*01	783	1388	gnl|Fabrus|O1_IGKJ1*01	832	1437
904	gnl|Fabrus|VH5-51_IGHD6-25*01_IGHJ4*01	784	1389	gnl|Fabrus|O1_IGKJ1*01	832	1437
905	gnl|Fabrus|VH5-51_IGHD7-27*01_IGHJ4*01	785	1390	gnl|Fabrus|O1_IGKJ1*01	832	1437
906	gnl|Fabrus|VH6-1_IGHD1-1*01_IGHJ4*01	786	1391	gnl|Fabrus|O1_IGKJ1*01	832	1437
907	gnl|Fabrus|VH6-1_IGHD2-15*01_IGHJ4*01	788	1393	gnl|Fabrus|O1_IGKJ1*01	832	1437
908	gnl|Fabrus|VH6-1_IGHD3-3*01_IGHJ4*01	791	1396	gnl|Fabrus|O1_IGKJ1*01	832	1437
909	gnl|Fabrus|VH6-1_IGHD4-23*01_IGHJ4*01	793	1398	gnl|Fabrus|O1_IGKJ1*01	832	1437
910	gnl|Fabrus|VH6-1_IGHD4-11*01_IGHJ6*01	792	1397	gnl|Fabrus|O1_IGKJ1*01	832	1437
911	gnl|Fabrus|VH6-1_IGHD5-5*01_IGHJ4*01	794	1399	gnl|Fabrus|O1_IGKJ1*01	832	1437

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
912	gnl|Fabrus|VH6-1_IGHD6-13*01_IGHJ4*01	795	1400	gnl|Fabrus|O1_IGKJ1*01	832	1437
913	gnl|Fabrus|VH6-1_IGHD6-25*01_IGHJ6*01	796	1401	gnl|Fabrus|O1_IGKJ1*01	832	1437
914	gnl|Fabrus|VH6-1_IGHD7-27*01_IGHJ4*01	797	1402	gnl|Fabrus|O1_IGKJ1*01	832	1437
915	gnl|Fabrus|VH4-59_IGHD6-25*01_IGHJ3*01	775	1380	gnl|Fabrus|O1_IGKJ1*01	832	1437
916	gnl|Fabrus|VH3-48_IGHD6-6*01_IGHJ1*01	655	1260	gnl|Fabrus|O1_IGKJ1*01	832	1437
917	gnl|Fabrus|VH3-30_IGHD6-6*01_IGHJ1*01	625	1230	gnl|Fabrus|O1_IGKJ1*01	832	1437
918	gnl|Fabrus|VH3-66_IGHD6-6*01_IGHJ1*01	681	1286	gnl|Fabrus|O1_IGKJ1*01	832	1437
919	gnl|Fabrus|VH3-53_IGHD5-5*01_IGHJ4*01	670	1275	gnl|Fabrus|O1_IGKJ1*01	832	1437
920	gnl|Fabrus|VH2-5_IGHD5-12*01_IGHJ4*01	536	1141	gnl|Fabrus|O1_IGKJ1*01	832	1437
921	gnl|Fabrus|VH2-70_IGHD5-12*01_IGHJ4*01	543	1148	gnl|Fabrus|O1_IGKJ1*01	832	1437
922	gnl|Fabrus|VH3-15_IGHD5-12*01_IGHJ4*01	567	1172	gnl|Fabrus|O1_IGKJ1*01	832	1437
923	gnl|Fabrus|VH3-15_IGHD3-10*01_IGHJ4*01	565	1170	gnl|Fabrus|O1_IGKJ1*01	832	1437
924	gnl|Fabrus|VH3-49_IGHD5-18*01_IGHJ4*01	662	1267	gnl|Fabrus|O1_IGKJ1*01	832	1437
925	gnl|Fabrus|VH3-49_IGHD6-13*01_IGHJ4*01	663	1268	gnl|Fabrus|O1_IGKJ1*01	832	1437
926	gnl|Fabrus|VH3-72_IGHD5-18*01_IGHJ4*01	699	1304	gnl|Fabrus|O1_IGKJ1*01	832	1437
927	gnl|Fabrus|VH3-72_IGHD6-6*01_IGHJ1*01	701	1306	gnl|Fabrus|O1_IGKJ1*01	832	1437
928	gnl|Fabrus|VH3-73_IGHD5-12*01_IGHJ4*01	709	1314	gnl|Fabrus|O1_IGKJ1*01	832	1437
929	gnl|Fabrus|VH3-73_IGHD4-23*01_IGHJ5*01	708	1313	gnl|Fabrus|O1_IGKJ1*01	832	1437
930	gnl|Fabrus|VH3-43_IGHD3-22*01_IGHJ4*01	650	1255	gnl|Fabrus|O1_IGKJ1*01	832	1437
931	gnl|Fabrus|VH3-43_IGHD6-13*01_IGHJ4*01	653	1258	gnl|Fabrus|O1_IGKJ1*01	832	1437
932	gnl|Fabrus|VH3-9_IGHD3-22*01_IGHJ4*01	724	1329	gnl|Fabrus|O1_IGKJ1*01	832	1437
933	gnl|Fabrus|VH3-9_IGHD1-7*01_IGHJ5*01	721	1326	gnl|Fabrus|O1_IGKJ1*01	832	1437
934	gnl|Fabrus|VH3-9_IGHD6-13*01_IGHJ4*01	727	1332	gnl|Fabrus|O1_IGKJ1*01	832	1437

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
935	gnl|Fabrus|VH4-39_IGHD3-10*01_IGHJ4*01	762	1367	gnl|Fabrus|O1_IGKJ1*01	832	1437
936	gnl|Fabrus|VH4-39_IGHD5-12*01_IGHJ4*01	766	1371	gnl|Fabrus|O1_IGKJ1*01	832	1437
937	gnl|Fabrus|VH1-18_IGHD6-6*01_IGHJ1*01	460	1065	gnl|Fabrus|O1_IGKJ1*01	832	1437
938	gnl|Fabrus|VH1-24_IGHD5-12*01_IGHJ4*01	467	1072	gnl|Fabrus|O1_IGKJ1*01	832	1437
939	gnl|Fabrus|VH1-2_IGHD1-1*01_IGHJ3*01	461	1066	gnl|Fabrus|O1_IGKJ1*01	832	1437
940	gnl|Fabrus|VH1-3_IGHD6-6*01_IGHJ1*01	475	1080	gnl|Fabrus|O1_IGKJ1*01	832	1437
941	gnl|Fabrus|VH1-45_IGHD3-10*01_IGHJ4*01	480	1085	gnl|Fabrus|O1_IGKJ1*01	832	1437
942	gnl|Fabrus|VH1-46_IGHD1-26*01_IGHJ4*01	486	1091	gnl|Fabrus|O1_IGKJ1*01	832	1437
943	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ6*01	800	1405	gnl|Fabrus|O1_IGKJ1*01	832	1437
944	gnl|Fabrus|VH2-70_IGHD3-9*01_IGHJ6*01	542	1147	gnl|Fabrus|O1_IGKJ1*01	832	1437
945	gnl|Fabrus|VH1-58_IGHD3-10*01_IGHJ6*01	496	1101	gnl|Fabrus|O1_IGKJ1*01	832	1437
946	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ2*01	799	1404	gnl|Fabrus|O1_IGKJ1*01	832	1437
947	gnl|Fabrus|VH4-28_IGHD3-9*01_IGHJ6*01	734	1339	gnl|Fabrus|O1_IGKJ1*01	832	1437
948	gnl|Fabrus|VH4-31_IGHD2-15*01_IGHJ2*01	740	1345	gnl|Fabrus|O1_IGKJ1*01	832	1437
949	gnl|Fabrus|VH2-5_IGHD3-9*01_IGHJ6*01	535	1140	gnl|Fabrus|O1_IGKJ1*01	832	1437
950	gnl|Fabrus|VH1-8_IGHD2-15*01_IGHJ6*01	515	1120	gnl|Fabrus|O1_IGKJ1*01	832	1437
951	gnl|Fabrus|VH2-70_IGHD2-15*01_IGHJ2*01	540	1145	gnl|Fabrus|O1_IGKJ1*01	832	1437
952	gnl|Fabrus|VH3-38_IGHD3-10*01_IGHJ4*01	639	1244	gnl|Fabrus|O1_IGKJ1*01	832	1437
953	gnl|Fabrus|VH3-16_IGHD1-7*01_IGHJ6*01	570	1175	gnl|Fabrus|O1_IGKJ1*01	832	1437
954	gnl|Fabrus|VH3-73_IGHD3-9*01_IGHJ6*01	706	1311	gnl|Fabrus|O1_IGKJ1*01	832	1437
955	gnl|Fabrus|VH3-11_IGHD3-9*01_IGHJ6*01	548	1153	gnl|Fabrus|O1_IGKJ1*01	832	1437
956	gnl|Fabrus|VH3-11_IGHD6-6*01_IGHJ1*01	552	1157	gnl|Fabrus|O1_IGKJ1*01	832	1437
957	gnl|Fabrus|VH3-20_IGHD5-12*01_IGHJ4*01	584	1189	gnl|Fabrus|O1_IGKJ1*01	832	1437

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
958	gnl|Fabrus|VH3-16_IGHD2-15*01_IGHJ2*01	571	1176	gnl|Fabrus|O1_IGKJ1*01	832	1437
959	gnl|Fabrus|VH3-7_IGHD6-6*01_IGHJ1*01	692	1297	gnl|Fabrus|O1_IGKJ1*01	832	1437
960	gnl|Fabrus|VH3-16_IGHD6-13*01_IGHJ4*01	576	1181	gnl|Fabrus|O1_IGKJ1*01	832	1437
961	gnl|Fabrus|VH3-23_IGHD1-1*01_IGHJ4*01	595	1200	gnl|Fabrus|L25_IGKJ3*01	826	1431
962	gnl|Fabrus|VH3-23_IGHD2-15*01_IGHJ4*01	598	1203	gnl|Fabrus|L25_IGKJ3*01	826	1431
963	gnl|Fabrus|VH3-23_IGHD3-22*01_IGHJ4*01	602	1207	gnl|Fabrus|L25_IGKJ3*01	826	1431
964	gnl|Fabrus|VH3-23_IGHD4-11*01_IGHJ4*01	604	1209	gnl|Fabrus|L25_IGKJ3*01	826	1431
965	gnl|Fabrus|VH3-23_IGHD5-12*01_IGHJ4*01	606	1211	gnl|Fabrus|L25_IGKJ3*01	826	1431
966	gnl|Fabrus|VH3-23_IGHD5-5*01_IGHJ4*01	608	1213	gnl|Fabrus|L25_IGKJ3*01	826	1431
967	gnl|Fabrus|VH3-23_IGHD6-13*01_IGHJ4*01	609	1214	gnl|Fabrus|L25_IGKJ3*01	826	1431
968	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ4*01	612	1217	gnl|Fabrus|L25_IGKJ3*01	826	1431
969	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ6*01	613	1218	gnl|Fabrus|L25_IGKJ3*01	826	1431
970	gnl|Fabrus|VH1-69_IGHD1-14*01_IGHJ4*01	502	1107	gnl|Fabrus|L25_IGKJ3*01	826	1431
971	gnl|Fabrus|VH1-69_IGHD2-2*01_IGHJ4*01	503	1108	gnl|Fabrus|L25_IGKJ3*01	826	1431
972	gnl|Fabrus|VH1-69_IGHD2-8*01_IGHJ6*01	504	1109	gnl|Fabrus|L25_IGKJ3*01	826	1431
973	gnl|Fabrus|VH1-69_IGHD3-16*01_IGHJ4*01	505	1110	gnl|Fabrus|L25_IGKJ3*01	826	1431
974	gnl|Fabrus|VH1-69_IGHD3-3*01_IGHJ4*01	506	1111	gnl|Fabrus|L25_IGKJ3*01	826	1431
975	gnl|Fabrus|VH1-69_IGHD4-17*01_IGHJ4*01	508	1113	gnl|Fabrus|L25_IGKJ3*01	826	1431
976	gnl|Fabrus|VH1-69_IGHD5-12*01_IGHJ4*01	509	1114	gnl|Fabrus|L25_IGKJ3*01	826	1431
977	gnl|Fabrus|VH1-69_IGHD6-19*01_IGHJ4*01	511	1116	gnl|Fabrus|L25_IGKJ3*01	826	1431
978	gnl|Fabrus|VH1-69_IGHD7-27*01_IGHJ4*01	513	1118	gnl|Fabrus|L25_IGKJ3*01	826	1431
979	gnl|Fabrus|VH4-34_IGHD1-7*01_IGHJ4*01	749	1354	gnl|Fabrus|L25_IGKJ3*01	826	1431
980	gnl|Fabrus|VH4-34_IGHD2-2*01_IGHJ4*01	750	1355	gnl|Fabrus|L25_IGKJ3*01	826	1431

Table 17. Exemplary Nucleic Acid Paired Library						
	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
981	gnl|Fabrus|VH4-34_IGHD3-16*01_IGHJ4*01	751	1356	gnl|Fabrus|L25_IGKJ3*01	826	1431
982	gnl|Fabrus|VH4-34_IGHD4-17*01_IGHJ4*01	753	1358	gnl|Fabrus|L25_IGKJ3*01	826	1431
983	gnl|Fabrus|VH4-34_IGHD5-12*01_IGHJ4*01	754	1359	gnl|Fabrus|L25_IGKJ3*01	826	1431
984	gnl|Fabrus|VH4-34_IGHD6-13*01_IGHJ4*01	755	1360	gnl|Fabrus|L25_IGKJ3*01	826	1431
985	gnl|Fabrus|VH4-34_IGHD6-25*01_IGHJ6*01	756	1361	gnl|Fabrus|L25_IGKJ3*01	826	1431
986	gnl|Fabrus|VH4-34_IGHD7-27*01_IGHJ4*01	758	1363	gnl|Fabrus|L25_IGKJ3*01	826	1431
987	gnl|Fabrus|VH2-26_IGHD1-20*01_IGHJ4*01	521	1126	gnl|Fabrus|L25_IGKJ3*01	826	1431
988	gnl|Fabrus|VH2-26_IGHD2-2*01_IGHJ4*01	523	1128	gnl|Fabrus|L25_IGKJ3*01	826	1431
989	gnl|Fabrus|VH2-26_IGHD3-10*01_IGHJ4*01	524	1129	gnl|Fabrus|L25_IGKJ3*01	826	1431
990	gnl|Fabrus|VH2-26_IGHD4-11*01_IGHJ4*01	526	1131	gnl|Fabrus|L25_IGKJ3*01	826	1431
991	gnl|Fabrus|VH2-26_IGHD5-18*01_IGHJ4*01	528	1133	gnl|Fabrus|L25_IGKJ3*01	826	1431
992	gnl|Fabrus|VH2-26_IGHD6-13*01_IGHJ4*01	529	1134	gnl|Fabrus|L25_IGKJ3*01	826	1431
993	gnl|Fabrus|VH2-26_IGHD7-27*01_IGHJ4*01	530	1135	gnl|Fabrus|L25_IGKJ3*01	826	1431
994	gnl|Fabrus|VH5-51_IGHD1-14*01_IGHJ4*01	776	1381	gnl|Fabrus|L25_IGKJ3*01	826	1431
995	gnl|Fabrus|VH5-51_IGHD2-8*01_IGHJ4*01	778	1383	gnl|Fabrus|L25_IGKJ3*01	826	1431
996	gnl|Fabrus|VH5-51_IGHD3-3*01_IGHJ4*01	780	1385	gnl|Fabrus|L25_IGKJ3*01	826	1431
997	gnl|Fabrus|VH5-51_IGHD4-17*01_IGHJ4*01	781	1386	gnl|Fabrus|L25_IGKJ3*01	826	1431
998	gnl|Fabrus|VH5-51_IGHD5-18*01>3_IGHJ4*01	782	1387	gnl|Fabrus|L25_IGKJ3*01	826	1431
999	gnl|Fabrus|VH5-51_IGHD5-18*01>1_IGHJ4*01	783	1388	gnl|Fabrus|L25_IGKJ3*01	826	1431
1000	gnl|Fabrus|VH5-51_IGHD6-25*01_IGHJ4*01	784	1389	gnl|Fabrus|L25_IGKJ3*01	826	1431
1001	gnl|Fabrus|VH5-51_IGHD7-27*01_IGHJ4*01	785	1390	gnl|Fabrus|L25_IGKJ3*01	826	1431
1002	gnl|Fabrus|VH6-1_IGHD1-1*01_IGHJ4*01	786	1391	gnl|Fabrus|L25_IGKJ3*01	826	1431
1003	gnl|Fabrus|VH6-1_IGHD2-15*01_IGHJ4*01	788	1393	gnl|Fabrus|L25_IGKJ3*01	826	1431

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
1004	gnl|Fabrus|VH6-1_IGHD3-3*01_IGHJ4*01	791	1396	gnl|Fabrus|L25_IGKJ3*01	826	1431
1005	gnl|Fabrus|VH6-1_IGHD4-23*01_IGHJ4*01	793	1398	gnl|Fabrus|L25_IGKJ3*01	826	1431
1006	gnl|Fabrus|VH6-1_IGHD4-11*01_IGHJ6*01	792	1397	gnl|Fabrus|L25_IGKJ3*01	826	1431
1007	gnl|Fabrus|VH6-1_IGHD5-5*01_IGHJ4*01	794	1399	gnl|Fabrus|L25_IGKJ3*01	826	1431
1008	gnl|Fabrus|VH6-1_IGHD6-13*01_IGHJ4*01	795	1400	gnl|Fabrus|L25_IGKJ3*01	826	1431
1009	gnl|Fabrus|VH6-1_IGHD6-25*01_IGHJ6*01	796	1401	gnl|Fabrus|L25_IGKJ3*01	826	1431
1010	gnl|Fabrus|VH6-1_IGHD7-27*01_IGHJ4*01	797	1402	gnl|Fabrus|L25_IGKJ3*01	826	1431
1011	gnl|Fabrus|VH4-59_IGHD6-25*01_IGHJ3*01	775	1380	gnl|Fabrus|L25_IGKJ3*01	826	1431
1012	gnl|Fabrus|VH3-48_IGHD6-6*01_IGHJ1*01	655	1260	gnl|Fabrus|L25_IGKJ3*01	826	1431
1013	gnl|Fabrus|VH3-30_IGHD6-6*01_IGHJ1*01	625	1230	gnl|Fabrus|L25_IGKJ3*01	826	1431
1014	gnl|Fabrus|VH3-66_IGHD6-6*01_IGHJ1*01	681	1286	gnl|Fabrus|L25_IGKJ3*01	826	1431
1015	gnl|Fabrus|VH3-53_IGHD5-5*01_IGHJ4*01	670	1275	gnl|Fabrus|L25_IGKJ3*01	826	1431
1016	gnl|Fabrus|VH2-5_IGHD5-12*01_IGHJ4*01	536	1141	gnl|Fabrus|L25_IGKJ3*01	826	1431
1017	gnl|Fabrus|VH2-70_IGHD5-12*01_IGHJ4*01	543	1148	gnl|Fabrus|L25_IGKJ3*01	826	1431
1018	gnl|Fabrus|VH3-15_IGHD5-12*01_IGHJ4*01	567	1172	gnl|Fabrus|L25_IGKJ3*01	826	1431
1019	gnl|Fabrus|VH3-15_IGHD3-10*01_IGHJ4*01	565	1170	gnl|Fabrus|L25_IGKJ3*01	826	1431
1020	gnl|Fabrus|VH3-49_IGHD5-18*01_IGHJ4*01	662	1267	gnl|Fabrus|L25_IGKJ3*01	826	1431
1021	gnl|Fabrus|VH3-49_IGHD6-13*01_IGHJ4*01	663	1268	gnl|Fabrus|L25_IGKJ3*01	826	1431
1022	gnl|Fabrus|VH3-72_IGHD5-18*01_IGHJ4*01	699	1304	gnl|Fabrus|L25_IGKJ3*01	826	1431
1023	gnl|Fabrus|VH3-72_IGHD6-6*01_IGHJ1*01	701	1306	gnl|Fabrus|L25_IGKJ3*01	826	1431
1024	gnl|Fabrus|VH3-73_IGHD5-12*01_IGHJ4*01	709	1314	gnl|Fabrus|L25_IGKJ3*01	826	1431
1025	gnl|Fabrus|VH3-73_IGHD4-23*01_IGHJ5*01	708	1313	gnl|Fabrus|L25_IGKJ3*01	826	1431
1026	gnl|Fabrus|VH3-43_IGHD3-22*01_IGHJ4*01	650	1255	gnl|Fabrus|L25_IGKJ3*01	826	1431

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
1027	gnl|Fabrus|VH3-43_IGHD6-13*01_IGHJ4*01	653	1258	gnl|Fabrus|L25_IGKJ3*01	826	1431
1028	gnl|Fabrus|VH3-9_IGHD3-22*01_IGHJ4*01	724	1329	gnl|Fabrus|L25_IGKJ3*01	826	1431
1029	gnl|Fabrus|VH3-9_IGHD1-7*01_IGHJ5*01	721	1326	gnl|Fabrus|L25_IGKJ3*01	826	1431
1030	gnl|Fabrus|VH3-9_IGHD6-13*01_IGHJ4*01	727	1332	gnl|Fabrus|L25_IGKJ3*01	826	1431
1031	gnl|Fabrus|VH4-39_IGHD3-10*01_IGHJ4*01	762	1367	gnl|Fabrus|L25_IGKJ3*01	826	1431
1032	gnl|Fabrus|VH4-39_IGHD5-12*01_IGHJ4*01	766	1371	gnl|Fabrus|L25_IGKJ3*01	826	1431
1033	gnl|Fabrus|VH1-18_IGHD6-6*01_IGHJ1*01	460	1065	gnl|Fabrus|L25_IGKJ3*01	826	1431
1034	gnl|Fabrus|VH1-24_IGHD5-12*01_IGHJ4*01	467	1072	gnl|Fabrus|L25_IGKJ3*01	826	1431
1035	gnl|Fabrus|VH1-2_IGHD1-1*01_IGHJ3*01	461	1066	gnl|Fabrus|L25_IGKJ3*01	826	1431
1036	gnl|Fabrus|VH1-3_IGHD6-6*01_IGHJ1*01	475	1080	gnl|Fabrus|L25_IGKJ3*01	826	1431
1037	gnl|Fabrus|VH1-45_IGHD3-10*01_IGHJ4*01	480	1085	gnl|Fabrus|L25_IGKJ3*01	826	1431
1038	gnl|Fabrus|VH1-46_IGHD1-26*01_IGHJ4*01	486	1091	gnl|Fabrus|L25_IGKJ3*01	826	1431
1039	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ6*01	800	1405	gnl|Fabrus|L25_IGKJ3*01	826	1431
1040	gnl|Fabrus|VH2-70_IGHD3-9*01_IGHJ6*01	542	1147	gnl|Fabrus|L25_IGKJ3*01	826	1431
1041	gnl|Fabrus|VH1-58_IGHD3-10*01_IGHJ6*01	496	1101	gnl|Fabrus|L25_IGKJ3*01	826	1431
1042	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ2*01	799	1404	gnl|Fabrus|L25_IGKJ3*01	826	1431
1043	gnl|Fabrus|VH4-28_IGHD3-9*01_IGHJ6*01	734	1339	gnl|Fabrus|L25_IGKJ3*01	826	1431
1044	gnl|Fabrus|VH4-31_IGHD2-15*01_IGHJ2*01	740	1345	gnl|Fabrus|L25_IGKJ3*01	826	1431
1045	gnl|Fabrus|VH2-5_IGHD3-9*01_IGHJ6*01	535	1140	gnl|Fabrus|L25_IGKJ3*01	826	1431
1046	gnl|Fabrus|VH1-8_IGHD2-15*01_IGHJ6*01	515	1120	gnl|Fabrus|L25_IGKJ3*01	826	1431
1047	gnl|Fabrus|VH2-70_IGHD2-15*01_IGHJ2*01	540	1145	gnl|Fabrus|L25_IGKJ3*01	826	1431
1048	gnl|Fabrus|VH3-38_IGHD3-10*01_IGHJ4*01	639	1244	gnl|Fabrus|L25_IGKJ3*01	826	1431
1049	gnl|Fabrus|VH3-16_IGHD1-7*01_IGHJ6*01	570	1175	gnl|Fabrus|L25_IGKJ3*01	826	1431

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
1050	gnl|Fabrus|VH3-73_IGHD3-9*01_IGHJ6*01	706	1311	gnl|Fabrus|L25_IGKJ3*01	826	1431
1051	gnl|Fabrus|VH3-11_IGHD3-9*01_IGHJ6*01	548	1153	gnl|Fabrus|L25_IGKJ3*01	826	1431
1052	gnl|Fabrus|VH3-11_IGHD6-6*01_IGHJ1*01	552	1157	gnl|Fabrus|L25_IGKJ3*01	826	1431
1053	gnl|Fabrus|VH3-20_IGHD5-12*01_IGHJ4*01	584	1189	gnl|Fabrus|L25_IGKJ3*01	826	1431
1054	gnl|Fabrus|VH3-16_IGHD2-15*01_IGHJ2*01	571	1176	gnl|Fabrus|L25_IGKJ3*01	826	1431
1055	gnl|Fabrus|VH3-7_IGHD6-6*01_IGHJ1*01	692	1297	gnl|Fabrus|L25_IGKJ3*01	826	1431
1056	gnl|Fabrus|VH3-16_IGHD6-13*01_IGHJ4*01	576	1181	gnl|Fabrus|L25_IGKJ3*01	826	1431
1057	gnl|Fabrus|VH3-23_IGHD1-1*01_IGHJ4*01	595	1200	gnl|Fabrus|A27_IGKJ1*01	812	1417
1058	gnl|Fabrus|VH3-23_IGHD2-15*01_IGHJ4*01	598	1203	gnl|Fabrus|A27_IGKJ1*01	812	1417
1059	gnl|Fabrus|VH3-23_IGHD3-22*01_IGHJ4*01	602	1207	gnl|Fabrus|A27_IGKJ1*01	812	1417
1060	gnl|Fabrus|VH3-23_IGHD4-11*01_IGHJ4*01	604	1209	gnl|Fabrus|A27_IGKJ1*01	812	1417
1061	gnl|Fabrus|VH3-23_IGHD5-12*01_IGHJ4*01	606	1211	gnl|Fabrus|A27_IGKJ1*01	812	1417
1062	gnl|Fabrus|VH3-23_IGHD5-5*01_IGHJ4*01	608	1213	gnl|Fabrus|A27_IGKJ1*01	812	1417
1063	gnl|Fabrus|VH3-23_IGHD6-13*01_IGHJ4*01	609	1214	gnl|Fabrus|A27_IGKJ1*01	812	1417
1064	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ4*01	612	1217	gnl|Fabrus|A27_IGKJ1*01	812	1417
1065	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ6*01	613	1218	gnl|Fabrus|A27_IGKJ1*01	812	1417
1066	gnl|Fabrus|VH1-69_IGHD1-14*01_IGHJ4*01	502	1107	gnl|Fabrus|A27_IGKJ1*01	812	1417
1067	gnl|Fabrus|VH1-69_IGHD2-2*01_IGHJ4*01	503	1108	gnl|Fabrus|A27_IGKJ1*01	812	1417
1068	gnl|Fabrus|VH1-69_IGHD2-8*01_IGHJ6*01	504	1109	gnl|Fabrus|A27_IGKJ1*01	812	1417
1069	gnl|Fabrus|VH1-69_IGHD3-16*01_IGHJ4*01	505	1110	gnl|Fabrus|A27_IGKJ1*01	812	1417
1070	gnl|Fabrus|VH1-69_IGHD3-3*01_IGHJ4*01	506	1111	gnl|Fabrus|A27_IGKJ1*01	812	1417
1071	gnl|Fabrus|VH1-69_IGHD4-17*01_IGHJ4*01	508	1113	gnl|Fabrus|A27_IGKJ1*01	812	1417
1072	gnl|Fabrus|VH1-69_IGHD5-12*01_IGHJ4*01	509	1114	gnl|Fabrus|A27_IGKJ1*01	812	1417

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
1073	gnl|Fabrus|VH1-69_IGHD6-19*01_IGHJ4*01	511	1116	gnl|Fabrus|A27_IGKJ1*01	812	1417
1074	gnl|Fabrus|VH1-69_IGHD7-27*01_IGHJ4*01	513	1118	gnl|Fabrus|A27_IGKJ1*01	812	1417
1075	gnl|Fabrus|VH4-34_IGHD1-7*01_IGHJ4*01	749	1354	gnl|Fabrus|A27_IGKJ1*01	812	1417
1076	gnl|Fabrus|VH4-34_IGHD2-2*01_IGHJ4*01	750	1355	gnl|Fabrus|A27_IGKJ1*01	812	1417
1077	gnl|Fabrus|VH4-34_IGHD3-16*01_IGHJ4*01	751	1356	gnl|Fabrus|A27_IGKJ1*01	812	1417
1078	gnl|Fabrus|VH4-34_IGHD4-17*01_IGHJ4*01	753	1358	gnl|Fabrus|A27_IGKJ1*01	812	1417
1079	gnl|Fabrus|VH4-34_IGHD5-12*01_IGHJ4*01	754	1359	gnl|Fabrus|A27_IGKJ1*01	812	1417
1080	gnl|Fabrus|VH4-34_IGHD6-13*01_IGHJ4*01	755	1360	gnl|Fabrus|A27_IGKJ1*01	812	1417
1081	gnl|Fabrus|VH4-34_IGHD6-25*01_IGHJ6*01	756	1361	gnl|Fabrus|A27_IGKJ1*01	812	1417
1082	gnl|Fabrus|VH4-34_IGHD7-27*01_IGHJ4*01	758	1363	gnl|Fabrus|A27_IGKJ1*01	812	1417
1083	gnl|Fabrus|VH2-26_IGHD1-20*01_IGHJ4*01	521	1126	gnl|Fabrus|A27_IGKJ1*01	812	1417
1084	gnl|Fabrus|VH2-26_IGHD2-2*01_IGHJ4*01	523	1128	gnl|Fabrus|A27_IGKJ1*01	812	1417
1085	gnl|Fabrus|VH2-26_IGHD3-10*01_IGHJ4*01	524	1129	gnl|Fabrus|A27_IGKJ1*01	812	1417
1086	gnl|Fabrus|VH2-26_IGHD4-11*01_IGHJ4*01	526	1131	gnl|Fabrus|A27_IGKJ1*01	812	1417
1087	gnl|Fabrus|VH2-26_IGHD5-18*01_IGHJ4*01	528	1133	gnl|Fabrus|A27_IGKJ1*01	812	1417
1088	gnl|Fabrus|VH2-26_IGHD6-13*01_IGHJ4*01	529	1134	gnl|Fabrus|A27_IGKJ1*01	812	1417
1089	gnl|Fabrus|VH2-26_IGHD7-27*01_IGHJ4*01	530	1135	gnl|Fabrus|A27_IGKJ1*01	812	1417
1090	gnl|Fabrus|VH5-51_IGHD1-14*01_IGHJ4*01	776	1381	gnl|Fabrus|A27_IGKJ1*01	812	1417
1091	gnl|Fabrus|VH5-51_IGHD2-8*01_IGHJ4*01	778	1383	gnl|Fabrus|A27_IGKJ1*01	812	1417
1092	gnl|Fabrus|VH5-51_IGHD3-3*01_IGHJ4*01	780	1385	gnl|Fabrus|A27_IGKJ1*01	812	1417
1093	gnl|Fabrus|VH5-51_IGHD4-17*01_IGHJ4*01	781	1386	gnl|Fabrus|A27_IGKJ1*01	812	1417
1094	gnl|Fabrus|VH5-51_IGHD5-18*01>3_IGHJ4*01	782	1387	gnl|Fabrus|A27_IGKJ1*01	812	1417
1095	gnl|Fabrus|VH5-51_IGHD5-18*01>1_IGHJ4*01	783	1388	gnl|Fabrus|A27_IGKJ1*01	812	1417

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
1096	gnl|Fabrus|VH5-51_IGHD6-25*01_IGHJ4*01	784	1389	gnl|Fabrus|A27_IGKJ1*01	812	1417
1097	gnl|Fabrus|VH5-51_IGHD7-27*01_IGHJ4*01	785	1390	gnl|Fabrus|A27_IGKJ1*01	812	1417
1098	gnl|Fabrus|VH6-1_IGHD1-1*01_IGHJ4*01	786	1391	gnl|Fabrus|A27_IGKJ1*01	812	1417
1099	gnl|Fabrus|VH6-1_IGHD2-15*01_IGHJ4*01	788	1393	gnl|Fabrus|A27_IGKJ1*01	812	1417
1100	gnl|Fabrus|VH6-1_IGHD3-3*01_IGHJ4*01	791	1396	gnl|Fabrus|A27_IGKJ1*01	812	1417
1101	gnl|Fabrus|VH6-1_IGHD4-23*01_IGHJ4*01	793	1398	gnl|Fabrus|A27_IGKJ1*01	812	1417
1102	gnl|Fabrus|VH6-1_IGHD4-11*01_IGHJ6*01	792	1397	gnl|Fabrus|A27_IGKJ1*01	812	1417
1103	gnl|Fabrus|VH6-1_IGHD5-5*01_IGHJ4*01	794	1399	gnl|Fabrus|A27_IGKJ1*01	812	1417
1104	gnl|Fabrus|VH6-1_IGHD6-13*01_IGHJ4*01	795	1400	gnl|Fabrus|A27_IGKJ1*01	812	1417
1105	gnl|Fabrus|VH6-1_IGHD6-25*01_IGHJ6*01	796	1401	gnl|Fabrus|A27_IGKJ1*01	812	1417
1106	gnl|Fabrus|VH6-1_IGHD7-27*01_IGHJ4*01	797	1402	gnl|Fabrus|A27_IGKJ1*01	812	1417
1107	gnl|Fabrus|VH4-59_IGHD6-25*01_IGHJ3*01	775	1380	gnl|Fabrus|A27_IGKJ1*01	812	1417
1108	gnl|Fabrus|VH3-48_IGHD6-6*01_IGHJ1*01	655	1260	gnl|Fabrus|A27_IGKJ1*01	812	1417
1109	gnl|Fabrus|VH3-30_IGHD6-6*01_IGHJ1*01	625	1230	gnl|Fabrus|A27_IGKJ1*01	812	1417
1110	gnl|Fabrus|VH3-66_IGHD6-6*01_IGHJ1*01	681	1286	gnl|Fabrus|A27_IGKJ1*01	812	1417
1111	gnl|Fabrus|VH3-53_IGHD5-5*01_IGHJ4*01	670	1275	gnl|Fabrus|A27_IGKJ1*01	812	1417
1112	gnl|Fabrus|VH2-5_IGHD5-12*01_IGHJ4*01	536	1141	gnl|Fabrus|A27_IGKJ1*01	812	1417
1113	gnl|Fabrus|VH2-70_IGHD5-12*01_IGHJ4*01	543	1148	gnl|Fabrus|A27_IGKJ1*01	812	1417
1114	gnl|Fabrus|VH3-15_IGHD5-12*01_IGHJ4*01	567	1172	gnl|Fabrus|A27_IGKJ1*01	812	1417
1115	gnl|Fabrus|VH3-15_IGHD3-10*01_IGHJ4*01	565	1170	gnl|Fabrus|A27_IGKJ1*01	812	1417
1116	gnl|Fabrus|VH3-49_IGHD5-18*01_IGHJ4*01	662	1267	gnl|Fabrus|A27_IGKJ1*01	812	1417
1117	gnl|Fabrus|VH3-49_IGHD6-13*01_IGHJ4*01	663	1268	gnl|Fabrus|A27_IGKJ1*01	812	1417
1118	gnl|Fabrus|VH3-72_IGHD5-18*01_IGHJ4*01	699	1304	gnl|Fabrus|A27_IGKJ1*01	812	1417

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
1119	gnl|Fabrus|VH3-72_IGHD6-6*01_IGHJ1*01	701	1306	gnl|Fabrus|A27_IGKJ1*01	812	1417
1120	gnl|Fabrus|VH3-73_IGHD5-12*01_IGHJ4*01	709	1314	gnl|Fabrus|A27_IGKJ1*01	812	1417
1121	gnl|Fabrus|VH3-73_IGHD4-23*01_IGHJ5*01	708	1313	gnl|Fabrus|A27_IGKJ1*01	812	1417
1122	gnl|Fabrus|VH3-43_IGHD3-22*01_IGHJ4*01	650	1255	gnl|Fabrus|A27_IGKJ1*01	812	1417
1123	gnl|Fabrus|VH3-43_IGHD6-13*01_IGHJ4*01	653	1258	gnl|Fabrus|A27_IGKJ1*01	812	1417
1124	gnl|Fabrus|VH3-9_IGHD3-22*01_IGHJ4*01	724	1329	gnl|Fabrus|A27_IGKJ1*01	812	1417
1125	gnl|Fabrus|VH3-9_IGHD1-7*01_IGHJ5*01	721	1326	gnl|Fabrus|A27_IGKJ1*01	812	1417
1126	gnl|Fabrus|VH3-9_IGHD6-13*01_IGHJ4*01	727	1332	gnl|Fabrus|A27_IGKJ1*01	812	1417
1127	gnl|Fabrus|VH4-39_IGHD3-10*01_IGHJ4*01	762	1367	gnl|Fabrus|A27_IGKJ1*01	812	1417
1128	gnl|Fabrus|VH4-39_IGHD5-12*01_IGHJ4*01	766	1371	gnl|Fabrus|A27_IGKJ1*01	812	1417
1129	gnl|Fabrus|VH1-18_IGHD6-6*01_IGHJ1*01	460	1065	gnl|Fabrus|A27_IGKJ1*01	812	1417
1130	gnl|Fabrus|VH1-24_IGHD5-12*01_IGHJ4*01	467	1072	gnl|Fabrus|A27_IGKJ1*01	812	1417
1131	gnl|Fabrus|VH1-2_IGHD1-1*01_IGHJ3*01	461	1066	gnl|Fabrus|A27_IGKJ1*01	812	1417
1132	gnl|Fabrus|VH1-3_IGHD6-6*01_IGHJ1*01	475	1080	gnl|Fabrus|A27_IGKJ1*01	812	1417
1133	gnl|Fabrus|VH1-45_IGHD3-10*01_IGHJ4*01	480	1085	gnl|Fabrus|A27_IGKJ1*01	812	1417
1134	gnl|Fabrus|VH1-46_IGHD1-26*01_IGHJ4*01	486	1091	gnl|Fabrus|A27_IGKJ1*01	812	1417
1135	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ6*01	800	1405	gnl|Fabrus|A27_IGKJ1*01	812	1417
1136	gnl|Fabrus|VH2-70_IGHD3-9*01_IGHJ6*01	542	1147	gnl|Fabrus|A27_IGKJ1*01	812	1417
1137	gnl|Fabrus|VH1-58_IGHD3-10*01_IGHJ6*01	496	1101	gnl|Fabrus|A27_IGKJ1*01	812	1417
1138	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ2*01	799	1404	gnl|Fabrus|A27_IGKJ1*01	812	1417
1139	gnl|Fabrus|VH4-28_IGHD3-9*01_IGHJ6*01	734	1339	gnl|Fabrus|A27_IGKJ1*01	812	1417
1140	gnl|Fabrus|VH4-31_IGHD2-15*01_IGHJ2*01	740	1345	gnl|Fabrus|A27_IGKJ1*01	812	1417
1141	gnl|Fabrus|VH2-5_IGHD3-9*01_IGHJ6*01	535	1140	gnl|Fabrus|A27_IGKJ1*01	812	1417

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
1142	gnl|Fabrus|VH1-8_IGHD2-15*01_IGHJ6*01	515	1120	gnl|Fabrus|A27_IGKJ1*01	812	1417
1143	gnl|Fabrus|VH2-70_IGHD2-15*01_IGHJ2*01	540	1145	gnl|Fabrus|A27_IGKJ1*01	812	1417
1144	gnl|Fabrus|VH3-38_IGHD3-10*01_IGHJ4*01	639	1244	gnl|Fabrus|A27_IGKJ1*01	812	1417
1145	gnl|Fabrus|VH3-16_IGHD1-7*01_IGHJ6*01	570	1175	gnl|Fabrus|A27_IGKJ1*01	812	1417
1146	gnl|Fabrus|VH3-73_IGHD3-9*01_IGHJ6*01	706	1311	gnl|Fabrus|A27_IGKJ1*01	812	1417
1147	gnl|Fabrus|VH3-11_IGHD3-9*01_IGHJ6*01	548	1153	gnl|Fabrus|A27_IGKJ1*01	812	1417
1148	gnl|Fabrus|VH3-11_IGHD6-6*01_IGHJ1*01	552	1157	gnl|Fabrus|A27_IGKJ1*01	812	1417
1149	gnl|Fabrus|VH3-20_IGHD5-12*01_IGHJ4*01	584	1189	gnl|Fabrus|A27_IGKJ1*01	812	1417
1150	gnl|Fabrus|VH3-16_IGHD2-15*01_IGHJ2*01	571	1176	gnl|Fabrus|A27_IGKJ1*01	812	1417
1151	gnl|Fabrus|VH3-7_IGHD6-6*01_IGHJ1*01	692	1297	gnl|Fabrus|A27_IGKJ1*01	812	1417
1152	gnl|Fabrus|VH3-16_IGHD6-13*01_IGHJ4*01	576	1181	gnl|Fabrus|A27_IGKJ1*01	812	1417
1153	gnl|Fabrus|VH3-23_IGHD1-1*01_IGHJ4*01	595	1200	gnl|Fabrus|A2_IGKJ1*01	808	1413
1154	gnl|Fabrus|VH3-23_IGHD2-15*01_IGHJ4*01	598	1203	gnl|Fabrus|A2_IGKJ1*01	808	1413
1155	gnl|Fabrus|VH3-23_IGHD3-22*01_IGHJ4*01	602	1207	gnl|Fabrus|A2_IGKJ1*01	808	1413
1156	gnl|Fabrus|VH3-23_IGHD4-11*01_IGHJ4*01	604	1209	gnl|Fabrus|A2_IGKJ1*01	808	1413
1157	gnl|Fabrus|VH3-23_IGHD5-12*01_IGHJ4*01	606	1211	gnl|Fabrus|A2_IGKJ1*01	808	1413
1158	gnl|Fabrus|VH3-23_IGHD5-5*01_IGHJ4*01	608	1213	gnl|Fabrus|A2_IGKJ1*01	808	1413
1159	gnl|Fabrus|VH3-23_IGHD6-13*01_IGHJ4*01	609	1214	gnl|Fabrus|A2_IGKJ1*01	808	1413
1160	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ4*01	612	1217	gnl|Fabrus|A2_IGKJ1*01	808	1413
1161	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ6*01	613	1218	gnl|Fabrus|A2_IGKJ1*01	808	1413
1162	gnl|Fabrus|VH1-69_IGHD1-14*01_IGHJ4*01	502	1107	gnl|Fabrus|A2_IGKJ1*01	808	1413
1163	gnl|Fabrus|VH1-69_IGHD2-2*01_IGHJ4*01	503	1108	gnl|Fabrus|A2_IGKJ1*01	808	1413
1164	gnl|Fabrus|VH1-69_IGHD2-8*01_IGHJ6*01	504	1109	gnl|Fabrus|A2_IGKJ1*01	808	1413

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
1165	gnl|Fabrus|VH1-69_IGHD3-16*01_IGHJ4*01	505	1110	gnl|Fabrus|A2_IGKJ1*01	808	1413
1166	gnl|Fabrus|VH1-69_IGHD3-3*01_IGHJ4*01	506	1111	gnl|Fabrus|A2_IGKJ1*01	808	1413
1167	gnl|Fabrus|VH1-69_IGHD4-17*01_IGHJ4*01	508	1113	gnl|Fabrus|A2_IGKJ1*01	808	1413
1168	gnl|Fabrus|VH1-69_IGHD5-12*01_IGHJ4*01	509	1114	gnl|Fabrus|A2_IGKJ1*01	808	1413
1169	gnl|Fabrus|VH1-69_IGHD6-19*01_IGHJ4*01	511	1116	gnl|Fabrus|A2_IGKJ1*01	808	1413
1170	gnl|Fabrus|VH1-69_IGHD7-27*01_IGHJ4*01	513	1118	gnl|Fabrus|A2_IGKJ1*01	808	1413
1171	gnl|Fabrus|VH4-34_IGHD1-7*01_IGHJ4*01	749	1354	gnl|Fabrus|A2_IGKJ1*01	808	1413
1172	gnl|Fabrus|VH4-34_IGHD2-2*01_IGHJ4*01	750	1355	gnl|Fabrus|A2_IGKJ1*01	808	1413
1173	gnl|Fabrus|VH4-34_IGHD3-16*01_IGHJ4*01	751	1356	gnl|Fabrus|A2_IGKJ1*01	808	1413
1174	gnl|Fabrus|VH4-34_IGHD4-17*01_IGHJ4*01	753	1358	gnl|Fabrus|A2_IGKJ1*01	808	1413
1175	gnl|Fabrus|VH4-34_IGHD5-12*01_IGHJ4*01	754	1359	gnl|Fabrus|A2_IGKJ1*01	808	1413
1176	gnl|Fabrus|VH4-34_IGHD6-13*01_IGHJ4*01	755	1360	gnl|Fabrus|A2_IGKJ1*01	808	1413
1177	gnl|Fabrus|VH4-34_IGHD6-25*01_IGHJ6*01	756	1361	gnl|Fabrus|A2_IGKJ1*01	808	1413
1178	gnl|Fabrus|VH4-34_IGHD7-27*01_IGHJ4*01	758	1363	gnl|Fabrus|A2_IGKJ1*01	808	1413
1179	gnl|Fabrus|VH2-26_IGHD1-20*01_IGHJ4*01	521	1126	gnl|Fabrus|A2_IGKJ1*01	808	1413
1180	gnl|Fabrus|VH2-26_IGHD2-2*01_IGHJ4*01	523	1128	gnl|Fabrus|A2_IGKJ1*01	808	1413
1181	gnl|Fabrus|VH2-26_IGHD3-10*01_IGHJ4*01	524	1129	gnl|Fabrus|A2_IGKJ1*01	808	1413
1182	gnl|Fabrus|VH2-26_IGHD4-11*01_IGHJ4*01	526	1131	gnl|Fabrus|A2_IGKJ1*01	808	1413
1183	gnl|Fabrus|VH2-26_IGHD5-18*01_IGHJ4*01	528	1133	gnl|Fabrus|A2_IGKJ1*01	808	1413
1184	gnl|Fabrus|VH2-26_IGHD6-13*01_IGHJ4*01	529	1134	gnl|Fabrus|A2_IGKJ1*01	808	1413
1185	gnl|Fabrus|VH2-26_IGHD7-27*01_IGHJ4*01	530	1135	gnl|Fabrus|A2_IGKJ1*01	808	1413
1186	gnl|Fabrus|VH5-51_IGHD1-14*01_IGHJ4*01	776	1381	gnl|Fabrus|A2_IGKJ1*01	808	1413
1187	gnl|Fabrus|VH5-51_IGHD2-8*01_IGHJ4*01	778	1383	gnl|Fabrus|A2_IGKJ1*01	808	1413

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
1188	gnl|Fabrus|VH5-51_IGHD3-3*01_IGHJ4*01	780	1385	gnl|Fabrus|A2_IGKJ1*01	808	1413
1189	gnl|Fabrus|VH5-51_IGHD4-17*01_IGHJ4*01	781	1386	gnl|Fabrus|A2_IGKJ1*01	808	1413
1190	gnl|Fabrus|VH5-51_IGHD5-18*01>3_IGHJ4*01	782	1387	gnl|Fabrus|A2_IGKJ1*01	808	1413
1191	gnl|Fabrus|VH5-51_IGHD5-18*01>1_IGHJ4*01	783	1388	gnl|Fabrus|A2_IGKJ1*01	808	1413
1192	gnl|Fabrus|VH5-51_IGHD6-25*01_IGHJ4*01	784	1389	gnl|Fabrus|A2_IGKJ1*01	808	1413
1193	gnl|Fabrus|VH5-51_IGHD7-27*01_IGHJ4*01	785	1390	gnl|Fabrus|A2_IGKJ1*01	808	1413
1194	gnl|Fabrus|VH6-1_IGHD1-1*01_IGHJ4*01	786	1391	gnl|Fabrus|A2_IGKJ1*01	808	1413
1195	gnl|Fabrus|VH6-1_IGHD2-15*01_IGHJ4*01	788	1393	gnl|Fabrus|A2_IGKJ1*01	808	1413
1196	gnl|Fabrus|VH6-1_IGHD3-3*01_IGHJ4*01	791	1396	gnl|Fabrus|A2_IGKJ1*01	808	1413
1197	gnl|Fabrus|VH6-1_IGHD4-23*01_IGHJ4*01	793	1398	gnl|Fabrus|A2_IGKJ1*01	808	1413
1198	gnl|Fabrus|VH6-1_IGHD4-11*01_IGHJ6*01	792	1397	gnl|Fabrus|A2_IGKJ1*01	808	1413
1199	gnl|Fabrus|VH6-1_IGHD5-5*01_IGHJ4*01	794	1399	gnl|Fabrus|A2_IGKJ1*01	808	1413
1200	gnl|Fabrus|VH6-1_IGHD6-13*01_IGHJ4*01	795	1400	gnl|Fabrus|A2_IGKJ1*01	808	1413
1201	gnl|Fabrus|VH6-1_IGHD6-25*01_IGHJ6*01	796	1401	gnl|Fabrus|A2_IGKJ1*01	808	1413
1202	gnl|Fabrus|VH6-1_IGHD7-27*01_IGHJ4*01	797	1402	gnl|Fabrus|A2_IGKJ1*01	808	1413
1203	gnl|Fabrus|VH4-59_IGHD6-25*01_IGHJ3*01	775	1380	gnl|Fabrus|A2_IGKJ1*01	808	1413
1204	gnl|Fabrus|VH3-48_IGHD6-6*01_IGHJ1*01	655	1260	gnl|Fabrus|A2_IGKJ1*01	808	1413
1205	gnl|Fabrus|VH3-30_IGHD6-6*01_IGHJ1*01	625	1230	gnl|Fabrus|A2_IGKJ1*01	808	1413
1206	gnl|Fabrus|VH3-66_IGHD6-6*01_IGHJ1*01	681	1286	gnl|Fabrus|A2_IGKJ1*01	808	1413
1207	gnl|Fabrus|VH3-53_IGHD5-5*01_IGHJ4*01	670	1275	gnl|Fabrus|A2_IGKJ1*01	808	1413
1208	gnl|Fabrus|VH2-5_IGHD5-12*01_IGHJ4*01	536	1141	gnl|Fabrus|A2_IGKJ1*01	808	1413
1209	gnl|Fabrus|VH2-70_IGHD5-12*01_IGHJ4*01	543	1148	gnl|Fabrus|A2_IGKJ1*01	808	1413
1210	gnl|Fabrus|VH3-15_IGHD5-12*01_IGHJ4*01	567	1172	gnl|Fabrus|A2_IGKJ1*01	808	1413

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
1211	gnl|Fabrus|VH3-15_IGHD3-10*01_IGHJ4*01	565	1170	gnl|Fabrus|A2_IGKJ1*01	808	1413
1212	gnl|Fabrus|VH3-49_IGHD5-18*01_IGHJ4*01	662	1267	gnl|Fabrus|A2_IGKJ1*01	808	1413
1213	gnl|Fabrus|VH3-49_IGHD6-13*01_IGHJ4*01	663	1268	gnl|Fabrus|A2_IGKJ1*01	808	1413
1214	gnl|Fabrus|VH3-72_IGHD5-18*01_IGHJ4*01	699	1304	gnl|Fabrus|A2_IGKJ1*01	808	1413
1215	gnl|Fabrus|VH3-72_IGHD6-6*01_IGHJ1*01	701	1306	gnl|Fabrus|A2_IGKJ1*01	808	1413
1216	gnl|Fabrus|VH3-73_IGHD5-12*01_IGHJ4*01	709	1314	gnl|Fabrus|A2_IGKJ1*01	808	1413
1217	gnl|Fabrus|VH3-73_IGHD4-23*01_IGHJ5*01	708	1313	gnl|Fabrus|A2_IGKJ1*01	808	1413
1218	gnl|Fabrus|VH3-43_IGHD3-22*01_IGHJ4*01	650	1255	gnl|Fabrus|A2_IGKJ1*01	808	1413
1219	gnl|Fabrus|VH3-43_IGHD6-13*01_IGHJ4*01	653	1258	gnl|Fabrus|A2_IGKJ1*01	808	1413
1220	gnl|Fabrus|VH3-9_IGHD3-22*01_IGHJ4*01	724	1329	gnl|Fabrus|A2_IGKJ1*01	808	1413
1221	gnl|Fabrus|VH3-9_IGHD1-7*01_IGHJ5*01	721	1326	gnl|Fabrus|A2_IGKJ1*01	808	1413
1222	gnl|Fabrus|VH3-9_IGHD6-13*01_IGHJ4*01	727	1332	gnl|Fabrus|A2_IGKJ1*01	808	1413
1223	gnl|Fabrus|VH4-39_IGHD3-10*01_IGHJ4*01	762	1367	gnl|Fabrus|A2_IGKJ1*01	808	1413
1224	gnl|Fabrus|VH4-39_IGHD5-12*01_IGHJ4*01	766	1371	gnl|Fabrus|A2_IGKJ1*01	808	1413
1225	gnl|Fabrus|VH1-18_IGHD6-6*01_IGHJ1*01	460	1065	gnl|Fabrus|A2_IGKJ1*01	808	1413
1226	gnl|Fabrus|VH1-24_IGHD5-12*01_IGHJ4*01	467	1072	gnl|Fabrus|A2_IGKJ1*01	808	1413
1227	gnl|Fabrus|VH1-2_IGHD1-1*01_IGHJ3*01	461	1066	gnl|Fabrus|A2_IGKJ1*01	808	1413
1228	gnl|Fabrus|VH1-3_IGHD6-6*01_IGHJ1*01	475	1080	gnl|Fabrus|A2_IGKJ1*01	808	1413
1229	gnl|Fabrus|VH1-45_IGHD3-10*01_IGHJ4*01	480	1085	gnl|Fabrus|A2_IGKJ1*01	808	1413
1230	gnl|Fabrus|VH1-46_IGHD1-26*01_IGHJ4*01	486	1091	gnl|Fabrus|A2_IGKJ1*01	808	1413
1231	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ6*01	800	1405	gnl|Fabrus|A2_IGKJ1*01	808	1413
1232	gnl|Fabrus|VH2-70_IGHD3-9*01_IGHJ6*01	542	1147	gnl|Fabrus|A2_IGKJ1*01	808	1413
1233	gnl|Fabrus|VH1-58_IGHD3-10*01_IGHJ6*01	496	1101	gnl|Fabrus|A2_IGKJ1*01	808	1413

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
1234	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ2*01	799	1404	gnl|Fabrus|A2_IGKJ1*01	808	1413
1235	gnl|Fabrus|VH4-28_IGHD3-9*01_IGHJ6*01	734	1339	gnl|Fabrus|A2_IGKJ1*01	808	1413
1236	gnl|Fabrus|VH4-31_IGHD2-15*01_IGHJ2*01	740	1345	gnl|Fabrus|A2_IGKJ1*01	808	1413
1237	gnl|Fabrus|VH2-5_IGHD3-9*01_IGHJ6*01	535	1140	gnl|Fabrus|A2_IGKJ1*01	808	1413
1238	gnl|Fabrus|VH1-8_IGHD2-15*01_IGHJ6*01	515	1120	gnl|Fabrus|A2_IGKJ1*01	808	1413
1239	gnl|Fabrus|VH2-70_IGHD2-15*01_IGHJ2*01	540	1145	gnl|Fabrus|A2_IGKJ1*01	808	1413
1240	gnl|Fabrus|VH3-38_IGHD3-10*01_IGHJ4*01	639	1244	gnl|Fabrus|A2_IGKJ1*01	808	1413
1241	gnl|Fabrus|VH3-16_IGHD1-7*01_IGHJ6*01	570	1175	gnl|Fabrus|A2_IGKJ1*01	808	1413
1242	gnl|Fabrus|VH3-73_IGHD3-9*01_IGHJ6*01	706	1311	gnl|Fabrus|A2_IGKJ1*01	808	1413
1243	gnl|Fabrus|VH3-11_IGHD3-9*01_IGHJ6*01	548	1153	gnl|Fabrus|A2_IGKJ1*01	808	1413
1244	gnl|Fabrus|VH3-11_IGHD6-6*01_IGHJ1*01	552	1157	gnl|Fabrus|A2_IGKJ1*01	808	1413
1245	gnl|Fabrus|VH3-20_IGHD5-12*01_IGHJ4*01	584	1189	gnl|Fabrus|A2_IGKJ1*01	808	1413
1246	gnl|Fabrus|VH3-16_IGHD2-15*01_IGHJ2*01	571	1176	gnl|Fabrus|A2_IGKJ1*01	808	1413
1247	gnl|Fabrus|VH3-7_IGHD6-6*01_IGHJ1*01	692	1297	gnl|Fabrus|A2_IGKJ1*01	808	1413
1248	gnl|Fabrus|VH3-16_IGHD6-13*01_IGHJ4*01	576	1181	gnl|Fabrus|A2_IGKJ1*01	808	1413
1249	gnl|Fabrus|VH3-23_IGHD1-1*01_IGHJ4*01	595	1200	gnl|Fabrus|HerceptinLC	818	1423
1250	gnl|Fabrus|VH3-23_IGHD2-15*01_IGHJ4*01	598	1203	gnl|Fabrus|HerceptinLC	818	1423
1251	gnl|Fabrus|VH3-23_IGHD3-22*01_IGHJ4*01	602	1207	gnl|Fabrus|HerceptinLC	818	1423
1252	gnl|Fabrus|VH3-23_IGHD4-11*01_IGHJ4*01	604	1209	gnl|Fabrus|HerceptinLC	818	1423
1253	gnl|Fabrus|VH3-23_IGHD5-12*01_IGHJ4*01	606	1211	gnl|Fabrus|HerceptinLC	818	1423
1254	gnl|Fabrus|VH3-23_IGHD5-5*01_IGHJ4*01	608	1213	gnl|Fabrus|HerceptinLC	818	1423
1255	gnl|Fabrus|VH3-23_IGHD6-13*01_IGHJ4*01	609	1214	gnl|Fabrus|HerceptinLC	818	1423
1256	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ4*01	612	1217	gnl|Fabrus|HerceptinLC	818	1423

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
1257	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ6*01	613	1218	gnl|Fabrus|HerceptinLC	818	1423
1258	gnl|Fabrus|VH1-69_IGHD1-14*01_IGHJ4*01	502	1107	gnl|Fabrus|HerceptinLC	818	1423
1259	gnl|Fabrus|VH1-69_IGHD2-2*01_IGHJ4*01	503	1108	gnl|Fabrus|HerceptinLC	818	1423
1260	gnl|Fabrus|VH1-69_IGHD2-8*01_IGHJ6*01	504	1109	gnl|Fabrus|HerceptinLC	818	1423
1261	gnl|Fabrus|VH1-69_IGHD3-16*01_IGHJ4*01	505	1110	gnl|Fabrus|HerceptinLC	818	1423
1262	gnl|Fabrus|VH1-69_IGHD3-3*01_IGHJ4*01	506	1111	gnl|Fabrus|HerceptinLC	818	1423
1263	gnl|Fabrus|VH1-69_IGHD4-17*01_IGHJ4*01	508	1113	gnl|Fabrus|HerceptinLC	818	1423
1264	gnl|Fabrus|VH1-69_IGHD5-12*01_IGHJ4*01	509	1114	gnl|Fabrus|HerceptinLC	818	1423
1265	gnl|Fabrus|VH1-69_IGHD6-19*01_IGHJ4*01	511	1116	gnl|Fabrus|HerceptinLC	818	1423
1266	gnl|Fabrus|VH1-69_IGHD7-27*01_IGHJ4*01	513	1118	gnl|Fabrus|HerceptinLC	818	1423
1267	gnl|Fabrus|VH4-34_IGHD1-7*01_IGHJ4*01	749	1354	gnl|Fabrus|HerceptinLC	818	1423
1268	gnl|Fabrus|VH4-34_IGHD2-2*01_IGHJ4*01	750	1355	gnl|Fabrus|HerceptinLC	818	1423
1269	gnl|Fabrus|VH4-34_IGHD3-16*01_IGHJ4*01	751	1356	gnl|Fabrus|HerceptinLC	818	1423
1270	gnl|Fabrus|VH4-34_IGHD4-17*01_IGHJ4*01	753	1358	gnl|Fabrus|HerceptinLC	818	1423
1271	gnl|Fabrus|VH4-34_IGHD5-12*01_IGHJ4*01	754	1359	gnl|Fabrus|HerceptinLC	818	1423
1272	gnl|Fabrus|VH4-34_IGHD6-13*01_IGHJ4*01	755	1360	gnl|Fabrus|HerceptinLC	818	1423
1273	gnl|Fabrus|VH4-34_IGHD6-25*01_IGHJ6*01	756	1361	gnl|Fabrus|HerceptinLC	818	1423
1274	gnl|Fabrus|VH4-34_IGHD7-27*01_IGHJ4*01	758	1363	gnl|Fabrus|HerceptinLC	818	1423
1275	gnl|Fabrus|VH2-26_IGHD1-20*01_IGHJ4*01	521	1126	gnl|Fabrus|HerceptinLC	818	1423
1276	gnl|Fabrus|VH2-26_IGHD2-2*01_IGHJ4*01	523	1128	gnl|Fabrus|HerceptinLC	818	1423
1277	gnl|Fabrus|VH2-26_IGHD3-10*01_IGHJ4*01	524	1129	gnl|Fabrus|HerceptinLC	818	1423
1278	gnl|Fabrus|VH2-26_IGHD4-11*01_IGHJ4*01	526	1131	gnl|Fabrus|HerceptinLC	818	1423
1279	gnl|Fabrus|VH2-26_IGHD5-18*01_IGHJ4*01	528	1133	gnl|Fabrus|HerceptinLC	818	1423

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
1280	gnl|Fabrus|VH2-26_IGHD6-13*01_IGHJ4*01	529	1134	gnl|Fabrus|HerceptinLC	818	1423
1281	gnl|Fabrus|VH2-26_IGHD7-27*01_IGHJ4*01	530	1135	gnl|Fabrus|HerceptinLC	818	1423
1282	gnl|Fabrus|VH5-51_IGHD1-14*01_IGHJ4*01	776	1381	gnl|Fabrus|HerceptinLC	818	1423
1283	gnl|Fabrus|VH5-51_IGHD2-8*01_IGHJ4*01	778	1383	gnl|Fabrus|HerceptinLC	818	1423
1284	gnl|Fabrus|VH5-51_IGHD3-3*01_IGHJ4*01	780	1385	gnl|Fabrus|HerceptinLC	818	1423
1285	gnl|Fabrus|VH5-51_IGHD4-17*01_IGHJ4*01	781	1386	gnl|Fabrus|HerceptinLC	818	1423
1286	gnl|Fabrus|VH5-51_IGHD5-18*01>3_IGHJ4*01	782	1387	gnl|Fabrus|HerceptinLC	818	1423
1287	gnl|Fabrus|VH5-51_IGHD5-18*01>1_IGHJ4*01	783	1388	gnl|Fabrus|HerceptinLC	818	1423
1288	gnl|Fabrus|VH5-51_IGHD6-25*01_IGHJ4*01	784	1389	gnl|Fabrus|HerceptinLC	818	1423
1289	gnl|Fabrus|VH5-51_IGHD7-27*01_IGHJ4*01	785	1390	gnl|Fabrus|HerceptinLC	818	1423
1290	gnl|Fabrus|VH6-1_IGHD1-1*01_IGHJ4*01	786	1391	gnl|Fabrus|HerceptinLC	818	1423
1291	gnl|Fabrus|VH6-1_IGHD2-15*01_IGHJ4*01	788	1393	gnl|Fabrus|HerceptinLC	818	1423
1292	gnl|Fabrus|VH6-1_IGHD3-3*01_IGHJ4*01	791	1396	gnl|Fabrus|HerceptinLC	818	1423
1293	gnl|Fabrus|VH6-1_IGHD4-23*01_IGHJ4*01	793	1398	gnl|Fabrus|HerceptinLC	818	1423
1294	gnl|Fabrus|VH6-1_IGHD4-11*01_IGHJ6*01	792	1397	gnl|Fabrus|HerceptinLC	818	1423
1295	gnl|Fabrus|VH6-1_IGHD5-5*01_IGHJ4*01	794	1399	gnl|Fabrus|HerceptinLC	818	1423
1296	gnl|Fabrus|VH6-1_IGHD6-13*01_IGHJ4*01	795	1400	gnl|Fabrus|HerceptinLC	818	1423
1297	gnl|Fabrus|VH6-1_IGHD6-25*01_IGHJ6*01	796	1401	gnl|Fabrus|HerceptinLC	818	1423
1298	gnl|Fabrus|VH6-1_IGHD7-27*01_IGHJ4*01	797	1402	gnl|Fabrus|HerceptinLC	818	1423
1299	gnl|Fabrus|VH4-59_IGHD6-25*01_IGHJ3*01	775	1380	gnl|Fabrus|HerceptinLC	818	1423
1300	gnl|Fabrus|VH3-48_IGHD6-6*01_IGHJ1*01	655	1260	gnl|Fabrus|HerceptinLC	818	1423
1301	gnl|Fabrus|VH3-30_IGHD6-6*01_IGHJ1*01	625	1230	gnl|Fabrus|HerceptinLC	818	1423
1302	gnl|Fabrus|VH3-66_IGHD6-6*01_IGHJ1*01	681	1286	gnl|Fabrus|HerceptinLC	818	1423

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
1303	gnl|Fabrus|VH3-53_IGHD5-5*01_IGHJ4*01	670	1275	gnl|Fabrus|HerceptinLC	818	1423
1304	gnl|Fabrus|VH2-5_IGHD5-12*01_IGHJ4*01	536	1141	gnl|Fabrus|HerceptinLC	818	1423
1305	gnl|Fabrus|VH2-70_IGHD5-12*01_IGHJ4*01	543	1148	gnl|Fabrus|HerceptinLC	818	1423
1306	gnl|Fabrus|VH3-15_IGHD5-12*01_IGHJ4*01	567	1172	gnl|Fabrus|HerceptinLC	818	1423
1307	gnl|Fabrus|VH3-15_IGHD3-10*01_IGHJ4*01	565	1170	gnl|Fabrus|HerceptinLC	818	1423
1308	gnl|Fabrus|VH3-49_IGHD5-18*01_IGHJ4*01	662	1267	gnl|Fabrus|HerceptinLC	818	1423
1309	gnl|Fabrus|VH3-49_IGHD6-13*01_IGHJ4*01	663	1268	gnl|Fabrus|HerceptinLC	818	1423
1310	gnl|Fabrus|VH3-72_IGHD5-18*01_IGHJ4*01	699	1304	gnl|Fabrus|HerceptinLC	818	1423
1311	gnl|Fabrus|VH3-72_IGHD6-6*01_IGHJ1*01	701	1306	gnl|Fabrus|HerceptinLC	818	1423
1312	gnl|Fabrus|VH3-73_IGHD5-12*01_IGHJ4*01	709	1314	gnl|Fabrus|HerceptinLC	818	1423
1313	gnl|Fabrus|VH3-73_IGHD4-23*01_IGHJ5*01	708	1313	gnl|Fabrus|HerceptinLC	818	1423
1314	gnl|Fabrus|VH3-43_IGHD3-22*01_IGHJ4*01	650	1255	gnl|Fabrus|HerceptinLC	818	1423
1315	gnl|Fabrus|VH3-43_IGHD6-13*01_IGHJ4*01	653	1258	gnl|Fabrus|HerceptinLC	818	1423
1316	gnl|Fabrus|VH3-9_IGHD3-22*01_IGHJ4*01	724	1329	gnl|Fabrus|HerceptinLC	818	1423
1317	gnl|Fabrus|VH3-9_IGHD1-7*01_IGHJ5*01	721	1326	gnl|Fabrus|HerceptinLC	818	1423
1318	gnl|Fabrus|VH3-9_IGHD6-13*01_IGHJ4*01	727	1332	gnl|Fabrus|HerceptinLC	818	1423
1319	gnl|Fabrus|VH4-39_IGHD3-10*01_IGHJ4*01	762	1367	gnl|Fabrus|HerceptinLC	818	1423
1320	gnl|Fabrus|VH4-39_IGHD5-12*01_IGHJ4*01	766	1371	gnl|Fabrus|HerceptinLC	818	1423
1321	gnl|Fabrus|VH1-18_IGHD6-6*01_IGHJ1*01	460	1065	gnl|Fabrus|HerceptinLC	818	1423
1322	gnl|Fabrus|VH1-24_IGHD5-12*01_IGHJ4*01	467	1072	gnl|Fabrus|HerceptinLC	818	1423
1323	gnl|Fabrus|VH1-2_IGHD1-1*01_IGHJ3*01	461	1066	gnl|Fabrus|HerceptinLC	818	1423
1324	gnl|Fabrus|VH1-3_IGHD6-6*01_IGHJ1*01	475	1080	gnl|Fabrus|HerceptinLC	818	1423
1325	gnl|Fabrus|VH1-45_IGHD3-10*01_IGHJ4*01	480	1085	gnl|Fabrus|HerceptinLC	818	1423

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
1326	gnl|Fabrus|VH1-46_IGHD1-26*01_IGHJ4*01	486	1091	gnl|Fabrus|HerceptinLC	818	1423
1327	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ6*01	800	1405	gnl|Fabrus|HerceptinLC	818	1423
1328	gnl|Fabrus|VH2-70_IGHD3-9*01_IGHJ6*01	542	1147	gnl|Fabrus|HerceptinLC	818	1423
1329	gnl|Fabrus|VH1-58_IGHD3-10*01_IGHJ6*01	496	1101	gnl|Fabrus|HerceptinLC	818	1423
1330	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ2*01	799	1404	gnl|Fabrus|HerceptinLC	818	1423
1331	gnl|Fabrus|VH4-28_IGHD3-9*01_IGHJ6*01	734	1339	gnl|Fabrus|HerceptinLC	818	1423
1332	gnl|Fabrus|VH4-31_IGHD2-15*01_IGHJ2*01	740	1345	gnl|Fabrus|HerceptinLC	818	1423
1333	gnl|Fabrus|VH2-5_IGHD3-9*01_IGHJ6*01	535	1140	gnl|Fabrus|HerceptinLC	818	1423
1334	gnl|Fabrus|VH1-8_IGHD2-15*01_IGHJ6*01	515	1120	gnl|Fabrus|HerceptinLC	818	1423
1335	gnl|Fabrus|VH2-70_IGHD2-15*01_IGHJ2*01	540	1145	gnl|Fabrus|HerceptinLC	818	1423
1336	gnl|Fabrus|VH3-38_IGHD3-10*01_IGHJ4*01	639	1244	gnl|Fabrus|HerceptinLC	818	1423
1337	gnl|Fabrus|VH3-16_IGHD1-7*01_IGHJ6*01	570	1175	gnl|Fabrus|HerceptinLC	818	1423
1338	gnl|Fabrus|VH3-73_IGHD3-9*01_IGHJ6*01	706	1311	gnl|Fabrus|HerceptinLC	818	1423
1339	gnl|Fabrus|VH3-11_IGHD3-9*01_IGHJ6*01	548	1153	gnl|Fabrus|HerceptinLC	818	1423
1340	gnl|Fabrus|VH3-11_IGHD6-6*01_IGHJ1*01	552	1157	gnl|Fabrus|HerceptinLC	818	1423
1341	gnl|Fabrus|VH3-20_IGHD5-12*01_IGHJ4*01	584	1189	gnl|Fabrus|HerceptinLC	818	1423
1342	gnl|Fabrus|VH3-16_IGHD2-15*01_IGHJ2*01	571	1176	gnl|Fabrus|HerceptinLC	818	1423
1343	gnl|Fabrus|VH3-7_IGHD6-6*01_IGHJ1*01	692	1297	gnl|Fabrus|HerceptinLC	818	1423
1344	gnl|Fabrus|VH3-16_IGHD6-13*01_IGHJ4*01	576	1181	gnl|Fabrus|HerceptinLC	818	1423
1345	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|O12_IGKJ1*01	833	1438
1346	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|O18_IGKJ1*01	834	1439
1347	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|A20_IGKJ1*01	809	1414
1348	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|A30_IGKJ1*01	814	1419

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
1349	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|L14_IGKJ1*01	821	1426
1350	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
1351	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|L5_IGKJ1*01	828	1433
1352	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|L8_IGKJ1*01	830	1435
1353	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|L23_IGKJ1*01	824	1429
1354	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|L11_IGKJ1*01	819	1424
1355	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|L12_IGKJ1*01	820	1425
1356	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|O1_IGKJ1*01	832	1437
1357	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|A17_IGKJ1*01	807	1412
1358	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|A2_IGKJ1*01	808	1413
1359	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|A23_IGKJ1*01	810	1415
1360	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|A27_IGKJ3*01	813	1418
1361	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|L2_IGKJ1*01	822	1427
1362	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|L6_IGKJ1*01	829	1434
1363	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|L25_IGKJ1*01	825	1430
1364	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|B3_IGKJ1*01	817	1422
1365	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|B2_IGKJ1*01	815	1420
1366	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|A26_IGKJ1*01	811	1416
1367	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|A14_IGKJ1*01	806	1411
1368	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|L9_IGKJ2*01	831	1436
1369	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|A27_IGKJ1*01	812	1417
1370	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|B2_IGKJ3*01	816	1421
1371	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|L25_IGKJ3*01	826	1431

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
1372	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|RituxanLC	835	1440
1373	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|L22_IGKJ3*01	823	1428
1374	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600	1205	gnl|Fabrus|HerceptinLC	818	1423
1375	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|O12_IGKJ1*01	833	1438
1376	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|O18_IGKJ1*01	834	1439
1377	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|A20_IGKJ1*01	809	1414
1378	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|A30_IGKJ1*01	814	1419
1379	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|L14_IGKJ1*01	821	1426
1380	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
1381	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|L5_IGKJ1*01	828	1433
1382	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|L8_IGKJ1*01	830	1435
1383	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|L23_IGKJ1*01	824	1429
1384	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|L11_IGKJ1*01	819	1424
1385	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|L12_IGKJ1*01	820	1425
1386	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|O1_IGKJ1*01	832	1437
1387	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|A17_IGKJ1*01	807	1412
1388	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|A2_IGKJ1*01	808	1413
1389	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|A23_IGKJ1*01	810	1415
1390	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|A27_IGKJ3*01	813	1418
1391	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|L2_IGKJ1*01	822	1427
1392	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|L6_IGKJ1*01	829	1434
1393	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|L25_IGKJ1*01	825	1430
1394	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|B3_IGKJ1*01	817	1422

Table 17. Exemplary Nucleic Acid Paired Library

	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
1395	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|B2_IGKJ1*01	815	1420
1396	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|A26_IGKJ1*01	811	1416
1397	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|A14_IGKJ1*01	806	1411
1398	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|L9_IGKJ2*01	831	1436
1399	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|A27_IGKJ1*01	812	1417
1400	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|B2_IGKJ3*01	816	1421
1401	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|L25_IGKJ3*01	826	1431
1402	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|RituxanLC	835	1440
1403	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|L22_IGKJ3*01	823	1428
1404	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747	1352	gnl|Fabrus|HerceptinLC	818	1423
1405	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|O12_IGKJ1*01	833	1438
1406	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|O18_IGKJ1*01	834	1439
1407	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|A20_IGKJ1*01	809	1414
1408	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|A30_IGKJ1*01	814	1419
1409	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|L14_IGKJ1*01	821	1426
1410	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
1411	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|L5_IGKJ1*01	828	1433
1412	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|L8_IGKJ1*01	830	1435
1413	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|L23_IGKJ1*01	824	1429
1414	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|L11_IGKJ1*01	819	1424
1415	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|L12_IGKJ1*01	820	1425
1416	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|O1_IGKJ1*01	832	1437
1417	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|A17_IGKJ1*01	807	1412
1418	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|A2_IGKJ1*01	808	1413
1419	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|A23_IGKJ1*01	810	1415
1420	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|A27_IGKJ3*01	813	1418
1421	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|L2_IGKJ1*01	822	1427
1422	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|L6_IGKJ1*01	829	1434
1423	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|L25_IGKJ1*01	825	1430
1424	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|B3_IGKJ1*01	817	1422
1425	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|B2_IGKJ1*01	815	1420
1426	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|A26_IGKJ1*01	811	1416
1427	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|A14_IGKJ1*01	806	1411
1428	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|L9_IGKJ2*01	831	1436
1429	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|A27_IGKJ1*01	812	1417
1430	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|B2_IGKJ3*01	816	1421
1431	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|L25_IGKJ3*01	826	1431

Table 17. Exemplary Nucleic Acid Paired Library						
	HEAVY CHAIN	RS	NO RS	LIGHT CHAIN	RS	NO RS
	Name	SEQ ID NO	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
1432	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|RituxanLC	835	1440
1433	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|L22_IGKJ3*01	823	1428
1434	gnl|Fabrus|RituxanHC	453	1058	gnl|Fabrus|HerceptinLC	818	1423
1435	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|O12_IGKJ1*01	833	1438
1436	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|O18_IGKJ1*01	834	1439
1437	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|A20_IGKJ1*01	809	1414
1438	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|A30_IGKJ1*01	814	1419
1439	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|L14_IGKJ1*01	821	1426
1440	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|L4/18a_IGKJ1*01	827	1432
1441	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|L5_IGKJ1*01	828	1433
1442	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|L8_IGKJ1*01	830	1435
1443	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|L23_IGKJ1*01	824	1429
1444	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|L11_IGKJ1*01	819	1424
1445	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|L12_IGKJ1*01	820	1425
1446	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|O1_IGKJ1*01	832	1437
1447	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|A17_IGKJ1*01	807	1412
1448	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|A2_IGKJ1*01	808	1413
1449	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|A23_IGKJ1*01	810	1415
1450	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|A27_IGKJ3*01	813	1418
1451	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|L2_IGKJ1*01	822	1427
1452	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|L6_IGKJ1*01	829	1434
1453	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|L25_IGKJ1*01	825	1430
1454	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|B3_IGKJ1*01	817	1422
1455	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|B2_IGKJ1*01	815	1420
1456	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|A26_IGKJ1*01	811	1416
1457	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|A14_IGKJ1*01	806	1411
1458	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|L9_IGKJ2*01	831	1436
1459	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|A27_IGKJ1*01	812	1417
1460	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|B2_IGKJ3*01	816	1421
1461	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|L25_IGKJ3*01	826	1431
1462	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|RituxanLC	835	1440
1463	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|L22_IGKJ3*01	823	1428
1464	gnl|Fabrus|HerceptinHC	452	1057	gnl|Fabrus|HerceptinLC	818	1423

An additional exemplary paired library is set forth in Table 17A, where each row sets forth a different loci of the library.

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	**RS**	**LIGHT CHAIN**	**RS**	**NO RS**
	Name	SEQ ID NO	Name	SEQ ID NO	SEQ ID NO
1	VH3-23_IGHD1-1*01>1_IGHJ1*01	2070	O12_IGKJ1*01	833	1438
2	VH3-23_IGHD1-1*01>2_IGHJ1*01	2071	O12_IGKJ1*01	833	1438
3	VH3-23_IGHD1-1*01>3_IGHJ1*01	2072	O12_IGKJ1*01	833	1438
4	VH3-23_IGHD1-7*01>1_IGHJ1*01	2073	O12_IGKJ1*01	833	1438
5	VH3-23_IGHD1-7*01>3_IGHJ1*01	2074	O12_IGKJ1*01	833	1438

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
6	VH3-23_IGHD1-14*01>1_IGHJ1*01	2075	O12_IGKJ1*01	833	1438
7	VH3-23_IGHD1-14*01>3_IGHJ1*01	2076	O12_IGKJ1*01	833	1438
8	VH3-23_IGHD1-20*01>1_IGHJ1*01	2077	O12_IGKJ1*01	833	1438
9	VH3-23_IGHD1-20*01>3_IGHJ1*01	2078	O12_IGKJ1*01	833	1438
10	VH3-23_IGHD1-26*01>1_IGHJ1*01	2079	O12_IGKJ1*01	833	1438
11	VH3-23_IGHD1-26*01>3_IGHJ1*01	2080	O12_IGKJ1*01	833	1438
12	VH3-23_IGHD2-2*01>2_IGHJ1*01	2081	O12_IGKJ1*01	833	1438
13	VH3-23_IGHD2-2*01>3_IGHJ1*01	2082	O12_IGKJ1*01	833	1438
14	VH3-23_IGHD2-8*01>2_IGHJ1*01	2083	O12_IGKJ1*01	833	1438
15	VH3-23_IGHD2-8*01>3_IGHJ1*01	2084	O12_IGKJ1*01	833	1438
16	VH3-23_IGHD2-15*01>2_IGHJ1*01	2085	O12_IGKJ1*01	833	1438
17	VH3-23_IGHD2-15*01>3_IGHJ1*01	2086	O12_IGKJ1*01	833	1438
18	VH3-23_IGHD2-21*01>2_IGHJ1*01	2087	O12_IGKJ1*01	833	1438
19	VH3-23_IGHD2-21*01>3_IGHJ1*01	2088	O12_IGKJ1*01	833	1438
20	VH3-23_IGHD3-3*01>1_IGHJ1*01	2089	O12_IGKJ1*01	833	1438
21	VH3-23_IGHD3-3*01>2_IGHJ1*01	2090	O12_IGKJ1*01	833	1438
22	VH3-23_IGHD3-3*01>3_IGHJ1*01	2091	O12_IGKJ1*01	833	1438
23	VH3-23_IGHD3-9*01>2_IGHJ1*01	2092	O12_IGKJ1*01	833	1438
24	VH3-23_IGHD3-10*01>2_IGHJ1*01	2093	O12_IGKJ1*01	833	1438
25	VH3-23_IGHD3-10*01>3_IGHJ1*01	2094	O12_IGKJ1*01	833	1438
26	VH3-23_IGHD3-16*01>2_IGHJ1*01	2095	O12_IGKJ1*01	833	1438
27	VH3-23_IGHD3-16*01>3_IGHJ1*01	2096	O12_IGKJ1*01	833	1438
28	VH3-23_IGHD3-22*01>2_IGHJ1*01	2097	O12_IGKJ1*01	833	1438
29	VH3-23_IGHD3-22*01>3_IGHJ1*01	2098	O12_IGKJ1*01	833	1438
30	VH3-23_IGHD4-4*01 (1) >2_IGHJ1*01	2099	O12_IGKJ1*01	833	1438
31	VH3-23_IGHD4-4*01 (1) >3_IGHJ1*01	2100	O12_IGKJ1*01	833	1438
32	VH3-23_IGHD4-11*01 (1) >2_IGHJ1*01	2101	O12_IGKJ1*01	833	1438
33	VH3-23_IGHD4-11*01 (1) >3_IGHJ1*01	2102	O12_IGKJ1*01	833	1438
34	VH3-23_IGHD4-17*01>2_IGHJ1*01	2103	O12_IGKJ1*01	833	1438
35	VH3-23_IGHD4-17*01>3_IGHJ1*01	2104	O12_IGKJ1*01	833	1438
36	VH3-23_IGHD4-23*01>2_IGHJ1*01	2105	O12_IGKJ1*01	833	1438
37	VH3-23_IGHD4-23*01>3_IGHJ1*01	2106	O12_IGKJ1*01	833	1438
38	VH3-23_IGHD5-5*01 (2) >1_IGHJ1*01	2107	O12_IGKJ1*01	833	1438
39	VH3-23_IGHD5-5*01 (2) >2_IGHJ1*01	2108	O12_IGKJ1*01	833	1438
40	VH3-23_IGHD5-5*01 (2) >3_IGHJ1*01	2109	O12_IGKJ1*01	833	1438
41	VH3-23_IGHD5-12*01>1_IGHJ1*01	2110	O12_IGKJ1*01	833	1438
42	VH3-23_IGHD5-12*01>3_IGHJ1*01	2111	O12_IGKJ1*01	833	1438
43	VH3-23_IGHD5-18*01 (2) >1_IGHJ1*01	2112	O12_IGKJ1*01	833	1438
44	VH3-23_IGHD5-18*01 (2) >2_IGHJ1*01	2113	O12_IGKJ1*01	833	1438
45	VH3-23_IGHD5-18*01 (2) >3_IGHJ1*01	2114	O12_IGKJ1*01	833	1438
46	VH3-23_IGHD5-24*01>1_IGHJ1*01	2115	O12_IGKJ1*01	833	1438
47	VH3-23_IGHD5-24*01>3_IGHJ1*01	2116	O12_IGKJ1*01	833	1438
48	VH3-23_IGHD6-6*01>1_IGHJ1*01	2117	O12_IGKJ1*01	833	1438
49	VH3-23_IGHD1-1*01>1'_IGHJ1*01	2127	O12_IGKJ1*01	833	1438

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
50	VH3-23_IGHD1-1*01>2'_IGHJ1*01	2128	O12_IGKJ1*01	833	1438
51	VH3-23_IGHD1-1*01>3'_IGHJ1*01	2129	O12_IGKJ1*01	833	1438
52	VH3-23_IGHD1-7*01>1'_IGHJ1*01	2130	O12_IGKJ1*01	833	1438
53	VH3-23_IGHD1-7*01>3'_IGHJ1*01	2131	O12_IGKJ1*01	833	1438
54	VH3-23_IGHD1-14*01>1'_IGHJ1*01	2132	O12_IGKJ1*01	833	1438
55	VH3-23_IGHD1-14*01>2'_IGHJ1*01	2133	O12_IGKJ1*01	833	1438
56	VH3-23_IGHD1-14*01>3'_IGHJ1*01	2134	O12_IGKJ1*01	833	1438
57	VH3-23_IGHD1-20*01>1'_IGHJ1*01	2135	O12_IGKJ1*01	833	1438
58	VH3-23_IGHD1-20*01>2'_IGHJ1*01	2136	O12_IGKJ1*01	833	1438
59	VH3-23_IGHD1-20*01>3'_IGHJ1*01	2137	O12_IGKJ1*01	833	1438
60	VH3-23_IGHD1-26*01>1'_IGHJ1*01	2138	O12_IGKJ1*01	833	1438
61	VH3-23_IGHD1-26*01>3'_IGHJ1*01	2139	O12_IGKJ1*01	833	1438
62	VH3-23_IGHD2-2*01>1'_IGHJ1*01	2140	O12_IGKJ1*01	833	1438
63	VH3-23_IGHD2-2*01>3'_IGHJ1*01	2141	O12_IGKJ1*01	833	1438
64	VH3-23_IGHD2-8*01>1'_IGHJ1*01	2142	O12_IGKJ1*01	833	1438
65	VH3-23_IGHD2-15*01>1'_IGHJ1*01	2143	O12_IGKJ1*01	833	1438
66	VH3-23_IGHD2-15*01>3'_IGHJ1*01	2144	O12_IGKJ1*01	833	1438
67	VH3-23_IGHD2-21*01>1'_IGHJ1*01	2145	O12_IGKJ1*01	833	1438
68	VH3-23_IGHD2-21*01>3'_IGHJ1*01	2146	O12_IGKJ1*01	833	1438
69	VH3-23_IGHD3-3*01>1'_IGHJ1*01	2147	O12_IGKJ1*01	833	1438
70	VH3-23_IGHD3-3*01>3'_IGHJ1*01	2148	O12_IGKJ1*01	833	1438
71	VH3-23_IGHD3-9*01>1'_IGHJ1*01	2149	O12_IGKJ1*01	833	1438
72	VH3-23_IGHD3-9*01>3'_IGHJ1*01	2150	O12_IGKJ1*01	833	1438
73	VH3-23_IGHD3-10*01>1'_IGHJ1*01	2151	O12_IGKJ1*01	833	1438
74	VH3-23_IGHD3-10*01>3'_IGHJ1*01	2152	O12_IGKJ1*01	833	1438
75	VH3-23_IGHD3-16*01>1'_IGHJ1*01	2153	O12_IGKJ1*01	833	1438
76	VH3-23_IGHD3-16*01>3'_IGHJ1*01	2154	O12_IGKJ1*01	833	1438
77	VH3-23_IGHD3-22*01>1'_IGHJ1*01	2155	O12_IGKJ1*01	833	1438
78	VH3-23_IGHD4-4*01 (1) >1'_IGHJ1*01	2156	O12_IGKJ1*01	833	1438
79	VH3-23_IGHD4-4*01 (1) >3'_IGHJ1*01	2157	O12_IGKJ1*01	833	1438
80	VH3-23_IGHD4-11*01 (1) >1'_IGHJ1*01	2158	O12_IGKJ1*01	833	1438
81	VH3-23_IGHD4-11*01 (1) >3'_IGHJ1*01	2159	O12_IGKJ1*01	833	1438
82	VH3-23_IGHD4-17*01>1'_IGHJ1*01	2160	O12_IGKJ1*01	833	1438
83	VH3-23_IGHD4-17*01>3'_IGHJ1*01	2161	O12_IGKJ1*01	833	1438
84	VH3-23_IGHD4-23*01>1'_IGHJ1*01	2162	O12_IGKJ1*01	833	1438
85	VH3-23_IGHD4-23*01>3'_IGHJ1*01	2163	O12_IGKJ1*01	833	1438
86	VH3-23_IGHD5-5*01 (2) >1'_IGHJ1*01	2164	O12_IGKJ1*01	833	1438
87	VH3-23_IGHD5-5*01 (2) >3'_IGHJ1*01	2165	O12_IGKJ1*01	833	1438
88	VH3-23_IGHD5-12*01>1'_IGHJ1*01	2166	O12_IGKJ1*01	833	1438
89	VH3-23_IGHD5-12*01>3'_IGHJ1*01	2167	O12_IGKJ1*01	833	1438
90	VH3-23_IGHD5-18*01 (2) >1'_IGHJ1*01	2168	O12_IGKJ1*01	833	1438
91	VH3-23_IGHD5-18*01 (2) >3'_IGHJ1*01	2169	O12_IGKJ1*01	833	1438
92	VH3-23_IGHD5-24*01>1'_IGHJ1*01	2170	O12_IGKJ1*01	833	1438
93	VH3-23_IGHD5-24*01>3'_IGHJ1*01	2171	O12_IGKJ1*01	833	1438

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
94	VH3-23_IGHD6-6*01>1'_IGHJ1*01	2172	O12_IGKJ1*01	833	1438
95	VH3-23_IGHD6-6*01>2'_IGHJ1*01	2173	O12_IGKJ1*01	833	1438
96	VH3-23_IGHD6-6*01>3'_IGHJ1*01	2174	O12_IGKJ1*01	833	1438
97	VH3-23_IGHD6-6*01>2_IGHJ1*01	2118	O12_IGKJ1*01	833	1438
98	VH3-23_IGHD6-13*01>1_IGHJ1*01	2119	O12_IGKJ1*01	833	1438
99	VH3-23_IGHD6-13*01>2_IGHJ1*01	2120	O12_IGKJ1*01	833	1438
100	VH3-23_IGHD6-19*01>1_IGHJ1*01	2121	O12_IGKJ1*01	833	1438
101	VH3-23_IGHD6-19*01>2_IGHJ1*01	2122	O12_IGKJ1*01	833	1438
102	VH3-23_IGHD6-25*01>1_IGHJ1*01	2123	O12_IGKJ1*01	833	1438
103	VH3-23_IGHD6-25*01>2_IGHJ1*01	2124	O12_IGKJ1*01	833	1438
104	VH3-23_IGHD7-27*01>1_IGHJ1*01	2125	O12_IGKJ1*01	833	1438
105	VH3-23_IGHD7-27*01>3_IGHJ1*01	2126	O12_IGKJ1*01	833	1438
106	VH3-23_IGHD6-13*01>1'_IGHJ1*01	2175	O12_IGKJ1*01	833	1438
107	VH3-23_IGHD6-13*01>2'_IGHJ1*01	2176	O12_IGKJ1*01	833	1438
108	VH3-23_IGHD6-13*01>2_IGHJ1*01_B	2177	O12_IGKJ1*01	833	1438
109	VH3-23_IGHD6-19*01>1'_IGHJ1*01	2178	O12_IGKJ1*01	833	1438
110	VH3-23_IGHD6-19*01>2'_IGHJ1*01	2179	O12_IGKJ1*01	833	1438
111	VH3-23_IGHD6-19*01>2_IGHJ1*01_B	2180	O12_IGKJ1*01	833	1438
112	VH3-23_IGHD6-25*01>1'_IGHJ1*01	2181	O12_IGKJ1*01	833	1438
113	VH3-23_IGHD6-25*01>3'_IGHJ1*01	2182	O12_IGKJ1*01	833	1438
114	VH3-23_IGHD7-27*01>1'_IGHJ1*01_B	2183	O12_IGKJ1*01	833	1438
115	VH3-23_IGHD7-27*01>2'_IGHJ1*01	2184	O12_IGKJ1*01	833	1438
116	VH3-23_IGHD1-1*01>1_IGHJ2*01	2185	O12_IGKJ1*01	833	1438
117	VH3-23_IGHD1-1*01>2_IGHJ2*01	2186	O12_IGKJ1*01	833	1438
118	VH3-23_IGHD1-1*01>3_IGHJ2*01	2187	O12_IGKJ1*01	833	1438
119	VH3-23_IGHD1-7*01>1_IGHJ2*01	2188	O12_IGKJ1*01	833	1438
120	VH3-23_IGHD1-7*01>3_IGHJ2*01	2189	O12_IGKJ1*01	833	1438
121	VH3-23_IGHD1-14*01>1_IGHJ2*01	2190	O12_IGKJ1*01	833	1438
122	VH3-23_IGHD1-14*01>3_IGHJ2*01	2191	O12_IGKJ1*01	833	1438
123	VH3-23_IGHD1-20*01>1_IGHJ2*01	2192	O12_IGKJ1*01	833	1438
124	VH3-23_IGHD1-20*01>3_IGHJ2*01	2193	O12_IGKJ1*01	833	1438
125	VH3-23_IGHD1-26*01>1_IGHJ2*01	2194	O12_IGKJ1*01	833	1438
126	VH3-23_IGHD1-26*01>3_IGHJ2*01	2195	O12_IGKJ1*01	833	1438
127	VH3-23_IGHD2-2*01>2_IGHJ2*01	2196	O12_IGKJ1*01	833	1438
128	VH3-23_IGHD2-2*01>3_IGHJ2*01	2197	O12_IGKJ1*01	833	1438
129	VH3-23_IGHD2-8*01>2_IGHJ2*01	2198	O12_IGKJ1*01	833	1438
130	VH3-23_IGHD2-8*01>3_IGHJ2*01	2199	O12_IGKJ1*01	833	1438
131	VH3-23_IGHD2-15*01>2_IGHJ2*01	2200	O12_IGKJ1*01	833	1438
132	VH3-23_IGHD2-15*01>3_IGHJ2*01	2201	O12_IGKJ1*01	833	1438
133	VH3-23_IGHD2-21*01>2_IGHJ2*01	2202	O12_IGKJ1*01	833	1438
134	VH3-23_IGHD2-21*01>3_IGHJ2*01	2203	O12_IGKJ1*01	833	1438
135	VH3-23_IGHD3-3*01>1_IGHJ2*01	2204	O12_IGKJ1*01	833	1438
136	VH3-23_IGHD3-3*01>2_IGHJ2*01	2205	O12_IGKJ1*01	833	1438
137	VH3-23_IGHD3-3*01>3_IGHJ2*01	2206	O12_IGKJ1*01	833	1438

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
138	VH3-23_IGHD3-9*01>2_IGHJ2*01	2207	O12_IGKJ1*01	833	1438
139	VH3-23_IGHD3-10*01>2_IGHJ2*01	2208	O12_IGKJ1*01	833	1438
140	VH3-23_IGHD3-10*01>3_IGHJ2*01	2209	O12_IGKJ1*01	833	1438
141	VH3-23_IGHD3-16*01>2_IGHJ2*01	2210	O12_IGKJ1*01	833	1438
142	VH3-23_IGHD3-16*01>3_IGHJ2*01	2211	O12_IGKJ1*01	833	1438
143	VH3-23_IGHD3-22*01>2_IGHJ2*01	2212	O12_IGKJ1*01	833	1438
144	VH3-23_IGHD3-22*01>3_IGHJ2*01	2213	O12_IGKJ1*01	833	1438
145	VH3-23_IGHD4-4*01 (1) >2_IGHJ2*01	2214	O12_IGKJ1*01	833	1438
146	VH3-23_IGHD4-4*01 (1) >3_IGHJ2*01	2215	O12_IGKJ1*01	833	1438
147	VH3-23_IGHD4-11*01 (1) >2_IGHJ2*01	2216	O12_IGKJ1*01	833	1438
148	VH3-23_IGHD4-11*01 (1) >3_IGHJ2*01	2217	O12_IGKJ1*01	833	1438
149	VH3-23_IGHD4-17*01>2_IGHJ2*01	2218	O12_IGKJ1*01	833	1438
150	VH3-23_IGHD4-17*01>3_IGHJ2*01	2219	O12_IGKJ1*01	833	1438
151	VH3-23_IGHD4-23*01>2_IGHJ2*01	2220	O12_IGKJ1*01	833	1438
152	VH3-23_IGHD4-23*01>3_IGHJ2*01	2221	O12_IGKJ1*01	833	1438
153	VH3-23_IGHD5-5*01 (2) >1_IGHJ2*01	2222	O12_IGKJ1*01	833	1438
154	VH3-23_IGHD5-5*01 (2) >2_IGHJ2*01	2223	O12_IGKJ1*01	833	1438
155	VH3-23_IGHD5-5*01 (2) >3_IGHJ2*01	2224	O12_IGKJ1*01	833	1438
156	VH3-23_IGHD5-12*01>1_IGHJ2*01	2225	O12_IGKJ1*01	833	1438
157	VH3-23_IGHD5-12*01>3_IGHJ2*01	2226	O12_IGKJ1*01	833	1438
158	VH3-23_IGHD5-18*01 (2) >1_IGHJ2*01	2227	O12_IGKJ1*01	833	1438
159	VH3-23_IGHD5-18*01 (2) >2_IGHJ2*01	2228	O12_IGKJ1*01	833	1438
160	VH3-23_IGHD5-18*01 (2) >3_IGHJ2*01	2229	O12_IGKJ1*01	833	1438
161	VH3-23_IGHD5-24*01>1_IGHJ2*01	2230	O12_IGKJ1*01	833	1438
162	VH3-23_IGHD5-24*01>3_IGHJ2*01	2231	O12_IGKJ1*01	833	1438
163	VH3-23_IGHD6-6*01>1_IGHJ2*01	2232	O12_IGKJ1*01	833	1438
164	VH3-23_IGHD1-1*01>1'_IGHJ2*01	2242	O12_IGKJ1*01	833	1438
165	VH3-23_IGHD1-1*01>2'_IGHJ2*01	2243	O12_IGKJ1*01	833	1438
166	VH3-23_IGHD1-1*01>3'_IGHJ2*01	2244	O12_IGKJ1*01	833	1438
167	VH3-23_IGHD1-7*01>1'_IGHJ2*01	2245	O12_IGKJ1*01	833	1438
168	VH3-23_IGHD1-7*01>3'_IGHJ2*01	2246	O12_IGKJ1*01	833	1438
169	VH3-23_IGHD1-14*01>1'_IGHJ2*01	2247	O12_IGKJ1*01	833	1438
170	VH3-23_IGHD1-14*01>2'_IGHJ2*01	2248	O12_IGKJ1*01	833	1438
171	VH3-23_IGHD1-14*01>3'_IGHJ2*01	2249	O12_IGKJ1*01	833	1438
172	VH3-23_IGHD1-20*01>1'_IGHJ2*01	2250	O12_IGKJ1*01	833	1438
173	VH3-23_IGHD1-20*01>2'_IGHJ2*01	2251	O12_IGKJ1*01	833	1438
174	VH3-23_IGHD1-20*01>3'_IGHJ2*01	2252	O12_IGKJ1*01	833	1438
175	VH3-23_IGHD1-26*01>1'_IGHJ2*01	2253	O12_IGKJ1*01	833	1438
176	VH3-23_IGHD1-26*01>1_IGHJ2*01_B	2254	O12_IGKJ1*01	833	1438
177	VH3-23_IGHD2-2*01>1'_IGHJ2*01	2255	O12_IGKJ1*01	833	1438
178	VH3-23_IGHD2-2*01>3'_IGHJ2*01	2256	O12_IGKJ1*01	833	1438
179	VH3-23_IGHD2-8*01>1'_IGHJ2*01	2257	O12_IGKJ1*01	833	1438
180	VH3-23_IGHD2-15*01>1'_IGHJ2*01	2258	O12_IGKJ1*01	833	1438
181	VH3-23_IGHD2-15*01>3'_IGHJ2*01	2259	O12_IGKJ1*01	833	1438

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
182	VH3-23_IGHD2-21*01>1'_IGHJ2*01	2260	O12_IGKJ1*01	833	1438
183	VH3-23_IGHD2-21*01>3'_IGHJ2*01	2261	O12_IGKJ1*01	833	1438
184	VH3-23_IGHD3-3*01>1'_IGHJ2*01	2262	O12_IGKJ1*01	833	1438
185	VH3-23_IGHD3-3*01>3'_IGHJ2*01	2263	O12_IGKJ1*01	833	1438
186	VH3-23_IGHD3-9*01>1'_IGHJ2*01	2264	O12_IGKJ1*01	833	1438
187	VH3-23_IGHD3-9*01>3'_IGHJ2*01	2265	O12_IGKJ1*01	833	1438
188	VH3-23_IGHD3-10*01>1'_IGHJ2*01	2266	O12_IGKJ1*01	833	1438
189	VH3-23_IGHD3-10*01>3'_IGHJ2*01	2267	O12_IGKJ1*01	833	1438
190	VH3-23_IGHD3-16*01>1'_IGHJ2*01	2268	O12_IGKJ1*01	833	1438
191	VH3-23_IGHD3-16*01>3'_IGHJ2*01	2269	O12_IGKJ1*01	833	1438
192	VH3-23_IGHD3-22*01>1'_IGHJ2*01	2270	O12_IGKJ1*01	833	1438
193	VH3-23_IGHD4-4*01 (1) >1'_IGHJ2*01	2271	O12_IGKJ1*01	833	1438
194	VH3-23_IGHD4-4*01 (1) >3'_IGHJ2*01	2272	O12_IGKJ1*01	833	1438
195	VH3-23_IGHD4-11*01 (1) >1'_IGHJ2*01	2273	O12_IGKJ1*01	833	1438
196	VH3-23_IGHD4-11*01 (1) >3'_IGHJ2*01	2274	O12_IGKJ1*01	833	1438
197	VH3-23_IGHD4-17*01>1'_IGHJ2*01	2275	O12_IGKJ1*01	833	1438
198	VH3-23_IGHD4-17*01>3'_IGHJ2*01	2276	O12_IGKJ1*01	833	1438
199	VH3-23_IGHD4-23*01>1'_IGHJ2*01	2277	O12_IGKJ1*01	833	1438
200	VH3-23_IGHD4-23*01>3'_IGHJ2*01	2278	O12_IGKJ1*01	833	1438
201	VH3-23_IGHD5-5*01 (2) >1'_IGHJ2*01	2279	O12_IGKJ1*01	833	1438
202	VH3-23_IGHD5-5*01 (2) >3'_IGHJ2*01	2280	O12_IGKJ1*01	833	1438
203	VH3-23_IGHD5-12*01>1'_IGHJ2*01	2281	O12_IGKJ1*01	833	1438
204	VH3-23_IGHD5-12*01>3'_IGHJ2*01	2282	O12_IGKJ1*01	833	1438
205	VH3-23_IGHD5-18*01 (2) >1'_IGHJ2*01	2283	O12_IGKJ1*01	833	1438
206	VH3-23_IGHD5-18*01 (2) >3'_IGHJ2*01	2284	O12_IGKJ1*01	833	1438
207	VH3-23_IGHD5-24*01>1'_IGHJ2*01	2285	O12_IGKJ1*01	833	1438
208	VH3-23_IGHD5-24*01>3'_IGHJ2*01	2286	O12_IGKJ1*01	833	1438
209	VH3-23_IGHD6-6*01>1'_IGHJ2*01	2287	O12_IGKJ1*01	833	1438
210	VH3-23_IGHD6-6*01>2'_IGHJ2*01	2288	O12_IGKJ1*01	833	1438
211	VH3-23_IGHD6-6*01>3'_IGHJ2*01	2289	O12_IGKJ1*01	833	1438
212	VH3-23_IGHD6-6*01>2_IGHJ2*01	2233	O12_IGKJ1*01	833	1438
213	VH3-23_IGHD6-13*01>1_IGHJ2*01	2234	O12_IGKJ1*01	833	1438
214	VH3-23_IGHD6-13*01>2_IGHJ2*01	2235	O12_IGKJ1*01	833	1438
215	VH3-23_IGHD6-19*01>1_IGHJ2*01	2236	O12_IGKJ1*01	833	1438
216	VH3-23_IGHD6-19*01>2_IGHJ2*01	2237	O12_IGKJ1*01	833	1438
217	VH3-23_IGHD6-25*01>1_IGHJ2*01	2238	O12_IGKJ1*01	833	1438
218	VH3-23_IGHD6-25*01>2_IGHJ2*01	2239	O12_IGKJ1*01	833	1438
219	VH3-23_IGHD7-27*01>1_IGHJ2*01	2240	O12_IGKJ1*01	833	1438
220	VH3-23_IGHD7-27*01>3_IGHJ2*01	2241	O12_IGKJ1*01	833	1438
221	VH3-23_IGHD6-13*01>1'_IGHJ2*01	2290	O12_IGKJ1*01	833	1438
222	VH3-23_IGHD6-13*01>2'_IGHJ2*01	2291	O12_IGKJ1*01	833	1438
223	VH3-23_IGHD6-13*01>2_IGHJ2*01_B	2292	O12_IGKJ1*01	833	1438
224	VH3-23_IGHD6-19*01>1'_IGHJ2*01	2293	O12_IGKJ1*01	833	1438
225	VH3-23_IGHD6-19*01>2'_IGHJ2*01	2294	O12_IGKJ1*01	833	1438

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
226	VH3-23_IGHD6-19*01>2_IGHJ2*01_B	2295	O12_IGKJ1*01	833	1438
227	VH3-23_IGHD6-25*01>1'_IGHJ2*01	2296	O12_IGKJ1*01	833	1438
228	VH3-23_IGHD6-25*01>3'_IGHJ2*01	2297	O12_IGKJ1*01	833	1438
229	VH3-23_IGHD7-27*01>1'_IGHJ2*01	2298	O12_IGKJ1*01	833	1438
230	VH3-23_IGHD7-27*01>2'_IGHJ2*01	2299	O12_IGKJ1*01	833	1438
231	VH3-23_IGHD1-1*01>1_IGHJ3*01	2300	O12_IGKJ1*01	833	1438
232	VH3-23_IGHD1-1*01>2_IGHJ3*01	2301	O12_IGKJ1*01	833	1438
233	VH3-23_IGHD1-1*01>3_IGHJ3*01	2302	O12_IGKJ1*01	833	1438
234	VH3-23_IGHD1-7*01>1_IGHJ3*01	2303	O12_IGKJ1*01	833	1438
235	VH3-23_IGHD1-7*01>3_IGHJ3*01	2304	O12_IGKJ1*01	833	1438
236	VH3-23_IGHD1-14*01>1_IGHJ3*01	2305	O12_IGKJ1*01	833	1438
237	VH3-23_IGHD1-14*01>3_IGHJ3*01	2306	O12_IGKJ1*01	833	1438
238	VH3-23_IGHD1-20*01>1_IGHJ3*01	2307	O12_IGKJ1*01	833	1438
239	VH3-23_IGHD1-20*01>3_IGHJ3*01	2308	O12_IGKJ1*01	833	1438
240	VH3-23_IGHD1-26*01>1_IGHJ3*01	2309	O12_IGKJ1*01	833	1438
241	VH3-23_IGHD1-26*01>3_IGHJ3*01	2310	O12_IGKJ1*01	833	1438
242	VH3-23_IGHD2-2*01>2_IGHJ3*01	2311	O12_IGKJ1*01	833	1438
243	VH3-23_IGHD2-2*01>3_IGHJ3*01	2312	O12_IGKJ1*01	833	1438
244	VH3-23_IGHD2-8*01>2_IGHJ3*01	2313	O12_IGKJ1*01	833	1438
245	VH3-23_IGHD2-8*01>3_IGHJ3*01	2314	O12_IGKJ1*01	833	1438
246	VH3-23_IGHD2-15*01>2_IGHJ3*01	2315	O12_IGKJ1*01	833	1438
247	VH3-23_IGHD2-15*01>3_IGHJ3*01	2316	O12_IGKJ1*01	833	1438
248	VH3-23_IGHD2-21*01>2_IGHJ3*01	2317	O12_IGKJ1*01	833	1438
249	VH3-23_IGHD2-21*01>3_IGHJ3*01	2318	O12_IGKJ1*01	833	1438
250	VH3-23_IGHD3-3*01>1_IGHJ3*01	2319	O12_IGKJ1*01	833	1438
251	VH3-23_IGHD3-3*01>2_IGHJ3*01	2320	O12_IGKJ1*01	833	1438
252	VH3-23_IGHD3-3*01>3_IGHJ3*01	2321	O12_IGKJ1*01	833	1438
253	VH3-23_IGHD3-9*01>2_IGHJ3*01	2322	O12_IGKJ1*01	833	1438
254	VH3-23_IGHD3-10*01>2_IGHJ3*01	2323	O12_IGKJ1*01	833	1438
255	VH3-23_IGHD3-10*01>3_IGHJ3*01	2324	O12_IGKJ1*01	833	1438
256	VH3-23_IGHD3-16*01>2_IGHJ3*01	2325	O12_IGKJ1*01	833	1438
257	VH3-23_IGHD3-16*01>3_IGHJ3*01	2326	O12_IGKJ1*01	833	1438
258	VH3-23_IGHD3-22*01>2_IGHJ3*01	2327	O12_IGKJ1*01	833	1438
259	VH3-23_IGHD3-22*01>3_IGHJ3*01	2328	O12_IGKJ1*01	833	1438
260	VH3-23_IGHD4-4*01 (1) >2_IGHJ3*01	2329	O12_IGKJ1*01	833	1438
261	VH3-23_IGHD4-4*01 (1) >3_IGHJ3*01	2330	O12_IGKJ1*01	833	1438
262	VH3-23_IGHD4-11*01 (1) >2_IGHJ3*01	2331	O12_IGKJ1*01	833	1438
263	VH3-23_IGHD4-11*01 (1) >3_IGHJ3*01	2332	O12_IGKJ1*01	833	1438
264	VH3-23_IGHD4-17*01>2_IGHJ3*01	2333	O12_IGKJ1*01	833	1438
265	VH3-23_IGHD4-17*01>3_IGHJ3*01	2334	O12_IGKJ1*01	833	1438
266	VH3-23_IGHD4-23*01>2_IGHJ3*01	2335	O12_IGKJ1*01	833	1438
267	VH3-23_IGHD4-23*01>3_IGHJ3*01	2336	O12_IGKJ1*01	833	1438
268	VH3-23_IGHD5-5*01 (2) >1_IGHJ3*01	2337	O12_IGKJ1*01	833	1438
269	VH3-23_IGHD5-5*01 (2) >2_IGHJ3*01	2338	O12_IGKJ1*01	833	1438

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
270	VH3-23_IGHD5-5*01 (2) >3_IGHJ3*01	2339	O12_IGKJ1*01	833	1438
271	VH3-23_IGHD5-12*01>1_IGHJ3*01	2340	O12_IGKJ1*01	833	1438
272	VH3-23_IGHD5-12*01>3_IGHJ3*01	2341	O12_IGKJ1*01	833	1438
273	VH3-23_IGHD5-18*01 (2) >1_IGHJ3*01	2342	O12_IGKJ1*01	833	1438
274	VH3-23_IGHD5-18*01 (2) >2_IGHJ3*01	2343	O12_IGKJ1*01	833	1438
275	VH3-23_IGHD5-18*01 (2) >3_IGHJ3*01	2344	O12_IGKJ1*01	833	1438
276	VH3-23_IGHD5-24*01>1_IGHJ3*01	2345	O12_IGKJ1*01	833	1438
277	VH3-23_IGHD5-24*01>3_IGHJ3*01	2346	O12_IGKJ1*01	833	1438
278	VH3-23_IGHD6-6*01>1_IGHJ3*01	2347	O12_IGKJ1*01	833	1438
279	VH3-23_IGHD1-1*01>1'_IGHJ3*01	2357	O12_IGKJ1*01	833	1438
280	VH3-23_IGHD1-1*01>2'_IGHJ3*01	2358	O12_IGKJ1*01	833	1438
281	VH3-23_IGHD1-1*01>3'_IGHJ3*01	2359	O12_IGKJ1*01	833	1438
282	VH3-23_IGHD1-7*01>1'_IGHJ3*01	2360	O12_IGKJ1*01	833	1438
283	VH3-23_IGHD1-7*01>3'_IGHJ3*01	2361	O12_IGKJ1*01	833	1438
284	VH3-23_IGHD1-14*01>1'_IGHJ3*01	2362	O12_IGKJ1*01	833	1438
285	VH3-23_IGHD1-14*01>2'_IGHJ3*01	2363	O12_IGKJ1*01	833	1438
286	VH3-23_IGHD1-14*01>3'_IGHJ3*01	2364	O12_IGKJ1*01	833	1438
287	VH3-23_IGHD1-20*01>1'_IGHJ3*01	2365	O12_IGKJ1*01	833	1438
288	VH3-23_IGHD1-20*01>2'_IGHJ3*01	2366	O12_IGKJ1*01	833	1438
289	VH3-23_IGHD1-20*01>3'_IGHJ3*01	2367	O12_IGKJ1*01	833	1438
290	VH3-23_IGHD1-26*01>1'_IGHJ3*01	2368	O12_IGKJ1*01	833	1438
291	VH3-23_IGHD1-26*01>3'_IGHJ3*01	2369	O12_IGKJ1*01	833	1438
292	VH3-23_IGHD2-2*01>1'_IGHJ3*01	2370	O12_IGKJ1*01	833	1438
293	VH3-23_IGHD2-2*01>3'_IGHJ3*01	2371	O12_IGKJ1*01	833	1438
294	VH3-23_IGHD2-8*01>1'_IGHJ3*01	2372	O12_IGKJ1*01	833	1438
295	VH3-23_IGHD2-15*01>1'_IGHJ3*01	2373	O12_IGKJ1*01	833	1438
296	VH3-23_IGHD2-15*01>3'_IGHJ3*01	2374	O12_IGKJ1*01	833	1438
297	VH3-23_IGHD2-21*01>1'_IGHJ3*01	2375	O12_IGKJ1*01	833	1438
298	VH3-23_IGHD2-21*01>3'_IGHJ3*01	2376	O12_IGKJ1*01	833	1438
299	VH3-23_IGHD3-3*01>1'_IGHJ3*01	2377	O12_IGKJ1*01	833	1438
300	VH3-23_IGHD3-3*01>3'_IGHJ3*01	2378	O12_IGKJ1*01	833	1438
301	VH3-23_IGHD3-9*01>1'_IGHJ3*01	2379	O12_IGKJ1*01	833	1438
302	VH3-23_IGHD3-9*01>3'_IGHJ3*01	2380	O12_IGKJ1*01	833	1438
303	VH3-23_IGHD3-10*01>1'_IGHJ3*01	2381	O12_IGKJ1*01	833	1438
304	VH3-23_IGHD3-10*01>3'_IGHJ3*01	2382	O12_IGKJ1*01	833	1438
305	VH3-23_IGHD3-16*01>1'_IGHJ3*01	2383	O12_IGKJ1*01	833	1438
306	VH3-23_IGHD3-16*01>3'_IGHJ3*01	2384	O12_IGKJ1*01	833	1438
307	VH3-23_IGHD3-22*01>1'_IGHJ3*01	2385	O12_IGKJ1*01	833	1438
308	VH3-23_IGHD4-4*01 (1) >1'_IGHJ3*01	2386	O12_IGKJ1*01	833	1438
309	VH3-23_IGHD4-4*01 (1) >3'_IGHJ3*01	2387	O12_IGKJ1*01	833	1438
310	VH3-23_IGHD4-11*01 (1) >1'_IGHJ3*01	2388	O12_IGKJ1*01	833	1438
311	VH3-23_IGHD4-11*01 (1) >3'_IGHJ3*01	2389	O12_IGKJ1*01	833	1438
312	VH3-23_IGHD4-17*01>1'_IGHJ3*01	2390	O12_IGKJ1*01	833	1438
313	VH3-23_IGHD4-17*01>3'_IGHJ3*01	2391	O12_IGKJ1*01	833	1438

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
314	VH3-23_IGHD4-23*01>1'_IGHJ3*01	2392	O12_IGKJ1*01	833	1438
315	VH3-23_IGHD4-23*01>3'_IGHJ3*01	2393	O12_IGKJ1*01	833	1438
316	VH3-23_IGHD5-5*01 (2) >1'_IGHJ3*01	2394	O12_IGKJ1*01	833	1438
317	VH3-23_IGHD5-5*01 (2) >3'_IGHJ3*01	2395	O12_IGKJ1*01	833	1438
318	VH3-23_IGHD5-12*01>1'_IGHJ3*01	2396	O12_IGKJ1*01	833	1438
319	VH3-23_IGHD5-12*01>3'_IGHJ3*01	2397	O12_IGKJ1*01	833	1438
320	VH3-23_IGHD5-18*01 (2) >1'_IGHJ3*01	2398	O12_IGKJ1*01	833	1438
321	VH3-23_IGHD5-18*01 (2) >3'_IGHJ3*01	2399	O12_IGKJ1*01	833	1438
322	VH3-23_IGHD5-24*01>1'_IGHJ3*01	2400	O12_IGKJ1*01	833	1438
323	VH3-23_IGHD5-24*01>3'_IGHJ3*01	2401	O12_IGKJ1*01	833	1438
324	VH3-23_IGHD6-6*01>1'_IGHJ3*01	2402	O12_IGKJ1*01	833	1438
325	VH3-23_IGHD6-6*01>2'_IGHJ3*01	2403	O12_IGKJ1*01	833	1438
326	VH3-23_IGHD6-6*01>3'_IGHJ3*01	2404	O12_IGKJ1*01	833	1438
327	VH3-23_IGHD6-6*01>2_IGHJ3*01	2348	O12_IGKJ1*01	833	1438
328	VH3-23_IGHD6-13*01>1_IGHJ3*01	2349	O12_IGKJ1*01	833	1438
329	VH3-23_IGHD6-13*01>2_IGHJ3*01	2350	O12_IGKJ1*01	833	1438
330	VH3-23_IGHD6-19*01>1_IGHJ3*01	2351	O12_IGKJ1*01	833	1438
331	VH3-23_IGHD6-19*01>2_IGHJ3*01	2352	O12_IGKJ1*01	833	1438
332	VH3-23_IGHD6-25*01>1_IGHJ3*01	2353	O12_IGKJ1*01	833	1438
333	VH3-23_IGHD6-25*01>2_IGHJ3*01	2354	O12_IGKJ1*01	833	1438
334	VH3-23_IGHD7-27*01>1_IGHJ3*01	2355	O12_IGKJ1*01	833	1438
335	VH3-23_IGHD7-27*01>3_IGHJ3*01	2356	O12_IGKJ1*01	833	1438
336	VH3-23_IGHD6-13*01>1'_IGHJ3*01	2405	O12_IGKJ1*01	833	1438
337	VH3-23_IGHD6-13*01>2'_IGHJ3*01	2406	O12_IGKJ1*01	833	1438
338	VH3-23_IGHD6-13*01>1_IGHJ6*01	2407	O12_IGKJ1*01	833	1438
339	VH3-23_IGHD6-19*01>1'_IGHJ3*01	2408	O12_IGKJ1*01	833	1438
340	VH3-23_IGHD6-19*01>2'_IGHJ3*01	2409	O12_IGKJ1*01	833	1438
341	VH3-23_IGHD6-19*01>3'_IGHJ3*01	2410	O12_IGKJ1*01	833	1438
342	VH3-23_IGHD6-25*01>1'_IGHJ3*01	2411	O12_IGKJ1*01	833	1438
343	VH3-23_IGHD6-25*01>3'_IGHJ3*01	2412	O12_IGKJ1*01	833	1438
344	VH3-23_IGHD7-27*01>1'_IGHJ3*01	2413	O12_IGKJ1*01	833	1438
345	VH3-23_IGHD7-27*01>2'_IGHJ3*01	2414	O12_IGKJ1*01	833	1438
346	VH3-23_IGHD1-1*01>1_IGHJ4*01	2415	O12_IGKJ1*01	833	1438
347	VH3-23_IGHD1-1*01>2_IGHJ4*01	2416	O12_IGKJ1*01	833	1438
348	VH3-23_IGHD1-1*01>3_IGHJ4*01	2417	O12_IGKJ1*01	833	1438
349	VH3-23_IGHD1-7*01>1_IGHJ4*01	2418	O12_IGKJ1*01	833	1438
350	VH3-23_IGHD1-7*01>3_IGHJ4*01	2419	O12_IGKJ1*01	833	1438
351	VH3-23_IGHD1-14*01>1_IGHJ4*01	2420	O12_IGKJ1*01	833	1438
352	VH3-23_IGHD1-14*01>3_IGHJ4*01	2421	O12_IGKJ1*01	833	1438
353	VH3-23_IGHD1-20*01>1_IGHJ4*01	2422	O12_IGKJ1*01	833	1438
354	VH3-23_IGHD1-20*01>3_IGHJ4*01	2423	O12_IGKJ1*01	833	1438
355	VH3-23_IGHD1-26*01>1_IGHJ4*01	2424	O12_IGKJ1*01	833	1438
356	VH3-23_IGHD1-26*01>3_IGHJ4*01	2425	O12_IGKJ1*01	833	1438
357	VH3-23_IGHD2-2*01>2_IGHJ4*01	2426	O12_IGKJ1*01	833	1438

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
358	VH3-23_IGHD2-2*01>3_IGHJ4*01	2427	O12_IGKJ1*01	833	1438
359	VH3-23_IGHD2-8*01>2_IGHJ4*01	2428	O12_IGKJ1*01	833	1438
360	VH3-23_IGHD2-8*01>3_IGHJ4*01	2429	O12_IGKJ1*01	833	1438
361	VH3-23_IGHD2-15*01>2_IGHJ4*01	2430	O12_IGKJ1*01	833	1438
362	VH3-23_IGHD2-15*01>3_IGHJ4*01	2431	O12_IGKJ1*01	833	1438
363	VH3-23_IGHD2-21*01>2_IGHJ4*01	2432	O12_IGKJ1*01	833	1438
364	VH3-23_IGHD2-21*01>3_IGHJ4*01	2433	O12_IGKJ1*01	833	1438
365	VH3-23_IGHD3-3*01>1_IGHJ4*01	2434	O12_IGKJ1*01	833	1438
366	VH3-23_IGHD3-3*01>2_IGHJ4*01	2435	O12_IGKJ1*01	833	1438
367	VH3-23_IGHD3-3*01>3_IGHJ4*01	2436	O12_IGKJ1*01	833	1438
368	VH3-23_IGHD3-9*01>2_IGHJ4*01	2437	O12_IGKJ1*01	833	1438
369	VH3-23_IGHD3-10*01>2_IGHJ4*01	2438	O12_IGKJ1*01	833	1438
370	VH3-23_IGHD3-10*01>3_IGHJ4*01	2439	O12_IGKJ1*01	833	1438
371	VH3-23_IGHD3-16*01>2_IGHJ4*01	2440	O12_IGKJ1*01	833	1438
372	VH3-23_IGHD3-16*01>3_IGHJ4*01	2441	O12_IGKJ1*01	833	1438
373	VH3-23_IGHD3-22*01>2_IGHJ4*01	2442	O12_IGKJ1*01	833	1438
374	VH3-23_IGHD3-22*01>3_IGHJ4*01	2443	O12_IGKJ1*01	833	1438
375	VH3-23_IGHD4-4*01 (1) >2_IGHJ4*01	2444	O12_IGKJ1*01	833	1438
376	VH3-23_IGHD4-4*01 (1) >3_IGHJ4*01	2445	O12_IGKJ1*01	833	1438
377	VH3-23_IGHD4-11*01 (1) >2_IGHJ4*01	2446	O12_IGKJ1*01	833	1438
378	VH3-23_IGHD4-11*01 (1) >3_IGHJ4*01	2447	O12_IGKJ1*01	833	1438
379	VH3-23_IGHD4-17*01>2_IGHJ4*01	2448	O12_IGKJ1*01	833	1438
380	VH3-23_IGHD4-17*01>3_IGHJ4*01	2449	O12_IGKJ1*01	833	1438
381	VH3-23_IGHD4-23*01>2_IGHJ4*01	2450	O12_IGKJ1*01	833	1438
382	VH3-23_IGHD4-23*01>3_IGHJ4*01	2451	O12_IGKJ1*01	833	1438
383	VH3-23_IGHD5-5*01 (2) >1_IGHJ4*01	2452	O12_IGKJ1*01	833	1438
384	VH3-23_IGHD5-5*01 (2) >2_IGHJ4*01	2453	O12_IGKJ1*01	833	1438
385	VH3-23_IGHD5-5*01 (2) >3_IGHJ4*01	2454	O12_IGKJ1*01	833	1438
386	VH3-23_IGHD5-12*01>1_IGHJ4*01	2455	O12_IGKJ1*01	833	1438
387	VH3-23_IGHD5-12*01>3_IGHJ4*01	2456	O12_IGKJ1*01	833	1438
388	VH3-23_IGHD5-18*01 (2) >1_IGHJ4*01	2457	O12_IGKJ1*01	833	1438
389	VH3-23_IGHD5-18*01 (2) >2_IGHJ4*01	2458	O12_IGKJ1*01	833	1438
390	VH3-23_IGHD5-18*01 (2) >3_IGHJ4*01	2459	O12_IGKJ1*01	833	1438
391	VH3-23_IGHD5-24*01>1_IGHJ4*01	2460	O12_IGKJ1*01	833	1438
392	VH3-23_IGHD5-24*01>3_IGHJ4*01	2461	O12_IGKJ1*01	833	1438
393	VH3-23_IGHD6-6*01>1_IGHJ4*01	2462	O12_IGKJ1*01	833	1438
394	VH3-23_IGHD1-1*01>1'_IGHJ4*01	2472	O12_IGKJ1*01	833	1438
395	VH3-23_IGHD1-1*01>2'_IGHJ4*01	2473	O12_IGKJ1*01	833	1438
396	VH3-23_IGHD1-1*01>3'_IGHJ4*01	2474	O12_IGKJ1*01	833	1438
397	VH3-23_IGHD1-7*01>1'_IGHJ4*01	2475	O12_IGKJ1*01	833	1438
398	VH3-23_IGHD1-7*01>3'_IGHJ4*01	2476	O12_IGKJ1*01	833	1438
399	VH3-23_IGHD1-14*01>1'_IGHJ4*01	2477	O12_IGKJ1*01	833	1438
400	VH3-23_IGHD1-14*01>2'_IGHJ4*01	2478	O12_IGKJ1*01	833	1438
401	VH3-23_IGHD1-14*01>3'_IGHJ4*01	2479	O12_IGKJ1*01	833	1438

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
402	VH3-23_IGHD1-20*01>1'_IGHJ4*01	2480	O12_IGKJ1*01	833	1438
403	VH3-23_IGHD1-20*01>2'_IGHJ4*01	2481	O12_IGKJ1*01	833	1438
404	VH3-23_IGHD1-20*01>3'_IGHJ4*01	2482	O12_IGKJ1*01	833	1438
405	VH3-23_IGHD1-26*01>1'_IGHJ4*01	2483	O12_IGKJ1*01	833	1438
406	VH3-23_IGHD1-26*01>1_IGHJ4*01_B	2484	O12_IGKJ1*01	833	1438
407	VH3-23_IGHD2-2*01>1'_IGHJ4*01	2485	O12_IGKJ1*01	833	1438
408	VH3-23_IGHD2-2*01>3'_IGHJ4*01	2486	O12_IGKJ1*01	833	1438
409	VH3-23_IGHD2-8*01>1'_IGHJ4*01	2487	O12_IGKJ1*01	833	1438
410	VH3-23_IGHD2-15*01>1'_IGHJ4*01	2488	O12_IGKJ1*01	833	1438
411	VH3-23_IGHD2-15*01>3'_IGHJ4*01	2489	O12_IGKJ1*01	833	1438
412	VH3-23_IGHD2-21*01>1'_IGHJ4*01	2490	O12_IGKJ1*01	833	1438
413	VH3-23_IGHD2-21*01>3'_IGHJ4*01	2491	O12_IGKJ1*01	833	1438
414	VH3-23_IGHD3-3*01>1'_IGHJ4*01	2492	O12_IGKJ1*01	833	1438
415	VH3-23_IGHD3-3*01>3'_IGHJ4*01	2493	O12_IGKJ1*01	833	1438
416	VH3-23_IGHD3-9*01>1'_IGHJ4*01	2494	O12_IGKJ1*01	833	1438
417	VH3-23_IGHD3-9*01>3'_IGHJ4*01	2495	O12_IGKJ1*01	833	1438
418	VH3-23_IGHD3-10*01>1'_IGHJ4*01	2496	O12_IGKJ1*01	833	1438
419	VH3-23_IGHD3-10*01>3'_IGHJ4*01	2497	O12_IGKJ1*01	833	1438
420	VH3-23_IGHD3-16*01>1'_IGHJ4*01	2498	O12_IGKJ1*01	833	1438
421	VH3-23_IGHD3-16*01>3'_IGHJ4*01	2499	O12_IGKJ1*01	833	1438
422	VH3-23_IGHD3-22*01>1'_IGHJ4*01	2500	O12_IGKJ1*01	833	1438
423	VH3-23_IGHD4-4*01 (1) >1'_IGHJ4*01	2501	O12_IGKJ1*01	833	1438
424	VH3-23_IGHD4-4*01 (1) >3'_IGHJ4*01	2502	O12_IGKJ1*01	833	1438
425	VH3-23_IGHD4-11*01 (1) >1'_IGHJ4*01	2503	O12_IGKJ1*01	833	1438
426	VH3-23_IGHD4-11*01 (1) >3'_IGHJ4*01	2504	O12_IGKJ1*01	833	1438
427	VH3-23_IGHD4-17*01>1'_IGHJ4*01	2505	O12_IGKJ1*01	833	1438
428	VH3-23_IGHD4-17*01>3'_IGHJ4*01	2506	O12_IGKJ1*01	833	1438
429	VH3-23_IGHD4-23*01>1'_IGHJ4*01	2507	O12_IGKJ1*01	833	1438
430	VH3-23_IGHD4-23*01>3'_IGHJ4*01	2508	O12_IGKJ1*01	833	1438
431	VH3-23_IGHD5-5*01 (2) >1'_IGHJ4*01	2509	O12_IGKJ1*01	833	1438
432	VH3-23_IGHD5-5*01 (2) >3'_IGHJ4*01	2510	O12_IGKJ1*01	833	1438
433	VH3-23_IGHD5-12*01>1'_IGHJ4*01	2511	O12_IGKJ1*01	833	1438
434	VH3-23_IGHD5-12*01>3'_IGHJ4*01	2512	O12_IGKJ1*01	833	1438
435	VH3-23_IGHD5-18*01 (2) >1'_IGHJ4*01	2513	O12_IGKJ1*01	833	1438
436	VH3-23_IGHD5-18*01 (2) >3'_IGHJ4*01	2514	O12_IGKJ1*01	833	1438
437	VH3-23_IGHD5-24*01>1'_IGHJ4*01	2515	O12_IGKJ1*01	833	1438
438	VH3-23_IGHD5-24*01>3'_IGHJ4*01	2516	O12_IGKJ1*01	833	1438
439	VH3-23_IGHD6-6*01>1'_IGHJ4*01	2517	O12_IGKJ1*01	833	1438
440	VH3-23_IGHD6-6*01>2'_IGHJ4*01	2518	O12_IGKJ1*01	833	1438
441	VH3-23_IGHD6-6*01>3'_IGHJ4*01	2519	O12_IGKJ1*01	833	1438
442	VH3-23_IGHD6-6*01>2_IGHJ4*01	2463	O12_IGKJ1*01	833	1438
443	VH3-23_IGHD6-13*01>1_IGHJ4*01	2464	O12_IGKJ1*01	833	1438
444	VH3-23_IGHD6-13*01>2_IGHJ4*01	2465	O12_IGKJ1*01	833	1438
445	VH3-23_IGHD6-19*01>1_IGHJ4*01	2466	O12_IGKJ1*01	833	1438

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
446	VH3-23_IGHD6-19*01>2_IGHJ4*01	2467	O12_IGKJ1*01	833	1438
447	VH3-23_IGHD6-25*01>1_IGHJ4*01	2468	O12_IGKJ1*01	833	1438
448	VH3-23_IGHD6-25*01>2_IGHJ4*01	2469	O12_IGKJ1*01	833	1438
449	VH3-23_IGHD7-27*01>1_IGHJ4*01	2470	O12_IGKJ1*01	833	1438
450	VH3-23_IGHD7-27*01>3_IGHJ4*01	2471	O12_IGKJ1*01	833	1438
451	VH3-23_IGHD6-13*01>1'_IGHJ4*01	2520	O12_IGKJ1*01	833	1438
452	VH3-23_IGHD6-13*01>2'_IGHJ4*01	2521	O12_IGKJ1*01	833	1438
453	VH3-23_IGHD6-13*01>2_IGHJ4*01_B	2522	O12_IGKJ1*01	833	1438
454	VH3-23_IGHD6-19*01>1'_IGHJ4*01	2523	O12_IGKJ1*01	833	1438
455	VH3-23_IGHD6-19*01>2'_IGHJ4*01	2524	O12_IGKJ1*01	833	1438
456	VH3-23_IGHD6-19*01>2_IGHJ4*01_B	2525	O12_IGKJ1*01	833	1438
457	VH3-23_IGHD6-25*01>1'_IGHJ4*01	2526	O12_IGKJ1*01	833	1438
458	VH3-23_IGHD6-25*01>3'_IGHJ4*01	2527	O12_IGKJ1*01	833	1438
459	VH3-23_IGHD7-27*01>1'_IGHJ4*01	2528	O12_IGKJ1*01	833	1438
460	VH3-23_IGHD7-27*01>2'_IGHJ4*01	2529	O12_IGKJ1*01	833	1438
461	VH3-23_IGHD1-1*01>1_IGHJ5*01	2530	O12_IGKJ1*01	833	1438
462	VH3-23_IGHD1-1*01>2_IGHJ5*01	2531	O12_IGKJ1*01	833	1438
463	VH3-23_IGHD1-1*01>3_IGHJ5*01	2532	O12_IGKJ1*01	833	1438
464	VH3-23_IGHD1-7*01>1_IGHJ5*01	2533	O12_IGKJ1*01	833	1438
465	VH3-23_IGHD1-7*01>3_IGHJ5*01	2534	O12_IGKJ1*01	833	1438
466	VH3-23_IGHD1-14*01>1_IGHJ5*01	2535	O12_IGKJ1*01	833	1438
467	VH3-23_IGHD1-14*01>3_IGHJ5*01	2536	O12_IGKJ1*01	833	1438
468	VH3-23_IGHD1-20*01>1_IGHJ5*01	2537	O12_IGKJ1*01	833	1438
469	VH3-23_IGHD1-20*01>3_IGHJ5*01	2538	O12_IGKJ1*01	833	1438
470	VH3-23_IGHD1-26*01>1_IGHJ5*01	2539	O12_IGKJ1*01	833	1438
471	VH3-23_IGHD1-26*01>3_IGHJ5*01	2540	O12_IGKJ1*01	833	1438
472	VH3-23_IGHD2-2*01>2_IGHJ5*01	2541	O12_IGKJ1*01	833	1438
473	VH3-23_IGHD2-2*01>3_IGHJ5*01	2542	O12_IGKJ1*01	833	1438
474	VH3-23_IGHD2-8*01>2_IGHJ5*01	2543	O12_IGKJ1*01	833	1438
475	VH3-23_IGHD2-8*01>3_IGHJ5*01	2544	O12_IGKJ1*01	833	1438
476	VH3-23_IGHD2-15*01>2_IGHJ5*01	2545	O12_IGKJ1*01	833	1438
477	VH3-23_IGHD2-15*01>3_IGHJ5*01	2546	O12_IGKJ1*01	833	1438
478	VH3-23_IGHD2-21*01>2_IGHJ5*01	2547	O12_IGKJ1*01	833	1438
479	VH3-23_IGHD2-21*01>3_IGHJ5*01	2548	O12_IGKJ1*01	833	1438
480	VH3-23_IGHD3-3*01>1_IGHJ5*01	2549	O12_IGKJ1*01	833	1438
481	VH3-23_IGHD3-3*01>2_IGHJ5*01	2550	O12_IGKJ1*01	833	1438
482	VH3-23_IGHD3-3*01>3_IGHJ5*01	2551	O12_IGKJ1*01	833	1438
483	VH3-23_IGHD3-9*01>2_IGHJ5*01	2552	O12_IGKJ1*01	833	1438
484	VH3-23_IGHD3-10*01>2_IGHJ5*01	2553	O12_IGKJ1*01	833	1438
485	VH3-23_IGHD3-10*01>3_IGHJ5*01	2554	O12_IGKJ1*01	833	1438
486	VH3-23_IGHD3-16*01>2_IGHJ5*01	2555	O12_IGKJ1*01	833	1438
487	VH3-23_IGHD3-16*01>3_IGHJ5*01	2556	O12_IGKJ1*01	833	1438
488	VH3-23_IGHD3-22*01>2_IGHJ5*01	2557	O12_IGKJ1*01	833	1438
489	VH3-23_IGHD3-22*01>3_IGHJ5*01	2558	O12_IGKJ1*01	833	1438

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
490	VH3-23_IGHD4-4*01 (1) >2_IGHJ5*01	2559	O12_IGKJ1*01	833	1438
491	VH3-23_IGHD4-4*01 (1) >3_IGHJ5*01	2560	O12_IGKJ1*01	833	1438
492	VH3-23_IGHD4-11*01 (1) >2_IGHJ5*01	2561	O12_IGKJ1*01	833	1438
493	VH3-23_IGHD4-11*01 (1) >3_IGHJ5*01	2562	O12_IGKJ1*01	833	1438
494	VH3-23_IGHD4-17*01>2_IGHJ5*01	2563	O12_IGKJ1*01	833	1438
495	VH3-23_IGHD4-17*01>3_IGHJ5*01	2564	O12_IGKJ1*01	833	1438
496	VH3-23_IGHD4-23*01>2_IGHJ5*01	2565	O12_IGKJ1*01	833	1438
497	VH3-23_IGHD4-23*01>3_IGHJ5*01	2566	O12_IGKJ1*01	833	1438
498	VH3-23_IGHD5-5*01 (2) >1_IGHJ5*01	2567	O12_IGKJ1*01	833	1438
499	VH3-23_IGHD5-5*01 (2) >2_IGHJ5*01	2568	O12_IGKJ1*01	833	1438
500	VH3-23_IGHD5-5*01 (2) >3_IGHJ5*01	2569	O12_IGKJ1*01	833	1438
501	VH3-23_IGHD5-12*01>1_IGHJ5*01	2570	O12_IGKJ1*01	833	1438
502	VH3-23_IGHD5-12*01>3_IGHJ5*01	2571	O12_IGKJ1*01	833	1438
503	VH3-23_IGHD5-18*01 (2) >1_IGHJ5*01	2572	O12_IGKJ1*01	833	1438
504	VH3-23_IGHD5-18*01 (2) >2_IGHJ5*01	2573	O12_IGKJ1*01	833	1438
505	VH3-23_IGHD5-18*01 (2) >3_IGHJ5*01	2574	O12_IGKJ1*01	833	1438
506	VH3-23_IGHD5-24*01>1_IGHJ5*01	2575	O12_IGKJ1*01	833	1438
507	VH3-23_IGHD5-24*01>3_IGHJ5*01	2576	O12_IGKJ1*01	833	1438
508	VH3-23_IGHD6-6*01>1_IGHJ5*01	2577	O12_IGKJ1*01	833	1438
509	VH3-23_IGHD1-1*01>1'_IGHJ5*01	2587	O12_IGKJ1*01	833	1438
510	VH3-23_IGHD1-1*01>2'_IGHJ5*01	2588	O12_IGKJ1*01	833	1438
511	VH3-23_IGHD1-1*01>3'_IGHJ5*01	2589	O12_IGKJ1*01	833	1438
512	VH3-23_IGHD1-7*01>1'_IGHJ5*01	2590	O12_IGKJ1*01	833	1438
513	VH3-23_IGHD1-7*01>3'_IGHJ5*01	2591	O12_IGKJ1*01	833	1438
514	VH3-23_IGHD1-14*01>1'_IGHJ5*01	2592	O12_IGKJ1*01	833	1438
515	VH3-23_IGHD1-14*01>2'_IGHJ5*01	2593	O12_IGKJ1*01	833	1438
516	VH3-23_IGHD1-14*01>3'_IGHJ5*01	2594	O12_IGKJ1*01	833	1438
517	VH3-23_IGHD1-20*01>1'_IGHJ5*01	2595	O12_IGKJ1*01	833	1438
518	VH3-23_IGHD1-20*01>2'_IGHJ5*01	2596	O12_IGKJ1*01	833	1438
519	VH3-23_IGHD1-20*01>3'_IGHJ5*01	2597	O12_IGKJ1*01	833	1438
520	VH3-23_IGHD1-26*01>1'_IGHJ5*01	2598	O12_IGKJ1*01	833	1438
521	VH3-23_IGHD1-26*01>3'_IGHJ5*01	2599	O12_IGKJ1*01	833	1438
522	VH3-23_IGHD2-2*01>1'_IGHJ5*01	2600	O12_IGKJ1*01	833	1438
523	VH3-23_IGHD2-2*01>3'_IGHJ5*01	2601	O12_IGKJ1*01	833	1438
524	VH3-23_IGHD2-8*01>1'_IGHJ5*01	2602	O12_IGKJ1*01	833	1438
525	VH3-23_IGHD2-15*01>1'_IGHJ5*01	2603	O12_IGKJ1*01	833	1438
526	VH3-23_IGHD2-15*01>3'_IGHJ5*01	2604	O12_IGKJ1*01	833	1438
527	VH3-23_IGHD2-21*01>1'_IGHJ5*01	2605	O12_IGKJ1*01	833	1438
528	VH3-23_IGHD2-21*01>3'_IGHJ5*01	2606	O12_IGKJ1*01	833	1438
529	VH3-23_IGHD3-3*01>1'_IGHJ5*01	2607	O12_IGKJ1*01	833	1438
530	VH3-23_IGHD3-3*01>3'_IGHJ5*01	2608	O12_IGKJ1*01	833	1438
531	VH3-23_IGHD3-9*01>1'_IGHJ5*01	2609	O12_IGKJ1*01	833	1438
532	VH3-23_IGHD3-9*01>3'_IGHJ5*01	2610	O12_IGKJ1*01	833	1438
533	VH3-23_IGHD3-10*01>1'_IGHJ5*01	2611	O12_IGKJ1*01	833	1438

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
534	VH3-23_IGHD3-10*01>3'_IGHJ5*01	2612	O12_IGKJ1*01	833	1438
535	VH3-23_IGHD3-16*01>1'_IGHJ5*01	2613	O12_IGKJ1*01	833	1438
536	VH3-23_IGHD3-16*01>3'_IGHJ5*01	2614	O12_IGKJ1*01	833	1438
537	VH3-23_IGHD3-22*01>1'_IGHJ5*01	2615	O12_IGKJ1*01	833	1438
538	VH3-23_IGHD4-4*01 (1) >1'_IGHJ5*01	2616	O12_IGKJ1*01	833	1438
539	VH3-23_IGHD4-4*01 (1) >3'_IGHJ5*01	2617	O12_IGKJ1*01	833	1438
540	VH3-23_IGHD4-11*01 (1) >1'_IGHJ5*01	2618	O12_IGKJ1*01	833	1438
541	VH3-23_IGHD4-11*01 (1) >3'_IGHJ5*01	2619	O12_IGKJ1*01	833	1438
542	VH3-23_IGHD4-17*01>1'_IGHJ5*01	2620	O12_IGKJ1*01	833	1438
543	VH3-23_IGHD4-17*01>3'_IGHJ5*01	2621	O12_IGKJ1*01	833	1438
544	VH3-23_IGHD4-23*01>1'_IGHJ5*01	2622	O12_IGKJ1*01	833	1438
545	VH3-23_IGHD4-23*01>3'_IGHJ5*01	2623	O12_IGKJ1*01	833	1438
546	VH3-23_IGHD5-5*01 (2) >1'_IGHJ5*01	2624	O12_IGKJ1*01	833	1438
547	VH3-23_IGHD5-5*01 (2) >3'_IGHJ5*01	2625	O12_IGKJ1*01	833	1438
548	VH3-23_IGHD5-12*01>1'_IGHJ5*01	2626	O12_IGKJ1*01	833	1438
549	VH3-23_IGHD5-12*01>3'_IGHJ5*01	2627	O12_IGKJ1*01	833	1438
550	VH3-23_IGHD5-18*01 (2) >1'_IGHJ5*01	2628	O12_IGKJ1*01	833	1438
551	VH3-23_IGHD5-18*01 (2) >3'_IGHJ5*01	2629	O12_IGKJ1*01	833	1438
552	VH3-23_IGHD5-24*01>1'_IGHJ5*01	2630	O12_IGKJ1*01	833	1438
553	VH3-23_IGHD5-24*01>3'_IGHJ5*01	2631	O12_IGKJ1*01	833	1438
554	VH3-23_IGHD6-6*01>1'_IGHJ5*01	2632	O12_IGKJ1*01	833	1438
555	VH3-23_IGHD6-6*01>2'_IGHJ5*01	2633	O12_IGKJ1*01	833	1438
556	VH3-23_IGHD6-6*01>3'_IGHJ5*01	2634	O12_IGKJ1*01	833	1438
557	VH3-23_IGHD6-6*01>2_IGHJ5*01	2578	O12_IGKJ1*01	833	1438
558	VH3-23_IGHD6-13*01>1_IGHJ5*01	2579	O12_IGKJ1*01	833	1438
559	VH3-23_IGHD6-13*01>2_IGHJ5*01	2580	O12_IGKJ1*01	833	1438
560	VH3-23_IGHD6-19*01>1_IGHJ5*01	2581	O12_IGKJ1*01	833	1438
561	VH3-23_IGHD6-19*01>2_IGHJ5*01	2582	O12_IGKJ1*01	833	1438
562	VH3-23_IGHD6-25*01>1_IGHJ5*01	2583	O12_IGKJ1*01	833	1438
563	VH3-23_IGHD6-25*01>2_IGHJ5*01	2584	O12_IGKJ1*01	833	1438
564	VH3-23_IGHD7-27*01>1_IGHJ5*01	2585	O12_IGKJ1*01	833	1438
565	VH3-23_IGHD7-27*01>3_IGHJ5*01	2586	O12_IGKJ1*01	833	1438
566	VH3-23_IGHD6-13*01>1'_IGHJ5*01	2635	O12_IGKJ1*01	833	1438
567	VH3-23_IGHD6-13*01>2'_IGHJ5*01	2636	O12_IGKJ1*01	833	1438
568	VH3-23_IGHD6-13*01>3'_IGHJ5*01	2637	O12_IGKJ1*01	833	1438
569	VH3-23_IGHD6-19*01>1'_IGHJ5*01	2638	O12_IGKJ1*01	833	1438
570	VH3-23_IGHD6-19*01>2'_IGHJ5*01	2639	O12_IGKJ1*01	833	1438
571	VH3-23_IGHD6-19*01>2_IGHJ5*01_B	2640	O12_IGKJ1*01	833	1438
572	VH3-23_IGHD6-25*01>1'_IGHJ5*01	2641	O12_IGKJ1*01	833	1438
573	VH3-23_IGHD6-25*01>3'_IGHJ5*01	2642	O12_IGKJ1*01	833	1438
574	VH3-23_IGHD7-27*01>1'_IGHJ5*01	2643	O12_IGKJ1*01	833	1438
575	VH3-23_IGHD7-27*01>2'_IGHJ5*01	2644	O12_IGKJ1*01	833	1438
576	VH3-23_IGHD1-1*01>1_IGHJ6*01	2645	O12_IGKJ1*01	833	1438
577	VH3-23_IGHD1-1*01>2_IGHJ6*01	2646	O12_IGKJ1*01	833	1438

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
578	VH3-23_IGHD1-1*01>3_IGHJ6*01	2647	O12_IGKJ1*01	833	1438
579	VH3-23_IGHD1-7*01>1_IGHJ6*01	2648	O12_IGKJ1*01	833	1438
580	VH3-23_IGHD1-7*01>3_IGHJ6*01	2649	O12_IGKJ1*01	833	1438
581	VH3-23_IGHD1-14*01>1_IGHJ6*01	2650	O12_IGKJ1*01	833	1438
582	VH3-23_IGHD1-14*01>3_IGHJ6*01	2651	O12_IGKJ1*01	833	1438
583	VH3-23_IGHD1-20*01>1_IGHJ6*01	2652	O12_IGKJ1*01	833	1438
584	VH3-23_IGHD1-20*01>3_IGHJ6*01	2653	O12_IGKJ1*01	833	1438
585	VH3-23_IGHD1-26*01>1_IGHJ6*01	2654	O12_IGKJ1*01	833	1438
586	VH3-23_IGHD1-26*01>3_IGHJ6*01	2655	O12_IGKJ1*01	833	1438
587	VH3-23_IGHD2-2*01>2_IGHJ6*01	2656	O12_IGKJ1*01	833	1438
588	VH3-23_IGHD2-2*01>3_IGHJ6*01	2657	O12_IGKJ1*01	833	1438
589	VH3-23_IGHD2-8*01>2_IGHJ6*01	2658	O12_IGKJ1*01	833	1438
590	VH3-23_IGHD2-8*01>3_IGHJ6*01	2659	O12_IGKJ1*01	833	1438
591	VH3-23_IGHD2-15*01>2_IGHJ6*01	2660	O12_IGKJ1*01	833	1438
592	VH3-23_IGHD2-15*01>3_IGHJ6*01	2661	O12_IGKJ1*01	833	1438
593	VH3-23_IGHD2-21*01>2_IGHJ6*01	2662	O12_IGKJ1*01	833	1438
594	VH3-23_IGHD2-21*01>3_IGHJ6*01	2663	O12_IGKJ1*01	833	1438
595	VH3-23_IGHD3-3*01>1_IGHJ6*01	2664	O12_IGKJ1*01	833	1438
596	VH3-23_IGHD3-3*01>2_IGHJ6*01	2665	O12_IGKJ1*01	833	1438
597	VH3-23_IGHD3-3*01>3_IGHJ6*01	2666	O12_IGKJ1*01	833	1438
598	VH3-23_IGHD3-9*01>2_IGHJ6*01	2667	O12_IGKJ1*01	833	1438
599	VH3-23_IGHD3-10*01>2_IGHJ6*01	2668	O12_IGKJ1*01	833	1438
600	VH3-23_IGHD3-10*01>3_IGHJ6*01	2669	O12_IGKJ1*01	833	1438
601	VH3-23_IGHD3-16*01>2_IGHJ6*01	2670	O12_IGKJ1*01	833	1438
602	VH3-23_IGHD3-16*01>3_IGHJ6*01	2671	O12_IGKJ1*01	833	1438
603	VH3-23_IGHD3-22*01>2_IGHJ6*01	2672	O12_IGKJ1*01	833	1438
604	VH3-23_IGHD3-22*01>3_IGHJ6*01	2673	O12_IGKJ1*01	833	1438
605	VH3-23_IGHD4-4*01 (1) >2_IGHJ6*01	2674	O12_IGKJ1*01	833	1438
606	VH3-23_IGHD4-4*01 (1) >3_IGHJ6*01	2675	O12_IGKJ1*01	833	1438
607	VH3-23_IGHD4-11*01 (1) >2_IGHJ6*01	2676	O12_IGKJ1*01	833	1438
608	VH3-23_IGHD4-11*01 (1) >3_IGHJ6*01	2677	O12_IGKJ1*01	833	1438
609	VH3-23_IGHD4-17*01>2_IGHJ6*01	2678	O12_IGKJ1*01	833	1438
610	VH3-23_IGHD4-17*01>3_IGHJ6*01	2679	O12_IGKJ1*01	833	1438
611	VH3-23_IGHD4-23*01>2_IGHJ6*01	2680	O12_IGKJ1*01	833	1438
612	VH3-23_IGHD4-23*01>3_IGHJ6*01	2681	O12_IGKJ1*01	833	1438
613	VH3-23_IGHD5-5*01 (2) >1_IGHJ6*01	2682	O12_IGKJ1*01	833	1438
614	VH3-23_IGHD5-5*01 (2) >2_IGHJ6*01	2683	O12_IGKJ1*01	833	1438
615	VH3-23_IGHD5-5*01 (2) >3_IGHJ6*01	2684	O12_IGKJ1*01	833	1438
616	VH3-23_IGHD5-12*01>1_IGHJ6*01	2685	O12_IGKJ1*01	833	1438
617	VH3-23_IGHD5-12*01>3_IGHJ6*01	2686	O12_IGKJ1*01	833	1438
618	VH3-23_IGHD5-18*01 (2) >1_IGHJ6*01	2687	O12_IGKJ1*01	833	1438
619	VH3-23_IGHD5-18*01 (2) >2_IGHJ6*01	2688	O12_IGKJ1*01	833	1438
620	VH3-23_IGHD5-18*01 (2) >3_IGHJ6*01	2689	O12_IGKJ1*01	833	1438
621	VH3-23_IGHD5-24*01>1_IGHJ6*01	2690	O12_IGKJ1*01	833	1438

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
622	VH3-23_IGHD5-24*01>3_IGHJ6*01	2691	O12_IGKJ1*01	833	1438
623	VH3-23_IGHD6-6*01>1_IGHJ6*01	2692	O12_IGKJ1*01	833	1438
624	VH3-23_IGHD6-6*01>2_IGHJ6*01	2693	O12_IGKJ1*01	833	1438
625	VH3-23_IGHD5-12*01>3'_IGHJ6*01	2742	O12_IGKJ1*01	833	1438
626	VH3-23_IGHD5-18*01(2)>1'_IGHJ6*01	2743	O12_IGKJ1*01	833	1438
627	VH3-23_IGHD5-18*01(2)>3'_IGHJ6*01	2744	O12_IGKJ1*01	833	1438
628	VH3-23_IGHD5-24*01>1'_IGHJ6*01	2745	O12_IGKJ1*01	833	1438
629	VH3-23_IGHD5-24*01>3'_IGHJ6*01	2746	O12_IGKJ1*01	833	1438
630	VH3-23_IGHD6-6*01>1'_IGHJ6*01	2747	O12_IGKJ1*01	833	1438
631	VH3-23_IGHD6-6*01>2'_IGHJ6*01	2748	O12_IGKJ1*01	833	1438
632	VH3-23_IGHD6-6*01>3'_IGHJ6*01	2749	O12_IGKJ1*01	833	1438
633	VH3-23_IGHD1-1*01>1'_IGHJ6*01	2702	O12_IGKJ1*01	833	1438
634	VH3-23_IGHD1-1*01>2'_IGHJ6*01	2703	O12_IGKJ1*01	833	1438
635	VH3-23_IGHD1-1*01>3'_IGHJ6*01	2704	O12_IGKJ1*01	833	1438
636	VH3-23_IGHD1-7*01>1'_IGHJ6*01	2705	O12_IGKJ1*01	833	1438
637	VH3-23_IGHD1-7*01>3'_IGHJ6*01	2706	O12_IGKJ1*01	833	1438
638	VH3-23_IGHD1-14*01>1'_IGHJ6*01	2707	O12_IGKJ1*01	833	1438
639	VH3-23_IGHD1-14*01>2'_IGHJ6*01	2708	O12_IGKJ1*01	833	1438
640	VH3-23_IGHD1-14*01>3'_IGHJ6*01	2709	O12_IGKJ1*01	833	1438
641	VH3-23_IGHD1-20*01>1'_IGHJ6*01	2710	O12_IGKJ1*01	833	1438
642	VH3-23_IGHD1-20*01>2'_IGHJ6*01	2711	O12_IGKJ1*01	833	1438
643	VH3-23_IGHD1-20*01>3'_IGHJ6*01	2712	O12_IGKJ1*01	833	1438
644	VH3-23_IGHD1-26*01>1'_IGHJ6*01	2713	O12_IGKJ1*01	833	1438
645	VH3-23_IGHD1-26*01>1_IGHJ6*01_B	2714	O12_IGKJ1*01	833	1438
646	VH3-23_IGHD2-2*01>2_IGHJ6*01_B	2715	O12_IGKJ1*01	833	1438
647	VH3-23_IGHD2-2*01>3'_IGHJ6*01	2716	O12_IGKJ1*01	833	1438
648	VH3-23_IGHD2-8*01>1'_IGHJ6*01	2717	O12_IGKJ1*01	833	1438
649	VH3-23_IGHD2-15*01>1'_IGHJ6*01	2718	O12_IGKJ1*01	833	1438
650	VH3-23_IGHD2-15*01>3'_IGHJ6*01	2719	O12_IGKJ1*01	833	1438
651	VH3-23_IGHD2-21*01>1'_IGHJ6*01	2720	O12_IGKJ1*01	833	1438
652	VH3-23_IGHD2-21*01>3'_IGHJ6*01	2721	O12_IGKJ1*01	833	1438
653	VH3-23_IGHD3-3*01>1'_IGHJ6*01	2722	O12_IGKJ1*01	833	1438
654	VH3-23_IGHD3-3*01>3'_IGHJ6*01	2723	O12_IGKJ1*01	833	1438
655	VH3-23_IGHD3-9*01>1'_IGHJ6*01	2724	O12_IGKJ1*01	833	1438
656	VH3-23_IGHD3-9*01>3'_IGHJ6*01	2725	O12_IGKJ1*01	833	1438
657	VH3-23_IGHD3-10*01>1'_IGHJ6*01	2726	O12_IGKJ1*01	833	1438
658	VH3-23_IGHD3-10*01>3'_IGHJ6*01	2727	O12_IGKJ1*01	833	1438
659	VH3-23_IGHD3-16*01>1'_IGHJ6*01	2728	O12_IGKJ1*01	833	1438
660	VH3-23_IGHD3-16*01>3'_IGHJ6*01	2729	O12_IGKJ1*01	833	1438
661	VH3-23_IGHD3-22*01>1'_IGHJ6*01	2730	O12_IGKJ1*01	833	1438
662	VH3-23_IGHD4-4*01 (1) >1'_IGHJ6*01	2731	O12_IGKJ1*01	833	1438
663	VH3-23_IGHD4-4*01 (1) >3'_IGHJ6*01	2732	O12_IGKJ1*01	833	1438
664	VH3-23_IGHD4-11*01 (1) >1'_IGHJ6*01	2733	O12_IGKJ1*01	833	1438
665	VH3-23_IGHD4-11*01 (1) >3'_IGHJ6*01	2734	O12_IGKJ1*01	833	1438

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
666	VH3-23_IGHD4-17*01>1'_IGHJ6*01	2735	O12_IGKJ1*01	833	1438
667	VH3-23_IGHD4-17*01>3'_IGHJ6*01	2736	O12_IGKJ1*01	833	1438
668	VH3-23_IGHD4-23*01>1'_IGHJ6*01	2737	O12_IGKJ1*01	833	1438
669	VH3-23_IGHD4-23*01>3'_IGHJ6*01	2738	O12_IGKJ1*01	833	1438
670	VH3-23_IGHD5-5*01 (2) >1'_IGHJ6*01	2739	O12_IGKJ1*01	833	1438
671	VH3-23_IGHD5-5*01 (2) >3'_IGHJ6*01	2740	O12_IGKJ1*01	833	1438
672	VH3-23_IGHD5-12*01>1'_IGHJ6*01	2741	O12_IGKJ1*01	833	1438
673	VH3-23_IGHD5-12*01>3'_IGHJ6*01	2742	O12_IGKJ1*01	833	1438
674	VH3-23_IGHD5-18*01 (2) >1'_IGHJ6*01	2743	O12_IGKJ1*01	833	1438
675	VH3-23_IGHD5-18*01 (2) >3'_IGHJ6*01	2744	O12_IGKJ1*01	833	1438
676	VH3-23_IGHD5-24*01>1'_IGHJ6*01	2745	O12_IGKJ1*01	833	1438
677	VH3-23_IGHD5-24*01>3'_IGHJ6*01	2746	O12_IGKJ1*01	833	1438
678	VH3-23_IGHD6-6*01>1'_IGHJ6*01	2747	O12_IGKJ1*01	833	1438
679	VH3-23_IGHD6-6*01>2'_IGHJ6*01	2748	O12_IGKJ1*01	833	1438
680	VH3-23_IGHD6-6*01>3'_IGHJ6*01	2749	O12_IGKJ1*01	833	1438
681	VH3-23_IGHD6-13*01>1'_IGHJ6*01	2750	O12_IGKJ1*01	833	1438
682	VH3-23_IGHD6-13*01>2'_IGHJ6*01	2751	O12_IGKJ1*01	833	1438
683	VH3-23_IGHD6-13*01>3'_IGHJ6*01	2752	O12_IGKJ1*01	833	1438
684	VH3-23_IGHD6-19*01>1'_IGHJ6*01	2753	O12_IGKJ1*01	833	1438
685	VH3-23_IGHD6-19*01>2'_IGHJ6*01	2754	O12_IGKJ1*01	833	1438
686	VH3-23_IGHD6-19*01>3'_IGHJ6*01	2755	O12_IGKJ1*01	833	1438
687	VH3-23_IGHD6-25*01>1'_IGHJ6*01	2756	O12_IGKJ1*01	833	1438
688	VH3-23_IGHD6-25*01>3'_IGHJ6*01	2757	O12_IGKJ1*01	833	1438
689	VH3-23_IGHD7-27*01>1'_IGHJ6*01	2758	O12_IGKJ1*01	833	1438
690	VH3-23_IGHD7-27*01>2'_IGHJ6*01	2759	O12_IGKJ1*01	833	1438
691	VH3-23_IGHD1-1*01>1_IGHJ1*01	2070	O18_IGKJ1*01	834	1439
692	VH3-23_IGHD1-1*01>2_IGHJ1*01	2071	O18_IGKJ1*01	834	1439
693	VH3-23_IGHD1-1*01>3_IGHJ1*01	2072	O18_IGKJ1*01	834	1439
694	VH3-23_IGHD1-7*01>1_IGHJ1*01	2073	O18_IGKJ1*01	834	1439
695	VH3-23_IGHD1-7*01>3_IGHJ1*01	2074	O18_IGKJ1*01	834	1439
696	VH3-23_IGHD1-14*01>1_IGHJ1*01	2075	O18_IGKJ1*01	834	1439
697	VH3-23_IGHD1-14*01>3_IGHJ1*01	2076	O18_IGKJ1*01	834	1439
698	VH3-23_IGHD1-20*01>1_IGHJ1*01	2077	O18_IGKJ1*01	834	1439
699	VH3-23_IGHD1-20*01>3_IGHJ1*01	2078	O18_IGKJ1*01	834	1439
700	VH3-23_IGHD1-26*01>1_IGHJ1*01	2079	O18_IGKJ1*01	834	1439
701	VH3-23_IGHD1-26*01>3_IGHJ1*01	2080	O18_IGKJ1*01	834	1439
702	VH3-23_IGHD2-2*01>2_IGHJ1*01	2081	O18_IGKJ1*01	834	1439
703	VH3-23_IGHD2-2*01>3_IGHJ1*01	2082	O18_IGKJ1*01	834	1439
704	VH3-23_IGHD2-8*01>2_IGHJ1*01	2083	O18_IGKJ1*01	834	1439
705	VH3-23_IGHD2-8*01>3_IGHJ1*01	2084	O18_IGKJ1*01	834	1439
706	VH3-23_IGHD2-15*01>2_IGHJ1*01	2085	O18_IGKJ1*01	834	1439
707	VH3-23_IGHD2-15*01>3_IGHJ1*01	2086	O18_IGKJ1*01	834	1439
708	VH3-23_IGHD2-21*01>2_IGHJ1*01	2087	O18_IGKJ1*01	834	1439
709	VH3-23_IGHD2-21*01>3_IGHJ1*01	2088	O18_IGKJ1*01	834	1439

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
710	VH3-23_IGHD3-3*01>1_IGHJ1*01	2089	O18_IGKJ1*01	834	1439
711	VH3-23_IGHD3-3*01>2_IGHJ1*01	2090	O18_IGKJ1*01	834	1439
712	VH3-23_IGHD3-3*01>3_IGHJ1*01	2091	O18_IGKJ1*01	834	1439
713	VH3-23_IGHD3-9*01>2_IGHJ1*01	2092	O18_IGKJ1*01	834	1439
714	VH3-23_IGHD3-10*01>2_IGHJ1*01	2093	O18_IGKJ1*01	834	1439
715	VH3-23_IGHD3-10*01>3_IGHJ1*01	2094	O18_IGKJ1*01	834	1439
716	VH3-23_IGHD3-16*01>2_IGHJ1*01	2095	O18_IGKJ1*01	834	1439
717	VH3-23_IGHD3-16*01>3_IGHJ1*01	2096	O18_IGKJ1*01	834	1439
718	VH3-23_IGHD3-22*01>2_IGHJ1*01	2097	O18_IGKJ1*01	834	1439
719	VH3-23_IGHD3-22*01>3_IGHJ1*01	2098	O18_IGKJ1*01	834	1439
720	VH3-23_IGHD4-4*01 (1) >2_IGHJ1*01	2099	O18_IGKJ1*01	834	1439
721	VH3-23_IGHD4-4*01 (1) >3_IGHJ1*01	2100	O18_IGKJ1*01	834	1439
722	VH3-23_IGHD4-11*01 (1) >2_IGHJ1*01	2101	O18_IGKJ1*01	834	1439
723	VH3-23_IGHD4-11*01 (1) >3_IGHJ1*01	2102	O18_IGKJ1*01	834	1439
724	VH3-23_IGHD4-17*01>2_IGHJ1*01	2103	O18_IGKJ1*01	834	1439
725	VH3-23_IGHD4-17*01>3_IGHJ1*01	2104	O18_IGKJ1*01	834	1439
726	VH3-23_IGHD4-23*01>2_IGHJ1*01	2105	O18_IGKJ1*01	834	1439
727	VH3-23_IGHD4-23*01>3_IGHJ1*01	2106	O18_IGKJ1*01	834	1439
728	VH3-23_IGHD5-5*01 (2) >1_IGHJ1*01	2107	O18_IGKJ1*01	834	1439
729	VH3-23_IGHD5-5*01 (2) >2_IGHJ1*01	2108	O18_IGKJ1*01	834	1439
730	VH3-23_IGHD5-5*01 (2) >3_IGHJ1*01	2109	O18_IGKJ1*01	834	1439
731	VH3-23_IGHD5-12*01>1_IGHJ1*01	2110	O18_IGKJ1*01	834	1439
732	VH3-23_IGHD5-12*01>3_IGHJ1*01	2111	O18_IGKJ1*01	834	1439
733	VH3-23_IGHD5-18*01 (2) >1_IGHJ1*01	2112	O18_IGKJ1*01	834	1439
734	VH3-23_IGHD5-18*01 (2) >2_IGHJ1*01	2113	O18_IGKJ1*01	834	1439
735	VH3-23_IGHD5-18*01 (2) >3_IGHJ1*01	2114	O18_IGKJ1*01	834	1439
736	VH3-23_IGHD5-24*01>1_IGHJ1*01	2115	O18_IGKJ1*01	834	1439
737	VH3-23_IGHD5-24*01>3_IGHJ1*01	2116	O18_IGKJ1*01	834	1439
738	VH3-23_IGHD6-6*01>1_IGHJ1*01	2117	O18_IGKJ1*01	834	1439
739	VH3-23_IGHD1-1*01>1'_IGHJ1*01	2127	O18_IGKJ1*01	834	1439
740	VH3-23_IGHD1-1*01>2'_IGHJ1*01	2128	O18_IGKJ1*01	834	1439
741	VH3-23_IGHD1-1*01>3'_IGHJ1*01	2129	O18_IGKJ1*01	834	1439
742	VH3-23_IGHD1-7*01>1'_IGHJ1*01	2130	O18_IGKJ1*01	834	1439
743	VH3-23_IGHD1-7*01>3'_IGHJ1*01	2131	O18_IGKJ1*01	834	1439
744	VH3-23_IGHD1-14*01>1'_IGHJ1*01	2132	O18_IGKJ1*01	834	1439
745	VH3-23_IGHD1-14*01>2'_IGHJ1*01	2133	O18_IGKJ1*01	834	1439
746	VH3-23_IGHD1-14*01>3'_IGHJ1*01	2134	O18_IGKJ1*01	834	1439
747	VH3-23_IGHD1-20*01>1'_IGHJ1*01	2135	O18_IGKJ1*01	834	1439
748	VH3-23_IGHD1-20*01>2'_IGHJ1*01	2136	O18_IGKJ1*01	834	1439
749	VH3-23_IGHD1-20*01>3'_IGHJ1*01	2137	O18_IGKJ1*01	834	1439
750	VH3-23_IGHD1-26*01>1'_IGHJ1*01	2138	O18_IGKJ1*01	834	1439
751	VH3-23_IGHD1-26*01>3'_IGHJ1*01	2139	O18_IGKJ1*01	834	1439
752	VH3-23_IGHD2-2*01>1'_IGHJ1*01	2140	O18_IGKJ1*01	834	1439
753	VH3-23_IGHD2-2*01>3'_IGHJ1*01	2141	O18_IGKJ1*01	834	1439

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
754	VH3-23_IGHD2-8*01>1'_IGHJ1*01	2142	O18_IGKJ1*01	834	1439
755	VH3-23_IGHD2-15*01>1'_IGHJ1*01	2143	O18_IGKJ1*01	834	1439
756	VH3-23_IGHD2-15*01>3'_IGHJ1*01	2144	O18_IGKJ1*01	834	1439
757	VH3-23_IGHD2-21*01>1'_IGHJ1*01	2145	O18_IGKJ1*01	834	1439
758	VH3-23_IGHD2-21*01>3'_IGHJ1*01	2146	O18_IGKJ1*01	834	1439
759	VH3-23_IGHD3-3*01>1'_IGHJ1*01	2147	O18_IGKJ1*01	834	1439
760	VH3-23_IGHD3-3*01>3'_IGHJ1*01	2148	O18_IGKJ1*01	834	1439
761	VH3-23_IGHD3-9*01>1'_IGHJ1*01	2149	O18_IGKJ1*01	834	1439
762	VH3-23_IGHD3-9*01>3'_IGHJ1*01	2150	O18_IGKJ1*01	834	1439
763	VH3-23_IGHD3-10*01>1'_IGHJ1*01	2151	O18_IGKJ1*01	834	1439
764	VH3-23_IGHD3-10*01>3'_IGHJ1*01	2152	O18_IGKJ1*01	834	1439
765	VH3-23_IGHD3-16*01>1'_IGHJ1*01	2153	O18_IGKJ1*01	834	1439
766	VH3-23_IGHD3-16*01>3'_IGHJ1*01	2154	O18_IGKJ1*01	834	1439
767	VH3-23_IGHD3-22*01>1'_IGHJ1*01	2155	O18_IGKJ1*01	834	1439
768	VH3-23_IGHD4-4*01 (1) >1'_IGHJ1*01	2156	O18_IGKJ1*01	834	1439
769	VH3-23_IGHD4-4*01 (1) >3'_IGHJ1*01	2157	O18_IGKJ1*01	834	1439
770	VH3-23_IGHD4-11*01 (1) >1'_IGHJ1*01	2158	O18_IGKJ1*01	834	1439
771	VH3-23_IGHD4-11*01 (1) >3'_IGHJ1*01	2159	O18_IGKJ1*01	834	1439
772	VH3-23_IGHD4-17*01>1'_IGHJ1*01	2160	O18_IGKJ1*01	834	1439
773	VH3-23_IGHD4-17*01>3'_IGHJ1*01	2161	O18_IGKJ1*01	834	1439
774	VH3-23_IGHD4-23*01>1'_IGHJ1*01	2162	O18_IGKJ1*01	834	1439
775	VH3-23_IGHD4-23*01>3'_IGHJ1*01	2163	O18_IGKJ1*01	834	1439
776	VH3-23_IGHD5-5*01 (2) >1'_IGHJ1*01	2164	O18_IGKJ1*01	834	1439
777	VH3-23_IGHD5-5*01 (2) >3'_IGHJ1*01	2165	O18_IGKJ1*01	834	1439
778	VH3-23_IGHD5-12*01>1'_IGHJ1*01	2166	O18_IGKJ1*01	834	1439
779	VH3-23_IGHD5-12*01>3'_IGHJ1*01	2167	O18_IGKJ1*01	834	1439
780	VH3-23_IGHD5-18*01 (2) >1'_IGHJ1*01	2168	O18_IGKJ1*01	834	1439
781	VH3-23_IGHD5-18*01 (2) >3'_IGHJ1*01	2169	O18_IGKJ1*01	834	1439
782	VH3-23_IGHD5-24*01>1'_IGHJ1*01	2170	O18_IGKJ1*01	834	1439
783	VH3-23_IGHD5-24*01>3'_IGHJ1*01	2171	O18_IGKJ1*01	834	1439
784	VH3-23_IGHD6-6*01>1'_IGHJ1*01	2172	O18_IGKJ1*01	834	1439
785	VH3-23_IGHD6-6*01>2'_IGHJ1*01	2173	O18_IGKJ1*01	834	1439
786	VH3-23_IGHD6-6*01>3'_IGHJ1*01	2174	O18_IGKJ1*01	834	1439
787	VH3-23_IGHD7-27*01>1'_IGHJ6*01	2758	O18_IGKJ1*01	834	1439
788	VH3-23_IGHD6-13*01>2_IGHJ6*01	2695	O18_IGKJ1*01	834	1439
789	VH3-23_IGHD6-19*01>1_IGHJ6*01	2696	O18_IGKJ1*01	834	1439
790	VH3-23_IGHD6-19*01>2_IGHJ6*01	2697	O18_IGKJ1*01	834	1439
791	VH3-23_IGHD6-25*01>1_IGHJ6*01	2698	O18_IGKJ1*01	834	1439
792	VH3-23_IGHD6-25*01>2_IGHJ6*01	2699	O18_IGKJ1*01	834	1439
793	VH3-23_IGHD7-27*01>1_IGHJ6*01	2700	O18_IGKJ1*01	834	1439
794	VH3-23_IGHD7-27*01>3_IGHJ6*01	2701	O18_IGKJ1*01	834	1439
795	VH3-23_IGHD6-13*01>1'_IGHJ6*01	2750	O18_IGKJ1*01	834	1439
796	VH3-23_IGHD6-13*01>2'_IGHJ6*01	2751	O18_IGKJ1*01	834	1439
797	VH3-23_IGHD6-13*01>2_IGHJ6*01_B	2695	O18_IGKJ1*01	834	1439

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
798	VH3-23_IGHD6-19*01>1'_IGHJ6*01	2753	O18_IGKJ1*01	834	1439
799	VH3-23_IGHD6-19*01>2'_IGHJ6*01	2754	O18_IGKJ1*01	834	1439
800	VH3-23_IGHD6-25*01>1_IGHJ6*01_B	2698	O18_IGKJ1*01	834	1439
801	VH3-23_IGHD6-25*01>1'_IGHJ6*01	2756	O18_IGKJ1*01	834	1439
802	VH3-23_IGHD6-25*01>3'_IGHJ6*01	2757	O18_IGKJ1*01	834	1439
803	VH3-23_IGHD7-27*01>1'_IGHJ6*01	2758	O18_IGKJ1*01	834	1439
804	VH3-23_IGHD7-27*01>2'_IGHJ6*01	2759	O18_IGKJ1*01	834	1439
805	VH3-23_IGHD7-27*01>1'_IGHJ6*01	2758	A20_IGKJ1*01	809	1414
806	VH3-23_IGHD6-13*01>2_IGHJ6*01	2695	A20_IGKJ1*01	809	1414
807	VH3-23_IGHD6-19*01>1_IGHJ6*01	2696	A20_IGKJ1*01	809	1414
808	VH3-23_IGHD6-19*01>2_IGHJ6*01	2697	A20_IGKJ1*01	809	1414
809	VH3-23_IGHD6-25*01>1_IGHJ6*01	2698	A20_IGKJ1*01	809	1414
810	VH3-23_IGHD6-25*01>2_IGHJ6*01	2699	A20_IGKJ1*01	809	1414
811	VH3-23_IGHD7-27*01>1_IGHJ6*01	2700	A20_IGKJ1*01	809	1414
812	VH3-23_IGHD7-27*01>3_IGHJ6*01	2701	A20_IGKJ1*01	809	1414
813	VH3-23_IGHD6-13*01>1'_IGHJ6*01	2750	A20_IGKJ1*01	809	1414
814	VH3-23_IGHD6-13*01>2'_IGHJ6*01	2751	A20_IGKJ1*01	809	1414
815	VH3-23_IGHD6-13*01>2_IGHJ6*01_B	2695	A20_IGKJ1*01	809	1414
816	VH3-23_IGHD6-19*01>1'_IGHJ6*01	2753	A20_IGKJ1*01	809	1414
817	VH3-23_IGHD6-19*01>2'_IGHJ6*01	2754	A20_IGKJ1*01	809	1414
818	VH3-23_IGHD6-25*01>1_IGHJ6*01_B	2698	A20_IGKJ1*01	809	1414
819	VH3-23_IGHD6-25*01>1'_IGHJ6*01	2756	A20_IGKJ1*01	809	1414
820	VH3-23_IGHD6-25*01>3'_IGHJ6*01	2757	A20_IGKJ1*01	809	1414
821	VH3-23_IGHD7-27*01>1'_IGHJ6*01	2758	A20_IGKJ1*01	809	1414
822	VH3-23_IGHD7-27*01>2'_IGHJ6*01	2759	A20_IGKJ1*01	809	1414
823	VH3-23_IGHD1-1*01>1_IGHJ6*01	2645	L11_IGKJ1*01	819	1424
824	VH3-23_IGHD1-1*01>2_IGHJ6*01	2646	L11_IGKJ1*01	819	1424
825	VH3-23_IGHD1-1*01>3_IGHJ6*01	2647	L11_IGKJ1*01	819	1424
826	VH3-23_IGHD1-7*01>1_IGHJ6*01	2648	L11_IGKJ1*01	819	1424
827	VH3-23_IGHD1-7*01>3_IGHJ6*01	2649	L11_IGKJ1*01	819	1424
828	VH3-23_IGHD1-14*01>1_IGHJ6*01	2650	L11_IGKJ1*01	819	1424
829	VH3-23_IGHD1-14*01>3_IGHJ6*01	2651	L11_IGKJ1*01	819	1424
830	VH3-23_IGHD1-20*01>1_IGHJ6*01	2652	L11_IGKJ1*01	819	1424
831	VH3-23_IGHD1-20*01>3_IGHJ6*01	2653	L11_IGKJ1*01	819	1424
832	VH3-23_IGHD1-26*01>1_IGHJ6*01	2654	L11_IGKJ1*01	819	1424
833	VH3-23_IGHD1-26*01>3_IGHJ6*01	2655	L11_IGKJ1*01	819	1424
834	VH3-23_IGHD2-2*01>2_IGHJ6*01	2656	L11_IGKJ1*01	819	1424
835	VH3-23_IGHD2-2*01>3_IGHJ6*01	2657	L11_IGKJ1*01	819	1424
836	VH3-23_IGHD2-8*01>2_IGHJ6*01	2658	L11_IGKJ1*01	819	1424
837	VH3-23_IGHD2-8*01>3_IGHJ6*01	2659	L11_IGKJ1*01	819	1424
838	VH3-23_IGHD2-15*01>2_IGHJ6*01	2660	L11_IGKJ1*01	819	1424
839	VH3-23_IGHD2-15*01>3_IGHJ6*01	2661	L11_IGKJ1*01	819	1424
840	VH3-23_IGHD2-21*01>2_IGHJ6*01	2662	L11_IGKJ1*01	819	1424
841	VH3-23_IGHD2-21*01>3_IGHJ6*01	2663	L11_IGKJ1*01	819	1424

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
842	VH3-23_IGHD3-3*01>1_IGHJ6*01	2664	L11_IGKJ1*01	819	1424
843	VH3-23_IGHD3-3*01>2_IGHJ6*01	2665	L11_IGKJ1*01	819	1424
844	VH3-23_IGHD3-3*01>3_IGHJ6*01	2666	L11_IGKJ1*01	819	1424
845	VH3-23_IGHD3-9*01>2_IGHJ6*01	2667	L11_IGKJ1*01	819	1424
846	VH3-23_IGHD3-10*01>2_IGHJ6*01	2668	L11_IGKJ1*01	819	1424
847	VH3-23_IGHD3-10*01>3_IGHJ6*01	2669	L11_IGKJ1*01	819	1424
848	VH3-23_IGHD3-16*01>2_IGHJ6*01	2670	L11_IGKJ1*01	819	1424
849	VH3-23_IGHD3-16*01>3_IGHJ6*01	2671	L11_IGKJ1*01	819	1424
850	VH3-23_IGHD3-22*01>2_IGHJ6*01	2672	L11_IGKJ1*01	819	1424
851	VH3-23_IGHD3-22*01>3_IGHJ6*01	2673	L11_IGKJ1*01	819	1424
852	VH3-23_IGHD4-4*01 (1) >2_IGHJ6*01	2674	L11_IGKJ1*01	819	1424
853	VH3-23_IGHD4-4*01 (1) >3_IGHJ6*01	2675	L11_IGKJ1*01	819	1424
854	VH3-23_IGHD4-11*01 (1) >2_IGHJ6*01	2676	L11_IGKJ1*01	819	1424
855	VH3-23_IGHD4-11*01 (1) >3_IGHJ6*01	2677	L11_IGKJ1*01	819	1424
856	VH3-23_IGHD4-17*01>2_IGHJ6*01	2678	L11_IGKJ1*01	819	1424
857	VH3-23_IGHD4-17*01>3_IGHJ6*01	2679	L11_IGKJ1*01	819	1424
858	VH3-23_IGHD4-23*01>2_IGHJ6*01	2680	L11_IGKJ1*01	819	1424
859	VH3-23_IGHD4-23*01>3_IGHJ6*01	2681	L11_IGKJ1*01	819	1424
860	VH3-23_IGHD5-5*01 (2) >1_IGHJ6*01	2682	L11_IGKJ1*01	819	1424
861	VH3-23_IGHD5-5*01 (2) >2_IGHJ6*01	2683	L11_IGKJ1*01	819	1424
862	VH3-23_IGHD5-5*01 (2) >3_IGHJ6*01	2684	L11_IGKJ1*01	819	1424
863	VH3-23_IGHD5-12*01>1_IGHJ6*01	2685	L11_IGKJ1*01	819	1424
864	VH3-23_IGHD5-12*01>3_IGHJ6*01	2686	L11_IGKJ1*01	819	1424
865	VH3-23_IGHD5-18*01 (2) >1_IGHJ6*01	2687	L11_IGKJ1*01	819	1424
866	VH3-23_IGHD5-18*01 (2) >2_IGHJ6*01	2688	L11_IGKJ1*01	819	1424
867	VH3-23_IGHD5-18*01 (2) >3_IGHJ6*01	2689	L11_IGKJ1*01	819	1424
868	VH3-23_IGHD5-24*01>1_IGHJ6*01	2690	L11_IGKJ1*01	819	1424
869	VH3-23_IGHD5-24*01>3_IGHJ6*01	2691	L11_IGKJ1*01	819	1424
870	VH3-23_IGHD6-6*01>1_IGHJ6*01	2692	L11_IGKJ1*01	819	1424
871	VH3-23_IGHD1-1*01>1'_IGHJ6*01	2702	L11_IGKJ1*01	819	1424
872	VH3-23_IGHD1-1*01>2'_IGHJ6*01	2703	L11_IGKJ1*01	819	1424
873	VH3-23_IGHD1-1*01>3'_IGHJ6*01	2704	L11_IGKJ1*01	819	1424
874	VH3-23_IGHD1-7*01>1'_IGHJ6*01	2705	L11_IGKJ1*01	819	1424
875	VH3-23_IGHD1-7*01>3'_IGHJ6*01	2706	L11_IGKJ1*01	819	1424
876	VH3-23_IGHD1-14*01>1'_IGHJ6*01	2707	L11_IGKJ1*01	819	1424
877	VH3-23_IGHD1-14*01>2'_IGHJ6*01	2708	L11_IGKJ1*01	819	1424
878	VH3-23_IGHD1-14*01>3'_IGHJ6*01	2709	L11_IGKJ1*01	819	1424
879	VH3-23_IGHD1-20*01>1'_IGHJ6*01	2710	L11_IGKJ1*01	819	1424
880	VH3-23_IGHD1-20*01>2'_IGHJ6*01	2711	L11_IGKJ1*01	819	1424
881	VH3-23_IGHD1-20*01>3'_IGHJ6*01	2712	L11_IGKJ1*01	819	1424
882	VH3-23_IGHD1-26*01>1'_IGHJ6*01	2713	L11_IGKJ1*01	819	1424
883	VH3-23_IGHD1-26*01>1_IGHJ6*01_B	2714	L11_IGKJ1*01	819	1424
884	VH3-23_IGHD2-2*01>2_IGHJ6*01_B	2715	L11_IGKJ1*01	819	1424
885	VH3-23_IGHD2-2*01>3'_IGHJ6*01	2716	L11_IGKJ1*01	819	1424

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
886	VH3-23_IGHD2-8*01>1'_IGHJ6*01	2717	L11_IGKJ1*01	819	1424
887	VH3-23_IGHD2-15*01>1'_IGHJ6*01	2718	L11_IGKJ1*01	819	1424
888	VH3-23_IGHD2-15*01>3'_IGHJ6*01	2719	L11_IGKJ1*01	819	1424
889	VH3-23_IGHD2-21*01>1'_IGHJ6*01	2720	L11_IGKJ1*01	819	1424
890	VH3-23_IGHD2-21*01>3'_IGHJ6*01	2721	L11_IGKJ1*01	819	1424
891	VH3-23_IGHD3-3*01>1'_IGHJ6*01	2722	L11_IGKJ1*01	819	1424
892	VH3-23_IGHD3-3*01>3'_IGHJ6*01	2723	L11_IGKJ1*01	819	1424
893	VH3-23_IGHD3-9*01>1'_IGHJ6*01	2724	L11_IGKJ1*01	819	1424
894	VH3-23_IGHD3-9*01>3'_IGHJ6*01	2725	L11_IGKJ1*01	819	1424
895	VH3-23_IGHD3-10*01>1'_IGHJ6*01	2726	L11_IGKJ1*01	819	1424
896	VH3-23_IGHD3-10*01>3'_IGHJ6*01	2727	L11_IGKJ1*01	819	1424
897	VH3-23_IGHD3-16*01>1'_IGHJ6*01	2728	L11_IGKJ1*01	819	1424
898	VH3-23_IGHD3-16*01>3'_IGHJ6*01	2729	L11_IGKJ1*01	819	1424
899	VH3-23_IGHD3-22*01>1'_IGHJ6*01	2730	L11_IGKJ1*01	819	1424
900	VH3-23_IGHD4-4*01 (1) >1'_IGHJ6*01	2731	L11_IGKJ1*01	819	1424
901	VH3-23_IGHD4-4*01 (1) >3'_IGHJ6*01	2732	L11_IGKJ1*01	819	1424
902	VH3-23_IGHD4-11*01 (1) >1'_IGHJ6*01	2733	L11_IGKJ1*01	819	1424
903	VH3-23_IGHD4-11*01 (1) >3'_IGHJ6*01	2734	L11_IGKJ1*01	819	1424
904	VH3-23_IGHD4-17*01>1'_IGHJ6*01	2735	L11_IGKJ1*01	819	1424
905	VH3-23_IGHD4-17*01>3'_IGHJ6*01	2736	L11_IGKJ1*01	819	1424
906	VH3-23_IGHD4-23*01>1'_IGHJ6*01	2737	L11_IGKJ1*01	819	1424
907	VH3-23_IGHD4-23*01>3'_IGHJ6*01	2738	L11_IGKJ1*01	819	1424
908	VH3-23_IGHD5-5*01 (2) >1'_IGHJ6*01	2739	L11_IGKJ1*01	819	1424
909	VH3-23_IGHD5-5*01 (2) >3'_IGHJ6*01	2740	L11_IGKJ1*01	819	1424
910	VH3-23_IGHD5-12*01>1'_IGHJ6*01	2741	L11_IGKJ1*01	819	1424
911	VH3-23_IGHD5-12*01>3'_IGHJ6*01	2742	L11_IGKJ1*01	819	1424
912	VH3-23_IGHD5-18*01 (2) >1'_IGHJ6*01	2743	L11_IGKJ1*01	819	1424
913	VH3-23_IGHD5-18*01 (2) >3'_IGHJ6*01	2744	L11_IGKJ1*01	819	1424
914	VH3-23_IGHD5-24*01>1'_IGHJ6*01	2745	L11_IGKJ1*01	819	1424
915	VH3-23_IGHD5-24*01>3'_IGHJ6*01	2746	L11_IGKJ1*01	819	1424
916	VH3-23_IGHD6-6*01>1'_IGHJ6*01	2747	L11_IGKJ1*01	819	1424
917	VH3-23_IGHD6-6*01>2'_IGHJ6*01	2748	L11_IGKJ1*01	819	1424
918	VH3-23_IGHD6-6*01>3'_IGHJ6*01	2749	L11_IGKJ1*01	819	1424
919	VH3-23_IGHD1-1*01>1_IGHJ6*01	2645	L12_IGKJ1*01	820	1425
920	VH3-23_IGHD1-1*01>2_IGHJ6*01	2646	L12_IGKJ1*01	820	1425
921	VH3-23_IGHD1-1*01>3_IGHJ6*01	2647	L12_IGKJ1*01	820	1425
922	VH3-23_IGHD1-7*01>1_IGHJ6*01	2648	L12_IGKJ1*01	820	1425
923	VH3-23_IGHD1-7*01>3_IGHJ6*01	2649	L12_IGKJ1*01	820	1425
924	VH3-23_IGHD1-14*01>1_IGHJ6*01	2650	L12_IGKJ1*01	820	1425
925	VH3-23_IGHD1-14*01>3_IGHJ6*01	2651	L12_IGKJ1*01	820	1425
926	VH3-23_IGHD1-20*01>1_IGHJ6*01	2652	L12_IGKJ1*01	820	1425
927	VH3-23_IGHD1-20*01>3_IGHJ6*01	2653	L12_IGKJ1*01	820	1425
928	VH3-23_IGHD1-26*01>1_IGHJ6*01	2654	L12_IGKJ1*01	820	1425
929	VH3-23_IGHD1-26*01>3_IGHJ6*01	2655	L12_IGKJ1*01	820	1425

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
930	VH3-23_IGHD2-2*01>2_IGHJ6*01	2656	L12_IGKJ1*01	820	1425
931	VH3-23_IGHD2-2*01>3_IGHJ6*01	2657	L12_IGKJ1*01	820	1425
932	VH3-23_IGHD2-8*01>2_IGHJ6*01	2658	L12_IGKJ1*01	820	1425
933	VH3-23_IGHD2-8*01>3_IGHJ6*01	2659	L12_IGKJ1*01	820	1425
934	VH3-23_IGHD2-15*01>2_IGHJ6*01	2660	L12_IGKJ1*01	820	1425
935	VH3-23_IGHD2-15*01>3_IGHJ6*01	2661	L12_IGKJ1*01	820	1425
936	VH3-23_IGHD2-21*01>2_IGHJ6*01	2662	L12_IGKJ1*01	820	1425
937	VH3-23_IGHD2-21*01>3_IGHJ6*01	2663	L12_IGKJ1*01	820	1425
938	VH3-23_IGHD3-3*01>1_IGHJ6*01	2664	L12_IGKJ1*01	820	1425
939	VH3-23_IGHD3-3*01>2_IGHJ6*01	2665	L12_IGKJ1*01	820	1425
940	VH3-23_IGHD3-3*01>3_IGHJ6*01	2666	L12_IGKJ1*01	820	1425
941	VH3-23_IGHD3-9*01>2_IGHJ6*01	2667	L12_IGKJ1*01	820	1425
942	VH3-23_IGHD3-10*01>2_IGHJ6*01	2668	L12_IGKJ1*01	820	1425
943	VH3-23_IGHD3-10*01>3_IGHJ6*01	2669	L12_IGKJ1*01	820	1425
944	VH3-23_IGHD3-16*01>2_IGHJ6*01	2670	L12_IGKJ1*01	820	1425
945	VH3-23_IGHD3-16*01>3_IGHJ6*01	2671	L12_IGKJ1*01	820	1425
946	VH3-23_IGHD3-22*01>2_IGHJ6*01	2672	L12_IGKJ1*01	820	1425
947	VH3-23_IGHD3-22*01>3_IGHJ6*01	2673	L12_IGKJ1*01	820	1425
948	VH3-23_IGHD4-4*01 (1) >2_IGHJ6*01	2674	L12_IGKJ1*01	820	1425
949	VH3-23_IGHD4-4*01 (1) >3_IGHJ6*01	2675	L12_IGKJ1*01	820	1425
950	VH3-23_IGHD4-11*01 (1) >2_IGHJ6*01	2676	L12_IGKJ1*01	820	1425
951	VH3-23_IGHD4-11*01 (1) >3_IGHJ6*01	2677	L12_IGKJ1*01	820	1425
952	VH3-23_IGHD4-17*01>2_IGHJ6*01	2678	L12_IGKJ1*01	820	1425
953	VH3-23_IGHD4-17*01>3_IGHJ6*01	2679	L12_IGKJ1*01	820	1425
954	VH3-23_IGHD4-23*01>2_IGHJ6*01	2680	L12_IGKJ1*01	820	1425
955	VH3-23_IGHD4-23*01>3_IGHJ6*01	2681	L12_IGKJ1*01	820	1425
956	VH3-23_IGHD5-5*01 (2) >1_IGHJ6*01	2682	L12_IGKJ1*01	820	1425
957	VH3-23_IGHD5-5*01 (2) >2_IGHJ6*01	2683	L12_IGKJ1*01	820	1425
958	VH3-23_IGHD5-5*01 (2) >3_IGHJ6*01	2684	L12_IGKJ1*01	820	1425
959	VH3-23_IGHD5-12*01>1_IGHJ6*01	2685	L12_IGKJ1*01	820	1425
960	VH3-23_IGHD5-12*01>3_IGHJ6*01	2686	L12_IGKJ1*01	820	1425
961	VH3-23_IGHD5-18*01 (2) >1_IGHJ6*01	2687	L12_IGKJ1*01	820	1425
962	VH3-23_IGHD5-18*01 (2) >2_IGHJ6*01	2688	L12_IGKJ1*01	820	1425
963	VH3-23_IGHD5-18*01 (2) >3_IGHJ6*01	2689	L12_IGKJ1*01	820	1425
964	VH3-23_IGHD5-24*01>1_IGHJ6*01	2690	L12_IGKJ1*01	820	1425
965	VH3-23_IGHD5-24*01>3_IGHJ6*01	2691	L12_IGKJ1*01	820	1425
966	VH3-23_IGHD6-6*01>1_IGHJ6*01	2692	L12_IGKJ1*01	820	1425
967	VH3-23_IGHD1-1*01>1'_IGHJ6*01	2702	L12_IGKJ1*01	820	1425
968	VH3-23_IGHD1-1*01>2'_IGHJ6*01	2703	L12_IGKJ1*01	820	1425
969	VH3-23_IGHD1-1*01>3'_IGHJ6*01	2704	L12_IGKJ1*01	820	1425
970	VH3-23_IGHD1-7*01>1'_IGHJ6*01	2705	L12_IGKJ1*01	820	1425
971	VH3-23_IGHD1-7*01>3'_IGHJ6*01	2706	L12_IGKJ1*01	820	1425
972	VH3-23_IGHD1-14*01>1'_IGHJ6*01	2707	L12_IGKJ1*01	820	1425
973	VH3-23_IGHD1-14*01>2'_IGHJ6*01	2708	L12_IGKJ1*01	820	1425

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
974	VH3-23_IGHD1-14*01>3'_IGHJ6*01	2709	L12_IGKJ1*01	820	1425
975	VH3-23_IGHD1-20*01>1'_IGHJ6*01	2710	L12_IGKJ1*01	820	1425
976	VH3-23_IGHD1-20*01>2'_IGHJ6*01	2711	L12_IGKJ1*01	820	1425
977	VH3-23_IGHD1-20*01>3'_IGHJ6*01	2712	L12_IGKJ1*01	820	1425
978	VH3-23_IGHD1-26*01>1'_IGHJ6*01	2713	L12_IGKJ1*01	820	1425
979	VH3-23_IGHD1-26*01>1_IGHJ6*01_B	2714	L12_IGKJ1*01	820	1425
980	VH3-23_IGHD2-2*01>2_IGHJ6*01_B	2715	L12_IGKJ1*01	820	1425
981	VH3-23_IGHD2-2*01>3'_IGHJ6*01	2716	L12_IGKJ1*01	820	1425
982	VH3-23_IGHD2-8*01>1'_IGHJ6*01	2717	L12_IGKJ1*01	820	1425
983	VH3-23_IGHD2-15*01>1'_IGHJ6*01	2718	L12_IGKJ1*01	820	1425
984	VH3-23_IGHD2-15*01>3'_IGHJ6*01	2719	L12_IGKJ1*01	820	1425
985	VH3-23_IGHD2-21*01>1'_IGHJ6*01	2720	L12_IGKJ1*01	820	1425
986	VH3-23_IGHD2-21*01>3'_IGHJ6*01	2721	L12_IGKJ1*01	820	1425
987	VH3-23_IGHD3-3*01>1'_IGHJ6*01	2722	L12_IGKJ1*01	820	1425
988	VH3-23_IGHD3-3*01>3'_IGHJ6*01	2723	L12_IGKJ1*01	820	1425
989	VH3-23_IGHD3-9*01>1'_IGHJ6*01	2724	L12_IGKJ1*01	820	1425
990	VH3-23_IGHD3-9*01>3'_IGHJ6*01	2725	L12_IGKJ1*01	820	1425
991	VH3-23_IGHD3-10*01>1'_IGHJ6*01	2726	L12_IGKJ1*01	820	1425
992	VH3-23_IGHD3-10*01>3'_IGHJ6*01	2727	L12_IGKJ1*01	820	1425
993	VH3-23_IGHD3-16*01>1'_IGHJ6*01	2728	L12_IGKJ1*01	820	1425
994	VH3-23_IGHD3-16*01>3'_IGHJ6*01	2729	L12_IGKJ1*01	820	1425
995	VH3-23_IGHD3-22*01>1'_IGHJ6*01	2730	L12_IGKJ1*01	820	1425
996	VH3-23_IGHD4-4*01 (1) >1'_IGHJ6*01	2731	L12_IGKJ1*01	820	1425
997	VH3-23_IGHD4-4*01 (1) >3'_IGHJ6*01	2732	L12_IGKJ1*01	820	1425
998	VH3-23_IGHD4-11*01 (1) >1'_IGHJ6*01	2733	L12_IGKJ1*01	820	1425
999	VH3-23_IGHD4-11*01 (1) >3'_IGHJ6*01	2734	L12_IGKJ1*01	820	1425
1000	VH3-23_IGHD4-17*01>1'_IGHJ6*01	2735	L12_IGKJ1*01	820	1425
1001	VH3-23_IGHD4-17*01>3'_IGHJ6*01	2736	L12_IGKJ1*01	820	1425
1002	VH3-23_IGHD4-23*01>1'_IGHJ6*01	2737	L12_IGKJ1*01	820	1425
1003	VH3-23_IGHD4-23*01>3'_IGHJ6*01	2738	L12_IGKJ1*01	820	1425
1004	VH3-23_IGHD5-5*01 (2) >1'_IGHJ6*01	2739	L12_IGKJ1*01	820	1425
1005	VH3-23_IGHD5-5*01 (2) >3'_IGHJ6*01	2740	L12_IGKJ1*01	820	1425
1006	VH3-23_IGHD5-12*01>1'_IGHJ6*01	2741	L12_IGKJ1*01	820	1425
1007	VH3-23_IGHD5-12*01>3'_IGHJ6*01	2742	L12_IGKJ1*01	820	1425
1008	VH3-23_IGHD5-18*01 (2) >1'_IGHJ6*01	2743	L12_IGKJ1*01	820	1425
1009	VH3-23_IGHD5-18*01 (2) >3'_IGHJ6*01	2744	L12_IGKJ1*01	820	1425
1010	VH3-23_IGHD5-24*01>1'_IGHJ6*01	2745	L12_IGKJ1*01	820	1425
1011	VH3-23_IGHD5-24*01>3'_IGHJ6*01	2746	L12_IGKJ1*01	820	1425
1012	VH3-23_IGHD6-6*01>1'_IGHJ6*01	2747	L12_IGKJ1*01	820	1425
1013	VH3-23_IGHD6-6*01>2'_IGHJ6*01	2748	L12_IGKJ1*01	820	1425
1014	VH3-23_IGHD6-6*01>3'_IGHJ6*01	2749	L12_IGKJ1*01	820	1425
1015	VH3-23_IGHD1-1*01>1_IGHJ6*01	2645	O1_IGKJ1*01	832	1437
1016	VH3-23_IGHD1-1*01>2_IGHJ6*01	2646	O1_IGKJ1*01	832	1437
1017	VH3-23_IGHD1-1*01>3_IGHJ6*01	2647	O1_IGKJ1*01	832	1437

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
1018	VH3-23_IGHD1-7*01>1_IGHJ6*01	2648	O1_IGKJ1*01	832	1437
1019	VH3-23_IGHD1-7*01>3_IGHJ6*01	2649	O1_IGKJ1*01	832	1437
1020	VH3-23_IGHD1-14*01>1_IGHJ6*01	2650	O1_IGKJ1*01	832	1437
1021	VH3-23_IGHD1-14*01>3_IGHJ6*01	2651	O1_IGKJ1*01	832	1437
1022	VH3-23_IGHD1-20*01>1_IGHJ6*01	2652	O1_IGKJ1*01	832	1437
1023	VH3-23_IGHD1-20*01>3_IGHJ6*01	2653	O1_IGKJ1*01	832	1437
1024	VH3-23_IGHD1-26*01>1_IGHJ6*01	2654	O1_IGKJ1*01	832	1437
1025	VH3-23_IGHD1-26*01>3_IGHJ6*01	2655	O1_IGKJ1*01	832	1437
1026	VH3-23_IGHD2-2*01>2_IGHJ6*01	2656	O1_IGKJ1*01	832	1437
1027	VH3-23_IGHD2-2*01>3_IGHJ6*01	2657	O1_IGKJ1*01	832	1437
1028	VH3-23_IGHD2-8*01>2_IGHJ6*01	2658	O1_IGKJ1*01	832	1437
1029	VH3-23_IGHD2-8*01>3_IGHJ6*01	2659	O1_IGKJ1*01	832	1437
1030	VH3-23_IGHD2-15*01>2_IGHJ6*01	2660	O1_IGKJ1*01	832	1437
1031	VH3-23_IGHD2-15*01>3_IGHJ6*01	2661	O1_IGKJ1*01	832	1437
1032	VH3-23_IGHD2-21*01>2_IGHJ6*01	2662	O1_IGKJ1*01	832	1437
1033	VH3-23_IGHD2-21*01>3_IGHJ6*01	2663	O1_IGKJ1*01	832	1437
1034	VH3-23_IGHD3-3*01>1_IGHJ6*01	2664	O1_IGKJ1*01	832	1437
1035	VH3-23_IGHD3-3*01>2_IGHJ6*01	2665	O1_IGKJ1*01	832	1437
1036	VH3-23_IGHD3-3*01>3_IGHJ6*01	2666	O1_IGKJ1*01	832	1437
1037	VH3-23_IGHD3-9*01>2_IGHJ6*01	2667	O1_IGKJ1*01	832	1437
1038	VH3-23_IGHD3-10*01>2_IGHJ6*01	2668	O1_IGKJ1*01	832	1437
1039	VH3-23_IGHD3-10*01>3_IGHJ6*01	2669	O1_IGKJ1*01	832	1437
1040	VH3-23_IGHD3-16*01>2_IGHJ6*01	2670	O1_IGKJ1*01	832	1437
1041	VH3-23_IGHD3-16*01>3_IGHJ6*01	2671	O1_IGKJ1*01	832	1437
1042	VH3-23_IGHD3-22*01>2_IGHJ6*01	2672	O1_IGKJ1*01	832	1437
1043	VH3-23_IGHD3-22*01>3_IGHJ6*01	2673	O1_IGKJ1*01	832	1437
1044	VH3-23_IGHD4-4*01 (1) >2_IGHJ6*01	2674	O1_IGKJ1*01	832	1437
1045	VH3-23_IGHD4-4*01 (1) >3_IGHJ6*01	2675	O1_IGKJ1*01	832	1437
1046	VH3-23_IGHD4-11*01 (1) >2_IGHJ6*01	2676	O1_IGKJ1*01	832	1437
1047	VH3-23_IGHD4-11*01 (1) >3_IGHJ6*01	2677	O1_IGKJ1*01	832	1437
1048	VH3-23_IGHD4-17*01>2_IGHJ6*01	2678	O1_IGKJ1*01	832	1437
1049	VH3-23_IGHD4-17*01>3_IGHJ6*01	2679	O1_IGKJ1*01	832	1437
1050	VH3-23_IGHD4-23*01>2_IGHJ6*01	2680	O1_IGKJ1*01	832	1437
1051	VH3-23_IGHD4-23*01>3_IGHJ6*01	2681	O1_IGKJ1*01	832	1437
1052	VH3-23_IGHD5-5*01 (2) >1_IGHJ6*01	2682	O1_IGKJ1*01	832	1437
1053	VH3-23_IGHD5-5*01 (2) >2_IGHJ6*01	2683	O1_IGKJ1*01	832	1437
1054	VH3-23_IGHD5-5*01 (2) >3_IGHJ6*01	2684	O1_IGKJ1*01	832	1437
1055	VH3-23_IGHD5-12*01>1_IGHJ6*01	2685	O1_IGKJ1*01	832	1437
1056	VH3-23_IGHD5-12*01>3_IGHJ6*01	2686	O1_IGKJ1*01	832	1437
1057	VH3-23_IGHD5-18*01 (2) >1_IGHJ6*01	2687	O1_IGKJ1*01	832	1437
1058	VH3-23_IGHD5-18*01 (2) >2_IGHJ6*01	2688	O1_IGKJ1*01	832	1437
1059	VH3-23_IGHD5-18*01 (2) >3_IGHJ6*01	2689	O1_IGKJ1*01	832	1437
1060	VH3-23_IGHD5-24*01>1_IGHJ6*01	2690	O1_IGKJ1*01	832	1437
1061	VH3-23_IGHD5-24*01>3_IGHJ6*01	2691	O1_IGKJ1*01	832	1437

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
1062	VH3-23_IGHD6-6*01>1_IGHJ6*01	2692	O1_IGKJ1*01	832	1437
1063	VH3-23_IGHD1-1*01>1'_IGHJ6*01	2702	O1_IGKJ1*01	832	1437
1064	VH3-23_IGHD1-1*01>2'_IGHJ6*01	2703	O1_IGKJ1*01	832	1437
1065	VH3-23_IGHD1-1*01>3'_IGHJ6*01	2704	O1_IGKJ1*01	832	1437
1066	VH3-23_IGHD1-7*01>1'_IGHJ6*01	2705	O1_IGKJ1*01	832	1437
1067	VH3-23_IGHD1-7*01>3'_IGHJ6*01	2706	O1_IGKJ1*01	832	1437
1068	VH3-23_IGHD1-14*01>1'_IGHJ6*01	2707	O1_IGKJ1*01	832	1437
1069	VH3-23_IGHD1-14*01>2'_IGHJ6*01	2708	O1_IGKJ1*01	832	1437
1070	VH3-23_IGHD1-14*01>3'_IGHJ6*01	2709	O1_IGKJ1*01	832	1437
1071	VH3-23_IGHD1-20*01>1'_IGHJ6*01	2710	O1_IGKJ1*01	832	1437
1072	VH3-23_IGHD1-20*01>2'_IGHJ6*01	2711	O1_IGKJ1*01	832	1437
1073	VH3-23_IGHD1-20*01>3'_IGHJ6*01	2712	O1_IGKJ1*01	832	1437
1074	VH3-23_IGHD1-26*01>1'_IGHJ6*01	2713	O1_IGKJ1*01	832	1437
1075	VH3-23_IGHD1-26*01>1_IGHJ6*01_B	2714	O1_IGKJ1*01	832	1437
1076	VH3-23_IGHD2-2*01>2_IGHJ6*01_B	2715	O1_IGKJ1*01	832	1437
1077	VH3-23_IGHD2-2*01>3'_IGHJ6*01	2716	O1_IGKJ1*01	832	1437
1078	VH3-23_IGHD2-8*01>1'_IGHJ6*01	2717	O1_IGKJ1*01	832	1437
1079	VH3-23_IGHD2-15*01>1'_IGHJ6*01	2718	O1_IGKJ1*01	832	1437
1080	VH3-23_IGHD2-15*01>3'_IGHJ6*01	2719	O1_IGKJ1*01	832	1437
1081	VH3-23_IGHD2-21*01>1'_IGHJ6*01	2720	O1_IGKJ1*01	832	1437
1082	VH3-23_IGHD2-21*01>3'_IGHJ6*01	2721	O1_IGKJ1*01	832	1437
1083	VH3-23_IGHD3-3*01>1'_IGHJ6*01	2722	O1_IGKJ1*01	832	1437
1084	VH3-23_IGHD3-3*01>3'_IGHJ6*01	2723	O1_IGKJ1*01	832	1437
1085	VH3-23_IGHD3-9*01>1'_IGHJ6*01	2724	O1_IGKJ1*01	832	1437
1086	VH3-23_IGHD3-9*01>3'_IGHJ6*01	2725	O1_IGKJ1*01	832	1437
1087	VH3-23_IGHD3-10*01>1'_IGHJ6*01	2726	O1_IGKJ1*01	832	1437
1088	VH3-23_IGHD3-10*01>3'_IGHJ6*01	2727	O1_IGKJ1*01	832	1437
1089	VH3-23_IGHD3-16*01>1'_IGHJ6*01	2728	O1_IGKJ1*01	832	1437
1090	VH3-23_IGHD3-16*01>3'_IGHJ6*01	2729	O1_IGKJ1*01	832	1437
1091	VH3-23_IGHD3-22*01>1'_IGHJ6*01	2730	O1_IGKJ1*01	832	1437
1092	VH3-23_IGHD4-4*01 (1) >1'_IGHJ6*01	2731	O1_IGKJ1*01	832	1437
1093	VH3-23_IGHD4-4*01 (1) >3'_IGHJ6*01	2732	O1_IGKJ1*01	832	1437
1094	VH3-23_IGHD4-11*01 (1) >1'_IGHJ6*01	2733	O1_IGKJ1*01	832	1437
1095	VH3-23_IGHD4-11*01 (1) >3'_IGHJ6*01	2734	O1_IGKJ1*01	832	1437
1096	VH3-23_IGHD4-17*01>1'_IGHJ6*01	2735	O1_IGKJ1*01	832	1437
1097	VH3-23_IGHD4-17*01>3'_IGHJ6*01	2736	O1_IGKJ1*01	832	1437
1098	VH3-23_IGHD4-23*01>1'_IGHJ6*01	2737	O1_IGKJ1*01	832	1437
1099	VH3-23_IGHD4-23*01>3'_IGHJ6*01	2738	O1_IGKJ1*01	832	1437
1100	VH3-23_IGHD5-5*01 (2) >1'_IGHJ6*01	2739	O1_IGKJ1*01	832	1437
1101	VH3-23_IGHD5-5*01 (2) >3'_IGHJ6*01	2740	O1_IGKJ1*01	832	1437
1102	VH3-23_IGHD5-12*01>1'_IGHJ6*01	2741	O1_IGKJ1*01	832	1437
1103	VH3-23_IGHD5-12*01>3'_IGHJ6*01	2742	O1_IGKJ1*01	832	1437
1104	VH3-23_IGHD5-18*01 (2) >1'_IGHJ6*01	2743	O1_IGKJ1*01	832	1437
1105	VH3-23_IGHD5-18*01 (2) >3'_IGHJ6*01	2744	O1_IGKJ1*01	832	1437

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
1106	VH3-23_IGHD5-24*01>1'_IGHJ6*01	2745	O1_IGKJ1*01	832	1437
1107	VH3-23_IGHD5-24*01>3'_IGHJ6*01	2746	O1_IGKJ1*01	832	1437
1108	VH3-23_IGHD6-6*01>1'_IGHJ6*01	2747	O1_IGKJ1*01	832	1437
1109	VH3-23_IGHD6-6*01>2'_IGHJ6*01	2748	O1_IGKJ1*01	832	1437
1110	VH3-23_IGHD6-6*01>3'_IGHJ6*01	2749	O1_IGKJ1*01	832	1437
1111	VH3-23_IGHD1-1*01>1_IGHJ5*01	2530	A2_IGKJ1*01	808	1413
1112	VH3-23_IGHD1-1*01>2_IGHJ5*01	2531	A2_IGKJ1*01	808	1413
1113	VH3-23_IGHD1-1*01>3_IGHJ5*01	2532	A2_IGKJ1*01	808	1413
1114	VH3-23_IGHD1-7*01>1_IGHJ5*01	2533	A2_IGKJ1*01	808	1413
1115	VH3-23_IGHD1-7*01>3_IGHJ5*01	2534	A2_IGKJ1*01	808	1413
1116	VH3-23_IGHD1-14*01>1_IGHJ5*01	2535	A2_IGKJ1*01	808	1413
1117	VH3-23_IGHD1-14*01>3_IGHJ5*01	2536	A2_IGKJ1*01	808	1413
1118	VH3-23_IGHD1-20*01>1_IGHJ5*01	2537	A2_IGKJ1*01	808	1413
1119	VH3-23_IGHD1-20*01>3_IGHJ5*01	2538	A2_IGKJ1*01	808	1413
1120	VH3-23_IGHD1-26*01>1_IGHJ5*01	2539	A2_IGKJ1*01	808	1413
1121	VH3-23_IGHD1-26*01>3_IGHJ5*01	2540	A2_IGKJ1*01	808	1413
1122	VH3-23_IGHD2-2*01>2_IGHJ5*01	2541	A2_IGKJ1*01	808	1413
1123	VH3-23_IGHD2-2*01>3_IGHJ5*01	2542	A2_IGKJ1*01	808	1413
1124	VH3-23_IGHD2-8*01>2_IGHJ5*01	2543	A2_IGKJ1*01	808	1413
1125	VH3-23_IGHD2-8*01>3_IGHJ5*01	2544	A2_IGKJ1*01	808	1413
1126	VH3-23_IGHD2-15*01>2_IGHJ5*01	2545	A2_IGKJ1*01	808	1413
1127	VH3-23_IGHD2-15*01>3_IGHJ5*01	2546	A2_IGKJ1*01	808	1413
1128	VH3-23_IGHD2-21*01>2_IGHJ5*01	2547	A2_IGKJ1*01	808	1413
1129	VH3-23_IGHD2-21*01>3_IGHJ5*01	2548	A2_IGKJ1*01	808	1413
1130	VH3-23_IGHD3-3*01>1_IGHJ5*01	2549	A2_IGKJ1*01	808	1413
1131	VH3-23_IGHD3-3*01>2_IGHJ5*01	2550	A2_IGKJ1*01	808	1413
1132	VH3-23_IGHD3-3*01>3_IGHJ5*01	2551	A2_IGKJ1*01	808	1413
1133	VH3-23_IGHD3-9*01>2_IGHJ5*01	2552	A2_IGKJ1*01	808	1413
1134	VH3-23_IGHD3-10*01>2_IGHJ5*01	2553	A2_IGKJ1*01	808	1413
1135	VH3-23_IGHD3-10*01>3_IGHJ5*01	2554	A2_IGKJ1*01	808	1413
1136	VH3-23_IGHD3-16*01>2_IGHJ5*01	2555	A2_IGKJ1*01	808	1413
1137	VH3-23_IGHD3-16*01>3_IGHJ5*01	2556	A2_IGKJ1*01	808	1413
1138	VH3-23_IGHD3-22*01>2_IGHJ5*01	2557	A2_IGKJ1*01	808	1413
1139	VH3-23_IGHD3-22*01>3_IGHJ5*01	2558	A2_IGKJ1*01	808	1413
1140	VH3-23_IGHD4-4*01 (1) >2_IGHJ5*01	2559	A2_IGKJ1*01	808	1413
1141	VH3-23_IGHD4-4*01 (1) >3_IGHJ5*01	2560	A2_IGKJ1*01	808	1413
1142	VH3-23_IGHD4-11*01 (1) >2_IGHJ5*01	2561	A2_IGKJ1*01	808	1413
1143	VH3-23_IGHD4-11*01 (1) >3_IGHJ5*01	2562	A2_IGKJ1*01	808	1413
1144	VH3-23_IGHD4-17*01>2_IGHJ5*01	2563	A2_IGKJ1*01	808	1413
1145	VH3-23_IGHD4-17*01>3_IGHJ5*01	2564	A2_IGKJ1*01	808	1413
1146	VH3-23_IGHD4-23*01>2_IGHJ5*01	2565	A2_IGKJ1*01	808	1413
1147	VH3-23_IGHD4-23*01>3_IGHJ5*01	2566	A2_IGKJ1*01	808	1413
1148	VH3-23_IGHD5-5*01 (2) >1_IGHJ5*01	2567	A2_IGKJ1*01	808	1413
1149	VH3-23_IGHD5-5*01 (2) >2_IGHJ5*01	2568	A2_IGKJ1*01	808	1413

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	**RS**	**LIGHT CHAIN**	**RS**	**NO RS**
1150	VH3-23_IGHD5-5*01 (2) >3_IGHJ5*01	2569	A2_IGKJ1*01	808	1413
1151	VH3-23_IGHD5-12*01>1_IGHJ5*01	2570	A2_IGKJ1*01	808	1413
1152	VH3-23_IGHD5-12*01>3_IGHJ5*01	2571	A2_IGKJ1*01	808	1413
1153	VH3-23_IGHD5-18*01 (2) >1_IGHJ5*01	2572	A2_IGKJ1*01	808	1413
1154	VH3-23_IGHD5-18*01 (2) >2_IGHJ5*01	2573	A2_IGKJ1*01	808	1413
1155	VH3-23_IGHD5-18*01 (2) >3_IGHJ5*01	2574	A2_IGKJ1*01	808	1413
1156	VH3-23_IGHD5-24*01>1_IGHJ5*01	2575	A2_IGKJ1*01	808	1413
1157	VH3-23_IGHD5-24*01>3_IGHJ5*01	2576	A2_IGKJ1*01	808	1413
1158	VH3-23_IGHD6-6*01>1_IGHJ5*01	2577	A2_IGKJ1*01	808	1413
1159	VH3-23_IGHD1-1*01>1'_IGHJ5*01	2587	A2_IGKJ1*01	808	1413
1160	VH3-23_IGHD1-1*01>2'_IGHJ5*01	2588	A2_IGKJ1*01	808	1413
1161	VH3-23_IGHD1-1*01>3'_IGHJ5*01	2589	A2_IGKJ1*01	808	1413
1162	VH3-23_IGHD1-7*01>1'_IGHJ5*01	2590	A2_IGKJ1*01	808	1413
1163	VH3-23_IGHD1-7*01>3'_IGHJ5*01	2591	A2_IGKJ1*01	808	1413
1164	VH3-23_IGHD1-14*01>1'_IGHJ5*01	2592	A2_IGKJ1*01	808	1413
1165	VH3-23_IGHD1-14*01>2'_IGHJ5*01	2593	A2_IGKJ1*01	808	1413
1166	VH3-23_IGHD1-14*01>3'_IGHJ5*01	2594	A2_IGKJ1*01	808	1413
1167	VH3-23_IGHD1-20*01>1'_IGHJ5*01	2595	A2_IGKJ1*01	808	1413
1168	VH3-23_IGHD1-20*01>2'_IGHJ5*01	2596	A2_IGKJ1*01	808	1413
1169	VH3-23_IGHD1-20*01>3'_IGHJ5*01	2597	A2_IGKJ1*01	808	1413
1170	VH3-23_IGHD1-26*01>1'_IGHJ5*01	2598	A2_IGKJ1*01	808	1413
1171	VH3-23_IGHD1-26*01>3'_IGHJ5*01	2599	A2_IGKJ1*01	808	1413
1172	VH3-23_IGHD2-2*01>1'_IGHJ5*01	2600	A2_IGKJ1*01	808	1413
1173	VH3-23_IGHD2-2*01>3'_IGHJ5*01	2601	A2_IGKJ1*01	808	1413
1174	VH3-23_IGHD2-8*01>1'_IGHJ5*01	2602	A2_IGKJ1*01	808	1413
1175	VH3-23_IGHD2-15*01>1'_IGHJ5*01	2603	A2_IGKJ1*01	808	1413
1176	VH3-23_IGHD2-15*01>3'_IGHJ5*01	2604	A2_IGKJ1*01	808	1413
1177	VH3-23_IGHD2-21*01>1'_IGHJ5*01	2605	A2_IGKJ1*01	808	1413
1178	VH3-23_IGHD2-21*01>3'_IGHJ5*01	2606	A2_IGKJ1*01	808	1413
1179	VH3-23_IGHD3-3*01>1'_IGHJ5*01	2607	A2_IGKJ1*01	808	1413
1180	VH3-23_IGHD3-3*01>3'_IGHJ5*01	2608	A2_IGKJ1*01	808	1413
1181	VH3-23_IGHD3-9*01>1'_IGHJ5*01	2609	A2_IGKJ1*01	808	1413
1182	VH3-23_IGHD3-9*01>3'_IGHJ5*01	2610	A2_IGKJ1*01	808	1413
1183	VH3-23_IGHD3-10*01>1'_IGHJ5*01	2611	A2_IGKJ1*01	808	1413
1184	VH3-23_IGHD3-10*01>3'_IGHJ5*01	2612	A2_IGKJ1*01	808	1413
1185	VH3-23_IGHD3-16*01>1'_IGHJ5*01	2613	A2_IGKJ1*01	808	1413
1186	VH3-23_IGHD3-16*01>3'_IGHJ5*01	2614	A2_IGKJ1*01	808	1413
1187	VH3-23_IGHD3-22*01>1'_IGHJ5*01	2615	A2_IGKJ1*01	808	1413
1188	VH3-23_IGHD4-4*01 (1) >1'_IGHJ5*01	2616	A2_IGKJ1*01	808	1413
1189	VH3-23_IGHD4-4*01 (1) >3'_IGHJ5*01	2617	A2_IGKJ1*01	808	1413
1190	VH3-23_IGHD4-11*01 (1) >1'_IGHJ5*01	2618	A2_IGKJ1*01	808	1413
1191	VH3-23_IGHD4-11*01 (1) >3'_IGHJ5*01	2619	A2_IGKJ1*01	808	1413
1192	VH3-23_IGHD4-17*01>1'_IGHJ5*01	2620	A2_IGKJ1*01	808	1413
1193	VH3-23_IGHD4-17*01>3'_IGHJ5*01	2621	A2_IGKJ1*01	808	1413

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
1194	VH3-23_IGHD4-23*01>1'_IGHJ5*01	2622	A2_IGKJ1*01	808	1413
1195	VH3-23_IGHD4-23*01>3'_IGHJ5*01	2623	A2_IGKJ1*01	808	1413
1196	VH3-23_IGHD5-5*01 (2) >1'_IGHJ5*01	2624	A2_IGKJ1*01	808	1413
1197	VH3-23_IGHD5-5*01 (2) >3'_IGHJ5*01	2625	A2_IGKJ1*01	808	1413
1198	VH3-23_IGHD5-12*01>1'_IGHJ5*01	2626	A2_IGKJ1*01	808	1413
1199	VH3-23_IGHD5-12*01>3'_IGHJ5*01	2627	A2_IGKJ1*01	808	1413
1200	VH3-23_IGHD5-18*01 (2) >1'_IGHJ5*01	2628	A2_IGKJ1*01	808	1413
1201	VH3-23_IGHD5-18*01 (2) >3'_IGHJ5*01	2629	A2_IGKJ1*01	808	1413
1202	VH3-23_IGHD5-24*01>1'_IGHJ5*01	2630	A2_IGKJ1*01	808	1413
1203	VH3-23_IGHD5-24*01>3'_IGHJ5*01	2631	A2_IGKJ1*01	808	1413
1204	VH3-23_IGHD6-6*01>1'_IGHJ5*01	2632	A2_IGKJ1*01	808	1413
1205	VH3-23_IGHD6-6*01>2'_IGHJ5*01	2633	A2_IGKJ1*01	808	1413
1206	VH3-23_IGHD6-6*01>3'_IGHJ5*01	2634	A2_IGKJ1*01	808	1413
1207	VH3-23_IGHD1-1*01>1_IGHJ6*01	2645	L2_IGKJ1*01	822	1427
1208	VH3-23_IGHD1-1*01>2_IGHJ6*01	2646	L2_IGKJ1*01	822	1427
1209	VH3-23_IGHD1-1*01>3_IGHJ6*01	2647	L2_IGKJ1*01	822	1427
1210	VH3-23_IGHD1-7*01>1_IGHJ6*01	2648	L2_IGKJ1*01	822	1427
1211	VH3-23_IGHD1-7*01>3_IGHJ6*01	2649	L2_IGKJ1*01	822	1427
1212	VH3-23_IGHD1-14*01>1_IGHJ6*01	2650	L2_IGKJ1*01	822	1427
1213	VH3-23_IGHD1-14*01>3_IGHJ6*01	2651	L2_IGKJ1*01	822	1427
1214	VH3-23_IGHD1-20*01>1_IGHJ6*01	2652	L2_IGKJ1*01	822	1427
1215	VH3-23_IGHD1-20*01>3_IGHJ6*01	2653	L2_IGKJ1*01	822	1427
1216	VH3-23_IGHD1-26*01>1_IGHJ6*01	2654	L2_IGKJ1*01	822	1427
1217	VH3-23_IGHD1-26*01>3_IGHJ6*01	2655	L2_IGKJ1*01	822	1427
1218	VH3-23_IGHD2-2*01>2_IGHJ6*01	2656	L2_IGKJ1*01	822	1427
1219	VH3-23_IGHD2-2*01>3_IGHJ6*01	2657	L2_IGKJ1*01	822	1427
1220	VH3-23_IGHD2-8*01>2_IGHJ6*01	2658	L2_IGKJ1*01	822	1427
1221	VH3-23_IGHD2-8*01>3_IGHJ6*01	2659	L2_IGKJ1*01	822	1427
1222	VH3-23_IGHD2-15*01>2_IGHJ6*01	2660	L2_IGKJ1*01	822	1427
1223	VH3-23_IGHD2-15*01>3_IGHJ6*01	2661	L2_IGKJ1*01	822	1427
1224	VH3-23_IGHD2-21*01>2_IGHJ6*01	2662	L2_IGKJ1*01	822	1427
1225	VH3-23_IGHD2-21*01>3_IGHJ6*01	2663	L2_IGKJ1*01	822	1427
1226	VH3-23_IGHD3-3*01>1_IGHJ6*01	2664	L2_IGKJ1*01	822	1427
1227	VH3-23_IGHD3-3*01>2_IGHJ6*01	2665	L2_IGKJ1*01	822	1427
1228	VH3-23_IGHD3-3*01>3_IGHJ6*01	2666	L2_IGKJ1*01	822	1427
1229	VH3-23_IGHD3-9*01>2_IGHJ6*01	2667	L2_IGKJ1*01	822	1427
1230	VH3-23_IGHD3-10*01>2_IGHJ6*01	2668	L2_IGKJ1*01	822	1427
1231	VH3-23_IGHD3-10*01>3_IGHJ6*01	2669	L2_IGKJ1*01	822	1427
1232	VH3-23_IGHD3-16*01>2_IGHJ6*01	2670	L2_IGKJ1*01	822	1427
1233	VH3-23_IGHD3-16*01>3_IGHJ6*01	2671	L2_IGKJ1*01	822	1427
1234	VH3-23_IGHD3-22*01>2_IGHJ6*01	2672	L2_IGKJ1*01	822	1427
1235	VH3-23_IGHD3-22*01>3_IGHJ6*01	2673	L2_IGKJ1*01	822	1427
1236	VH3-23_IGHD4-4*01 (1) >2_IGHJ6*01	2674	L2_IGKJ1*01	822	1427
1237	VH3-23_IGHD4-4*01 (1) >3_IGHJ6*01	2675	L2_IGKJ1*01	822	1427

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
1238	VH3-23_IGHD4-11*01 (1) >2_IGHJ6*01	2676	L2_IGKJ1*01	822	1427
1239	VH3-23_IGHD4-11*01 (1) >3_IGHJ6*01	2677	L2_IGKJ1*01	822	1427
1240	VH3-23_IGHD4-17*01>2_IGHJ6*01	2678	L2_IGKJ1*01	822	1427
1241	VH3-23_IGHD4-17*01>3_IGHJ6*01	2679	L2_IGKJ1*01	822	1427
1242	VH3-23_IGHD4-23*01>2_IGHJ6*01	2680	L2_IGKJ1*01	822	1427
1243	VH3-23_IGHD4-23*01>3_IGHJ6*01	2681	L2_IGKJ1*01	822	1427
1244	VH3-23_IGHD5-5*01 (2) >1_IGHJ6*01	2682	L2_IGKJ1*01	822	1427
1245	VH3-23_IGHD5-5*01 (2) >2_IGHJ6*01	2683	L2_IGKJ1*01	822	1427
1246	VH3-23_IGHD5-5*01 (2) >3_IGHJ6*01	2684	L2_IGKJ1*01	822	1427
1247	VH3-23_IGHD5-12*01>1_IGHJ6*01	2685	L2_IGKJ1*01	822	1427
1248	VH3-23_IGHD5-12*01>3_IGHJ6*01	2686	L2_IGKJ1*01	822	1427
1249	VH3-23_IGHD5-18*01 (2) >1_IGHJ6*01	2687	L2_IGKJ1*01	822	1427
1250	VH3-23_IGHD5-18*01 (2) >2_IGHJ6*01	2688	L2_IGKJ1*01	822	1427
1251	VH3-23_IGHD5-18*01 (2) >3_IGHJ6*01	2689	L2_IGKJ1*01	822	1427
1252	VH3-23_IGHD5-24*01>1_IGHJ6*01	2690	L2_IGKJ1*01	822	1427
1253	VH3-23_IGHD5-24*01>3_IGHJ6*01	2691	L2_IGKJ1*01	822	1427
1254	VH3-23_IGHD6-6*01>1_IGHJ6*01	2692	L2_IGKJ1*01	822	1427
1255	VH3-23_IGHD1-1*01>1'_IGHJ6*01	2702	L2_IGKJ1*01	822	1427
1256	VH3-23_IGHD1-1*01>2'_IGHJ6*01	2703	L2_IGKJ1*01	822	1427
1257	VH3-23_IGHD1-1*01>3'_IGHJ6*01	2704	L2_IGKJ1*01	822	1427
1258	VH3-23_IGHD1-7*01>1'_IGHJ6*01	2705	L2_IGKJ1*01	822	1427
1259	VH3-23_IGHD1-7*01>3'_IGHJ6*01	2706	L2_IGKJ1*01	822	1427
1260	VH3-23_IGHD1-14*01>1'_IGHJ6*01	2707	L2_IGKJ1*01	822	1427
1261	VH3-23_IGHD1-14*01>2'_IGHJ6*01	2708	L2_IGKJ1*01	822	1427
1262	VH3-23_IGHD1-14*01>3'_IGHJ6*01	2709	L2_IGKJ1*01	822	1427
1263	VH3-23_IGHD1-20*01>1'_IGHJ6*01	2710	L2_IGKJ1*01	822	1427
1264	VH3-23_IGHD1-20*01>2'_IGHJ6*01	2711	L2_IGKJ1*01	822	1427
1265	VH3-23_IGHD1-20*01>3'_IGHJ6*01	2712	L2_IGKJ1*01	822	1427
1266	VH3-23_IGHD1-26*01>1'_IGHJ6*01	2713	L2_IGKJ1*01	822	1427
1267	VH3-23_IGHD1-26*01>1_IGHJ6*01_B	2714	L2_IGKJ1*01	822	1427
1268	VH3-23_IGHD2-2*01>2_IGHJ6*01_B	2715	L2_IGKJ1*01	822	1427
1269	VH3-23_IGHD2-2*01>3'_IGHJ6*01	2716	L2_IGKJ1*01	822	1427
1270	VH3-23_IGHD2-8*01>1'_IGHJ6*01	2717	L2_IGKJ1*01	822	1427
1271	VH3-23_IGHD2-15*01>1'_IGHJ6*01	2718	L2_IGKJ1*01	822	1427
1272	VH3-23_IGHD2-15*01>3'_IGHJ6*01	2719	L2_IGKJ1*01	822	1427
1273	VH3-23_IGHD2-21*01>1'_IGHJ6*01	2720	L2_IGKJ1*01	822	1427
1274	VH3-23_IGHD2-21*01>3'_IGHJ6*01	2721	L2_IGKJ1*01	822	1427
1275	VH3-23_IGHD3-3*01>1'_IGHJ6*01	2722	L2_IGKJ1*01	822	1427
1276	VH3-23_IGHD3-3*01>3'_IGHJ6*01	2723	L2_IGKJ1*01	822	1427
1277	VH3-23_IGHD3-9*01>1'_IGHJ6*01	2724	L2_IGKJ1*01	822	1427
1278	VH3-23_IGHD3-9*01>3'_IGHJ6*01	2725	L2_IGKJ1*01	822	1427
1279	VH3-23_IGHD3-10*01>1'_IGHJ6*01	2726	L2_IGKJ1*01	822	1427
1280	VH3-23_IGHD3-10*01>3'_IGHJ6*01	2727	L2_IGKJ1*01	822	1427
1281	VH3-23_IGHD3-16*01>1'_IGHJ6*01	2728	L2_IGKJ1*01	822	1427

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
1282	VH3-23_IGHD3-16*01>3'_IGHJ6*01	2729	L2_IGKJ1*01	822	1427
1283	VH3-23_IGHD3-22*01>1'_IGHJ6*01	2730	L2_IGKJ1*01	822	1427
1284	VH3-23_IGHD4-4*01 (1) >1'_IGHJ6*01	2731	L2_IGKJ1*01	822	1427
1285	VH3-23_IGHD4-4*01 (1) >3'_IGHJ6*01	2732	L2_IGKJ1*01	822	1427
1286	VH3-23_IGHD4-11*01 (1) >1'_IGHJ6*01	2733	L2_IGKJ1*01	822	1427
1287	VH3-23_IGHD4-11*01 (1) >3'_IGHJ6*01	2734	L2_IGKJ1*01	822	1427
1288	VH3-23_IGHD4-17*01>1'_IGHJ6*01	2735	L2_IGKJ1*01	822	1427
1289	VH3-23_IGHD4-17*01>3'_IGHJ6*01	2736	L2_IGKJ1*01	822	1427
1290	VH3-23_IGHD4-23*01>1'_IGHJ6*01	2737	L2_IGKJ1*01	822	1427
1291	VH3-23_IGHD4-23*01>3'_IGHJ6*01	2738	L2_IGKJ1*01	822	1427
1292	VH3-23_IGHD5-5*01 (2) >1'_IGHJ6*01	2739	L2_IGKJ1*01	822	1427
1293	VH3-23_IGHD5-5*01 (2) >3'_IGHJ6*01	2740	L2_IGKJ1*01	822	1427
1294	VH3-23_IGHD5-12*01>1'_IGHJ6*01	2741	L2_IGKJ1*01	822	1427
1295	VH3-23_IGHD5-12*01>3'_IGHJ6*01	2742	L2_IGKJ1*01	822	1427
1296	VH3-23_IGHD5-18*01 (2) >1'_IGHJ6*01	2743	L2_IGKJ1*01	822	1427
1297	VH3-23_IGHD5-18*01 (2) >3'_IGHJ6*01	2744	L2_IGKJ1*01	822	1427
1298	VH3-23_IGHD5-24*01>1'_IGHJ6*01	2745	L2_IGKJ1*01	822	1427
1299	VH3-23_IGHD5-24*01>3'_IGHJ6*01	2746	L2_IGKJ1*01	822	1427
1300	VH3-23_IGHD6-6*01>1'_IGHJ6*01	2747	L2_IGKJ1*01	822	1427
1301	VH3-23_IGHD6-6*01>2'_IGHJ6*01	2748	L2_IGKJ1*01	822	1427
1302	VH3-23_IGHD6-6*01>3'_IGHJ6*01	2749	L2_IGKJ1*01	822	1427
1303	VH3-23_IGHD1-1*01>1_IGHJ6*01	2645	L6_IGKJ1*01	829	1434
1304	VH3-23_IGHD1-1*01>2_IGHJ6*01	2646	L6_IGKJ1*01	829	1434
1305	VH3-23_IGHD1-1*01>3_IGHJ6*01	2647	L6_IGKJ1*01	829	1434
1306	VH3-23_IGHD1-7*01>1_IGHJ6*01	2648	L6_IGKJ1*01	829	1434
1307	VH3-23_IGHD1-7*01>3_IGHJ6*01	2649	L6_IGKJ1*01	829	1434
1308	VH3-23_IGHD1-14*01>1_IGHJ6*01	2650	L6_IGKJ1*01	829	1434
1309	VH3-23_IGHD1-14*01>3_IGHJ6*01	2651	L6_IGKJ1*01	829	1434
1310	VH3-23_IGHD1-20*01>1_IGHJ6*01	2652	L6_IGKJ1*01	829	1434
1311	VH3-23_IGHD1-20*01>3_IGHJ6*01	2653	L6_IGKJ1*01	829	1434
1312	VH3-23_IGHD1-26*01>1_IGHJ6*01	2654	L6_IGKJ1*01	829	1434
1313	VH3-23_IGHD1-26*01>3_IGHJ6*01	2655	L6_IGKJ1*01	829	1434
1314	VH3-23_IGHD2-2*01>2_IGHJ6*01	2656	L6_IGKJ1*01	829	1434
1315	VH3-23_IGHD2-2*01>3_IGHJ6*01	2657	L6_IGKJ1*01	829	1434
1316	VH3-23_IGHD2-8*01>2_IGHJ6*01	2658	L6_IGKJ1*01	829	1434
1317	VH3-23_IGHD2-8*01>3_IGHJ6*01	2659	L6_IGKJ1*01	829	1434
1318	VH3-23_IGHD2-15*01>2_IGHJ6*01	2660	L6_IGKJ1*01	829	1434
1319	VH3-23_IGHD2-15*01>3_IGHJ6*01	2661	L6_IGKJ1*01	829	1434
1320	VH3-23_IGHD2-21*01>2_IGHJ6*01	2662	L6_IGKJ1*01	829	1434
1321	VH3-23_IGHD2-21*01>3_IGHJ6*01	2663	L6_IGKJ1*01	829	1434
1322	VH3-23_IGHD3-3*01>1_IGHJ6*01	2664	L6_IGKJ1*01	829	1434
1323	VH3-23_IGHD3-3*01>2_IGHJ6*01	2665	L6_IGKJ1*01	829	1434
1324	VH3-23_IGHD3-3*01>3_IGHJ6*01	2666	L6_IGKJ1*01	829	1434
1325	VH3-23_IGHD3-9*01>2_IGHJ6*01	2667	L6_IGKJ1*01	829	1434

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
1326	VH3-23_IGHD3-10*01>2_IGHJ6*01	2668	L6_IGKJ1*01	829	1434
1327	VH3-23_IGHD3-10*01>3_IGHJ6*01	2669	L6_IGKJ1*01	829	1434
1328	VH3-23_IGHD3-16*01>2_IGHJ6*01	2670	L6_IGKJ1*01	829	1434
1329	VH3-23_IGHD3-16*01>3_IGHJ6*01	2671	L6_IGKJ1*01	829	1434
1330	VH3-23_IGHD3-22*01>2_IGHJ6*01	2672	L6_IGKJ1*01	829	1434
1331	VH3-23_IGHD3-22*01>3_IGHJ6*01	2673	L6_IGKJ1*01	829	1434
1332	VH3-23_IGHD4-4*01 (1) >2_IGHJ6*01	2674	L6_IGKJ1*01	829	1434
1333	VH3-23_IGHD4-4*01 (1) >3_IGHJ6*01	2675	L6_IGKJ1*01	829	1434
1334	VH3-23_IGHD4-11*01 (1) >2_IGHJ6*01	2676	L6_IGKJ1*01	829	1434
1335	VH3-23_IGHD4-11*01 (1) >3_IGHJ6*01	2677	L6_IGKJ1*01	829	1434
1336	VH3-23_IGHD4-17*01>2_IGHJ6*01	2678	L6_IGKJ1*01	829	1434
1337	VH3-23_IGHD4-17*01>3_IGHJ6*01	2679	L6_IGKJ1*01	829	1434
1338	VH3-23_IGHD4-23*01>2_IGHJ6*01	2680	L6_IGKJ1*01	829	1434
1339	VH3-23_IGHD4-23*01>3_IGHJ6*01	2681	L6_IGKJ1*01	829	1434
1340	VH3-23_IGHD5-5*01 (2) >1_IGHJ6*01	2682	L6_IGKJ1*01	829	1434
1341	VH3-23_IGHD5-5*01 (2) >2_IGHJ6*01	2683	L6_IGKJ1*01	829	1434
1342	VH3-23_IGHD5-5*01 (2) >3_IGHJ6*01	2684	L6_IGKJ1*01	829	1434
1343	VH3-23_IGHD5-12*01>1_IGHJ6*01	2685	L6_IGKJ1*01	829	1434
1344	VH3-23_IGHD5-12*01>3_IGHJ6*01	2686	L6_IGKJ1*01	829	1434
1345	VH3-23_IGHD5-18*01 (2) >1_IGHJ6*01	2687	L6_IGKJ1*01	829	1434
1346	VH3-23_IGHD5-18*01 (2) >2_IGHJ6*01	2688	L6_IGKJ1*01	829	1434
1347	VH3-23_IGHD5-18*01 (2) >3_IGHJ6*01	2689	L6_IGKJ1*01	829	1434
1348	VH3-23_IGHD5-24*01>1_IGHJ6*01	2690	L6_IGKJ1*01	829	1434
1349	VH3-23_IGHD5-24*01>3_IGHJ6*01	2691	L6_IGKJ1*01	829	1434
1350	VH3-23_IGHD6-6*01>1_IGHJ6*01	2692	L6_IGKJ1*01	829	1434
1351	VH3-23_IGHD1-1*01>1'_IGHJ6*01	2702	L6_IGKJ1*01	829	1434
1352	VH3-23_IGHD1-1*01>2'_IGHJ6*01	2703	L6_IGKJ1*01	829	1434
1353	VH3-23_IGHD1-1*01>3'_IGHJ6*01	2704	L6_IGKJ1*01	829	1434
1354	VH3-23_IGHD1-7*01>1'_IGHJ6*01	2705	L6_IGKJ1*01	829	1434
1355	VH3-23_IGHD1-7*01>3'_IGHJ6*01	2706	L6_IGKJ1*01	829	1434
1356	VH3-23_IGHD1-14*01>1'_IGHJ6*01	2707	L6_IGKJ1*01	829	1434
1357	VH3-23_IGHD1-14*01>2'_IGHJ6*01	2708	L6_IGKJ1*01	829	1434
1358	VH3-23_IGHD1-14*01>3'_IGHJ6*01	2709	L6_IGKJ1*01	829	1434
1359	VH3-23_IGHD1-20*01>1'_IGHJ6*01	2710	L6_IGKJ1*01	829	1434
1360	VH3-23_IGHD1-20*01>2'_IGHJ6*01	2711	L6_IGKJ1*01	829	1434
1361	VH3-23_IGHD1-20*01>3'_IGHJ6*01	2712	L6_IGKJ1*01	829	1434
1362	VH3-23_IGHD1-26*01>1'_IGHJ6*01	2713	L6_IGKJ1*01	829	1434
1363	VH3-23_IGHD1-26*01>1_IGHJ6*01_B	2714	L6_IGKJ1*01	829	1434
1364	VH3-23_IGHD2-2*01>2_IGHJ6*01_B	2715	L6_IGKJ1*01	829	1434
1365	VH3-23_IGHD2-2*01>3'_IGHJ6*01	2716	L6_IGKJ1*01	829	1434
1366	VH3-23_IGHD2-8*01>1'_IGHJ6*01	2717	L6_IGKJ1*01	829	1434
1367	VH3-23_IGHD2-15*01>1'_IGHJ6*01	2718	L6_IGKJ1*01	829	1434
1368	VH3-23_IGHD2-15*01>3'_IGHJ6*01	2719	L6_IGKJ1*01	829	1434
1369	VH3-23_IGHD2-21*01>1'_IGHJ6*01	2720	L6_IGKJ1*01	829	1434

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
1370	VH3-23_IGHD2-21*01>3'_IGHJ6*01	2721	L6_IGKJ1*01	829	1434
1371	VH3-23_IGHD3-3*01>1'_IGHJ6*01	2722	L6_IGKJ1*01	829	1434
1372	VH3-23_IGHD3-3*01>3'_IGHJ6*01	2723	L6_IGKJ1*01	829	1434
1373	VH3-23_IGHD3-9*01>1'_IGHJ6*01	2724	L6_IGKJ1*01	829	1434
1374	VH3-23_IGHD3-9*01>3'_IGHJ6*01	2725	L6_IGKJ1*01	829	1434
1375	VH3-23_IGHD3-10*01>1'_IGHJ6*01	2726	L6_IGKJ1*01	829	1434
1376	VH3-23_IGHD3-10*01>3'_IGHJ6*01	2727	L6_IGKJ1*01	829	1434
1377	VH3-23_IGHD3-16*01>1'_IGHJ6*01	2728	L6_IGKJ1*01	829	1434
1378	VH3-23_IGHD3-16*01>3'_IGHJ6*01	2729	L6_IGKJ1*01	829	1434
1379	VH3-23_IGHD3-22*01>1'_IGHJ6*01	2730	L6_IGKJ1*01	829	1434
1380	VH3-23_IGHD4-4*01 (1) >1'_IGHJ6*01	2731	L6_IGKJ1*01	829	1434
1381	VH3-23_IGHD4-4*01 (1) >3'_IGHJ6*01	2732	L6_IGKJ1*01	829	1434
1382	VH3-23_IGHD4-11*01 (1) >1'_IGHJ6*01	2733	L6_IGKJ1*01	829	1434
1383	VH3-23_IGHD4-11*01 (1) >3'_IGHJ6*01	2734	L6_IGKJ1*01	829	1434
1384	VH3-23_IGHD4-17*01>1'_IGHJ6*01	2735	L6_IGKJ1*01	829	1434
1385	VH3-23_IGHD4-17*01>3'_IGHJ6*01	2736	L6_IGKJ1*01	829	1434
1386	VH3-23_IGHD4-23*01>1'_IGHJ6*01	2737	L6_IGKJ1*01	829	1434
1387	VH3-23_IGHD4-23*01>3'_IGHJ6*01	2738	L6_IGKJ1*01	829	1434
1388	VH3-23_IGHD5-5*01 (2) >1'_IGHJ6*01	2739	L6_IGKJ1*01	829	1434
1389	VH3-23_IGHD5-5*01 (2) >3'_IGHJ6*01	2740	L6_IGKJ1*01	829	1434
1390	VH3-23_IGHD5-12*01>1'_IGHJ6*01	2741	L6_IGKJ1*01	829	1434
1391	VH3-23_IGHD5-12*01>3'_IGHJ6*01	2742	L6_IGKJ1*01	829	1434
1392	VH3-23_IGHD5-18*01 (2) >1'_IGHJ6*01	2743	L6_IGKJ1*01	829	1434
1393	VH3-23_IGHD5-18*01 (2) >3'_IGHJ6*01	2744	L6_IGKJ1*01	829	1434
1394	VH3-23_IGHD5-24*01>1'_IGHJ6*01	2745	L6_IGKJ1*01	829	1434
1395	VH3-23_IGHD5-24*01>3'_IGHJ6*01	2746	L6_IGKJ1*01	829	1434
1396	VH3-23_IGHD6-6*01>1'_IGHJ6*01	2747	L6_IGKJ1*01	829	1434
1397	VH3-23_IGHD6-6*01>2'_IGHJ6*01	2748	L6_IGKJ1*01	829	1434
1398	VH3-23_IGHD6-6*01>3'_IGHJ6*01	2749	L6_IGKJ1*01	829	1434
1399	VH3-23_IGHD1-1*01>1_IGHJ5*01	2530	L25_IGKJ1*01	826	1431
1400	VH3-23_IGHD1-1*01>2_IGHJ5*01	2531	L25_IGKJ1*01	826	1431
1401	VH3-23_IGHD1-1*01>3_IGHJ5*01	2532	L25_IGKJ1*01	826	1431
1402	VH3-23_IGHD1-7*01>1_IGHJ5*01	2533	L25_IGKJ1*01	826	1431
1403	VH3-23_IGHD1-7*01>3_IGHJ5*01	2534	L25_IGKJ1*01	826	1431
1404	VH3-23_IGHD1-14*01>1_IGHJ5*01	2535	L25_IGKJ1*01	826	1431
1405	VH3-23_IGHD1-14*01>3_IGHJ5*01	2536	L25_IGKJ1*01	826	1431
1406	VH3-23_IGHD1-20*01>1_IGHJ5*01	2537	L25_IGKJ1*01	826	1431
1407	VH3-23_IGHD1-20*01>3_IGHJ5*01	2538	L25_IGKJ1*01	826	1431
1408	VH3-23_IGHD1-26*01>1_IGHJ5*01	2539	L25_IGKJ1*01	826	1431
1409	VH3-23_IGHD1-26*01>3_IGHJ5*01	2540	L25_IGKJ1*01	826	1431
1410	VH3-23_IGHD2-2*01>2_IGHJ5*01	2541	L25_IGKJ1*01	826	1431
1411	VH3-23_IGHD2-2*01>3_IGHJ5*01	2542	L25_IGKJ1*01	826	1431
1412	VH3-23_IGHD2-8*01>2_IGHJ5*01	2543	L25_IGKJ1*01	826	1431
1413	VH3-23_IGHD2-8*01>3_IGHJ5*01	2544	L25_IGKJ1*01	826	1431

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
1414	VH3-23_IGHD2-15*01>2_IGHJ5*01	2545	L25_IGKJ1*01	826	1431
1415	VH3-23_IGHD2-15*01>3_IGHJ5*01	2546	L25_IGKJ1*01	826	1431
1416	VH3-23_IGHD2-21*01>2_IGHJ5*01	2547	L25_IGKJ1*01	826	1431
1417	VH3-23_IGHD2-21*01>3_IGHJ5*01	2548	L25_IGKJ1*01	826	1431
1418	VH3-23_IGHD3-3*01>1_IGHJ5*01	2549	L25_IGKJ1*01	826	1431
1419	VH3-23_IGHD3-3*01>2_IGHJ5*01	2550	L25_IGKJ1*01	826	1431
1420	VH3-23_IGHD3-3*01>3_IGHJ5*01	2551	L25_IGKJ1*01	826	1431
1421	VH3-23_IGHD3-9*01>2_IGHJ5*01	2552	L25_IGKJ1*01	826	1431
1422	VH3-23_IGHD3-10*01>2_IGHJ5*01	2553	L25_IGKJ1*01	826	1431
1423	VH3-23_IGHD3-10*01>3_IGHJ5*01	2554	L25_IGKJ1*01	826	1431
1424	VH3-23_IGHD3-16*01>2_IGHJ5*01	2555	L25_IGKJ1*01	826	1431
1425	VH3-23_IGHD3-16*01>3_IGHJ5*01	2556	L25_IGKJ1*01	826	1431
1426	VH3-23_IGHD3-22*01>2_IGHJ5*01	2557	L25_IGKJ1*01	826	1431
1427	VH3-23_IGHD3-22*01>3_IGHJ5*01	2558	L25_IGKJ1*01	826	1431
1428	VH3-23_IGHD4-4*01 (1) >2_IGHJ5*01	2559	L25_IGKJ1*01	826	1431
1429	VH3-23_IGHD4-4*01 (1) >3_IGHJ5*01	2560	L25_IGKJ1*01	826	1431
1430	VH3-23_IGHD4-11*01 (1) >2_IGHJ5*01	2561	L25_IGKJ1*01	826	1431
1431	VH3-23_IGHD4-11*01 (1) >3_IGHJ5*01	2562	L25_IGKJ1*01	826	1431
1432	VH3-23_IGHD4-17*01>2_IGHJ5*01	2563	L25_IGKJ1*01	826	1431
1433	VH3-23_IGHD4-17*01>3_IGHJ5*01	2564	L25_IGKJ1*01	826	1431
1434	VH3-23_IGHD4-23*01>2_IGHJ5*01	2565	L25_IGKJ1*01	826	1431
1435	VH3-23_IGHD4-23*01>3_IGHJ5*01	2566	L25_IGKJ1*01	826	1431
1436	VH3-23_IGHD5-5*01 (2) >1_IGHJ5*01	2567	L25_IGKJ1*01	826	1431
1437	VH3-23_IGHD5-5*01 (2) >2_IGHJ5*01	2568	L25_IGKJ1*01	826	1431
1438	VH3-23_IGHD5-5*01 (2) >3_IGHJ5*01	2569	L25_IGKJ1*01	826	1431
1439	VH3-23_IGHD5-12*01>1_IGHJ5*01	2570	L25_IGKJ1*01	826	1431
1440	VH3-23_IGHD5-12*01>3_IGHJ5*01	2571	L25_IGKJ1*01	826	1431
1441	VH3-23_IGHD5-18*01 (2) >1_IGHJ5*01	2572	L25_IGKJ1*01	826	1431
1442	VH3-23_IGHD5-18*01 (2) >2_IGHJ5*01	2573	L25_IGKJ1*01	826	1431
1443	VH3-23_IGHD5-18*01 (2) >3_IGHJ5*01	2574	L25_IGKJ1*01	826	1431
1444	VH3-23_IGHD5-24*01>1_IGHJ5*01	2575	L25_IGKJ1*01	826	1431
1445	VH3-23_IGHD5-24*01>3_IGHJ5*01	2576	L25_IGKJ1*01	826	1431
1446	VH3-23_IGHD6-6*01>1_IGHJ5*01	2577	L25_IGKJ1*01	826	1431
1447	VH3-23_IGHD1-1*01>1'_IGHJ5*01	2587	L25_IGKJ1*01	826	1431
1448	VH3-23_IGHD1-1*01>2'_IGHJ5*01	2588	L25_IGKJ1*01	826	1431
1449	VH3-23_IGHD1-1*01>3'_IGHJ5*01	2589	L25_IGKJ1*01	826	1431
1450	VH3-23_IGHD1-7*01>1'_IGHJ5*01	2590	L25_IGKJ1*01	826	1431
1451	VH3-23_IGHD1-7*01>3'_IGHJ5*01	2591	L25_IGKJ1*01	826	1431
1452	VH3-23_IGHD1-14*01>1'_IGHJ5*01	2592	L25_IGKJ1*01	826	1431
1453	VH3-23_IGHD1-14*01>2'_IGHJ5*01	2593	L25_IGKJ1*01	826	1431
1454	VH3-23_IGHD1-14*01>3'_IGHJ5*01	2594	L25_IGKJ1*01	826	1431
1455	VH3-23_IGHD1-20*01>1'_IGHJ5*01	2595	L25_IGKJ1*01	826	1431
1456	VH3-23_IGHD1-20*01>2'_IGHJ5*01	2596	L25_IGKJ1*01	826	1431
1457	VH3-23_IGHD1-20*01>3'_IGHJ5*01	2597	L25_IGKJ1*01	826	1431

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
1458	VH3-23_IGHD1-26*01>1'_IGHJ5*01	2598	L25_IGKJ1*01	826	1431
1459	VH3-23_IGHD1-26*01>3'_IGHJ5*01	2599	L25_IGKJ1*01	826	1431
1460	VH3-23_IGHD2-2*01>1'_IGHJ5*01	2600	L25_IGKJ1*01	826	1431
1461	VH3-23_IGHD2-2*01>3'_IGHJ5*01	2601	L25_IGKJ1*01	826	1431
1462	VH3-23_IGHD2-8*01>1'_IGHJ5*01	2602	L25_IGKJ1*01	826	1431
1463	VH3-23_IGHD2-15*01>1'_IGHJ5*01	2603	L25_IGKJ1*01	826	1431
1464	VH3-23_IGHD2-15*01>3'_IGHJ5*01	2604	L25_IGKJ1*01	826	1431
1465	VH3-23_IGHD2-21*01>1'_IGHJ5*01	2605	L25_IGKJ1*01	826	1431
1466	VH3-23_IGHD2-21*01>3'_IGHJ5*01	2606	L25_IGKJ1*01	826	1431
1467	VH3-23_IGHD3-3*01>1'_IGHJ5*01	2607	L25_IGKJ1*01	826	1431
1468	VH3-23_IGHD3-3*01>3'_IGHJ5*01	2608	L25_IGKJ1*01	826	1431
1469	VH3-23_IGHD3-9*01>1'_IGHJ5*01	2609	L25_IGKJ1*01	826	1431
1470	VH3-23_IGHD3-9*01>3'_IGHJ5*01	2610	L25_IGKJ1*01	826	1431
1471	VH3-23_IGHD3-10*01>1'_IGHJ5*01	2611	L25_IGKJ1*01	826	1431
1472	VH3-23_IGHD3-10*01>3'_IGHJ5*01	2612	L25_IGKJ1*01	826	1431
1473	VH3-23_IGHD3-16*01>1'_IGHJ5*01	2613	L25_IGKJ1*01	826	1431
1474	VH3-23_IGHD3-16*01>3'_IGHJ5*01	2614	L25_IGKJ1*01	826	1431
1475	VH3-23_IGHD3-22*01>1'_IGHJ5*01	2615	L25_IGKJ1*01	826	1431
1476	VH3-23_IGHD4-4*01 (1) >1'_IGHJ5*01	2616	L25_IGKJ1*01	826	1431
1477	VH3-23_IGHD4-4*01 (1) >3'_IGHJ5*01	2617	L25_IGKJ1*01	826	1431
1478	VH3-23_IGHD4-11*01 (1) >1'_IGHJ5*01	2618	L25_IGKJ1*01	826	1431
1479	VH3-23_IGHD4-11*01 (1) >3'_IGHJ5*01	2619	L25_IGKJ1*01	826	1431
1480	VH3-23_IGHD4-17*01>1'_IGHJ5*01	2620	L25_IGKJ1*01	826	1431
1481	VH3-23_IGHD4-17*01>3'_IGHJ5*01	2621	L25_IGKJ1*01	826	1431
1482	VH3-23_IGHD4-23*01>1'_IGHJ5*01	2622	L25_IGKJ1*01	826	1431
1483	VH3-23_IGHD4-23*01>3'_IGHJ5*01	2623	L25_IGKJ1*01	826	1431
1484	VH3-23_IGHD5-5*01 (2) >1'_IGHJ5*01	2624	L25_IGKJ1*01	826	1431
1485	VH3-23_IGHD5-5*01 (2) >3'_IGHJ5*01	2625	L25_IGKJ1*01	826	1431
1486	VH3-23_IGHD5-12*01>1'_IGHJ5*01	2626	L25_IGKJ1*01	826	1431
1487	VH3-23_IGHD5-12*01>3'_IGHJ5*01	2627	L25_IGKJ1*01	826	1431
1488	VH3-23_IGHD5-18*01 (2) >1'_IGHJ5*01	2628	L25_IGKJ1*01	826	1431
1489	VH3-23_IGHD5-18*01 (2) >3'_IGHJ5*01	2629	L25_IGKJ1*01	826	1431
1490	VH3-23_IGHD5-24*01>1'_IGHJ5*01	2630	L25_IGKJ1*01	826	1431
1491	VH3-23_IGHD5-24*01>3'_IGHJ5*01	2631	L25_IGKJ1*01	826	1431
1492	VH3-23_IGHD6-6*01>1'_IGHJ5*01	2632	L25_IGKJ1*01	826	1431
1493	VH3-23_IGHD6-6*01>2'_IGHJ5*01	2633	L25_IGKJ1*01	826	1431
1494	VH3-23_IGHD6-6*01>3'_IGHJ5*01	2634	L25_IGKJ1*01	826	1431
1495	VH3-23_IGHD1-1*01>1_IGHJ5*01	2530	B3_IGKJ1*01	817	1422
1496	VH3-23_IGHD1-1*01>2_IGHJ5*01	2531	B3_IGKJ1*01	817	1422
1497	VH3-23_IGHD1-1*01>3_IGHJ5*01	2532	B3_IGKJ1*01	817	1422
1498	VH3-23_IGHD1-7*01>1_IGHJ5*01	2533	B3_IGKJ1*01	817	1422
1499	VH3-23_IGHD1-7*01>3_IGHJ5*01	2534	B3_IGKJ1*01	817	1422
1500	VH3-23_IGHD1-14*01>1_IGHJ5*01	2535	B3_IGKJ1*01	817	1422
1501	VH3-23_IGHD1-14*01>3_IGHJ5*01	2536	B3_IGKJ1*01	817	1422

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
1502	VH3-23_IGHD1-20*01>1_IGHJ5*01	2537	B3_IGKJ1*01	817	1422
1503	VH3-23_IGHD1-20*01>3_IGHJ5*01	2538	B3_IGKJ1*01	817	1422
1504	VH3-23_IGHD1-26*01>1_IGHJ5*01	2539	B3_IGKJ1*01	817	1422
1505	VH3-23_IGHD1-26*01>3_IGHJ5*01	2540	B3_IGKJ1*01	817	1422
1506	VH3-23_IGHD2-2*01>2_IGHJ5*01	2541	B3_IGKJ1*01	817	1422
1507	VH3-23_IGHD2-2*01>3_IGHJ5*01	2542	B3_IGKJ1*01	817	1422
1508	VH3-23_IGHD2-8*01>2_IGHJ5*01	2543	B3_IGKJ1*01	817	1422
1509	VH3-23_IGHD2-8*01>3_IGHJ5*01	2544	B3_IGKJ1*01	817	1422
1510	VH3-23_IGHD2-15*01>2_IGHJ5*01	2545	B3_IGKJ1*01	817	1422
1511	VH3-23_IGHD2-15*01>3_IGHJ5*01	2546	B3_IGKJ1*01	817	1422
1512	VH3-23_IGHD2-21*01>2_IGHJ5*01	2547	B3_IGKJ1*01	817	1422
1513	VH3-23_IGHD2-21*01>3_IGHJ5*01	2548	B3_IGKJ1*01	817	1422
1514	VH3-23_IGHD3-3*01>1_IGHJ5*01	2549	B3_IGKJ1*01	817	1422
1515	VH3-23_IGHD3-3*01>2_IGHJ5*01	2550	B3_IGKJ1*01	817	1422
1516	VH3-23_IGHD3-3*01>3_IGHJ5*01	2551	B3_IGKJ1*01	817	1422
1517	VH3-23_IGHD3-9*01>2_IGHJ5*01	2552	B3_IGKJ1*01	817	1422
1518	VH3-23_IGHD3-10*01>2_IGHJ5*01	2553	B3_IGKJ1*01	817	1422
1519	VH3-23_IGHD3-10*01>3_IGHJ5*01	2554	B3_IGKJ1*01	817	1422
1520	VH3-23_IGHD3-16*01>2_IGHJ5*01	2555	B3_IGKJ1*01	817	1422
1521	VH3-23_IGHD3-16*01>3_IGHJ5*01	2556	B3_IGKJ1*01	817	1422
1522	VH3-23_IGHD3-22*01>2_IGHJ5*01	2557	B3_IGKJ1*01	817	1422
1523	VH3-23_IGHD3-22*01>3_IGHJ5*01	2558	B3_IGKJ1*01	817	1422
1524	VH3-23_IGHD4-4*01 (1) >2_IGHJ5*01	2559	B3_IGKJ1*01	817	1422
1525	VH3-23_IGHD4-4*01 (1) >3_IGHJ5*01	2560	B3_IGKJ1*01	817	1422
1526	VH3-23_IGHD4-11*01 (1) >2_IGHJ5*01	2561	B3_IGKJ1*01	817	1422
1527	VH3-23_IGHD4-11*01 (1) >3_IGHJ5*01	2562	B3_IGKJ1*01	817	1422
1528	VH3-23_IGHD4-17*01>2_IGHJ5*01	2563	B3_IGKJ1*01	817	1422
1529	VH3-23_IGHD4-17*01>3_IGHJ5*01	2564	B3_IGKJ1*01	817	1422
1530	VH3-23_IGHD4-23*01>2_IGHJ5*01	2565	B3_IGKJ1*01	817	1422
1531	VH3-23_IGHD4-23*01>3_IGHJ5*01	2566	B3_IGKJ1*01	817	1422
1532	VH3-23_IGHD5-5*01 (2) >1_IGHJ5*01	2567	B3_IGKJ1*01	817	1422
1533	VH3-23_IGHD5-5*01 (2) >2_IGHJ5*01	2568	B3_IGKJ1*01	817	1422
1534	VH3-23_IGHD5-5*01 (2) >3_IGHJ5*01	2569	B3_IGKJ1*01	817	1422
1535	VH3-23_IGHD5-12*01>1_IGHJ5*01	2570	B3_IGKJ1*01	817	1422
1536	VH3-23_IGHD5-12*01>3_IGHJ5*01	2571	B3_IGKJ1*01	817	1422
1537	VH3-23_IGHD5-18*01 (2) >1_IGHJ5*01	2572	B3_IGKJ1*01	817	1422
1538	VH3-23_IGHD5-18*01 (2) >2_IGHJ5*01	2573	B3_IGKJ1*01	817	1422
1539	VH3-23_IGHD5-18*01 (2) >3_IGHJ5*01	2574	B3_IGKJ1*01	817	1422
1540	VH3-23_IGHD5-24*01>1_IGHJ5*01	2575	B3_IGKJ1*01	817	1422
1541	VH3-23_IGHD5-24*01>3_IGHJ5*01	2576	B3_IGKJ1*01	817	1422
1542	VH3-23_IGHD6-6*01>1_IGHJ5*01	2577	B3_IGKJ1*01	817	1422
1543	VH3-23_IGHD1-1*01>1'_IGHJ5*01	2587	B3_IGKJ1*01	817	1422
1544	VH3-23_IGHD1-1*01>2'_IGHJ5*01	2588	B3_IGKJ1*01	817	1422
1545	VH3-23_IGHD1-1*01>3'_IGHJ5*01	2589	B3_IGKJ1*01	817	1422

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
1546	VH3-23_IGHD1-7*01>1'_IGHJ5*01	2590	B3_IGKJ1*01	817	1422
1547	VH3-23_IGHD1-7*01>3'_IGHJ5*01	2591	B3_IGKJ1*01	817	1422
1548	VH3-23_IGHD1-14*01>1'_IGHJ5*01	2592	B3_IGKJ1*01	817	1422
1549	VH3-23_IGHD1-14*01>2'_IGHJ5*01	2593	B3_IGKJ1*01	817	1422
1550	VH3-23_IGHD1-14*01>3'_IGHJ5*01	2594	B3_IGKJ1*01	817	1422
1551	VH3-23_IGHD1-20*01>1'_IGHJ5*01	2595	B3_IGKJ1*01	817	1422
1552	VH3-23_IGHD1-20*01>2'_IGHJ5*01	2596	B3_IGKJ1*01	817	1422
1553	VH3-23_IGHD1-20*01>3'_IGHJ5*01	2597	B3_IGKJ1*01	817	1422
1554	VH3-23_IGHD1-26*01>1'_IGHJ5*01	2598	B3_IGKJ1*01	817	1422
1555	VH3-23_IGHD1-26*01>3'_IGHJ5*01	2599	B3_IGKJ1*01	817	1422
1556	VH3-23_IGHD2-2*01>1'_IGHJ5*01	2600	B3_IGKJ1*01	817	1422
1557	VH3-23_IGHD2-2*01>3'_IGHJ5*01	2601	B3_IGKJ1*01	817	1422
1558	VH3-23_IGHD2-8*01>1'_IGHJ5*01	2602	B3_IGKJ1*01	817	1422
1559	VH3-23_IGHD2-15*01>1'_IGHJ5*01	2603	B3_IGKJ1*01	817	1422
1560	VH3-23_IGHD2-15*01>3'_IGHJ5*01	2604	B3_IGKJ1*01	817	1422
1561	VH3-23_IGHD2-21*01>1'_IGHJ5*01	2605	B3_IGKJ1*01	817	1422
1562	VH3-23_IGHD2-21*01>3'_IGHJ5*01	2606	B3_IGKJ1*01	817	1422
1563	VH3-23_IGHD3-3*01>1'_IGHJ5*01	2607	B3_IGKJ1*01	817	1422
1564	VH3-23_IGHD3-3*01>3'_IGHJ5*01	2608	B3_IGKJ1*01	817	1422
1565	VH3-23_IGHD3-9*01>1'_IGHJ5*01	2609	B3_IGKJ1*01	817	1422
1566	VH3-23_IGHD3-9*01>3'_IGHJ5*01	2610	B3_IGKJ1*01	817	1422
1567	VH3-23_IGHD3-10*01>1'_IGHJ5*01	2611	B3_IGKJ1*01	817	1422
1568	VH3-23_IGHD3-10*01>3'_IGHJ5*01	2612	B3_IGKJ1*01	817	1422
1569	VH3-23_IGHD3-16*01>1'_IGHJ5*01	2613	B3_IGKJ1*01	817	1422
1570	VH3-23_IGHD3-16*01>3'_IGHJ5*01	2614	B3_IGKJ1*01	817	1422
1571	VH3-23_IGHD3-22*01>1'_IGHJ5*01	2615	B3_IGKJ1*01	817	1422
1572	VH3-23_IGHD4-4*01 (1) >1'_IGHJ5*01	2616	B3_IGKJ1*01	817	1422
1573	VH3-23_IGHD4-4*01 (1) >3'_IGHJ5*01	2617	B3_IGKJ1*01	817	1422
1574	VH3-23_IGHD4-11*01 (1) >1'_IGHJ5*01	2618	B3_IGKJ1*01	817	1422
1575	VH3-23_IGHD4-11*01 (1) >3'_IGHJ5*01	2619	B3_IGKJ1*01	817	1422
1576	VH3-23_IGHD4-17*01>1'_IGHJ5*01	2620	B3_IGKJ1*01	817	1422
1577	VH3-23_IGHD4-17*01>3'_IGHJ5*01	2621	B3_IGKJ1*01	817	1422
1578	VH3-23_IGHD4-23*01>1'_IGHJ5*01	2622	B3_IGKJ1*01	817	1422
1579	VH3-23_IGHD4-23*01>3'_IGHJ5*01	2623	B3_IGKJ1*01	817	1422
1580	VH3-23_IGHD5-5*01 (2) >1'_IGHJ5*01	2624	B3_IGKJ1*01	817	1422
1581	VH3-23_IGHD5-5*01 (2) >3'_IGHJ5*01	2625	B3_IGKJ1*01	817	1422
1582	VH3-23_IGHD5-12*01>1'_IGHJ5*01	2626	B3_IGKJ1*01	817	1422
1583	VH3-23_IGHD5-12*01>3'_IGHJ5*01	2627	B3_IGKJ1*01	817	1422
1584	VH3-23_IGHD5-18*01 (2) >1'_IGHJ5*01	2628	B3_IGKJ1*01	817	1422
1585	VH3-23_IGHD5-18*01 (2) >3'_IGHJ5*01	2629	B3_IGKJ1*01	817	1422
1586	VH3-23_IGHD5-24*01>1'_IGHJ5*01	2630	B3_IGKJ1*01	817	1422
1587	VH3-23_IGHD5-24*01>3'_IGHJ5*01	2631	B3_IGKJ1*01	817	1422
1588	VH3-23_IGHD6-6*01>1'_IGHJ5*01	2632	B3_IGKJ1*01	817	1422
1589	VH3-23_IGHD6-6*01>2'_IGHJ5*01	2633	B3_IGKJ1*01	817	1422

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
1590	VH3-23_IGHD6-6*01>3'_IGHJ5*01	2634	B3_IGKJ1*01	817	1422
1591	VH3-23_IGHD1-1*01>1_IGHJ5*01	2530	A26_IGKJ1*01	811	1416
1592	VH3-23_IGHD1-1*01>2_IGHJ5*01	2531	A26_IGKJ1*01	811	1416
1593	VH3-23_IGHD1-1*01>3_IGHJ5*01	2532	A26_IGKJ1*01	811	1416
1594	VH3-23_IGHD1-7*01>1_IGHJ5*01	2533	A26_IGKJ1*01	811	1416
1595	VH3-23_IGHD1-7*01>3_IGHJ5*01	2534	A26_IGKJ1*01	811	1416
1596	VH3-23_IGHD1-14*01>1_IGHJ5*01	2535	A26_IGKJ1*01	811	1416
1597	VH3-23_IGHD1-14*01>3_IGHJ5*01	2536	A26_IGKJ1*01	811	1416
1598	VH3-23_IGHD1-20*01>1_IGHJ5*01	2537	A26_IGKJ1*01	811	1416
1599	VH3-23_IGHD1-20*01>3_IGHJ5*01	2538	A26_IGKJ1*01	811	1416
1600	VH3-23_IGHD1-26*01>1_IGHJ5*01	2539	A26_IGKJ1*01	811	1416
1601	VH3-23_IGHD1-26*01>3_IGHJ5*01	2540	A26_IGKJ1*01	811	1416
1602	VH3-23_IGHD2-2*01>2_IGHJ5*01	2541	A26_IGKJ1*01	811	1416
1603	VH3-23_IGHD2-2*01>3_IGHJ5*01	2542	A26_IGKJ1*01	811	1416
1604	VH3-23_IGHD2-8*01>2_IGHJ5*01	2543	A26_IGKJ1*01	811	1416
1605	VH3-23_IGHD2-8*01>3_IGHJ5*01	2544	A26_IGKJ1*01	811	1416
1606	VH3-23_IGHD2-15*01>2_IGHJ5*01	2545	A26_IGKJ1*01	811	1416
1607	VH3-23_IGHD2-15*01>3_IGHJ5*01	2546	A26_IGKJ1*01	811	1416
1608	VH3-23_IGHD2-21*01>2_IGHJ5*01	2547	A26_IGKJ1*01	811	1416
1609	VH3-23_IGHD2-21*01>3_IGHJ5*01	2548	A26_IGKJ1*01	811	1416
1610	VH3-23_IGHD3-3*01>1_IGHJ5*01	2549	A26_IGKJ1*01	811	1416
1611	VH3-23_IGHD3-3*01>2_IGHJ5*01	2550	A26_IGKJ1*01	811	1416
1612	VH3-23_IGHD3-3*01>3_IGHJ5*01	2551	A26_IGKJ1*01	811	1416
1613	VH3-23_IGHD3-9*01>2_IGHJ5*01	2552	A26_IGKJ1*01	811	1416
1614	VH3-23_IGHD3-10*01>2_IGHJ5*01	2553	A26_IGKJ1*01	811	1416
1615	VH3-23_IGHD3-10*01>3_IGHJ5*01	2554	A26_IGKJ1*01	811	1416
1616	VH3-23_IGHD3-16*01>2_IGHJ5*01	2555	A26_IGKJ1*01	811	1416
1617	VH3-23_IGHD3-16*01>3_IGHJ5*01	2556	A26_IGKJ1*01	811	1416
1618	VH3-23_IGHD3-22*01>2_IGHJ5*01	2557	A26_IGKJ1*01	811	1416
1619	VH3-23_IGHD3-22*01>3_IGHJ5*01	2558	A26_IGKJ1*01	811	1416
1620	VH3-23_IGHD4-4*01 (1) >2_IGHJ5*01	2559	A26_IGKJ1*01	811	1416
1621	VH3-23_IGHD4-4*01 (1) >3_IGHJ5*01	2560	A26_IGKJ1*01	811	1416
1622	VH3-23_IGHD4-11*01 (1) >2_IGHJ5*01	2561	A26_IGKJ1*01	811	1416
1623	VH3-23_IGHD4-11*01 (1) >3_IGHJ5*01	2562	A26_IGKJ1*01	811	1416
1624	VH3-23_IGHD4-17*01>2_IGHJ5*01	2563	A26_IGKJ1*01	811	1416
1625	VH3-23_IGHD4-17*01>3_IGHJ5*01	2564	A26_IGKJ1*01	811	1416
1626	VH3-23_IGHD4-23*01>2_IGHJ5*01	2565	A26_IGKJ1*01	811	1416
1627	VH3-23_IGHD4-23*01>3_IGHJ5*01	2566	A26_IGKJ1*01	811	1416
1628	VH3-23_IGHD5-5*01 (2) >1_IGHJ5*01	2567	A26_IGKJ1*01	811	1416
1629	VH3-23_IGHD5-5*01 (2) >2_IGHJ5*01	2568	A26_IGKJ1*01	811	1416
1630	VH3-23_IGHD5-5*01 (2) >3_IGHJ5*01	2569	A26_IGKJ1*01	811	1416
1631	VH3-23_IGHD5-12*01>1_IGHJ5*01	2570	A26_IGKJ1*01	811	1416
1632	VH3-23_IGHD5-12*01>3_IGHJ5*01	2571	A26_IGKJ1*01	811	1416
1633	VH3-23_IGHD5-18*01 (2) >1_IGHJ5*01	2572	A26_IGKJ1*01	811	1416

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
1634	VH3-23_IGHD5-18*01 (2) >2_IGHJ5*01	2573	A26_IGKJ1*01	811	1416
1635	VH3-23_IGHD5-18*01 (2) >3_IGHJ5*01	2574	A26_IGKJ1*01	811	1416
1636	VH3-23_IGHD5-24*01>1_IGHJ5*01	2575	A26_IGKJ1*01	811	1416
1637	VH3-23_IGHD5-24*01>3_IGHJ5*01	2576	A26_IGKJ1*01	811	1416
1638	VH3-23_IGHD6-6*01>1_IGHJ5*01	2577	A26_IGKJ1*01	811	1416
1639	VH3-23_IGHD1-1*01>1'_IGHJ5*01	2587	A26_IGKJ1*01	811	1416
1640	VH3-23_IGHD1-1*01>2'_IGHJ5*01	2588	A26_IGKJ1*01	811	1416
1641	VH3-23_IGHD1-1*01>3'_IGHJ5*01	2589	A26_IGKJ1*01	811	1416
1642	VH3-23_IGHD1-7*01>1'_IGHJ5*01	2590	A26_IGKJ1*01	811	1416
1643	VH3-23_IGHD1-7*01>3'_IGHJ5*01	2591	A26_IGKJ1*01	811	1416
1644	VH3-23_IGHD1-14*01>1'_IGHJ5*01	2592	A26_IGKJ1*01	811	1416
1645	VH3-23_IGHD1-14*01>2'_IGHJ5*01	2593	A26_IGKJ1*01	811	1416
1646	VH3-23_IGHD1-14*01>3'_IGHJ5*01	2594	A26_IGKJ1*01	811	1416
1647	VH3-23_IGHD1-20*01>1'_IGHJ5*01	2595	A26_IGKJ1*01	811	1416
1648	VH3-23_IGHD1-20*01>2'_IGHJ5*01	2596	A26_IGKJ1*01	811	1416
1649	VH3-23_IGHD1-20*01>3'_IGHJ5*01	2597	A26_IGKJ1*01	811	1416
1650	VH3-23_IGHD1-26*01>1'_IGHJ5*01	2598	A26_IGKJ1*01	811	1416
1651	VH3-23_IGHD1-26*01>3'_IGHJ5*01	2599	A26_IGKJ1*01	811	1416
1652	VH3-23_IGHD2-2*01>1'_IGHJ5*01	2600	A26_IGKJ1*01	811	1416
1653	VH3-23_IGHD2-2*01>3'_IGHJ5*01	2601	A26_IGKJ1*01	811	1416
1654	VH3-23_IGHD2-8*01>1'_IGHJ5*01	2602	A26_IGKJ1*01	811	1416
1655	VH3-23_IGHD2-15*01>1'_IGHJ5*01	2603	A26_IGKJ1*01	811	1416
1656	VH3-23_IGHD2-15*01>3'_IGHJ5*01	2604	A26_IGKJ1*01	811	1416
1657	VH3-23_IGHD2-21*01>1'_IGHJ5*01	2605	A26_IGKJ1*01	811	1416
1658	VH3-23_IGHD2-21*01>3'_IGHJ5*01	2606	A26_IGKJ1*01	811	1416
1659	VH3-23_IGHD3-3*01>1'_IGHJ5*01	2607	A26_IGKJ1*01	811	1416
1660	VH3-23_IGHD3-3*01>3'_IGHJ5*01	2608	A26_IGKJ1*01	811	1416
1661	VH3-23_IGHD3-9*01>1'_IGHJ5*01	2609	A26_IGKJ1*01	811	1416
1662	VH3-23_IGHD3-9*01>3'_IGHJ5*01	2610	A26_IGKJ1*01	811	1416
1663	VH3-23_IGHD3-10*01>1'_IGHJ5*01	2611	A26_IGKJ1*01	811	1416
1664	VH3-23_IGHD3-10*01>3'_IGHJ5*01	2612	A26_IGKJ1*01	811	1416
1665	VH3-23_IGHD3-16*01>1'_IGHJ5*01	2613	A26_IGKJ1*01	811	1416
1666	VH3-23_IGHD3-16*01>3'_IGHJ5*01	2614	A26_IGKJ1*01	811	1416
1667	VH3-23_IGHD3-22*01>1'_IGHJ5*01	2615	A26_IGKJ1*01	811	1416
1668	VH3-23_IGHD4-4*01 (1) >1'_IGHJ5*01	2616	A26_IGKJ1*01	811	1416
1669	VH3-23_IGHD4-4*01 (1) >3'_IGHJ5*01	2617	A26_IGKJ1*01	811	1416
1670	VH3-23_IGHD4-11*01 (1) >1'_IGHJ5*01	2618	A26_IGKJ1*01	811	1416
1671	VH3-23_IGHD4-11*01 (1) >3'_IGHJ5*01	2619	A26_IGKJ1*01	811	1416
1672	VH3-23_IGHD4-17*01>1'_IGHJ5*01	2620	A26_IGKJ1*01	811	1416
1673	VH3-23_IGHD4-17*01>3'_IGHJ5*01	2621	A26_IGKJ1*01	811	1416
1674	VH3-23_IGHD4-23*01>1'_IGHJ5*01	2622	A26_IGKJ1*01	811	1416
1675	VH3-23_IGHD4-23*01>3'_IGHJ5*01	2623	A26_IGKJ1*01	811	1416
1676	VH3-23_IGHD5-5*01 (2) >1'_IGHJ5*01	2624	A26_IGKJ1*01	811	1416
1677	VH3-23_IGHD5-5*01 (2) >3'_IGHJ5*01	2625	A26_IGKJ1*01	811	1416

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
1678	VH3-23_IGHD5-12*01>1'_IGHJ5*01	2626	A26_IGKJ1*01	811	1416
1679	VH3-23_IGHD5-12*01>3'_IGHJ5*01	2627	A26_IGKJ1*01	811	1416
1680	VH3-23_IGHD5-18*01 (2) >1'_IGHJ5*01	2628	A26_IGKJ1*01	811	1416
1681	VH3-23_IGHD5-18*01 (2) >3'_IGHJ5*01	2629	A26_IGKJ1*01	811	1416
1682	VH3-23_IGHD5-24*01>1'_IGHJ5*01	2630	A26_IGKJ1*01	811	1416
1683	VH3-23_IGHD5-24*01>3'_IGHJ5*01	2631	A26_IGKJ1*01	811	1416
1684	VH3-23_IGHD6-6*01>1'_IGHJ5*01	2632	A26_IGKJ1*01	811	1416
1685	VH3-23_IGHD6-6*01>2'_IGHJ5*01	2633	A26_IGKJ1*01	811	1416
1686	VH3-23_IGHD6-6*01>3'_IGHJ5*01	2634	A26_IGKJ1*01	811	1416
1687	VH3-23_IGHD1-1*01>1_IGHJ5*01	2530	A14_IGKJ1*01	806	1411
1688	VH3-23_IGHD1-1*01>2_IGHJ5*01	2531	A14_IGKJ1*01	806	1411
1689	VH3-23_IGHD1-1*01>3_IGHJ5*01	2532	A14_IGKJ1*01	806	1411
1690	VH3-23_IGHD1-7*01>1_IGHJ5*01	2533	A14_IGKJ1*01	806	1411
1691	VH3-23_IGHD1-7*01>3_IGHJ5*01	2534	A14_IGKJ1*01	806	1411
1692	VH3-23_IGHD1-14*01>1_IGHJ5*01	2535	A14_IGKJ1*01	806	1411
1693	VH3-23_IGHD1-14*01>3_IGHJ5*01	2536	A14_IGKJ1*01	806	1411
1694	VH3-23_IGHD1-20*01>1_IGHJ5*01	2537	A14_IGKJ1*01	806	1411
1695	VH3-23_IGHD1-20*01>3_IGHJ5*01	2538	A14_IGKJ1*01	806	1411
1696	VH3-23_IGHD1-26*01>1_IGHJ5*01	2539	A14_IGKJ1*01	806	1411
1697	VH3-23_IGHD1-26*01>3_IGHJ5*01	2540	A14_IGKJ1*01	806	1411
1698	VH3-23_IGHD2-2*01>2_IGHJ5*01	2541	A14_IGKJ1*01	806	1411
1699	VH3-23_IGHD2-2*01>3_IGHJ5*01	2542	A14_IGKJ1*01	806	1411
1700	VH3-23_IGHD2-8*01>2_IGHJ5*01	2543	A14_IGKJ1*01	806	1411
1701	VH3-23_IGHD2-8*01>3_IGHJ5*01	2544	A14_IGKJ1*01	806	1411
1702	VH3-23_IGHD2-15*01>2_IGHJ5*01	2545	A14_IGKJ1*01	806	1411
1703	VH3-23_IGHD2-15*01>3_IGHJ5*01	2546	A14_IGKJ1*01	806	1411
1704	VH3-23_IGHD2-21*01>2_IGHJ5*01	2547	A14_IGKJ1*01	806	1411
1705	VH3-23_IGHD2-21*01>3_IGHJ5*01	2548	A14_IGKJ1*01	806	1411
1706	VH3-23_IGHD3-3*01>1_IGHJ5*01	2549	A14_IGKJ1*01	806	1411
1707	VH3-23_IGHD3-3*01>2_IGHJ5*01	2550	A14_IGKJ1*01	806	1411
1708	VH3-23_IGHD3-3*01>3_IGHJ5*01	2551	A14_IGKJ1*01	806	1411
1709	VH3-23_IGHD3-9*01>2_IGHJ5*01	2552	A14_IGKJ1*01	806	1411
1710	VH3-23_IGHD3-10*01>2_IGHJ5*01	2553	A14_IGKJ1*01	806	1411
1711	VH3-23_IGHD3-10*01>3_IGHJ5*01	2554	A14_IGKJ1*01	806	1411
1712	VH3-23_IGHD3-16*01>2_IGHJ5*01	2555	A14_IGKJ1*01	806	1411
1713	VH3-23_IGHD3-16*01>3_IGHJ5*01	2556	A14_IGKJ1*01	806	1411
1714	VH3-23_IGHD3-22*01>2_IGHJ5*01	2557	A14_IGKJ1*01	806	1411
1715	VH3-23_IGHD3-22*01>3_IGHJ5*01	2558	A14_IGKJ1*01	806	1411
1716	VH3-23_IGHD4-4*01 (1) >2_IGHJ5*01	2559	A14_IGKJ1*01	806	1411
1717	VH3-23_IGHD4-4*01 (1) >3_IGHJ5*01	2560	A14_IGKJ1*01	806	1411
1718	VH3-23_IGHD4-11*01 (1) >2_IGHJ5*01	2561	A14_IGKJ1*01	806	1411
1719	VH3-23_IGHD4-11*01 (1) >3_IGHJ5*01	2562	A14_IGKJ1*01	806	1411
1720	VH3-23_IGHD4-17*01>2_IGHJ5*01	2563	A14_IGKJ1*01	806	1411
1721	VH3-23_IGHD4-17*01>3_IGHJ5*01	2564	A14_IGKJ1*01	806	1411

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
1722	VH3-23_IGHD4-23*01>2_IGHJ5*01	2565	A14_IGKJ1*01	806	1411
1723	VH3-23_IGHD4-23*01>3_IGHJ5*01	2566	A14_IGKJ1*01	806	1411
1724	VH3-23_IGHD5-5*01 (2) >1_IGHJ5*01	2567	A14_IGKJ1*01	806	1411
1725	VH3-23_IGHD5-5*01 (2) >2_IGHJ5*01	2568	A14_IGKJ1*01	806	1411
1726	VH3-23_IGHD5-5*01 (2) >3_IGHJ5*01	2569	A14_IGKJ1*01	806	1411
1727	VH3-23_IGHD5-12*01>1_IGHJ5*01	2570	A14_IGKJ1*01	806	1411
1728	VH3-23_IGHD5-12*01>3_IGHJ5*01	2571	A14_IGKJ1*01	806	1411
1729	VH3-23_IGHD5-18*01 (2) >1_IGHJ5*01	2572	A14_IGKJ1*01	806	1411
1730	VH3-23_IGHD5-18*01 (2) >2_IGHJ5*01	2573	A14_IGKJ1*01	806	1411
1731	VH3-23_IGHD5-18*01 (2) >3_IGHJ5*01	2574	A14_IGKJ1*01	806	1411
1732	VH3-23_IGHD5-24*01>1_IGHJ5*01	2575	A14_IGKJ1*01	806	1411
1733	VH3-23_IGHD5-24*01>3_IGHJ5*01	2576	A14_IGKJ1*01	806	1411
1734	VH3-23_IGHD6-6*01>1_IGHJ5*01	2577	A14_IGKJ1*01	806	1411
1735	VH3-23_IGHD1-1*01>1'_IGHJ5*01	2587	A14_IGKJ1*01	806	1411
1736	VH3-23_IGHD1-1*01>2'_IGHJ5*01	2588	A14_IGKJ1*01	806	1411
1737	VH3-23_IGHD1-1*01>3'_IGHJ5*01	2589	A14_IGKJ1*01	806	1411
1738	VH3-23_IGHD1-7*01>1'_IGHJ5*01	2590	A14_IGKJ1*01	806	1411
1739	VH3-23_IGHD1-7*01>3'_IGHJ5*01	2591	A14_IGKJ1*01	806	1411
1740	VH3-23_IGHD1-14*01>1'_IGHJ5*01	2592	A14_IGKJ1*01	806	1411
1741	VH3-23_IGHD1-14*01>2'_IGHJ5*01	2593	A14_IGKJ1*01	806	1411
1742	VH3-23_IGHD1-14*01>3'_IGHJ5*01	2594	A14_IGKJ1*01	806	1411
1743	VH3-23_IGHD1-20*01>1'_IGHJ5*01	2595	A14_IGKJ1*01	806	1411
1744	VH3-23_IGHD1-20*01>2'_IGHJ5*01	2596	A14_IGKJ1*01	806	1411
1745	VH3-23_IGHD1-20*01>3'_IGHJ5*01	2597	A14_IGKJ1*01	806	1411
1746	VH3-23_IGHD1-26*01>1'_IGHJ5*01	2598	A14_IGKJ1*01	806	1411
1747	VH3-23_IGHD1-26*01>3'_IGHJ5*01	2599	A14_IGKJ1*01	806	1411
1748	VH3-23_IGHD2-2*01>1'_IGHJ5*01	2600	A14_IGKJ1*01	806	1411
1749	VH3-23_IGHD2-2*01>3'_IGHJ5*01	2601	A14_IGKJ1*01	806	1411
1750	VH3-23_IGHD2-8*01>1'_IGHJ5*01	2602	A14_IGKJ1*01	806	1411
1751	VH3-23_IGHD2-15*01>1'_IGHJ5*01	2603	A14_IGKJ1*01	806	1411
1752	VH3-23_IGHD2-15*01>3'_IGHJ5*01	2604	A14_IGKJ1*01	806	1411
1753	VH3-23_IGHD2-21*01>1'_IGHJ5*01	2605	A14_IGKJ1*01	806	1411
1754	VH3-23_IGHD2-21*01>3'_IGHJ5*01	2606	A14_IGKJ1*01	806	1411
1755	VH3-23_IGHD3-3*01>1'_IGHJ5*01	2607	A14_IGKJ1*01	806	1411
1756	VH3-23_IGHD3-3*01>3'_IGHJ5*01	2608	A14_IGKJ1*01	806	1411
1757	VH3-23_IGHD3-9*01>1'_IGHJ5*01	2609	A14_IGKJ1*01	806	1411
1758	VH3-23_IGHD3-9*01>3'_IGHJ5*01	2610	A14_IGKJ1*01	806	1411
1759	VH3-23_IGHD3-10*01>1'_IGHJ5*01	2611	A14_IGKJ1*01	806	1411
1760	VH3-23_IGHD3-10*01>3'_IGHJ5*01	2612	A14_IGKJ1*01	806	1411
1761	VH3-23_IGHD3-16*01>1'_IGHJ5*01	2613	A14_IGKJ1*01	806	1411
1762	VH3-23_IGHD3-16*01>3'_IGHJ5*01	2614	A14_IGKJ1*01	806	1411
1763	VH3-23_IGHD3-22*01>1'_IGHJ5*01	2615	A14_IGKJ1*01	806	1411
1764	VH3-23_IGHD4-4*01 (1) >1'_IGHJ5*01	2616	A14_IGKJ1*01	806	1411
1765	VH3-23_IGHD4-4*01 (1) >3'_IGHJ5*01	2617	A14_IGKJ1*01	806	1411

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
1766	VH3-23_IGHD4-11*01 (1) >1'_IGHJ5*01	2618	A14_IGKJ1*01	806	1411
1767	VH3-23_IGHD4-11*01 (1) >3'_IGHJ5*01	2619	A14_IGKJ1*01	806	1411
1768	VH3-23_IGHD4-17*01>1'_IGHJ5*01	2620	A14_IGKJ1*01	806	1411
1769	VH3-23_IGHD4-17*01>3'_IGHJ5*01	2621	A14_IGKJ1*01	806	1411
1770	VH3-23_IGHD4-23*01>1'_IGHJ5*01	2622	A14_IGKJ1*01	806	1411
1771	VH3-23_IGHD4-23*01>3'_IGHJ5*01	2623	A14_IGKJ1*01	806	1411
1772	VH3-23_IGHD5-5*01 (2) >1'_IGHJ5*01	2624	A14_IGKJ1*01	806	1411
1773	VH3-23_IGHD5-5*01 (2) >3'_IGHJ5*01	2625	A14_IGKJ1*01	806	1411
1774	VH3-23_IGHD5-12*01>1'_IGHJ5*01	2626	A14_IGKJ1*01	806	1411
1775	VH3-23_IGHD5-12*01>3'_IGHJ5*01	2627	A14_IGKJ1*01	806	1411
1776	VH3-23_IGHD5-18*01 (2) >1'_IGHJ5*01	2628	A14_IGKJ1*01	806	1411
1777	VH3-23_IGHD5-18*01 (2) >3'_IGHJ5*01	2629	A14_IGKJ1*01	806	1411
1778	VH3-23_IGHD5-24*01>1'_IGHJ5*01	2630	A14_IGKJ1*01	806	1411
1779	VH3-23_IGHD5-24*01>3'_IGHJ5*01	2631	A14_IGKJ1*01	806	1411
1780	VH3-23_IGHD6-6*01>1'_IGHJ5*01	2632	A14_IGKJ1*01	806	1411
1781	VH3-23_IGHD6-6*01>2'_IGHJ5*01	2633	A14_IGKJ1*01	806	1411
1782	VH3-23_IGHD6-6*01>3'_IGHJ5*01	2634	A14_IGKJ1*01	806	1411
1783	VH3-23_IGHD1-1*01>1_IGHJ5*01	2530	A27_IGKJ1*01	812	1417
1784	VH3-23_IGHD1-1*01>2_IGHJ5*01	2531	A27_IGKJ1*01	812	1417
1785	VH3-23_IGHD1-1*01>3_IGHJ5*01	2532	A27_IGKJ1*01	812	1417
1786	VH3-23_IGHD1-7*01>1_IGHJ5*01	2533	A27_IGKJ1*01	812	1417
1787	VH3-23_IGHD1-7*01>3_IGHJ5*01	2534	A27_IGKJ1*01	812	1417
1788	VH3-23_IGHD1-14*01>1_IGHJ5*01	2535	A27_IGKJ1*01	812	1417
1789	VH3-23_IGHD1-14*01>3_IGHJ5*01	2536	A27_IGKJ1*01	812	1417
1790	VH3-23_IGHD1-20*01>1_IGHJ5*01	2537	A27_IGKJ1*01	812	1417
1791	VH3-23_IGHD1-20*01>3_IGHJ5*01	2538	A27_IGKJ1*01	812	1417
1792	VH3-23_IGHD1-26*01>1_IGHJ5*01	2539	A27_IGKJ1*01	812	1417
1793	VH3-23_IGHD1-26*01>3_IGHJ5*01	2540	A27_IGKJ1*01	812	1417
1794	VH3-23_IGHD2-2*01>2_IGHJ5*01	2541	A27_IGKJ1*01	812	1417
1795	VH3-23_IGHD2-2*01>3_IGHJ5*01	2542	A27_IGKJ1*01	812	1417
1796	VH3-23_IGHD2-8*01>2_IGHJ5*01	2543	A27_IGKJ1*01	812	1417
1797	VH3-23_IGHD2-8*01>3_IGHJ5*01	2544	A27_IGKJ1*01	812	1417
1798	VH3-23_IGHD2-15*01>2_IGHJ5*01	2545	A27_IGKJ1*01	812	1417
1799	VH3-23_IGHD2-15*01>3_IGHJ5*01	2546	A27_IGKJ1*01	812	1417
1800	VH3-23_IGHD2-21*01>2_IGHJ5*01	2547	A27_IGKJ1*01	812	1417
1801	VH3-23_IGHD2-21*01>3_IGHJ5*01	2548	A27_IGKJ1*01	812	1417
1802	VH3-23_IGHD3-3*01>1_IGHJ5*01	2549	A27_IGKJ1*01	812	1417
1803	VH3-23_IGHD3-3*01>2_IGHJ5*01	2550	A27_IGKJ1*01	812	1417
1804	VH3-23_IGHD3-3*01>3_IGHJ5*01	2551	A27_IGKJ1*01	812	1417
1805	VH3-23_IGHD3-9*01>2_IGHJ5*01	2552	A27_IGKJ1*01	812	1417
1806	VH3-23_IGHD3-10*01>2_IGHJ5*01	2553	A27_IGKJ1*01	812	1417
1807	VH3-23_IGHD3-10*01>3_IGHJ5*01	2554	A27_IGKJ1*01	812	1417
1808	VH3-23_IGHD3-16*01>2_IGHJ5*01	2555	A27_IGKJ1*01	812	1417
1809	VH3-23_IGHD3-16*01>3_IGHJ5*01	2556	A27_IGKJ1*01	812	1417

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
1810	VH3-23_IGHD3-22*01>2_IGHJ5*01	2557	A27_IGKJ1*01	812	1417
1811	VH3-23_IGHD3-22*01>3_IGHJ5*01	2558	A27_IGKJ1*01	812	1417
1812	VH3-23_IGHD4-4*01 (1) >2_IGHJ5*01	2559	A27_IGKJ1*01	812	1417
1813	VH3-23_IGHD4-4*01 (1) >3_IGHJ5*01	2560	A27_IGKJ1*01	812	1417
1814	VH3-23_IGHD4-11*01 (1) >2_IGHJ5*01	2561	A27_IGKJ1*01	812	1417
1815	VH3-23_IGHD4-11*01 (1) >3_IGHJ5*01	2562	A27_IGKJ1*01	812	1417
1816	VH3-23_IGHD4-17*01>2_IGHJ5*01	2563	A27_IGKJ1*01	812	1417
1817	VH3-23_IGHD4-17*01>3_IGHJ5*01	2564	A27_IGKJ1*01	812	1417
1818	VH3-23_IGHD4-23*01>2_IGHJ5*01	2565	A27_IGKJ1*01	812	1417
1819	VH3-23_IGHD4-23*01>3_IGHJ5*01	2566	A27_IGKJ1*01	812	1417
1820	VH3-23_IGHD5-5*01 (2) >1_IGHJ5*01	2567	A27_IGKJ1*01	812	1417
1821	VH3-23_IGHD5-5*01 (2) >2_IGHJ5*01	2568	A27_IGKJ1*01	812	1417
1822	VH3-23_IGHD5-5*01 (2) >3_IGHJ5*01	2569	A27_IGKJ1*01	812	1417
1823	VH3-23_IGHD5-12*01>1_IGHJ5*01	2570	A27_IGKJ1*01	812	1417
1824	VH3-23_IGHD5-12*01>3_IGHJ5*01	2571	A27_IGKJ1*01	812	1417
1825	VH3-23_IGHD5-18*01 (2) >1_IGHJ5*01	2572	A27_IGKJ1*01	812	1417
1826	VH3-23_IGHD5-18*01 (2) >2_IGHJ5*01	2573	A27_IGKJ1*01	812	1417
1827	VH3-23_IGHD5-18*01 (2) >3_IGHJ5*01	2574	A27_IGKJ1*01	812	1417
1828	VH3-23_IGHD5-24*01>1_IGHJ5*01	2575	A27_IGKJ1*01	812	1417
1829	VH3-23_IGHD5-24*01>3_IGHJ5*01	2576	A27_IGKJ1*01	812	1417
1830	VH3-23_IGHD6-6*01>1_IGHJ5*01	2577	A27_IGKJ1*01	812	1417
1831	VH3-23_IGHD1-1*01>1'_IGHJ5*01	2587	A27_IGKJ1*01	812	1417
1832	VH3-23_IGHD1-1*01>2'_IGHJ5*01	2588	A27_IGKJ1*01	812	1417
1833	VH3-23_IGHD1-1*01>3'_IGHJ5*01	2589	A27_IGKJ1*01	812	1417
1834	VH3-23_IGHD1-7*01>1'_IGHJ5*01	2590	A27_IGKJ1*01	812	1417
1835	VH3-23_IGHD1-7*01>3'_IGHJ5*01	2591	A27_IGKJ1*01	812	1417
1836	VH3-23_IGHD1-14*01>1'_IGHJ5*01	2592	A27_IGKJ1*01	812	1417
1837	VH3-23_IGHD1-14*01>2'_IGHJ5*01	2593	A27_IGKJ1*01	812	1417
1838	VH3-23_IGHD1-14*01>3'_IGHJ5*01	2594	A27_IGKJ1*01	812	1417
1839	VH3-23_IGHD1-20*01>1'_IGHJ5*01	2595	A27_IGKJ1*01	812	1417
1840	VH3-23_IGHD1-20*01>2'_IGHJ5*01	2596	A27_IGKJ1*01	812	1417
1841	VH3-23_IGHD1-20*01>3'_IGHJ5*01	2597	A27_IGKJ1*01	812	1417
1842	VH3-23_IGHD1-26*01>1'_IGHJ5*01	2598	A27_IGKJ1*01	812	1417
1843	VH3-23_IGHD1-26*01>3'_IGHJ5*01	2599	A27_IGKJ1*01	812	1417
1844	VH3-23_IGHD2-2*01>1'_IGHJ5*01	2600	A27_IGKJ1*01	812	1417
1845	VH3-23_IGHD2-2*01>3'_IGHJ5*01	2601	A27_IGKJ1*01	812	1417
1846	VH3-23_IGHD2-8*01>1'_IGHJ5*01	2602	A27_IGKJ1*01	812	1417
1847	VH3-23_IGHD2-15*01>1'_IGHJ5*01	2603	A27_IGKJ1*01	812	1417
1848	VH3-23_IGHD2-15*01>3'_IGHJ5*01	2604	A27_IGKJ1*01	812	1417
1849	VH3-23_IGHD2-21*01>1'_IGHJ5*01	2605	A27_IGKJ1*01	812	1417
1850	VH3-23_IGHD2-21*01>3'_IGHJ5*01	2606	A27_IGKJ1*01	812	1417
1851	VH3-23_IGHD3-3*01>1'_IGHJ5*01	2607	A27_IGKJ1*01	812	1417
1852	VH3-23_IGHD3-3*01>3'_IGHJ5*01	2608	A27_IGKJ1*01	812	1417
1853	VH3-23_IGHD3-9*01>1'_IGHJ5*01	2609	A27_IGKJ1*01	812	1417

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
1854	VH3-23_IGHD3-9*01>3'_IGHJ5*01	2610	A27_IGKJ1*01	812	1417
1855	VH3-23_IGHD3-10*01>1'_IGHJ5*01	2611	A27_IGKJ1*01	812	1417
1856	VH3-23_IGHD3-10*01>3'_IGHJ5*01	2612	A27_IGKJ1*01	812	1417
1857	VH3-23_IGHD3-16*01>1'_IGHJ5*01	2613	A27_IGKJ1*01	812	1417
1858	VH3-23_IGHD3-16*01>3'_IGHJ5*01	2614	A27_IGKJ1*01	812	1417
1859	VH3-23_IGHD3-22*01>1'_IGHJ5*01	2615	A27_IGKJ1*01	812	1417
1860	VH3-23_IGHD4-4*01 (1) >1'_IGHJ5*01	2616	A27_IGKJ1*01	812	1417
1861	VH3-23_IGHD4-4*01 (1) >3'_IGHJ5*01	2617	A27_IGKJ1*01	812	1417
1862	VH3-23_IGHD4-11*01 (1) >1'_IGHJ5*01	2618	A27_IGKJ1*01	812	1417
1863	VH3-23_IGHD4-11*01 (1) >3'_IGHJ5*01	2619	A27_IGKJ1*01	812	1417
1864	VH3-23_IGHD4-17*01>1'_IGHJ5*01	2620	A27_IGKJ1*01	812	1417
1865	VH3-23_IGHD4-17*01>3'_IGHJ5*01	2621	A27_IGKJ1*01	812	1417
1866	VH3-23_IGHD4-23*01>1'_IGHJ5*01	2622	A27_IGKJ1*01	812	1417
1867	VH3-23_IGHD4-23*01>3'_IGHJ5*01	2623	A27_IGKJ1*01	812	1417
1868	VH3-23_IGHD5-5*01 (2) >1'_IGHJ5*01	2624	A27_IGKJ1*01	812	1417
1869	VH3-23_IGHD5-5*01 (2) >3'_IGHJ5*01	2625	A27_IGKJ1*01	812	1417
1870	VH3-23_IGHD5-12*01>1'_IGHJ5*01	2626	A27_IGKJ1*01	812	1417
1871	VH3-23_IGHD5-12*01>3'_IGHJ5*01	2627	A27_IGKJ1*01	812	1417
1872	VH3-23_IGHD5-18*01 (2) >1'_IGHJ5*01	2628	A27_IGKJ1*01	812	1417
1873	VH3-23_IGHD5-18*01 (2) >3'_IGHJ5*01	2629	A27_IGKJ1*01	812	1417
1874	VH3-23_IGHD5-24*01>1'_IGHJ5*01	2630	A27_IGKJ1*01	812	1417
1875	VH3-23_IGHD5-24*01>3'_IGHJ5*01	2631	A27_IGKJ1*01	812	1417
1876	VH3-23_IGHD6-6*01>1'_IGHJ5*01	2632	A27_IGKJ1*01	812	1417
1877	VH3-23_IGHD6-6*01>2'_IGHJ5*01	2633	A27_IGKJ1*01	812	1417
1878	VH3-23_IGHD6-6*01>3'_IGHJ5*01	2634	A27_IGKJ1*01	812	1417
1879	VH3-23_IGHD6-6*01>2_IGHJ1*01	2118	V1-11_IGLJ2*01	836	1441
1880	VH3-23_IGHD6-13*01>1_IGHJ1*01	2119	V1-11_IGLJ2*01	836	1441
1881	VH3-23_IGHD6-13*01>2_IGHJ1*01	2120	V1-11_IGLJ2*01	836	1441
1882	VH3-23_IGHD6-19*01>1_IGHJ1*01	2121	V1-11_IGLJ2*01	836	1441
1883	VH3-23_IGHD6-19*01>2_IGHJ1*01	2122	V1-11_IGLJ2*01	836	1441
1884	VH3-23_IGHD6-25*01>1_IGHJ1*01	2123	V1-11_IGLJ2*01	836	1441
1885	VH3-23_IGHD6-25*01>2_IGHJ1*01	2124	V1-11_IGLJ2*01	836	1441
1886	VH3-23_IGHD7-27*01>1_IGHJ1*01	2125	V1-11_IGLJ2*01	836	1441
1887	VH3-23_IGHD7-27*01>3_IGHJ1*01	2126	V1-11_IGLJ2*01	836	1441
1888	VH3-23_IGHD6-13*01>1'_IGHJ1*01	2175	V1-11_IGLJ2*01	836	1441
1889	VH3-23_IGHD6-13*01>2'_IGHJ1*01	2176	V1-11_IGLJ2*01	836	1441
1890	VH3-23_IGHD6-13*01>2_IGHJ1*01_B	2177	V1-11_IGLJ2*01	836	1441
1891	VH3-23_IGHD6-19*01>1'_IGHJ1*01	2178	V1-11_IGLJ2*01	836	1441
1892	VH3-23_IGHD6-19*01>2'_IGHJ1*01	2179	V1-11_IGLJ2*01	836	1441
1893	VH3-23_IGHD6-19*01>2_IGHJ1*01_B	2180	V1-11_IGLJ2*01	836	1441
1894	VH3-23_IGHD6-25*01>1'_IGHJ1*01	2181	V1-11_IGLJ2*01	836	1441
1895	VH3-23_IGHD6-25*01>3'_IGHJ1*01	2182	V1-11_IGLJ2*01	836	1441
1896	VH3-23_IGHD7-27*01>1'_IGHJ1*01_B	2183	V1-11_IGLJ2*01	836	1441
1897	VH3-23_IGHD7-27*01>2'_IGHJ1*01	2184	V1-11_IGLJ2*01	836	1441

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
1898	VH3-23_IGHD6-6*01>2_IGHJ2*01	2233	V1-11_IGLJ2*01	836	1441
1899	VH3-23_IGHD6-13*01>1_IGHJ2*01	2234	V1-11_IGLJ2*01	836	1441
1900	VH3-23_IGHD6-13*01>2_IGHJ2*01	2235	V1-11_IGLJ2*01	836	1441
1901	VH3-23_IGHD6-19*01>1_IGHJ2*01	2236	V1-11_IGLJ2*01	836	1441
1902	VH3-23_IGHD6-19*01>2_IGHJ2*01	2237	V1-11_IGLJ2*01	836	1441
1903	VH3-23_IGHD6-25*01>1_IGHJ2*01	2238	V1-11_IGLJ2*01	836	1441
1904	VH3-23_IGHD6-25*01>2_IGHJ2*01	2239	V1-11_IGLJ2*01	836	1441
1905	VH3-23_IGHD7-27*01>1_IGHJ2*01	2240	V1-11_IGLJ2*01	836	1441
1906	VH3-23_IGHD7-27*01>3_IGHJ2*01	2241	V1-11_IGLJ2*01	836	1441
1907	VH3-23_IGHD6-13*01>1'_IGHJ2*01	2290	V1-11_IGLJ2*01	836	1441
1908	VH3-23_IGHD6-13*01>2'_IGHJ2*01	2291	V1-11_IGLJ2*01	836	1441
1909	VH3-23_IGHD6-13*01>2_IGHJ2*01_B	2292	V1-11_IGLJ2*01	836	1441
1910	VH3-23_IGHD6-19*01>1'_IGHJ2*01	2293	V1-11_IGLJ2*01	836	1441
1911	VH3-23_IGHD6-19*01>2'_IGHJ2*01	2294	V1-11_IGLJ2*01	836	1441
1912	VH3-23_IGHD6-19*01>2_IGHJ2*01_B	2295	V1-11_IGLJ2*01	836	1441
1913	VH3-23_IGHD6-25*01>1'_IGHJ2*01	2296	V1-11_IGLJ2*01	836	1441
1914	VH3-23_IGHD6-25*01>3'_IGHJ2*01	2297	V1-11_IGLJ2*01	836	1441
1915	VH3-23_IGHD7-27*01>1'_IGHJ2*01	2298	V1-11_IGLJ2*01	836	1441
1916	VH3-23_IGHD7-27*01>2'_IGHJ2*01	2299	V1-11_IGLJ2*01	836	1441
1917	VH3-23_IGHD6-6*01>2_IGHJ3*01	2348	V1-11_IGLJ2*01	836	1441
1918	VH3-23_IGHD6-13*01>1_IGHJ3*01	2349	V1-11_IGLJ2*01	836	1441
1919	VH3-23_IGHD6-13*01>2_IGHJ3*01	2350	V1-11_IGLJ2*01	836	1441
1920	VH3-23_IGHD6-19*01>1_IGHJ3*01	2351	V1-11_IGLJ2*01	836	1441
1921	VH3-23_IGHD6-19*01>2_IGHJ3*01	2352	V1-11_IGLJ2*01	836	1441
1922	VH3-23_IGHD6-25*01>1_IGHJ3*01	2353	V1-11_IGLJ2*01	836	1441
1923	VH3-23_IGHD6-25*01>2_IGHJ3*01	2354	V1-11_IGLJ2*01	836	1441
1924	VH3-23_IGHD7-27*01>1_IGHJ3*01	2355	V1-11_IGLJ2*01	836	1441
1925	VH3-23_IGHD7-27*01>3_IGHJ3*01	2356	V1-11_IGLJ2*01	836	1441
1926	VH3-23_IGHD6-13*01>1'_IGHJ3*01	2405	V1-11_IGLJ2*01	836	1441
1927	VH3-23_IGHD6-13*01>2'_IGHJ3*01	2406	V1-11_IGLJ2*01	836	1441
1928	VH3-23_IGHD6-13*01>1_IGHJ6*01	2407	V1-11_IGLJ2*01	836	1441
1929	VH3-23_IGHD6-19*01>1'_IGHJ3*01	2408	V1-11_IGLJ2*01	836	1441
1930	VH3-23_IGHD6-19*01>2'_IGHJ3*01	2409	V1-11_IGLJ2*01	836	1441
1931	VH3-23_IGHD6-19*01>3'_IGHJ3*01	2410	V1-11_IGLJ2*01	836	1441
1932	VH3-23_IGHD6-25*01>1'_IGHJ3*01	2411	V1-11_IGLJ2*01	836	1441
1933	VH3-23_IGHD6-25*01>3'_IGHJ3*01	2412	V1-11_IGLJ2*01	836	1441
1934	VH3-23_IGHD7-27*01>1'_IGHJ3*01	2413	V1-11_IGLJ2*01	836	1441
1935	VH3-23_IGHD7-27*01>2'_IGHJ3*01	2414	V1-11_IGLJ2*01	836	1441
1936	VH3-23_IGHD6-6*01>2_IGHJ4*01	2463	V1-11_IGLJ2*01	836	1441
1937	VH3-23_IGHD6-13*01>1_IGHJ4*01	2464	V1-11_IGLJ2*01	836	1441
1938	VH3-23_IGHD6-13*01>2_IGHJ4*01	2465	V1-11_IGLJ2*01	836	1441
1939	VH3-23_IGHD6-19*01>1_IGHJ4*01	2466	V1-11_IGLJ2*01	836	1441
1940	VH3-23_IGHD6-19*01>2_IGHJ4*01	2467	V1-11_IGLJ2*01	836	1441
1941	VH3-23_IGHD6-25*01>1_IGHJ4*01	2468	V1-11_IGLJ2*01	836	1441

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
1942	VH3-23_IGHD6-25*01>2_IGHJ4*01	2469	V1-11_IGLJ2*01	836	1441
1943	VH3-23_IGHD7-27*01>1_IGHJ4*01	2470	V1-11_IGLJ2*01	836	1441
1944	VH3-23_IGHD7-27*01>3_IGHJ4*01	2471	V1-11_IGLJ2*01	836	1441
1945	VH3-23_IGHD6-13*01>1'_IGHJ4*01	2520	V1-11_IGLJ2*01	836	1441
1946	VH3-23_IGHD6-13*01>2'_IGHJ4*01	2521	V1-11_IGLJ2*01	836	1441
1947	VH3-23_IGHD6-13*01>2_IGHJ4*01_B	2522	V1-11_IGLJ2*01	836	1441
1948	VH3-23_IGHD6-19*01>1'_IGHJ4*01	2523	V1-11_IGLJ2*01	836	1441
1949	VH3-23_IGHD6-19*01>2'_IGHJ4*01	2524	V1-11_IGLJ2*01	836	1441
1950	VH3-23_IGHD6-19*01>2_IGHJ4*01_B	2525	V1-11_IGLJ2*01	836	1441
1951	VH3-23_IGHD6-25*01>1'_IGHJ4*01	2526	V1-11_IGLJ2*01	836	1441
1952	VH3-23_IGHD6-25*01>3'_IGHJ4*01	2527	V1-11_IGLJ2*01	836	1441
1953	VH3-23_IGHD7-27*01>1'_IGHJ4*01	2528	V1-11_IGLJ2*01	836	1441
1954	VH3-23_IGHD7-27*01>2'_IGHJ4*01	2529	V1-11_IGLJ2*01	836	1441
1955	VH3-23_IGHD6-6*01>2_IGHJ5*01	2578	V1-11_IGLJ2*01	836	1441
1956	VH3-23_IGHD6-13*01>1_IGHJ5*01	2579	V1-11_IGLJ2*01	836	1441
1957	VH3-23_IGHD6-13*01>2_IGHJ5*01	2580	V1-11_IGLJ2*01	836	1441
1958	VH3-23_IGHD6-19*01>1_IGHJ5*01	2581	V1-11_IGLJ2*01	836	1441
1959	VH3-23_IGHD6-19*01>2_IGHJ5*01	2582	V1-11_IGLJ2*01	836	1441
1960	VH3-23_IGHD6-25*01>1_IGHJ5*01	2583	V1-11_IGLJ2*01	836	1441
1961	VH3-23_IGHD6-25*01>2_IGHJ5*01	2584	V1-11_IGLJ2*01	836	1441
1962	VH3-23_IGHD7-27*01>1_IGHJ5*01	2585	V1-11_IGLJ2*01	836	1441
1963	VH3-23_IGHD7-27*01>3_IGHJ5*01	2586	V1-11_IGLJ2*01	836	1441
1964	VH3-23_IGHD6-13*01>1'_IGHJ5*01	2635	V1-11_IGLJ2*01	836	1441
1965	VH3-23_IGHD6-13*01>2'_IGHJ5*01	2636	V1-11_IGLJ2*01	836	1441
1966	VH3-23_IGHD6-13*01>3'_IGHJ5*01	2637	V1-11_IGLJ2*01	836	1441
1967	VH3-23_IGHD6-19*01>1'_IGHJ5*01	2638	V1-11_IGLJ2*01	836	1441
1968	VH3-23_IGHD6-19*01>2'_IGHJ5*01	2639	V1-11_IGLJ2*01	836	1441
1969	VH3-23_IGHD6-19*01>2_IGHJ5*01_B	2640	V1-11_IGLJ2*01	836	1441
1970	VH3-23_IGHD6-25*01>1'_IGHJ5*01	2641	V1-11_IGLJ2*01	836	1441
1971	VH3-23_IGHD6-25*01>3'_IGHJ5*01	2642	V1-11_IGLJ2*01	836	1441
1972	VH3-23_IGHD7-27*01>1'_IGHJ5*01	2643	V1-11_IGLJ2*01	836	1441
1973	VH3-23_IGHD7-27*01>2'_IGHJ5*01	2644	V1-11_IGLJ2*01	836	1441
1974	VH3-23_IGHD6-6*01>2_IGHJ6*01	2693	V1-11_IGLJ2*01	836	1441
1975	VH3-23_IGHD6-6*01>2_IGHJ1*01	2118	V1-13_IGLJ5*01	837	1442
1976	VH3-23_IGHD6-13*01>1_IGHJ1*01	2119	V1-13_IGLJ5*01	837	1442
1977	VH3-23_IGHD6-13*01>2_IGHJ1*01	2120	V1-13_IGLJ5*01	837	1442
1978	VH3-23_IGHD6-19*01>1_IGHJ1*01	2121	V1-13_IGLJ5*01	837	1442
1979	VH3-23_IGHD6-19*01>2_IGHJ1*01	2122	V1-13_IGLJ5*01	837	1442
1980	VH3-23_IGHD6-25*01>1_IGHJ1*01	2123	V1-13_IGLJ5*01	837	1442
1981	VH3-23_IGHD6-25*01>2_IGHJ1*01	2124	V1-13_IGLJ5*01	837	1442
1982	VH3-23_IGHD7-27*01>1_IGHJ1*01	2125	V1-13_IGLJ5*01	837	1442
1983	VH3-23_IGHD7-27*01>3_IGHJ1*01	2126	V1-13_IGLJ5*01	837	1442
1984	VH3-23_IGHD6-13*01>1'_IGHJ1*01	2175	V1-13_IGLJ5*01	837	1442
1985	VH3-23_IGHD6-13*01>2'_IGHJ1*01	2176	V1-13_IGLJ5*01	837	1442

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
1986	VH3-23_IGHD6-13*01>2_IGHJ1*01_B	2177	V1-13_IGLJ5*01	837	1442
1987	VH3-23_IGHD6-19*01>1'_IGHJ1*01	2178	V1-13_IGLJ5*01	837	1442
1988	VH3-23_IGHD6-19*01>2'_IGHJ1*01	2179	V1-13_IGLJ5*01	837	1442
1989	VH3-23_IGHD6-19*01>2_IGHJ1*01_B	2180	V1-13_IGLJ5*01	837	1442
1990	VH3-23_IGHD6-25*01>1'_IGHJ1*01	2181	V1-13_IGLJ5*01	837	1442
1991	VH3-23_IGHD6-25*01>3'_IGHJ1*01	2182	V1-13_IGLJ5*01	837	1442
1992	VH3-23_IGHD7-27*01>1'_IGHJ1*01_B	2183	V1-13_IGLJ5*01	837	1442
1993	VH3-23_IGHD7-27*01>2'_IGHJ1*01	2184	V1-13_IGLJ5*01	837	1442
1994	VH3-23_IGHD6-6*01>2_IGHJ2*01	2233	V1-13_IGLJ5*01	837	1442
1995	VH3-23_IGHD6-13*01>1_IGHJ2*01	2234	V1-13_IGLJ5*01	837	1442
1996	VH3-23_IGHD6-13*01>2_IGHJ2*01	2235	V1-13_IGLJ5*01	837	1442
1997	VH3-23_IGHD6-19*01>1_IGHJ2*01	2236	V1-13_IGLJ5*01	837	1442
1998	VH3-23_IGHD6-19*01>2_IGHJ2*01	2237	V1-13_IGLJ5*01	837	1442
1999	VH3-23_IGHD6-25*01>1_IGHJ2*01	2238	V1-13_IGLJ5*01	837	1442
2000	VH3-23_IGHD6-25*01>2_IGHJ2*01	2239	V1-13_IGLJ5*01	837	1442
2001	VH3-23_IGHD7-27*01>1_IGHJ2*01	2240	V1-13_IGLJ5*01	837	1442
2002	VH3-23_IGHD7-27*01>3_IGHJ2*01	2241	V1-13_IGLJ5*01	837	1442
2003	VH3-23_IGHD6-13*01>1'_IGHJ2*01	2290	V1-13_IGLJ5*01	837	1442
2004	VH3-23_IGHD6-13*01>2'_IGHJ2*01	2291	V1-13_IGLJ5*01	837	1442
2005	VH3-23_IGHD6-13*01>2_IGHJ2*01_B	2292	V1-13_IGLJ5*01	837	1442
2006	VH3-23_IGHD6-19*01>1'_IGHJ2*01	2293	V1-13_IGLJ5*01	837	1442
2007	VH3-23_IGHD6-19*01>2'_IGHJ2*01	2294	V1-13_IGLJ5*01	837	1442
2008	VH3-23_IGHD6-19*01>2_IGHJ2*01_B	2295	V1-13_IGLJ5*01	837	1442
2009	VH3-23_IGHD6-25*01>1'_IGHJ2*01	2296	V1-13_IGLJ5*01	837	1442
2010	VH3-23_IGHD6-25*01>3'_IGHJ2*01	2297	V1-13_IGLJ5*01	837	1442
2011	VH3-23_IGHD7-27*01>1'_IGHJ2*01	2298	V1-13_IGLJ5*01	837	1442
2012	VH3-23_IGHD7-27*01>2'_IGHJ2*01	2299	V1-13_IGLJ5*01	837	1442
2013	VH3-23_IGHD6-6*01>2_IGHJ3*01	2348	V1-13_IGLJ5*01	837	1442
2014	VH3-23_IGHD6-13*01>1_IGHJ3*01	2349	V1-13_IGLJ5*01	837	1442
2015	VH3-23_IGHD6-13*01>2_IGHJ3*01	2350	V1-13_IGLJ5*01	837	1442
2016	VH3-23_IGHD6-19*01>1_IGHJ3*01	2351	V1-13_IGLJ5*01	837	1442
2017	VH3-23_IGHD6-19*01>2_IGHJ3*01	2352	V1-13_IGLJ5*01	837	1442
2018	VH3-23_IGHD6-25*01>1_IGHJ3*01	2353	V1-13_IGLJ5*01	837	1442
2019	VH3-23_IGHD6-25*01>2_IGHJ3*01	2354	V1-13_IGLJ5*01	837	1442
2020	VH3-23_IGHD7-27*01>1_IGHJ3*01	2355	V1-13_IGLJ5*01	837	1442
2021	VH3-23_IGHD7-27*01>3_IGHJ3*01	2356	V1-13_IGLJ5*01	837	1442
2022	VH3-23_IGHD6-13*01>1'_IGHJ3*01	2405	V1-13_IGLJ5*01	837	1442
2023	VH3-23_IGHD6-13*01>2'_IGHJ3*01	2406	V1-13_IGLJ5*01	837	1442
2024	VH3-23_IGHD6-13*01>1_IGHJ6*01	2407	V1-13_IGLJ5*01	837	1442
2025	VH3-23_IGHD6-19*01>1'_IGHJ3*01	2408	V1-13_IGLJ5*01	837	1442
2026	VH3-23_IGHD6-19*01>2'_IGHJ3*01	2409	V1-13_IGLJ5*01	837	1442
2027	VH3-23_IGHD6-19*01>3'_IGHJ3*01	2410	V1-13_IGLJ5*01	837	1442
2028	VH3-23_IGHD6-25*01>1'_IGHJ3*01	2411	V1-13_IGLJ5*01	837	1442
2029	VH3-23_IGHD6-25*01>3'_IGHJ3*01	2412	V1-13_IGLJ5*01	837	1442

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
2030	VH3-23_IGHD7-27*01>1'_IGHJ3*01	2413	V1-13_IGLJ5*01	837	1442
2031	VH3-23_IGHD7-27*01>2'_IGHJ3*01	2414	V1-13_IGLJ5*01	837	1442
2032	VH3-23_IGHD6-6*01>2_IGHJ4*01	2463	V1-13_IGLJ5*01	837	1442
2033	VH3-23_IGHD6-13*01>1_IGHJ4*01	2464	V1-13_IGLJ5*01	837	1442
2034	VH3-23_IGHD6-13*01>2_IGHJ4*01	2465	V1-13_IGLJ5*01	837	1442
2035	VH3-23_IGHD6-19*01>1_IGHJ4*01	2466	V1-13_IGLJ5*01	837	1442
2036	VH3-23_IGHD6-19*01>2_IGHJ4*01	2467	V1-13_IGLJ5*01	837	1442
2037	VH3-23_IGHD6-25*01>1_IGHJ4*01	2468	V1-13_IGLJ5*01	837	1442
2038	VH3-23_IGHD6-25*01>2_IGHJ4*01	2469	V1-13_IGLJ5*01	837	1442
2039	VH3-23_IGHD7-27*01>1_IGHJ4*01	2470	V1-13_IGLJ5*01	837	1442
2040	VH3-23_IGHD7-27*01>3_IGHJ4*01	2471	V1-13_IGLJ5*01	837	1442
2041	VH3-23_IGHD6-13*01>1'_IGHJ4*01	2520	V1-13_IGLJ5*01	837	1442
2042	VH3-23_IGHD6-13*01>2'_IGHJ4*01	2521	V1-13_IGLJ5*01	837	1442
2043	VH3-23_IGHD6-13*01>2_IGHJ4*01_B	2522	V1-13_IGLJ5*01	837	1442
2044	VH3-23_IGHD6-19*01>1'_IGHJ4*01	2523	V1-13_IGLJ5*01	837	1442
2045	VH3-23_IGHD6-19*01>2'_IGHJ4*01	2524	V1-13_IGLJ5*01	837	1442
2046	VH3-23_IGHD6-19*01>2_IGHJ4*01_B	2525	V1-13_IGLJ5*01	837	1442
2047	VH3-23_IGHD6-25*01>1'_IGHJ4*01	2526	V1-13_IGLJ5*01	837	1442
2048	VH3-23_IGHD6-25*01>3'_IGHJ4*01	2527	V1-13_IGLJ5*01	837	1442
2049	VH3-23_IGHD7-27*01>1'_IGHJ4*01	2528	V1-13_IGLJ5*01	837	1442
2050	VH3-23_IGHD7-27*01>2'_IGHJ4*01	2529	V1-13_IGLJ5*01	837	1442
2051	VH3-23_IGHD6-6*01>2_IGHJ5*01	2578	V1-13_IGLJ5*01	837	1442
2052	VH3-23_IGHD6-13*01>1_IGHJ5*01	2579	V1-13_IGLJ5*01	837	1442
2053	VH3-23_IGHD6-13*01>2_IGHJ5*01	2580	V1-13_IGLJ5*01	837	1442
2054	VH3-23_IGHD6-19*01>1_IGHJ5*01	2581	V1-13_IGLJ5*01	837	1442
2055	VH3-23_IGHD6-19*01>2_IGHJ5*01	2582	V1-13_IGLJ5*01	837	1442
2056	VH3-23_IGHD6-25*01>1_IGHJ5*01	2583	V1-13_IGLJ5*01	837	1442
2057	VH3-23_IGHD6-25*01>2_IGHJ5*01	2584	V1-13_IGLJ5*01	837	1442
2058	VH3-23_IGHD7-27*01>1_IGHJ5*01	2585	V1-13_IGLJ5*01	837	1442
2059	VH3-23_IGHD7-27*01>3_IGHJ5*01	2586	V1-13_IGLJ5*01	837	1442
2060	VH3-23_IGHD6-13*01>1'_IGHJ5*01	2635	V1-13_IGLJ5*01	837	1442
2061	VH3-23_IGHD6-13*01>2'_IGHJ5*01	2636	V1-13_IGLJ5*01	837	1442
2062	VH3-23_IGHD6-13*01>3'_IGHJ5*01	2637	V1-13_IGLJ5*01	837	1442
2063	VH3-23_IGHD6-19*01>1'_IGHJ5*01	2638	V1-13_IGLJ5*01	837	1442
2064	VH3-23_IGHD6-19*01>2'_IGHJ5*01	2639	V1-13_IGLJ5*01	837	1442
2065	VH3-23_IGHD6-19*01>2_IGHJ5*01_B	2640	V1-13_IGLJ5*01	837	1442
2066	VH3-23_IGHD6-25*01>1'_IGHJ5*01	2641	V1-13_IGLJ5*01	837	1442
2067	VH3-23_IGHD6-25*01>3'_IGHJ5*01	2642	V1-13_IGLJ5*01	837	1442
2068	VH3-23_IGHD7-27*01>1'_IGHJ5*01	2643	V1-13_IGLJ5*01	837	1442
2069	VH3-23_IGHD7-27*01>2'_IGHJ5*01	2644	V1-13_IGLJ5*01	837	1442
2070	VH3-23_IGHD6-6*01>2_IGHJ6*01	2693	V1-13_IGLJ5*01	837	1442
2071	VH3-23_IGHD6-6*01>2_IGHJ1*01	2118	V1-16_IGLJ6*01	838	1443
2072	VH3-23_IGHD6-13*01>1_IGHJ1*01	2119	V1-16_IGLJ6*01	838	1443
2073	VH3-23_IGHD6-13*01>2_IGHJ1*01	2120	V1-16_IGLJ6*01	838	1443

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
2074	VH3-23_IGHD6-19*01>1_IGHJ1*01	2121	V1-16_IGLJ6*01	838	1443
2075	VH3-23_IGHD6-19*01>2_IGHJ1*01	2122	V1-16_IGLJ6*01	838	1443
2076	VH3-23_IGHD6-25*01>1_IGHJ1*01	2123	V1-16_IGLJ6*01	838	1443
2077	VH3-23_IGHD6-25*01>2_IGHJ1*01	2124	V1-16_IGLJ6*01	838	1443
2078	VH3-23_IGHD7-27*01>1_IGHJ1*01	2125	V1-16_IGLJ6*01	838	1443
2079	VH3-23_IGHD7-27*01>3_IGHJ1*01	2126	V1-16_IGLJ6*01	838	1443
2080	VH3-23_IGHD6-13*01>1'_IGHJ1*01	2175	V1-16_IGLJ6*01	838	1443
2081	VH3-23_IGHD6-13*01>2'_IGHJ1*01	2176	V1-16_IGLJ6*01	838	1443
2082	VH3-23_IGHD6-13*01>2_IGHJ1*01_B	2177	V1-16_IGLJ6*01	838	1443
2083	VH3-23_IGHD6-19*01>1'_IGHJ1*01	2178	V1-16_IGLJ6*01	838	1443
2084	VH3-23_IGHD6-19*01>2'_IGHJ1*01	2179	V1-16_IGLJ6*01	838	1443
2085	VH3-23_IGHD6-19*01>2_IGHJ1*01_B	2180	V1-16_IGLJ6*01	838	1443
2086	VH3-23_IGHD6-25*01>1'_IGHJ1*01	2181	V1-16_IGLJ6*01	838	1443
2087	VH3-23_IGHD6-25*01>3'_IGHJ1*01	2182	V1-16_IGLJ6*01	838	1443
2088	VH3-23_IGHD7-27*01>1'_IGHJ1*01_B	2183	V1-16_IGLJ6*01	838	1443
2089	VH3-23_IGHD7-27*01>2'_IGHJ1*01	2184	V1-16_IGLJ6*01	838	1443
2090	VH3-23_IGHD6-6*01>2_IGHJ2*01	2233	V1-16_IGLJ6*01	838	1443
2091	VH3-23_IGHD6-13*01>1_IGHJ2*01	2234	V1-16_IGLJ6*01	838	1443
2092	VH3-23_IGHD6-13*01>2_IGHJ2*01	2235	V1-16_IGLJ6*01	838	1443
2093	VH3-23_IGHD6-19*01>1_IGHJ2*01	2236	V1-16_IGLJ6*01	838	1443
2094	VH3-23_IGHD6-19*01>2_IGHJ2*01	2237	V1-16_IGLJ6*01	838	1443
2095	VH3-23_IGHD6-25*01>1_IGHJ2*01	2238	V1-16_IGLJ6*01	838	1443
2096	VH3-23_IGHD6-25*01>2_IGHJ2*01	2239	V1-16_IGLJ6*01	838	1443
2097	VH3-23_IGHD7-27*01>1_IGHJ2*01	2240	V1-16_IGLJ6*01	838	1443
2098	VH3-23_IGHD7-27*01>3_IGHJ2*01	2241	V1-16_IGLJ6*01	838	1443
2099	VH3-23_IGHD6-13*01>1'_IGHJ2*01	2290	V1-16_IGLJ6*01	838	1443
2100	VH3-23_IGHD6-13*01>2'_IGHJ2*01	2291	V1-16_IGLJ6*01	838	1443
2101	VH3-23_IGHD6-13*01>2_IGHJ2*01_B	2292	V1-16_IGLJ6*01	838	1443
2102	VH3-23_IGHD6-19*01>1'_IGHJ2*01	2293	V1-16_IGLJ6*01	838	1443
2103	VH3-23_IGHD6-19*01>2'_IGHJ2*01	2294	V1-16_IGLJ6*01	838	1443
2104	VH3-23_IGHD6-19*01>2_IGHJ2*01_B	2295	V1-16_IGLJ6*01	838	1443
2105	VH3-23_IGHD6-25*01>1'_IGHJ2*01	2296	V1-16_IGLJ6*01	838	1443
2106	VH3-23_IGHD6-25*01>3'_IGHJ2*01	2297	V1-16_IGLJ6*01	838	1443
2107	VH3-23_IGHD7-27*01>1'_IGHJ2*01	2298	V1-16_IGLJ6*01	838	1443
2108	VH3-23_IGHD7-27*01>2'_IGHJ2*01	2299	V1-16_IGLJ6*01	838	1443
2109	VH3-23_IGHD6-6*01>2_IGHJ3*01	2348	V1-16_IGLJ6*01	838	1443
2110	VH3-23_IGHD6-13*01>1_IGHJ3*01	2349	V1-16_IGLJ6*01	838	1443
2111	VH3-23_IGHD6-13*01>2_IGHJ3*01	2350	V1-16_IGLJ6*01	838	1443
2112	VH3-23_IGHD6-19*01>1_IGHJ3*01	2351	V1-16_IGLJ6*01	838	1443
2113	VH3-23_IGHD6-19*01>2_IGHJ3*01	2352	V1-16_IGLJ6*01	838	1443
2114	VH3-23_IGHD6-25*01>1_IGHJ3*01	2353	V1-16_IGLJ6*01	838	1443
2115	VH3-23_IGHD6-25*01>2_IGHJ3*01	2354	V1-16_IGLJ6*01	838	1443
2116	VH3-23_IGHD7-27*01>1_IGHJ3*01	2355	V1-16_IGLJ6*01	838	1443
2117	VH3-23_IGHD7-27*01>3_IGHJ3*01	2356	V1-16_IGLJ6*01	838	1443

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
2118	VH3-23_IGHD6-13*01>1'_IGHJ3*01	2405	V1-16_IGLJ6*01	838	1443
2119	VH3-23_IGHD6-13*01>2'_IGHJ3*01	2406	V1-16_IGLJ6*01	838	1443
2120	VH3-23_IGHD6-13*01>1_IGHJ6*01	2407	V1-16_IGLJ6*01	838	1443
2121	VH3-23_IGHD6-19*01>1'_IGHJ3*01	2408	V1-16_IGLJ6*01	838	1443
2122	VH3-23_IGHD6-19*01>2'_IGHJ3*01	2409	V1-16_IGLJ6*01	838	1443
2123	VH3-23_IGHD6-19*01>3'_IGHJ3*01	2410	V1-16_IGLJ6*01	838	1443
2124	VH3-23_IGHD6-25*01>1'_IGHJ3*01	2411	V1-16_IGLJ6*01	838	1443
2125	VH3-23_IGHD6-25*01>3'_IGHJ3*01	2412	V1-16_IGLJ6*01	838	1443
2126	VH3-23_IGHD7-27*01>1'_IGHJ3*01	2413	V1-16_IGLJ6*01	838	1443
2127	VH3-23_IGHD7-27*01>2'_IGHJ3*01	2414	V1-16_IGLJ6*01	838	1443
2128	VH3-23_IGHD6-6*01>2_IGHJ4*01	2463	V1-16_IGLJ6*01	838	1443
2129	VH3-23_IGHD6-13*01>1_IGHJ4*01	2464	V1-16_IGLJ6*01	838	1443
2130	VH3-23_IGHD6-13*01>2_IGHJ4*01	2465	V1-16_IGLJ6*01	838	1443
2131	VH3-23_IGHD6-19*01>1_IGHJ4*01	2466	V1-16_IGLJ6*01	838	1443
2132	VH3-23_IGHD6-19*01>2_IGHJ4*01	2467	V1-16_IGLJ6*01	838	1443
2133	VH3-23_IGHD6-25*01>1_IGHJ4*01	2468	V1-16_IGLJ6*01	838	1443
2134	VH3-23_IGHD6-25*01>2_IGHJ4*01	2469	V1-16_IGLJ6*01	838	1443
2135	VH3-23_IGHD7-27*01>1_IGHJ4*01	2470	V1-16_IGLJ6*01	838	1443
2136	VH3-23_IGHD7-27*01>3_IGHJ4*01	2471	V1-16_IGLJ6*01	838	1443
2137	VH3-23_IGHD6-13*01>1'_IGHJ4*01	2520	V1-16_IGLJ6*01	838	1443
2138	VH3-23_IGHD6-13*01>2'_IGHJ4*01	2521	V1-16_IGLJ6*01	838	1443
2139	VH3-23_IGHD6-13*01>2_IGHJ4*01_B	2522	V1-16_IGLJ6*01	838	1443
2140	VH3-23_IGHD6-19*01>1'_IGHJ4*01	2523	V1-16_IGLJ6*01	838	1443
2141	VH3-23_IGHD6-19*01>2'_IGHJ4*01	2524	V1-16_IGLJ6*01	838	1443
2142	VH3-23_IGHD6-19*01>2_IGHJ4*01_B	2525	V1-16_IGLJ6*01	838	1443
2143	VH3-23_IGHD6-25*01>1'_IGHJ4*01	2526	V1-16_IGLJ6*01	838	1443
2144	VH3-23_IGHD6-25*01>3'_IGHJ4*01	2527	V1-16_IGLJ6*01	838	1443
2145	VH3-23_IGHD7-27*01>1'_IGHJ4*01	2528	V1-16_IGLJ6*01	838	1443
2146	VH3-23_IGHD7-27*01>2'_IGHJ4*01	2529	V1-16_IGLJ6*01	838	1443
2147	VH3-23_IGHD6-6*01>2_IGHJ5*01	2578	V1-16_IGLJ6*01	838	1443
2148	VH3-23_IGHD6-13*01>1_IGHJ5*01	2579	V1-16_IGLJ6*01	838	1443
2149	VH3-23_IGHD6-13*01>2_IGHJ5*01	2580	V1-16_IGLJ6*01	838	1443
2150	VH3-23_IGHD6-19*01>1_IGHJ5*01	2581	V1-16_IGLJ6*01	838	1443
2151	VH3-23_IGHD6-19*01>2_IGHJ5*01	2582	V1-16_IGLJ6*01	838	1443
2152	VH3-23_IGHD6-25*01>1_IGHJ5*01	2583	V1-16_IGLJ6*01	838	1443
2153	VH3-23_IGHD6-25*01>2_IGHJ5*01	2584	V1-16_IGLJ6*01	838	1443
2154	VH3-23_IGHD7-27*01>1_IGHJ5*01	2585	V1-16_IGLJ6*01	838	1443
2155	VH3-23_IGHD7-27*01>3_IGHJ5*01	2586	V1-16_IGLJ6*01	838	1443
2156	VH3-23_IGHD6-13*01>1'_IGHJ5*01	2635	V1-16_IGLJ6*01	838	1443
2157	VH3-23_IGHD6-13*01>2'_IGHJ5*01	2636	V1-16_IGLJ6*01	838	1443
2158	VH3-23_IGHD6-13*01>3'_IGHJ5*01	2637	V1-16_IGLJ6*01	838	1443
2159	VH3-23_IGHD6-19*01>1'_IGHJ5*01	2638	V1-16_IGLJ6*01	838	1443
2160	VH3-23_IGHD6-19*01>2'_IGHJ5*01	2639	V1-16_IGLJ6*01	838	1443
2161	VH3-23_IGHD6-19*01>2_IGHJ5*01_B	2640	V1-16_IGLJ6*01	838	1443

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
2162	VH3-23_IGHD6-25*01>1'_IGHJ5*01	2641	V1-16_IGLJ6*01	838	1443
2163	VH3-23_IGHD6-25*01>3'_IGHJ5*01	2642	V1-16_IGLJ6*01	838	1443
2164	VH3-23_IGHD7-27*01>1'_IGHJ5*01	2643	V1-16_IGLJ6*01	838	1443
2165	VH3-23_IGHD7-27*01>2'_IGHJ5*01	2644	V1-16_IGLJ6*01	838	1443
2166	VH3-23_IGHD6-6*01>2_IGHJ6*01	2693	V1-16_IGLJ6*01	838	1443
2167	VH3-23_IGHD6-6*01>2_IGHJ1*01	2118	V1-2_IGLJ7*01	840	1445
2168	VH3-23_IGHD6-13*01>1_IGHJ1*01	2119	V1-2_IGLJ7*01	840	1445
2169	VH3-23_IGHD6-13*01>2_IGHJ1*01	2120	V1-2_IGLJ7*01	840	1445
2170	VH3-23_IGHD6-19*01>1_IGHJ1*01	2121	V1-2_IGLJ7*01	840	1445
2171	VH3-23_IGHD6-19*01>2_IGHJ1*01	2122	V1-2_IGLJ7*01	840	1445
2172	VH3-23_IGHD6-25*01>1_IGHJ1*01	2123	V1-2_IGLJ7*01	840	1445
2173	VH3-23_IGHD6-25*01>2_IGHJ1*01	2124	V1-2_IGLJ7*01	840	1445
2174	VH3-23_IGHD7-27*01>1_IGHJ1*01	2125	V1-2_IGLJ7*01	840	1445
2175	VH3-23_IGHD7-27*01>3_IGHJ1*01	2126	V1-2_IGLJ7*01	840	1445
2176	VH3-23_IGHD6-13*01>1'_IGHJ1*01	2175	V1-2_IGLJ7*01	840	1445
2177	VH3-23_IGHD6-13*01>2'_IGHJ1*01	2176	V1-2_IGLJ7*01	840	1445
2178	VH3-23_IGHD6-13*01>2_IGHJ1*01_B	2177	V1-2_IGLJ7*01	840	1445
2179	VH3-23_IGHD6-19*01>1'_IGHJ1*01	2178	V1-2_IGLJ7*01	840	1445
2180	VH3-23_IGHD6-19*01>2'_IGHJ1*01	2179	V1-2_IGLJ7*01	840	1445
2181	VH3-23_IGHD6-19*01>2_IGHJ1*01_B	2180	V1-2_IGLJ7*01	840	1445
2182	VH3-23_IGHD6-25*01>1'_IGHJ1*01	2181	V1-2_IGLJ7*01	840	1445
2183	VH3-23_IGHD6-25*01>3'_IGHJ1*01	2182	V1-2_IGLJ7*01	840	1445
2184	VH3-23_IGHD7-27*01>1'_IGHJ1*01_B	2183	V1-2_IGLJ7*01	840	1445
2185	VH3-23_IGHD7-27*01>2'_IGHJ1*01	2184	V1-2_IGLJ7*01	840	1445
2186	VH3-23_IGHD6-6*01>2_IGHJ2*01	2233	V1-2_IGLJ7*01	840	1445
2187	VH3-23_IGHD6-13*01>1_IGHJ2*01	2234	V1-2_IGLJ7*01	840	1445
2188	VH3-23_IGHD6-13*01>2_IGHJ2*01	2235	V1-2_IGLJ7*01	840	1445
2189	VH3-23_IGHD6-19*01>1_IGHJ2*01	2236	V1-2_IGLJ7*01	840	1445
2190	VH3-23_IGHD6-19*01>2_IGHJ2*01	2237	V1-2_IGLJ7*01	840	1445
2191	VH3-23_IGHD6-25*01>1_IGHJ2*01	2238	V1-2_IGLJ7*01	840	1445
2192	VH3-23_IGHD6-25*01>2_IGHJ2*01	2239	V1-2_IGLJ7*01	840	1445
2193	VH3-23_IGHD7-27*01>1_IGHJ2*01	2240	V1-2_IGLJ7*01	840	1445
2194	VH3-23_IGHD7-27*01>3_IGHJ2*01	2241	V1-2_IGLJ7*01	840	1445
2195	VH3-23_IGHD6-13*01>1'_IGHJ2*01	2290	V1-2_IGLJ7*01	840	1445
2196	VH3-23_IGHD6-13*01>2'_IGHJ2*01	2291	V1-2_IGLJ7*01	840	1445
2197	VH3-23_IGHD6-13*01>2_IGHJ2*01_B	2292	V1-2_IGLJ7*01	840	1445
2198	VH3-23_IGHD6-19*01>1'_IGHJ2*01	2293	V1-2_IGLJ7*01	840	1445
2199	VH3-23_IGHD6-19*01>2'_IGHJ2*01	2294	V1-2_IGLJ7*01	840	1445
2200	VH3-23_IGHD6-19*01>2_IGHJ2*01_B	2295	V1-2_IGLJ7*01	840	1445
2201	VH3-23_IGHD6-25*01>1'_IGHJ2*01	2296	V1-2_IGLJ7*01	840	1445
2202	VH3-23_IGHD6-25*01>3'_IGHJ2*01	2297	V1-2_IGLJ7*01	840	1445
2203	VH3-23_IGHD7-27*01>1'_IGHJ2*01	2298	V1-2_IGLJ7*01	840	1445
2204	VH3-23_IGHD7-27*01>2'_IGHJ2*01	2299	V1-2_IGLJ7*01	840	1445
2205	VH3-23_IGHD6-6*01>2_IGHJ3*01	2348	V1-2_IGLJ7*01	840	1445

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
2206	VH3-23_IGHD6-13*01>1_IGHJ3*01	2349	V1-2_IGLJ7*01	840	1445
2207	VH3-23_IGHD6-13*01>2_IGHJ3*01	2350	V1-2_IGLJ7*01	840	1445
2208	VH3-23_IGHD6-19*01>1_IGHJ3*01	2351	V1-2_IGLJ7*01	840	1445
2209	VH3-23_IGHD6-19*01>2_IGHJ3*01	2352	V1-2_IGLJ7*01	840	1445
2210	VH3-23_IGHD6-25*01>1_IGHJ3*01	2353	V1-2_IGLJ7*01	840	1445
2211	VH3-23_IGHD6-25*01>2_IGHJ3*01	2354	V1-2_IGLJ7*01	840	1445
2212	VH3-23_IGHD7-27*01>1_IGHJ3*01	2355	V1-2_IGLJ7*01	840	1445
2213	VH3-23_IGHD7-27*01>3_IGHJ3*01	2356	V1-2_IGLJ7*01	840	1445
2214	VH3-23_IGHD6-13*01>1'_IGHJ3*01	2405	V1-2_IGLJ7*01	840	1445
2215	VH3-23_IGHD6-13*01>2'_IGHJ3*01	2406	V1-2_IGLJ7*01	840	1445
2216	VH3-23_IGHD6-13*01>1_IGHJ6*01	2407	V1-2_IGLJ7*01	840	1445
2217	VH3-23_IGHD6-19*01>1'_IGHJ3*01	2408	V1-2_IGLJ7*01	840	1445
2218	VH3-23_IGHD6-19*01>2'_IGHJ3*01	2409	V1-2_IGLJ7*01	840	1445
2219	VH3-23_IGHD6-19*01>3'_IGHJ3*01	2410	V1-2_IGLJ7*01	840	1445
2220	VH3-23_IGHD6-25*01>1'_IGHJ3*01	2411	V1-2_IGLJ7*01	840	1445
2221	VH3-23_IGHD6-25*01>3'_IGHJ3*01	2412	V1-2_IGLJ7*01	840	1445
2222	VH3-23_IGHD7-27*01>1'_IGHJ3*01	2413	V1-2_IGLJ7*01	840	1445
2223	VH3-23_IGHD7-27*01>2'_IGHJ3*01	2414	V1-2_IGLJ7*01	840	1445
2224	VH3-23_IGHD6-6*01>2_IGHJ4*01	2463	V1-2_IGLJ7*01	840	1445
2225	VH3-23_IGHD6-13*01>1_IGHJ4*01	2464	V1-2_IGLJ7*01	840	1445
2226	VH3-23_IGHD6-13*01>2_IGHJ4*01	2465	V1-2_IGLJ7*01	840	1445
2227	VH3-23_IGHD6-19*01>1_IGHJ4*01	2466	V1-2_IGLJ7*01	840	1445
2228	VH3-23_IGHD6-19*01>2_IGHJ4*01	2467	V1-2_IGLJ7*01	840	1445
2229	VH3-23_IGHD6-25*01>1_IGHJ4*01	2468	V1-2_IGLJ7*01	840	1445
2230	VH3-23_IGHD6-25*01>2_IGHJ4*01	2469	V1-2_IGLJ7*01	840	1445
2231	VH3-23_IGHD7-27*01>1_IGHJ4*01	2470	V1-2_IGLJ7*01	840	1445
2232	VH3-23_IGHD7-27*01>3_IGHJ4*01	2471	V1-2_IGLJ7*01	840	1445
2233	VH3-23_IGHD6-13*01>1'_IGHJ4*01	2520	V1-2_IGLJ7*01	840	1445
2234	VH3-23_IGHD6-13*01>2'_IGHJ4*01	2521	V1-2_IGLJ7*01	840	1445
2235	VH3-23_IGHD6-13*01>2_IGHJ4*01_B	2522	V1-2_IGLJ7*01	840	1445
2236	VH3-23_IGHD6-19*01>1'_IGHJ4*01	2523	V1-2_IGLJ7*01	840	1445
2237	VH3-23_IGHD6-19*01>2'_IGHJ4*01	2524	V1-2_IGLJ7*01	840	1445
2238	VH3-23_IGHD6-19*01>2_IGHJ4*01_B	2525	V1-2_IGLJ7*01	840	1445
2239	VH3-23_IGHD6-25*01>1'_IGHJ4*01	2526	V1-2_IGLJ7*01	840	1445
2240	VH3-23_IGHD6-25*01>3'_IGHJ4*01	2527	V1-2_IGLJ7*01	840	1445
2241	VH3-23_IGHD7-27*01>1'_IGHJ4*01	2528	V1-2_IGLJ7*01	840	1445
2242	VH3-23_IGHD7-27*01>2'_IGHJ4*01	2529	V1-2_IGLJ7*01	840	1445
2243	VH3-23_IGHD6-6*01>2_IGHJ5*01	2578	V1-2_IGLJ7*01	840	1445
2244	VH3-23_IGHD6-13*01>1_IGHJ5*01	2579	V1-2_IGLJ7*01	840	1445
2245	VH3-23_IGHD6-13*01>2_IGHJ5*01	2580	V1-2_IGLJ7*01	840	1445
2246	VH3-23_IGHD6-19*01>1_IGHJ5*01	2581	V1-2_IGLJ7*01	840	1445
2247	VH3-23_IGHD6-19*01>2_IGHJ5*01	2582	V1-2_IGLJ7*01	840	1445
2248	VH3-23_IGHD6-25*01>1_IGHJ5*01	2583	V1-2_IGLJ7*01	840	1445
2249	VH3-23_IGHD6-25*01>2_IGHJ5*01	2584	V1-2_IGLJ7*01	840	1445

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
2250	VH3-23_IGHD7-27*01>1_IGHJ5*01	2585	V1-2_IGLJ7*01	840	1445
2251	VH3-23_IGHD7-27*01>3_IGHJ5*01	2586	V1-2_IGLJ7*01	840	1445
2252	VH3-23_IGHD6-13*01>1'_IGHJ5*01	2635	V1-2_IGLJ7*01	840	1445
2253	VH3-23_IGHD6-13*01>2'_IGHJ5*01	2636	V1-2_IGLJ7*01	840	1445
2254	VH3-23_IGHD6-13*01>3'_IGHJ5*01	2637	V1-2_IGLJ7*01	840	1445
2255	VH3-23_IGHD6-19*01>1'_IGHJ5*01	2638	V1-2_IGLJ7*01	840	1445
2256	VH3-23_IGHD6-19*01>2'_IGHJ5*01	2639	V1-2_IGLJ7*01	840	1445
2257	VH3-23_IGHD6-19*01>2_IGHJ5*01_B	2640	V1-2_IGLJ7*01	840	1445
2258	VH3-23_IGHD6-25*01>1'_IGHJ5*01	2641	V1-2_IGLJ7*01	840	1445
2259	VH3-23_IGHD6-25*01>3'_IGHJ5*01	2642	V1-2_IGLJ7*01	840	1445
2260	VH3-23_IGHD7-27*01>1'_IGHJ5*01	2643	V1-2_IGLJ7*01	840	1445
2261	VH3-23_IGHD7-27*01>2'_IGHJ5*01	2644	V1-2_IGLJ7*01	840	1445
2262	VH3-23_IGHD6-6*01>2_IGHJ6*01	2693	V1-2_IGLJ7*01	840	1445
2263	VH3-23_IGHD6-6*01>2_IGHJ1*01	2118	V1-20_IGLJ6*01	841	1446
2264	VH3-23_IGHD6-13*01>1_IGHJ1*01	2119	V1-20_IGLJ6*01	841	1446
2265	VH3-23_IGHD6-13*01>2_IGHJ1*01	2120	V1-20_IGLJ6*01	841	1446
2266	VH3-23_IGHD6-19*01>1_IGHJ1*01	2121	V1-20_IGLJ6*01	841	1446
2267	VH3-23_IGHD6-19*01>2_IGHJ1*01	2122	V1-20_IGLJ6*01	841	1446
2268	VH3-23_IGHD6-25*01>1_IGHJ1*01	2123	V1-20_IGLJ6*01	841	1446
2269	VH3-23_IGHD6-25*01>2_IGHJ1*01	2124	V1-20_IGLJ6*01	841	1446
2270	VH3-23_IGHD7-27*01>1_IGHJ1*01	2125	V1-20_IGLJ6*01	841	1446
2271	VH3-23_IGHD7-27*01>3_IGHJ1*01	2126	V1-20_IGLJ6*01	841	1446
2272	VH3-23_IGHD6-13*01>1'_IGHJ1*01	2175	V1-20_IGLJ6*01	841	1446
2273	VH3-23_IGHD6-13*01>2'_IGHJ1*01	2176	V1-20_IGLJ6*01	841	1446
2274	VH3-23_IGHD6-13*01>2_IGHJ1*01_B	2177	V1-20_IGLJ6*01	841	1446
2275	VH3-23_IGHD6-19*01>1'_IGHJ1*01	2178	V1-20_IGLJ6*01	841	1446
2276	VH3-23_IGHD6-19*01>2'_IGHJ1*01	2179	V1-20_IGLJ6*01	841	1446
2277	VH3-23_IGHD6-19*01>2_IGHJ1*01_B	2180	V1-20_IGLJ6*01	841	1446
2278	VH3-23_IGHD6-25*01>1'_IGHJ1*01	2181	V1-20_IGLJ6*01	841	1446
2279	VH3-23_IGHD6-25*01>3'_IGHJ1*01	2182	V1-20_IGLJ6*01	841	1446
2280	VH3-23_IGHD7-27*01>1'_IGHJ1*01_B	2183	V1-20_IGLJ6*01	841	1446
2281	VH3-23_IGHD7-27*01>2'_IGHJ1*01	2184	V1-20_IGLJ6*01	841	1446
2282	VH3-23_IGHD6-6*01>2_IGHJ2*01	2233	V1-20_IGLJ6*01	841	1446
2283	VH3-23_IGHD6-13*01>1_IGHJ2*01	2234	V1-20_IGLJ6*01	841	1446
2284	VH3-23_IGHD6-13*01>2_IGHJ2*01	2235	V1-20_IGLJ6*01	841	1446
2285	VH3-23_IGHD6-19*01>1_IGHJ2*01	2236	V1-20_IGLJ6*01	841	1446
2286	VH3-23_IGHD6-19*01>2_IGHJ2*01	2237	V1-20_IGLJ6*01	841	1446
2287	VH3-23_IGHD6-25*01>1_IGHJ2*01	2238	V1-20_IGLJ6*01	841	1446
2288	VH3-23_IGHD6-25*01>2_IGHJ2*01	2239	V1-20_IGLJ6*01	841	1446
2289	VH3-23_IGHD7-27*01>1_IGHJ2*01	2240	V1-20_IGLJ6*01	841	1446
2290	VH3-23_IGHD7-27*01>3_IGHJ2*01	2241	V1-20_IGLJ6*01	841	1446
2291	VH3-23_IGHD6-13*01>1'_IGHJ2*01	2290	V1-20_IGLJ6*01	841	1446
2292	VH3-23_IGHD6-13*01>2'_IGHJ2*01	2291	V1-20_IGLJ6*01	841	1446
2293	VH3-23_IGHD6-13*01>2_IGHJ2*01_B	2292	V1-20_IGLJ6*01	841	1446

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
2294	VH3-23_IGHD6-19*01>1'_IGHJ2*01	2293	V1-20_IGLJ6*01	841	1446
2295	VH3-23_IGHD6-19*01>2'_IGHJ2*01	2294	V1-20_IGLJ6*01	841	1446
2296	VH3-23_IGHD6-19*01>2_IGHJ2*01_B	2295	V1-20_IGLJ6*01	841	1446
2297	VH3-23_IGHD6-25*01>1'_IGHJ2*01	2296	V1-20_IGLJ6*01	841	1446
2298	VH3-23_IGHD6-25*01>3'_IGHJ2*01	2297	V1-20_IGLJ6*01	841	1446
2299	VH3-23_IGHD7-27*01>1'_IGHJ2*01	2298	V1-20_IGLJ6*01	841	1446
2300	VH3-23_IGHD7-27*01>2'_IGHJ2*01	2299	V1-20_IGLJ6*01	841	1446
2301	VH3-23_IGHD6-6*01>2_IGHJ3*01	2348	V1-20_IGLJ6*01	841	1446
2302	VH3-23_IGHD6-13*01>1_IGHJ3*01	2349	V1-20_IGLJ6*01	841	1446
2303	VH3-23_IGHD6-13*01>2_IGHJ3*01	2350	V1-20_IGLJ6*01	841	1446
2304	VH3-23_IGHD6-19*01>1_IGHJ3*01	2351	V1-20_IGLJ6*01	841	1446
2305	VH3-23_IGHD6-19*01>2_IGHJ3*01	2352	V1-20_IGLJ6*01	841	1446
2306	VH3-23_IGHD6-25*01>1_IGHJ3*01	2353	V1-20_IGLJ6*01	841	1446
2307	VH3-23_IGHD6-25*01>2_IGHJ3*01	2354	V1-20_IGLJ6*01	841	1446
2308	VH3-23_IGHD7-27*01>1_IGHJ3*01	2355	V1-20_IGLJ6*01	841	1446
2309	VH3-23_IGHD7-27*01>3_IGHJ3*01	2356	V1-20_IGLJ6*01	841	1446
2310	VH3-23_IGHD6-13*01>1'_IGHJ3*01	2405	V1-20_IGLJ6*01	841	1446
2311	VH3-23_IGHD6-13*01>2'_IGHJ3*01	2406	V1-20_IGLJ6*01	841	1446
2312	VH3-23_IGHD6-13*01>1_IGHJ6*01	2407	V1-20_IGLJ6*01	841	1446
2313	VH3-23_IGHD6-19*01>1'_IGHJ3*01	2408	V1-20_IGLJ6*01	841	1446
2314	VH3-23_IGHD6-19*01>2'_IGHJ3*01	2409	V1-20_IGLJ6*01	841	1446
2315	VH3-23_IGHD6-19*01>3'_IGHJ3*01	2410	V1-20_IGLJ6*01	841	1446
2316	VH3-23_IGHD6-25*01>1'_IGHJ3*01	2411	V1-20_IGLJ6*01	841	1446
2317	VH3-23_IGHD6-25*01>3'_IGHJ3*01	2412	V1-20_IGLJ6*01	841	1446
2318	VH3-23_IGHD7-27*01>1'_IGHJ3*01	2413	V1-20_IGLJ6*01	841	1446
2319	VH3-23_IGHD7-27*01>2'_IGHJ3*01	2414	V1-20_IGLJ6*01	841	1446
2320	VH3-23_IGHD6-6*01>2_IGHJ4*01	2463	V1-20_IGLJ6*01	841	1446
2321	VH3-23_IGHD6-13*01>1_IGHJ4*01	2464	V1-20_IGLJ6*01	841	1446
2322	VH3-23_IGHD6-13*01>2_IGHJ4*01	2465	V1-20_IGLJ6*01	841	1446
2323	VH3-23_IGHD6-19*01>1_IGHJ4*01	2466	V1-20_IGLJ6*01	841	1446
2324	VH3-23_IGHD6-19*01>2_IGHJ4*01	2467	V1-20_IGLJ6*01	841	1446
2325	VH3-23_IGHD6-25*01>1_IGHJ4*01	2468	V1-20_IGLJ6*01	841	1446
2326	VH3-23_IGHD6-25*01>2_IGHJ4*01	2469	V1-20_IGLJ6*01	841	1446
2327	VH3-23_IGHD7-27*01>1_IGHJ4*01	2470	V1-20_IGLJ6*01	841	1446
2328	VH3-23_IGHD7-27*01>3_IGHJ4*01	2471	V1-20_IGLJ6*01	841	1446
2329	VH3-23_IGHD6-13*01>1'_IGHJ4*01	2520	V1-20_IGLJ6*01	841	1446
2330	VH3-23_IGHD6-13*01>2'_IGHJ4*01	2521	V1-20_IGLJ6*01	841	1446
2331	VH3-23_IGHD6-13*01>2_IGHJ4*01_B	2522	V1-20_IGLJ6*01	841	1446
2332	VH3-23_IGHD6-19*01>1'_IGHJ4*01	2523	V1-20_IGLJ6*01	841	1446
2333	VH3-23_IGHD6-19*01>2'_IGHJ4*01	2524	V1-20_IGLJ6*01	841	1446
2334	VH3-23_IGHD6-19*01>2_IGHJ4*01_B	2525	V1-20_IGLJ6*01	841	1446
2335	VH3-23_IGHD6-25*01>1'_IGHJ4*01	2526	V1-20_IGLJ6*01	841	1446
2336	VH3-23_IGHD6-25*01>3'_IGHJ4*01	2527	V1-20_IGLJ6*01	841	1446
2337	VH3-23_IGHD7-27*01>1'_IGHJ4*01	2528	V1-20_IGLJ6*01	841	1446

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
2338	VH3-23_IGHD7-27*01>2'_IGHJ4*01	2529	V1-20_IGLJ6*01	841	1446
2339	VH3-23_IGHD6-6*01>2_IGHJ5*01	2578	V1-20_IGLJ6*01	841	1446
2340	VH3-23_IGHD6-13*01>1_IGHJ5*01	2579	V1-20_IGLJ6*01	841	1446
2341	VH3-23_IGHD6-13*01>2_IGHJ5*01	2580	V1-20_IGLJ6*01	841	1446
2342	VH3-23_IGHD6-19*01>1_IGHJ5*01	2581	V1-20_IGLJ6*01	841	1446
2343	VH3-23_IGHD6-19*01>2_IGHJ5*01	2582	V1-20_IGLJ6*01	841	1446
2344	VH3-23_IGHD6-25*01>1_IGHJ5*01	2583	V1-20_IGLJ6*01	841	1446
2345	VH3-23_IGHD6-25*01>2_IGHJ5*01	2584	V1-20_IGLJ6*01	841	1446
2346	VH3-23_IGHD7-27*01>1_IGHJ5*01	2585	V1-20_IGLJ6*01	841	1446
2347	VH3-23_IGHD7-27*01>3_IGHJ5*01	2586	V1-20_IGLJ6*01	841	1446
2348	VH3-23_IGHD6-13*01>1'_IGHJ5*01	2635	V1-20_IGLJ6*01	841	1446
2349	VH3-23_IGHD6-13*01>2'_IGHJ5*01	2636	V1-20_IGLJ6*01	841	1446
2350	VH3-23_IGHD6-13*01>3'_IGHJ5*01	2637	V1-20_IGLJ6*01	841	1446
2351	VH3-23_IGHD6-19*01>1'_IGHJ5*01	2638	V1-20_IGLJ6*01	841	1446
2352	VH3-23_IGHD6-19*01>2'_IGHJ5*01	2639	V1-20_IGLJ6*01	841	1446
2353	VH3-23_IGHD6-19*01>2_IGHJ5*01_B	2640	V1-20_IGLJ6*01	841	1446
2354	VH3-23_IGHD6-25*01>1'_IGHJ5*01	2641	V1-20_IGLJ6*01	841	1446
2355	VH3-23_IGHD6-25*01>3'_IGHJ5*01	2642	V1-20_IGLJ6*01	841	1446
2356	VH3-23_IGHD7-27*01>1'_IGHJ5*01	2643	V1-20_IGLJ6*01	841	1446
2357	VH3-23_IGHD7-27*01>2'_IGHJ5*01	2644	V1-20_IGLJ6*01	841	1446
2358	VH3-23_IGHD6-6*01>2_IGHJ6*01	2693	V1-20_IGLJ6*01	841	1446
2359	VH3-23_IGHD6-6*01>2_IGHJ1*01	2118	V1-3_IGLJ1*01	842	1447
2360	VH3-23_IGHD6-13*01>1_IGHJ1*01	2119	V1-3_IGLJ1*01	842	1447
2361	VH3-23_IGHD6-13*01>2_IGHJ1*01	2120	V1-3_IGLJ1*01	842	1447
2362	VH3-23_IGHD6-19*01>1_IGHJ1*01	2121	V1-3_IGLJ1*01	842	1447
2363	VH3-23_IGHD6-19*01>2_IGHJ1*01	2122	V1-3_IGLJ1*01	842	1447
2364	VH3-23_IGHD6-25*01>1_IGHJ1*01	2123	V1-3_IGLJ1*01	842	1447
2365	VH3-23_IGHD6-25*01>2_IGHJ1*01	2124	V1-3_IGLJ1*01	842	1447
2366	VH3-23_IGHD7-27*01>1_IGHJ1*01	2125	V1-3_IGLJ1*01	842	1447
2367	VH3-23_IGHD7-27*01>3_IGHJ1*01	2126	V1-3_IGLJ1*01	842	1447
2368	VH3-23_IGHD6-13*01>1'_IGHJ1*01	2175	V1-3_IGLJ1*01	842	1447
2369	VH3-23_IGHD6-13*01>2'_IGHJ1*01	2176	V1-3_IGLJ1*01	842	1447
2370	VH3-23_IGHD6-13*01>2_IGHJ1*01_B	2177	V1-3_IGLJ1*01	842	1447
2371	VH3-23_IGHD6-19*01>1'_IGHJ1*01	2178	V1-3_IGLJ1*01	842	1447
2372	VH3-23_IGHD6-19*01>2'_IGHJ1*01	2179	V1-3_IGLJ1*01	842	1447
2373	VH3-23_IGHD6-19*01>2_IGHJ1*01_B	2180	V1-3_IGLJ1*01	842	1447
2374	VH3-23_IGHD6-25*01>1'_IGHJ1*01	2181	V1-3_IGLJ1*01	842	1447
2375	VH3-23_IGHD6-25*01>3'_IGHJ1*01	2182	V1-3_IGLJ1*01	842	1447
2376	VH3-23_IGHD7-27*01>1'_IGHJ1*01_B	2183	V1-3_IGLJ1*01	842	1447
2377	VH3-23_IGHD7-27*01>2'_IGHJ1*01	2184	V1-3_IGLJ1*01	842	1447
2378	VH3-23_IGHD6-6*01>2_IGHJ2*01	2233	V1-3_IGLJ1*01	842	1447
2379	VH3-23_IGHD6-13*01>1_IGHJ2*01	2234	V1-3_IGLJ1*01	842	1447
2380	VH3-23_IGHD6-13*01>2_IGHJ2*01	2235	V1-3_IGLJ1*01	842	1447
2381	VH3-23_IGHD6-19*01>1_IGHJ2*01	2236	V1-3_IGLJ1*01	842	1447

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
2382	VH3-23_IGHD6-19*01>2_IGHJ2*01	2237	V1-3_IGLJ1*01	842	1447
2383	VH3-23_IGHD6-25*01>1_IGHJ2*01	2238	V1-3_IGLJ1*01	842	1447
2384	VH3-23_IGHD6-25*01>2_IGHJ2*01	2239	V1-3_IGLJ1*01	842	1447
2385	VH3-23_IGHD7-27*01>1_IGHJ2*01	2240	V1-3_IGLJ1*01	842	1447
2386	VH3-23_IGHD7-27*01>3_IGHJ2*01	2241	V1-3_IGLJ1*01	842	1447
2387	VH3-23_IGHD6-13*01>1'_IGHJ2*01	2290	V1-3_IGLJ1*01	842	1447
2388	VH3-23_IGHD6-13*01>2'_IGHJ2*01	2291	V1-3_IGLJ1*01	842	1447
2389	VH3-23_IGHD6-13*01>2_IGHJ2*01_B	2292	V1-3_IGLJ1*01	842	1447
2390	VH3-23_IGHD6-19*01>1'_IGHJ2*01	2293	V1-3_IGLJ1*01	842	1447
2391	VH3-23_IGHD6-19*01>2'_IGHJ2*01	2294	V1-3_IGLJ1*01	842	1447
2392	VH3-23_IGHD6-19*01>2_IGHJ2*01_B	2295	V1-3_IGLJ1*01	842	1447
2393	VH3-23_IGHD6-25*01>1'_IGHJ2*01	2296	V1-3_IGLJ1*01	842	1447
2394	VH3-23_IGHD6-25*01>3'_IGHJ2*01	2297	V1-3_IGLJ1*01	842	1447
2395	VH3-23_IGHD7-27*01>1'_IGHJ2*01	2298	V1-3_IGLJ1*01	842	1447
2396	VH3-23_IGHD7-27*01>2'_IGHJ2*01	2299	V1-3_IGLJ1*01	842	1447
2397	VH3-23_IGHD6-6*01>2_IGHJ3*01	2348	V1-3_IGLJ1*01	842	1447
2398	VH3-23_IGHD6-13*01>1_IGHJ3*01	2349	V1-3_IGLJ1*01	842	1447
2399	VH3-23_IGHD6-13*01>2_IGHJ3*01	2350	V1-3_IGLJ1*01	842	1447
2400	VH3-23_IGHD6-19*01>1_IGHJ3*01	2351	V1-3_IGLJ1*01	842	1447
2401	VH3-23_IGHD6-19*01>2_IGHJ3*01	2352	V1-3_IGLJ1*01	842	1447
2402	VH3-23_IGHD6-25*01>1_IGHJ3*01	2353	V1-3_IGLJ1*01	842	1447
2403	VH3-23_IGHD6-25*01>2_IGHJ3*01	2354	V1-3_IGLJ1*01	842	1447
2404	VH3-23_IGHD7-27*01>1_IGHJ3*01	2355	V1-3_IGLJ1*01	842	1447
2405	VH3-23_IGHD7-27*01>3_IGHJ3*01	2356	V1-3_IGLJ1*01	842	1447
2406	VH3-23_IGHD6-13*01>1'_IGHJ3*01	2405	V1-3_IGLJ1*01	842	1447
2407	VH3-23_IGHD6-13*01>2'_IGHJ3*01	2406	V1-3_IGLJ1*01	842	1447
2408	VH3-23_IGHD6-13*01>1_IGHJ6*01	2407	V1-3_IGLJ1*01	842	1447
2409	VH3-23_IGHD6-19*01>1'_IGHJ3*01	2408	V1-3_IGLJ1*01	842	1447
2410	VH3-23_IGHD6-19*01>2'_IGHJ3*01	2409	V1-3_IGLJ1*01	842	1447
2411	VH3-23_IGHD6-19*01>3'_IGHJ3*01	2410	V1-3_IGLJ1*01	842	1447
2412	VH3-23_IGHD6-25*01>1'_IGHJ3*01	2411	V1-3_IGLJ1*01	842	1447
2413	VH3-23_IGHD6-25*01>3'_IGHJ3*01	2412	V1-3_IGLJ1*01	842	1447
2414	VH3-23_IGHD7-27*01>1'_IGHJ3*01	2413	V1-3_IGLJ1*01	842	1447
2415	VH3-23_IGHD7-27*01>2'_IGHJ3*01	2414	V1-3_IGLJ1*01	842	1447
2416	VH3-23_IGHD6-6*01>2_IGHJ4*01	2463	V1-3_IGLJ1*01	842	1447
2417	VH3-23_IGHD6-13*01>1_IGHJ4*01	2464	V1-3_IGLJ1*01	842	1447
2418	VH3-23_IGHD6-13*01>2_IGHJ4*01	2465	V1-3_IGLJ1*01	842	1447
2419	VH3-23_IGHD6-19*01>1_IGHJ4*01	2466	V1-3_IGLJ1*01	842	1447
2420	VH3-23_IGHD6-19*01>2_IGHJ4*01	2467	V1-3_IGLJ1*01	842	1447
2421	VH3-23_IGHD6-25*01>1_IGHJ4*01	2468	V1-3_IGLJ1*01	842	1447
2422	VH3-23_IGHD6-25*01>2_IGHJ4*01	2469	V1-3_IGLJ1*01	842	1447
2423	VH3-23_IGHD7-27*01>1_IGHJ4*01	2470	V1-3_IGLJ1*01	842	1447
2424	VH3-23_IGHD7-27*01>3_IGHJ4*01	2471	V1-3_IGLJ1*01	842	1447
2425	VH3-23_IGHD6-13*01>1'_IGHJ4*01	2520	V1-3_IGLJ1*01	842	1447

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
2426	VH3-23_IGHD6-13*01>2'_IGHJ4*01	2521	V1-3_IGLJ1*01	842	1447
2427	VH3-23_IGHD6-13*01>2_IGHJ4*01_B	2522	V1-3_IGLJ1*01	842	1447
2428	VH3-23_IGHD6-19*01>1'_IGHJ4*01	2523	V1-3_IGLJ1*01	842	1447
2429	VH3-23_IGHD6-19*01>2'_IGHJ4*01	2524	V1-3_IGLJ1*01	842	1447
2430	VH3-23_IGHD6-19*01>2_IGHJ4*01_B	2525	V1-3_IGLJ1*01	842	1447
2431	VH3-23_IGHD6-25*01>1'_IGHJ4*01	2526	V1-3_IGLJ1*01	842	1447
2432	VH3-23_IGHD6-25*01>3'_IGHJ4*01	2527	V1-3_IGLJ1*01	842	1447
2433	VH3-23_IGHD7-27*01>1'_IGHJ4*01	2528	V1-3_IGLJ1*01	842	1447
2434	VH3-23_IGHD7-27*01>2'_IGHJ4*01	2529	V1-3_IGLJ1*01	842	1447
2435	VH3-23_IGHD6-6*01>2_IGHJ5*01	2578	V1-3_IGLJ1*01	842	1447
2436	VH3-23_IGHD6-13*01>1_IGHJ5*01	2579	V1-3_IGLJ1*01	842	1447
2437	VH3-23_IGHD6-13*01>2_IGHJ5*01	2580	V1-3_IGLJ1*01	842	1447
2438	VH3-23_IGHD6-19*01>1_IGHJ5*01	2581	V1-3_IGLJ1*01	842	1447
2439	VH3-23_IGHD6-19*01>2_IGHJ5*01	2582	V1-3_IGLJ1*01	842	1447
2440	VH3-23_IGHD6-25*01>1_IGHJ5*01	2583	V1-3_IGLJ1*01	842	1447
2441	VH3-23_IGHD6-25*01>2_IGHJ5*01	2584	V1-3_IGLJ1*01	842	1447
2442	VH3-23_IGHD7-27*01>1_IGHJ5*01	2585	V1-3_IGLJ1*01	842	1447
2443	VH3-23_IGHD7-27*01>3_IGHJ5*01	2586	V1-3_IGLJ1*01	842	1447
2444	VH3-23_IGHD6-13*01>1'_IGHJ5*01	2635	V1-3_IGLJ1*01	842	1447
2445	VH3-23_IGHD6-13*01>2'_IGHJ5*01	2636	V1-3_IGLJ1*01	842	1447
2446	VH3-23_IGHD6-13*01>3'_IGHJ5*01	2637	V1-3_IGLJ1*01	842	1447
2447	VH3-23_IGHD6-19*01>1'_IGHJ5*01	2638	V1-3_IGLJ1*01	842	1447
2448	VH3-23_IGHD6-19*01>2'_IGHJ5*01	2639	V1-3_IGLJ1*01	842	1447
2449	VH3-23_IGHD6-19*01>2_IGHJ5*01_B	2640	V1-3_IGLJ1*01	842	1447
2450	VH3-23_IGHD6-25*01>1'_IGHJ5*01	2641	V1-3_IGLJ1*01	842	1447
2451	VH3-23_IGHD6-25*01>3'_IGHJ5*01	2642	V1-3_IGLJ1*01	842	1447
2452	VH3-23_IGHD7-27*01>1'_IGHJ5*01	2643	V1-3_IGLJ1*01	842	1447
2453	VH3-23_IGHD7-27*01>2'_IGHJ5*01	2644	V1-3_IGLJ1*01	842	1447
2454	VH3-23_IGHD6-6*01>2_IGHJ6*01	2693	V1-3_IGLJ1*01	842	1447
2455	VH3-23_IGHD1-1*01>1_IGHJ6*01	2645	V2-13_IGLJ2*01	849	1454
2456	VH3-23_IGHD1-1*01>2_IGHJ6*01	2646	V2-13_IGLJ2*01	849	1454
2457	VH3-23_IGHD1-1*01>3_IGHJ6*01	2647	V2-13_IGLJ2*01	849	1454
2458	VH3-23_IGHD1-7*01>1_IGHJ6*01	2648	V2-13_IGLJ2*01	849	1454
2459	VH3-23_IGHD1-7*01>3_IGHJ6*01	2649	V2-13_IGLJ2*01	849	1454
2460	VH3-23_IGHD1-14*01>1_IGHJ6*01	2650	V2-13_IGLJ2*01	849	1454
2461	VH3-23_IGHD1-14*01>3_IGHJ6*01	2651	V2-13_IGLJ2*01	849	1454
2462	VH3-23_IGHD1-20*01>1_IGHJ6*01	2652	V2-13_IGLJ2*01	849	1454
2463	VH3-23_IGHD1-20*01>3_IGHJ6*01	2653	V2-13_IGLJ2*01	849	1454
2464	VH3-23_IGHD1-26*01>1_IGHJ6*01	2654	V2-13_IGLJ2*01	849	1454
2465	VH3-23_IGHD1-26*01>3_IGHJ6*01	2655	V2-13_IGLJ2*01	849	1454
2466	VH3-23_IGHD2-2*01>2_IGHJ6*01	2656	V2-13_IGLJ2*01	849	1454
2467	VH3-23_IGHD2-2*01>3_IGHJ6*01	2657	V2-13_IGLJ2*01	849	1454
2468	VH3-23_IGHD2-8*01>2_IGHJ6*01	2658	V2-13_IGLJ2*01	849	1454
2469	VH3-23_IGHD2-8*01>3_IGHJ6*01	2659	V2-13_IGLJ2*01	849	1454

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
2470	VH3-23_IGHD2-15*01>2_IGHJ6*01	2660	V2-13_IGLJ2*01	849	1454
2471	VH3-23_IGHD2-15*01>3_IGHJ6*01	2661	V2-13_IGLJ2*01	849	1454
2472	VH3-23_IGHD2-21*01>2_IGHJ6*01	2662	V2-13_IGLJ2*01	849	1454
2473	VH3-23_IGHD2-21*01>3_IGHJ6*01	2663	V2-13_IGLJ2*01	849	1454
2474	VH3-23_IGHD3-3*01>1_IGHJ6*01	2664	V2-13_IGLJ2*01	849	1454
2475	VH3-23_IGHD3-3*01>2_IGHJ6*01	2665	V2-13_IGLJ2*01	849	1454
2476	VH3-23_IGHD3-3*01>3_IGHJ6*01	2666	V2-13_IGLJ2*01	849	1454
2477	VH3-23_IGHD3-9*01>2_IGHJ6*01	2667	V2-13_IGLJ2*01	849	1454
2478	VH3-23_IGHD3-10*01>2_IGHJ6*01	2668	V2-13_IGLJ2*01	849	1454
2479	VH3-23_IGHD3-10*01>3_IGHJ6*01	2669	V2-13_IGLJ2*01	849	1454
2480	VH3-23_IGHD3-16*01>2_IGHJ6*01	2670	V2-13_IGLJ2*01	849	1454
2481	VH3-23_IGHD3-16*01>3_IGHJ6*01	2671	V2-13_IGLJ2*01	849	1454
2482	VH3-23_IGHD3-22*01>2_IGHJ6*01	2672	V2-13_IGLJ2*01	849	1454
2483	VH3-23_IGHD3-22*01>3_IGHJ6*01	2673	V2-13_IGLJ2*01	849	1454
2484	VH3-23_IGHD4-4*01 (1) >2_IGHJ6*01	2674	V2-13_IGLJ2*01	849	1454
2485	VH3-23_IGHD4-4*01 (1) >3_IGHJ6*01	2675	V2-13_IGLJ2*01	849	1454
2486	VH3-23_IGHD4-11*01 (1) >2_IGHJ6*01	2676	V2-13_IGLJ2*01	849	1454
2487	VH3-23_IGHD4-11*01 (1) >3_IGHJ6*01	2677	V2-13_IGLJ2*01	849	1454
2488	VH3-23_IGHD4-17*01>2_IGHJ6*01	2678	V2-13_IGLJ2*01	849	1454
2489	VH3-23_IGHD4-17*01>3_IGHJ6*01	2679	V2-13_IGLJ2*01	849	1454
2490	VH3-23_IGHD4-23*01>2_IGHJ6*01	2680	V2-13_IGLJ2*01	849	1454
2491	VH3-23_IGHD4-23*01>3_IGHJ6*01	2681	V2-13_IGLJ2*01	849	1454
2492	VH3-23_IGHD5-5*01 (2) >1_IGHJ6*01	2682	V2-13_IGLJ2*01	849	1454
2493	VH3-23_IGHD5-5*01 (2) >2_IGHJ6*01	2683	V2-13_IGLJ2*01	849	1454
2494	VH3-23_IGHD5-5*01 (2) >3_IGHJ6*01	2684	V2-13_IGLJ2*01	849	1454
2495	VH3-23_IGHD5-12*01>1_IGHJ6*01	2685	V2-13_IGLJ2*01	849	1454
2496	VH3-23_IGHD5-12*01>3_IGHJ6*01	2686	V2-13_IGLJ2*01	849	1454
2497	VH3-23_IGHD5-18*01 (2) >1_IGHJ6*01	2687	V2-13_IGLJ2*01	849	1454
2498	VH3-23_IGHD5-18*01 (2) >2_IGHJ6*01	2688	V2-13_IGLJ2*01	849	1454
2499	VH3-23_IGHD5-18*01 (2) >3_IGHJ6*01	2689	V2-13_IGLJ2*01	849	1454
2500	VH3-23_IGHD5-24*01>1_IGHJ6*01	2690	V2-13_IGLJ2*01	849	1454
2501	VH3-23_IGHD5-24*01>3_IGHJ6*01	2691	V2-13_IGLJ2*01	849	1454
2502	VH3-23_IGHD6-6*01>1_IGHJ6*01	2692	V2-13_IGLJ2*01	849	1454
2503	VH3-23_IGHD1-1*01>1'_IGHJ6*01	2702	V2-13_IGLJ2*01	849	1454
2504	VH3-23_IGHD1-1*01>2'_IGHJ6*01	2703	V2-13_IGLJ2*01	849	1454
2505	VH3-23_IGHD1-1*01>3'_IGHJ6*01	2704	V2-13_IGLJ2*01	849	1454
2506	VH3-23_IGHD1-7*01>1'_IGHJ6*01	2705	V2-13_IGLJ2*01	849	1454
2507	VH3-23_IGHD1-7*01>3'_IGHJ6*01	2706	V2-13_IGLJ2*01	849	1454
2508	VH3-23_IGHD1-14*01>1'_IGHJ6*01	2707	V2-13_IGLJ2*01	849	1454
2509	VH3-23_IGHD1-14*01>2'_IGHJ6*01	2708	V2-13_IGLJ2*01	849	1454
2510	VH3-23_IGHD1-14*01>3'_IGHJ6*01	2709	V2-13_IGLJ2*01	849	1454
2511	VH3-23_IGHD1-20*01>1'_IGHJ6*01	2710	V2-13_IGLJ2*01	849	1454
2512	VH3-23_IGHD1-20*01>2'_IGHJ6*01	2711	V2-13_IGLJ2*01	849	1454
2513	VH3-23_IGHD1-20*01>3'_IGHJ6*01	2712	V2-13_IGLJ2*01	849	1454

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
2514	VH3-23_IGHD1-26*01>1'_IGHJ6*01	2713	V2-13_IGLJ2*01	849	1454
2515	VH3-23_IGHD1-26*01>1_IGHJ6*01_B	2714	V2-13_IGLJ2*01	849	1454
2516	VH3-23_IGHD2-2*01>2_IGHJ6*01_B	2715	V2-13_IGLJ2*01	849	1454
2517	VH3-23_IGHD2-2*01>3'_IGHJ6*01	2716	V2-13_IGLJ2*01	849	1454
2518	VH3-23_IGHD2-8*01>1'_IGHJ6*01	2717	V2-13_IGLJ2*01	849	1454
2519	VH3-23_IGHD2-15*01>1'_IGHJ6*01	2718	V2-13_IGLJ2*01	849	1454
2520	VH3-23_IGHD2-15*01>3'_IGHJ6*01	2719	V2-13_IGLJ2*01	849	1454
2521	VH3-23_IGHD2-21*01>1'_IGHJ6*01	2720	V2-13_IGLJ2*01	849	1454
2522	VH3-23_IGHD2-21*01>3'_IGHJ6*01	2721	V2-13_IGLJ2*01	849	1454
2523	VH3-23_IGHD3-3*01>1'_IGHJ6*01	2722	V2-13_IGLJ2*01	849	1454
2524	VH3-23_IGHD3-3*01>3'_IGHJ6*01	2723	V2-13_IGLJ2*01	849	1454
2525	VH3-23_IGHD3-9*01>1'_IGHJ6*01	2724	V2-13_IGLJ2*01	849	1454
2526	VH3-23_IGHD3-9*01>3'_IGHJ6*01	2725	V2-13_IGLJ2*01	849	1454
2527	VH3-23_IGHD3-10*01>1'_IGHJ6*01	2726	V2-13_IGLJ2*01	849	1454
2528	VH3-23_IGHD3-10*01>3'_IGHJ6*01	2727	V2-13_IGLJ2*01	849	1454
2529	VH3-23_IGHD3-16*01>1'_IGHJ6*01	2728	V2-13_IGLJ2*01	849	1454
2530	VH3-23_IGHD3-16*01>3'_IGHJ6*01	2729	V2-13_IGLJ2*01	849	1454
2531	VH3-23_IGHD3-22*01>1'_IGHJ6*01	2730	V2-13_IGLJ2*01	849	1454
2532	VH3-23_IGHD4-4*01 (1) >1'_IGHJ6*01	2731	V2-13_IGLJ2*01	849	1454
2533	VH3-23_IGHD4-4*01 (1) >3'_IGHJ6*01	2732	V2-13_IGLJ2*01	849	1454
2534	VH3-23_IGHD4-11*01 (1) >1'_IGHJ6*01	2733	V2-13_IGLJ2*01	849	1454
2535	VH3-23_IGHD4-11*01 (1) >3'_IGHJ6*01	2734	V2-13_IGLJ2*01	849	1454
2536	VH3-23_IGHD4-17*01>1'_IGHJ6*01	2735	V2-13_IGLJ2*01	849	1454
2537	VH3-23_IGHD4-17*01>3'_IGHJ6*01	2736	V2-13_IGLJ2*01	849	1454
2538	VH3-23_IGHD4-23*01>1'_IGHJ6*01	2737	V2-13_IGLJ2*01	849	1454
2539	VH3-23_IGHD4-23*01>3'_IGHJ6*01	2738	V2-13_IGLJ2*01	849	1454
2540	VH3-23_IGHD5-5*01 (2) >1'_IGHJ6*01	2739	V2-13_IGLJ2*01	849	1454
2541	VH3-23_IGHD5-5*01 (2) >3'_IGHJ6*01	2740	V2-13_IGLJ2*01	849	1454
2542	VH3-23_IGHD5-12*01>1'_IGHJ6*01	2741	V2-13_IGLJ2*01	849	1454
2543	VH3-23_IGHD5-12*01>3'_IGHJ6*01	2742	V2-13_IGLJ2*01	849	1454
2544	VH3-23_IGHD5-18*01 (2) >1'_IGHJ6*01	2743	V2-13_IGLJ2*01	849	1454
2545	VH3-23_IGHD5-18*01 (2) >3'_IGHJ6*01	2744	V2-13_IGLJ2*01	849	1454
2546	VH3-23_IGHD5-24*01>1'_IGHJ6*01	2745	V2-13_IGLJ2*01	849	1454
2547	VH3-23_IGHD5-24*01>3'_IGHJ6*01	2746	V2-13_IGLJ2*01	849	1454
2548	VH3-23_IGHD6-6*01>1'_IGHJ6*01	2747	V2-13_IGLJ2*01	849	1454
2549	VH3-23_IGHD6-6*01>2'_IGHJ6*01	2748	V2-13_IGLJ2*01	849	1454
2550	VH3-23_IGHD6-6*01>3'_IGHJ6*01	2749	V2-13_IGLJ2*01	849	1454
2551	VH3-23_IGHD1-1*01>1_IGHJ6*01	2645	V2-14_IGLJ4*01	850	1455
2552	VH3-23_IGHD1-1*01>2_IGHJ6*01	2646	V2-14_IGLJ4*01	850	1455
2553	VH3-23_IGHD1-1*01>3_IGHJ6*01	2647	V2-14_IGLJ4*01	850	1455
2554	VH3-23_IGHD1-7*01>1_IGHJ6*01	2648	V2-14_IGLJ4*01	850	1455
2555	VH3-23_IGHD1-7*01>3_IGHJ6*01	2649	V2-14_IGLJ4*01	850	1455
2556	VH3-23_IGHD1-14*01>1_IGHJ6*01	2650	V2-14_IGLJ4*01	850	1455
2557	VH3-23_IGHD1-14*01>3_IGHJ6*01	2651	V2-14_IGLJ4*01	850	1455

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
2558	VH3-23_IGHD1-20*01>1_IGHJ6*01	2652	V2-14_IGLJ4*01	850	1455
2559	VH3-23_IGHD1-20*01>3_IGHJ6*01	2653	V2-14_IGLJ4*01	850	1455
2560	VH3-23_IGHD1-26*01>1_IGHJ6*01	2654	V2-14_IGLJ4*01	850	1455
2561	VH3-23_IGHD1-26*01>3_IGHJ6*01	2655	V2-14_IGLJ4*01	850	1455
2562	VH3-23_IGHD2-2*01>2_IGHJ6*01	2656	V2-14_IGLJ4*01	850	1455
2563	VH3-23_IGHD2-2*01>3_IGHJ6*01	2657	V2-14_IGLJ4*01	850	1455
2564	VH3-23_IGHD2-8*01>2_IGHJ6*01	2658	V2-14_IGLJ4*01	850	1455
2565	VH3-23_IGHD2-8*01>3_IGHJ6*01	2659	V2-14_IGLJ4*01	850	1455
2566	VH3-23_IGHD2-15*01>2_IGHJ6*01	2660	V2-14_IGLJ4*01	850	1455
2567	VH3-23_IGHD2-15*01>3_IGHJ6*01	2661	V2-14_IGLJ4*01	850	1455
2568	VH3-23_IGHD2-21*01>2_IGHJ6*01	2662	V2-14_IGLJ4*01	850	1455
2569	VH3-23_IGHD2-21*01>3_IGHJ6*01	2663	V2-14_IGLJ4*01	850	1455
2570	VH3-23_IGHD3-3*01>1_IGHJ6*01	2664	V2-14_IGLJ4*01	850	1455
2571	VH3-23_IGHD3-3*01>2_IGHJ6*01	2665	V2-14_IGLJ4*01	850	1455
2572	VH3-23_IGHD3-3*01>3_IGHJ6*01	2666	V2-14_IGLJ4*01	850	1455
2573	VH3-23_IGHD3-9*01>2_IGHJ6*01	2667	V2-14_IGLJ4*01	850	1455
2574	VH3-23_IGHD3-10*01>2_IGHJ6*01	2668	V2-14_IGLJ4*01	850	1455
2575	VH3-23_IGHD3-10*01>3_IGHJ6*01	2669	V2-14_IGLJ4*01	850	1455
2576	VH3-23_IGHD3-16*01>2_IGHJ6*01	2670	V2-14_IGLJ4*01	850	1455
2577	VH3-23_IGHD3-16*01>3_IGHJ6*01	2671	V2-14_IGLJ4*01	850	1455
2578	VH3-23_IGHD3-22*01>2_IGHJ6*01	2672	V2-14_IGLJ4*01	850	1455
2579	VH3-23_IGHD3-22*01>3_IGHJ6*01	2673	V2-14_IGLJ4*01	850	1455
2580	VH3-23_IGHD4-4*01 (1) >2_IGHJ6*01	2674	V2-14_IGLJ4*01	850	1455
2581	VH3-23_IGHD4-4*01 (1) >3_IGHJ6*01	2675	V2-14_IGLJ4*01	850	1455
2582	VH3-23_IGHD4-11*01 (1) >2_IGHJ6*01	2676	V2-14_IGLJ4*01	850	1455
2583	VH3-23_IGHD4-11*01 (1) >3_IGHJ6*01	2677	V2-14_IGLJ4*01	850	1455
2584	VH3-23_IGHD4-17*01>2_IGHJ6*01	2678	V2-14_IGLJ4*01	850	1455
2585	VH3-23_IGHD4-17*01>3_IGHJ6*01	2679	V2-14_IGLJ4*01	850	1455
2586	VH3-23_IGHD4-23*01>2_IGHJ6*01	2680	V2-14_IGLJ4*01	850	1455
2587	VH3-23_IGHD4-23*01>3_IGHJ6*01	2681	V2-14_IGLJ4*01	850	1455
2588	VH3-23_IGHD5-5*01 (2) >1_IGHJ6*01	2682	V2-14_IGLJ4*01	850	1455
2589	VH3-23_IGHD5-5*01 (2) >2_IGHJ6*01	2683	V2-14_IGLJ4*01	850	1455
2590	VH3-23_IGHD5-5*01 (2) >3_IGHJ6*01	2684	V2-14_IGLJ4*01	850	1455
2591	VH3-23_IGHD5-12*01>1_IGHJ6*01	2685	V2-14_IGLJ4*01	850	1455
2592	VH3-23_IGHD5-12*01>3_IGHJ6*01	2686	V2-14_IGLJ4*01	850	1455
2593	VH3-23_IGHD5-18*01 (2) >1_IGHJ6*01	2687	V2-14_IGLJ4*01	850	1455
2594	VH3-23_IGHD5-18*01 (2) >2_IGHJ6*01	2688	V2-14_IGLJ4*01	850	1455
2595	VH3-23_IGHD5-18*01 (2) >3_IGHJ6*01	2689	V2-14_IGLJ4*01	850	1455
2596	VH3-23_IGHD5-24*01>1_IGHJ6*01	2690	V2-14_IGLJ4*01	850	1455
2597	VH3-23_IGHD5-24*01>3_IGHJ6*01	2691	V2-14_IGLJ4*01	850	1455
2598	VH3-23_IGHD6-6*01>1_IGHJ6*01	2692	V2-14_IGLJ4*01	850	1455
2599	VH3-23_IGHD1-1*01>1'_IGHJ6*01	2702	V2-14_IGLJ4*01	850	1455
2600	VH3-23_IGHD1-1*01>2'_IGHJ6*01	2703	V2-14_IGLJ4*01	850	1455
2601	VH3-23_IGHD1-1*01>3'_IGHJ6*01	2704	V2-14_IGLJ4*01	850	1455

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
2602	VH3-23_IGHD1-7*01>1'_IGHJ6*01	2705	V2-14_IGLJ4*01	850	1455
2603	VH3-23_IGHD1-7*01>3'_IGHJ6*01	2706	V2-14_IGLJ4*01	850	1455
2604	VH3-23_IGHD1-14*01>1'_IGHJ6*01	2707	V2-14_IGLJ4*01	850	1455
2605	VH3-23_IGHD1-14*01>2'_IGHJ6*01	2708	V2-14_IGLJ4*01	850	1455
2606	VH3-23_IGHD1-14*01>3'_IGHJ6*01	2709	V2-14_IGLJ4*01	850	1455
2607	VH3-23_IGHD1-20*01>1'_IGHJ6*01	2710	V2-14_IGLJ4*01	850	1455
2608	VH3-23_IGHD1-20*01>2'_IGHJ6*01	2711	V2-14_IGLJ4*01	850	1455
2609	VH3-23_IGHD1-20*01>3'_IGHJ6*01	2712	V2-14_IGLJ4*01	850	1455
2610	VH3-23_IGHD1-26*01>1'_IGHJ6*01	2713	V2-14_IGLJ4*01	850	1455
2611	VH3-23_IGHD1-26*01>1_IGHJ6*01_B	2714	V2-14_IGLJ4*01	850	1455
2612	VH3-23_IGHD2-2*01>2_IGHJ6*01_B	2715	V2-14_IGLJ4*01	850	1455
2613	VH3-23_IGHD2-2*01>3'_IGHJ6*01	2716	V2-14_IGLJ4*01	850	1455
2614	VH3-23_IGHD2-8*01>1'_IGHJ6*01	2717	V2-14_IGLJ4*01	850	1455
2615	VH3-23_IGHD2-15*01>1'_IGHJ6*01	2718	V2-14_IGLJ4*01	850	1455
2616	VH3-23_IGHD2-15*01>3'_IGHJ6*01	2719	V2-14_IGLJ4*01	850	1455
2617	VH3-23_IGHD2-21*01>1'_IGHJ6*01	2720	V2-14_IGLJ4*01	850	1455
2618	VH3-23_IGHD2-21*01>3'_IGHJ6*01	2721	V2-14_IGLJ4*01	850	1455
2619	VH3-23_IGHD3-3*01>1'_IGHJ6*01	2722	V2-14_IGLJ4*01	850	1455
2620	VH3-23_IGHD3-3*01>3'_IGHJ6*01	2723	V2-14_IGLJ4*01	850	1455
2621	VH3-23_IGHD3-9*01>1'_IGHJ6*01	2724	V2-14_IGLJ4*01	850	1455
2622	VH3-23_IGHD3-9*01>3'_IGHJ6*01	2725	V2-14_IGLJ4*01	850	1455
2623	VH3-23_IGHD3-10*01>1'_IGHJ6*01	2726	V2-14_IGLJ4*01	850	1455
2624	VH3-23_IGHD3-10*01>3'_IGHJ6*01	2727	V2-14_IGLJ4*01	850	1455
2625	VH3-23_IGHD3-16*01>1'_IGHJ6*01	2728	V2-14_IGLJ4*01	850	1455
2626	VH3-23_IGHD3-16*01>3'_IGHJ6*01	2729	V2-14_IGLJ4*01	850	1455
2627	VH3-23_IGHD3-22*01>1'_IGHJ6*01	2730	V2-14_IGLJ4*01	850	1455
2628	VH3-23_IGHD4-4*01 (1) >1'_IGHJ6*01	2731	V2-14_IGLJ4*01	850	1455
2629	VH3-23_IGHD4-4*01 (1) >3'_IGHJ6*01	2732	V2-14_IGLJ4*01	850	1455
2630	VH3-23_IGHD4-11*01 (1) >1'_IGHJ6*01	2733	V2-14_IGLJ4*01	850	1455
2631	VH3-23_IGHD4-11*01 (1) >3'_IGHJ6*01	2734	V2-14_IGLJ4*01	850	1455
2632	VH3-23_IGHD4-17*01>1'_IGHJ6*01	2735	V2-14_IGLJ4*01	850	1455
2633	VH3-23_IGHD4-17*01>3'_IGHJ6*01	2736	V2-14_IGLJ4*01	850	1455
2634	VH3-23_IGHD4-23*01>1'_IGHJ6*01	2737	V2-14_IGLJ4*01	850	1455
2635	VH3-23_IGHD4-23*01>3'_IGHJ6*01	2738	V2-14_IGLJ4*01	850	1455
2636	VH3-23_IGHD5-5*01 (2) >1'_IGHJ6*01	2739	V2-14_IGLJ4*01	850	1455
2637	VH3-23_IGHD5-5*01 (2) >3'_IGHJ6*01	2740	V2-14_IGLJ4*01	850	1455
2638	VH3-23_IGHD5-12*01>1'_IGHJ6*01	2741	V2-14_IGLJ4*01	850	1455
2639	VH3-23_IGHD5-12*01>3'_IGHJ6*01	2742	V2-14_IGLJ4*01	850	1455
2640	VH3-23_IGHD5-18*01 (2) >1'_IGHJ6*01	2743	V2-14_IGLJ4*01	850	1455
2641	VH3-23_IGHD5-18*01 (2) >3'_IGHJ6*01	2744	V2-14_IGLJ4*01	850	1455
2642	VH3-23_IGHD5-24*01>1'_IGHJ6*01	2745	V2-14_IGLJ4*01	850	1455
2643	VH3-23_IGHD5-24*01>3'_IGHJ6*01	2746	V2-14_IGLJ4*01	850	1455
2644	VH3-23_IGHD6-6*01>1'_IGHJ6*01	2747	V2-14_IGLJ4*01	850	1455
2645	VH3-23_IGHD6-6*01>2'_IGHJ6*01	2748	V2-14_IGLJ4*01	850	1455

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
2646	VH3-23_IGHD6-6*01>3'_IGHJ6*01	2749	V2-14_IGLJ4*01	850	1455
2647	VH3-23_IGHD1-1*01>1_IGHJ6*01	2645	V2-15_IGLJ7*01	850	1455
2648	VH3-23_IGHD1-1*01>2_IGHJ6*01	2646	V2-15_IGLJ7*01	851	1456
2649	VH3-23_IGHD1-1*01>3_IGHJ6*01	2647	V2-15_IGLJ7*01	851	1456
2650	VH3-23_IGHD1-7*01>1_IGHJ6*01	2648	V2-15_IGLJ7*01	851	1456
2651	VH3-23_IGHD1-7*01>3_IGHJ6*01	2649	V2-15_IGLJ7*01	851	1456
2652	VH3-23_IGHD1-14*01>1_IGHJ6*01	2650	V2-15_IGLJ7*01	851	1456
2653	VH3-23_IGHD1-14*01>3_IGHJ6*01	2651	V2-15_IGLJ7*01	851	1456
2654	VH3-23_IGHD1-20*01>1_IGHJ6*01	2652	V2-15_IGLJ7*01	851	1456
2655	VH3-23_IGHD1-20*01>3_IGHJ6*01	2653	V2-15_IGLJ7*01	851	1456
2656	VH3-23_IGHD1-26*01>1_IGHJ6*01	2654	V2-15_IGLJ7*01	851	1456
2657	VH3-23_IGHD1-26*01>3_IGHJ6*01	2655	V2-15_IGLJ7*01	851	1456
2658	VH3-23_IGHD2-2*01>2_IGHJ6*01	2656	V2-15_IGLJ7*01	851	1456
2659	VH3-23_IGHD2-2*01>3_IGHJ6*01	2657	V2-15_IGLJ7*01	851	1456
2660	VH3-23_IGHD2-8*01>2_IGHJ6*01	2658	V2-15_IGLJ7*01	851	1456
2661	VH3-23_IGHD2-8*01>3_IGHJ6*01	2659	V2-15_IGLJ7*01	851	1456
2662	VH3-23_IGHD2-15*01>2_IGHJ6*01	2660	V2-15_IGLJ7*01	851	1456
2663	VH3-23_IGHD2-15*01>3_IGHJ6*01	2661	V2-15_IGLJ7*01	851	1456
2664	VH3-23_IGHD2-21*01>2_IGHJ6*01	2662	V2-15_IGLJ7*01	851	1456
2665	VH3-23_IGHD2-21*01>3_IGHJ6*01	2663	V2-15_IGLJ7*01	851	1456
2666	VH3-23_IGHD3-3*01>1_IGHJ6*01	2664	V2-15_IGLJ7*01	851	1456
2667	VH3-23_IGHD3-3*01>2_IGHJ6*01	2665	V2-15_IGLJ7*01	851	1456
2668	VH3-23_IGHD3-3*01>3_IGHJ6*01	2666	V2-15_IGLJ7*01	851	1456
2669	VH3-23_IGHD3-9*01>2_IGHJ6*01	2667	V2-15_IGLJ7*01	851	1456
2670	VH3-23_IGHD3-10*01>2_IGHJ6*01	2668	V2-15_IGLJ7*01	851	1456
2671	VH3-23_IGHD3-10*01>3_IGHJ6*01	2669	V2-15_IGLJ7*01	851	1456
2672	VH3-23_IGHD3-16*01>2_IGHJ6*01	2670	V2-15_IGLJ7*01	851	1456
2673	VH3-23_IGHD3-16*01>3_IGHJ6*01	2671	V2-15_IGLJ7*01	851	1456
2674	VH3-23_IGHD3-22*01>2_IGHJ6*01	2672	V2-15_IGLJ7*01	851	1456
2675	VH3-23_IGHD3-22*01>3_IGHJ6*01	2673	V2-15_IGLJ7*01	851	1456
2676	VH3-23_IGHD4-4*01 (1) >2_IGHJ6*01	2674	V2-15_IGLJ7*01	851	1456
2677	VH3-23_IGHD4-4*01 (1) >3_IGHJ6*01	2675	V2-15_IGLJ7*01	851	1456
2678	VH3-23_IGHD4-11*01 (1) >2_IGHJ6*01	2676	V2-15_IGLJ7*01	851	1456
2679	VH3-23_IGHD4-11*01 (1) >3_IGHJ6*01	2677	V2-15_IGLJ7*01	851	1456
2680	VH3-23_IGHD4-17*01>2_IGHJ6*01	2678	V2-15_IGLJ7*01	851	1456
2681	VH3-23_IGHD4-17*01>3_IGHJ6*01	2679	V2-15_IGLJ7*01	851	1456
2682	VH3-23_IGHD4-23*01>2_IGHJ6*01	2680	V2-15_IGLJ7*01	851	1456
2683	VH3-23_IGHD4-23*01>3_IGHJ6*01	2681	V2-15_IGLJ7*01	851	1456
2684	VH3-23_IGHD5-5*01 (2) >1_IGHJ6*01	2682	V2-15_IGLJ7*01	851	1456
2685	VH3-23_IGHD5-5*01 (2) >2_IGHJ6*01	2683	V2-15_IGLJ7*01	851	1456
2686	VH3-23_IGHD5-5*01 (2) >3_IGHJ6*01	2684	V2-15_IGLJ7*01	851	1456
2687	VH3-23_IGHD5-12*01>1_IGHJ6*01	2685	V2-15_IGLJ7*01	851	1456
2688	VH3-23_IGHD5-12*01>3_IGHJ6*01	2686	V2-15_IGLJ7*01	851	1456
2689	VH3-23_IGHD5-18*01 (2) >1_IGHJ6*01	2687	V2-15_IGLJ7*01	851	1456

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
2690	VH3-23_IGHD5-18*01 (2) >2_IGHJ6*01	2688	V2-15_IGLJ7*01	851	1456
2691	VH3-23_IGHD5-18*01 (2) >3_IGHJ6*01	2689	V2-15_IGLJ7*01	851	1456
2692	VH3-23_IGHD5-24*01>1_IGHJ6*01	2690	V2-15_IGLJ7*01	851	1456
2693	VH3-23_IGHD5-24*01>3_IGHJ6*01	2691	V2-15_IGLJ7*01	851	1456
2694	VH3-23_IGHD6-6*01>1_IGHJ6*01	2692	V2-15_IGLJ7*01	851	1456
2695	VH3-23_IGHD1-1*01>1'_IGHJ6*01	2702	V2-15_IGLJ7*01	851	1456
2696	VH3-23_IGHD1-1*01>2'_IGHJ6*01	2703	V2-15_IGLJ7*01	851	1456
2697	VH3-23_IGHD1-1*01>3'_IGHJ6*01	2704	V2-15_IGLJ7*01	851	1456
2698	VH3-23_IGHD1-7*01>1'_IGHJ6*01	2705	V2-15_IGLJ7*01	851	1456
2699	VH3-23_IGHD1-7*01>3'_IGHJ6*01	2706	V2-15_IGLJ7*01	851	1456
2700	VH3-23_IGHD1-14*01>1'_IGHJ6*01	2707	V2-15_IGLJ7*01	851	1456
2701	VH3-23_IGHD1-14*01>2'_IGHJ6*01	2708	V2-15_IGLJ7*01	851	1456
2702	VH3-23_IGHD1-14*01>3'_IGHJ6*01	2709	V2-15_IGLJ7*01	851	1456
2703	VH3-23_IGHD1-20*01>1'_IGHJ6*01	2710	V2-15_IGLJ7*01	851	1456
2704	VH3-23_IGHD1-20*01>2'_IGHJ6*01	2711	V2-15_IGLJ7*01	851	1456
2705	VH3-23_IGHD1-20*01>3'_IGHJ6*01	2712	V2-15_IGLJ7*01	851	1456
2706	VH3-23_IGHD1-26*01>1'_IGHJ6*01	2713	V2-15_IGLJ7*01	851	1456
2707	VH3-23_IGHD1-26*01>1_IGHJ6*01_B	2714	V2-15_IGLJ7*01	851	1456
2708	VH3-23_IGHD2-2*01>2_IGHJ6*01_B	2715	V2-15_IGLJ7*01	851	1456
2709	VH3-23_IGHD2-2*01>3'_IGHJ6*01	2716	V2-15_IGLJ7*01	851	1456
2710	VH3-23_IGHD2-8*01>1'_IGHJ6*01	2717	V2-15_IGLJ7*01	851	1456
2711	VH3-23_IGHD2-15*01>1'_IGHJ6*01	2718	V2-15_IGLJ7*01	851	1456
2712	VH3-23_IGHD2-15*01>3'_IGHJ6*01	2719	V2-15_IGLJ7*01	851	1456
2713	VH3-23_IGHD2-21*01>1'_IGHJ6*01	2720	V2-15_IGLJ7*01	851	1456
2714	VH3-23_IGHD2-21*01>3'_IGHJ6*01	2721	V2-15_IGLJ7*01	851	1456
2715	VH3-23_IGHD3-3*01>1'_IGHJ6*01	2722	V2-15_IGLJ7*01	851	1456
2716	VH3-23_IGHD3-3*01>3'_IGHJ6*01	2723	V2-15_IGLJ7*01	851	1456
2717	VH3-23_IGHD3-9*01>1'_IGHJ6*01	2724	V2-15_IGLJ7*01	851	1456
2718	VH3-23_IGHD3-9*01>3'_IGHJ6*01	2725	V2-15_IGLJ7*01	851	1456
2719	VH3-23_IGHD3-10*01>1'_IGHJ6*01	2726	V2-15_IGLJ7*01	851	1456
2720	VH3-23_IGHD3-10*01>3'_IGHJ6*01	2727	V2-15_IGLJ7*01	851	1456
2721	VH3-23_IGHD3-16*01>1'_IGHJ6*01	2728	V2-15_IGLJ7*01	851	1456
2722	VH3-23_IGHD3-16*01>3'_IGHJ6*01	2729	V2-15_IGLJ7*01	851	1456
2723	VH3-23_IGHD3-22*01>1'_IGHJ6*01	2730	V2-15_IGLJ7*01	851	1456
2724	VH3-23_IGHD4-4*01 (1) >1'_IGHJ6*01	2731	V2-15_IGLJ7*01	851	1456
2725	VH3-23_IGHD4-4*01 (1) >3'_IGHJ6*01	2732	V2-15_IGLJ7*01	851	1456
2726	VH3-23_IGHD4-11*01 (1) >1'_IGHJ6*01	2733	V2-15_IGLJ7*01	851	1456
2727	VH3-23_IGHD4-11*01 (1) >3'_IGHJ6*01	2734	V2-15_IGLJ7*01	851	1456
2728	VH3-23_IGHD4-17*01>1'_IGHJ6*01	2735	V2-15_IGLJ7*01	851	1456
2729	VH3-23_IGHD4-17*01>3'_IGHJ6*01	2736	V2-15_IGLJ7*01	851	1456
2730	VH3-23_IGHD4-23*01>1'_IGHJ6*01	2737	V2-15_IGLJ7*01	851	1456
2731	VH3-23_IGHD4-23*01>3'_IGHJ6*01	2738	V2-15_IGLJ7*01	851	1456
2732	VH3-23_IGHD5-5*01 (2) >1'_IGHJ6*01	2739	V2-15_IGLJ7*01	851	1456
2733	VH3-23_IGHD5-5*01 (2) >3'_IGHJ6*01	2740	V2-15_IGLJ7*01	851	1456

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
2734	VH3-23_IGHD5-12*01>1'_IGHJ6*01	2741	V2-15_IGLJ7*01	851	1456
2735	VH3-23_IGHD5-12*01>3'_IGHJ6*01	2742	V2-15_IGLJ7*01	851	1456
2736	VH3-23_IGHD5-18*01 (2) >1'_IGHJ6*01	2743	V2-15_IGLJ7*01	851	1456
2737	VH3-23_IGHD5-18*01 (2) >3'_IGHJ6*01	2744	V2-15_IGLJ7*01	851	1456
2738	VH3-23_IGHD5-24*01>1'_IGHJ6*01	2745	V2-15_IGLJ7*01	851	1456
2739	VH3-23_IGHD5-24*01>3'_IGHJ6*01	2746	V2-15_IGLJ7*01	851	1456
2740	VH3-23_IGHD6-6*01>1'_IGHJ6*01	2747	V2-15_IGLJ7*01	851	1456
2741	VH3-23_IGHD6-6*01>2'_IGHJ6*01	2748	V2-15_IGLJ7*01	851	1456
2742	VH3-23_IGHD6-6*01>3'_IGHJ6*01	2749	V2-15_IGLJ7*01	851	1456
2743	VH3-23_IGHD1-1*01>1_IGHJ6*01	2645	V2-17_IGLJ2*01	852	1457
2744	VH3-23_IGHD1-1*01>2_IGHJ6*01	2646	V2-17_IGLJ2*01	852	1457
2745	VH3-23_IGHD1-1*01>3_IGHJ6*01	2647	V2-17_IGLJ2*01	852	1457
2746	VH3-23_IGHD1-7*01>1_IGHJ6*01	2648	V2-17_IGLJ2*01	852	1457
2747	VH3-23_IGHD1-7*01>3_IGHJ6*01	2649	V2-17_IGLJ2*01	852	1457
2748	VH3-23_IGHD1-14*01>1_IGHJ6*01	2650	V2-17_IGLJ2*01	852	1457
2749	VH3-23_IGHD1-14*01>3_IGHJ6*01	2651	V2-17_IGLJ2*01	852	1457
2750	VH3-23_IGHD1-20*01>1_IGHJ6*01	2652	V2-17_IGLJ2*01	852	1457
2751	VH3-23_IGHD1-20*01>3_IGHJ6*01	2653	V2-17_IGLJ2*01	852	1457
2752	VH3-23_IGHD1-26*01>1_IGHJ6*01	2654	V2-17_IGLJ2*01	852	1457
2753	VH3-23_IGHD1-26*01>3_IGHJ6*01	2655	V2-17_IGLJ2*01	852	1457
2754	VH3-23_IGHD2-2*01>2_IGHJ6*01	2656	V2-17_IGLJ2*01	852	1457
2755	VH3-23_IGHD2-2*01>3_IGHJ6*01	2657	V2-17_IGLJ2*01	852	1457
2756	VH3-23_IGHD2-8*01>2_IGHJ6*01	2658	V2-17_IGLJ2*01	852	1457
2757	VH3-23_IGHD2-8*01>3_IGHJ6*01	2659	V2-17_IGLJ2*01	852	1457
2758	VH3-23_IGHD2-15*01>2_IGHJ6*01	2660	V2-17_IGLJ2*01	852	1457
2759	VH3-23_IGHD2-15*01>3_IGHJ6*01	2661	V2-17_IGLJ2*01	852	1457
2760	VH3-23_IGHD2-21*01>2_IGHJ6*01	2662	V2-17_IGLJ2*01	852	1457
2761	VH3-23_IGHD2-21*01>3_IGHJ6*01	2663	V2-17_IGLJ2*01	852	1457
2762	VH3-23_IGHD3-3*01>1_IGHJ6*01	2664	V2-17_IGLJ2*01	852	1457
2763	VH3-23_IGHD3-3*01>2_IGHJ6*01	2665	V2-17_IGLJ2*01	852	1457
2764	VH3-23_IGHD3-3*01>3_IGHJ6*01	2666	V2-17_IGLJ2*01	852	1457
2765	VH3-23_IGHD3-9*01>2_IGHJ6*01	2667	V2-17_IGLJ2*01	852	1457
2766	VH3-23_IGHD3-10*01>2_IGHJ6*01	2668	V2-17_IGLJ2*01	852	1457
2767	VH3-23_IGHD3-10*01>3_IGHJ6*01	2669	V2-17_IGLJ2*01	852	1457
2768	VH3-23_IGHD3-16*01>2_IGHJ6*01	2670	V2-17_IGLJ2*01	852	1457
2769	VH3-23_IGHD3-16*01>3_IGHJ6*01	2671	V2-17_IGLJ2*01	852	1457
2770	VH3-23_IGHD3-22*01>2_IGHJ6*01	2672	V2-17_IGLJ2*01	852	1457
2771	VH3-23_IGHD3-22*01>3_IGHJ6*01	2673	V2-17_IGLJ2*01	852	1457
2772	VH3-23_IGHD4-4*01 (1) >2_IGHJ6*01	2674	V2-17_IGLJ2*01	852	1457
2773	VH3-23_IGHD4-4*01 (1) >3_IGHJ6*01	2675	V2-17_IGLJ2*01	852	1457
2774	VH3-23_IGHD4-11*01 (1) >2_IGHJ6*01	2676	V2-17_IGLJ2*01	852	1457
2775	VH3-23_IGHD4-11*01 (1) >3_IGHJ6*01	2677	V2-17_IGLJ2*01	852	1457
2776	VH3-23_IGHD4-17*01>2_IGHJ6*01	2678	V2-17_IGLJ2*01	852	1457
2777	VH3-23_IGHD4-17*01>3_IGHJ6*01	2679	V2-17_IGLJ2*01	852	1457

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
2778	VH3-23_IGHD4-23*01>2_IGHJ6*01	2680	V2-17_IGLJ2*01	852	1457
2779	VH3-23_IGHD4-23*01>3_IGHJ6*01	2681	V2-17_IGLJ2*01	852	1457
2780	VH3-23_IGHD5-5*01 (2) >1_IGHJ6*01	2682	V2-17_IGLJ2*01	852	1457
2781	VH3-23_IGHD5-5*01 (2) >2_IGHJ6*01	2683	V2-17_IGLJ2*01	852	1457
2782	VH3-23_IGHD5-5*01 (2) >3_IGHJ6*01	2684	V2-17_IGLJ2*01	852	1457
2783	VH3-23_IGHD5-12*01>1_IGHJ6*01	2685	V2-17_IGLJ2*01	852	1457
2784	VH3-23_IGHD5-12*01>3_IGHJ6*01	2686	V2-17_IGLJ2*01	852	1457
2785	VH3-23_IGHD5-18*01 (2) >1_IGHJ6*01	2687	V2-17_IGLJ2*01	852	1457
2786	VH3-23_IGHD5-18*01 (2) >2_IGHJ6*01	2688	V2-17_IGLJ2*01	852	1457
2787	VH3-23_IGHD5-18*01 (2) >3_IGHJ6*01	2689	V2-17_IGLJ2*01	852	1457
2788	VH3-23_IGHD5-24*01>1_IGHJ6*01	2690	V2-17_IGLJ2*01	852	1457
2789	VH3-23_IGHD5-24*01>3_IGHJ6*01	2691	V2-17_IGLJ2*01	852	1457
2790	VH3-23_IGHD6-6*01>1_IGHJ6*01	2692	V2-17_IGLJ2*01	852	1457
2791	VH3-23_IGHD1-1*01>1'_IGHJ6*01	2702	V2-17_IGLJ2*01	852	1457
2792	VH3-23_IGHD1-1*01>2'_IGHJ6*01	2703	V2-17_IGLJ2*01	852	1457
2793	VH3-23_IGHD1-1*01>3'_IGHJ6*01	2704	V2-17_IGLJ2*01	852	1457
2794	VH3-23_IGHD1-7*01>1'_IGHJ6*01	2705	V2-17_IGLJ2*01	852	1457
2795	VH3-23_IGHD1-7*01>3'_IGHJ6*01	2706	V2-17_IGLJ2*01	852	1457
2796	VH3-23_IGHD1-14*01>1'_IGHJ6*01	2707	V2-17_IGLJ2*01	852	1457
2797	VH3-23_IGHD1-14*01>2'_IGHJ6*01	2708	V2-17_IGLJ2*01	852	1457
2798	VH3-23_IGHD1-14*01>3'_IGHJ6*01	2709	V2-17_IGLJ2*01	852	1457
2799	VH3-23_IGHD1-20*01>1'_IGHJ6*01	2710	V2-17_IGLJ2*01	852	1457
2800	VH3-23_IGHD1-20*01>2'_IGHJ6*01	2711	V2-17_IGLJ2*01	852	1457
2801	VH3-23_IGHD1-20*01>3'_IGHJ6*01	2712	V2-17_IGLJ2*01	852	1457
2802	VH3-23_IGHD1-26*01>1'_IGHJ6*01	2713	V2-17_IGLJ2*01	852	1457
2803	VH3-23_IGHD1-26*01>1_IGHJ6*01_B	2714	V2-17_IGLJ2*01	852	1457
2804	VH3-23_IGHD2-2*01>2_IGHJ6*01_B	2715	V2-17_IGLJ2*01	852	1457
2805	VH3-23_IGHD2-2*01>3'_IGHJ6*01	2716	V2-17_IGLJ2*01	852	1457
2806	VH3-23_IGHD2-8*01>1'_IGHJ6*01	2717	V2-17_IGLJ2*01	852	1457
2807	VH3-23_IGHD2-15*01>1'_IGHJ6*01	2718	V2-17_IGLJ2*01	852	1457
2808	VH3-23_IGHD2-15*01>3'_IGHJ6*01	2719	V2-17_IGLJ2*01	852	1457
2809	VH3-23_IGHD2-21*01>1'_IGHJ6*01	2720	V2-17_IGLJ2*01	852	1457
2810	VH3-23_IGHD2-21*01>3'_IGHJ6*01	2721	V2-17_IGLJ2*01	852	1457
2811	VH3-23_IGHD3-3*01>1'_IGHJ6*01	2722	V2-17_IGLJ2*01	852	1457
2812	VH3-23_IGHD3-3*01>3'_IGHJ6*01	2723	V2-17_IGLJ2*01	852	1457
2813	VH3-23_IGHD3-9*01>1'_IGHJ6*01	2724	V2-17_IGLJ2*01	852	1457
2814	VH3-23_IGHD3-9*01>3'_IGHJ6*01	2725	V2-17_IGLJ2*01	852	1457
2815	VH3-23_IGHD3-10*01>1'_IGHJ6*01	2726	V2-17_IGLJ2*01	852	1457
2816	VH3-23_IGHD3-10*01>3'_IGHJ6*01	2727	V2-17_IGLJ2*01	852	1457
2817	VH3-23_IGHD3-16*01>1'_IGHJ6*01	2728	V2-17_IGLJ2*01	852	1457
2818	VH3-23_IGHD3-16*01>3'_IGHJ6*01	2729	V2-17_IGLJ2*01	852	1457
2819	VH3-23_IGHD3-22*01>1'_IGHJ6*01	2730	V2-17_IGLJ2*01	852	1457
2820	VH3-23_IGHD4-4*01 (1) >1'_IGHJ6*01	2731	V2-17_IGLJ2*01	852	1457
2821	VH3-23_IGHD4-4*01 (1) >3'_IGHJ6*01	2732	V2-17_IGLJ2*01	852	1457

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
2822	VH3-23_IGHD4-11*01 (1) >1'_IGHJ6*01	2733	V2-17_IGLJ2*01	852	1457
2823	VH3-23_IGHD4-11*01 (1) >3'_IGHJ6*01	2734	V2-17_IGLJ2*01	852	1457
2824	VH3-23_IGHD4-17*01>1'_IGHJ6*01	2735	V2-17_IGLJ2*01	852	1457
2825	VH3-23_IGHD4-17*01>3'_IGHJ6*01	2736	V2-17_IGLJ2*01	852	1457
2826	VH3-23_IGHD4-23*01>1'_IGHJ6*01	2737	V2-17_IGLJ2*01	852	1457
2827	VH3-23_IGHD4-23*01>3'_IGHJ6*01	2738	V2-17_IGLJ2*01	852	1457
2828	VH3-23_IGHD5-5*01 (2) >1'_IGHJ6*01	2739	V2-17_IGLJ2*01	852	1457
2829	VH3-23_IGHD5-5*01 (2) >3'_IGHJ6*01	2740	V2-17_IGLJ2*01	852	1457
2830	VH3-23_IGHD5-12*01>1'_IGHJ6*01	2741	V2-17_IGLJ2*01	852	1457
2831	VH3-23_IGHD5-12*01>3'_IGHJ6*01	2742	V2-17_IGLJ2*01	852	1457
2832	VH3-23_IGHD5-18*01 (2) >1'_IGHJ6*01	2743	V2-17_IGLJ2*01	852	1457
2833	VH3-23_IGHD5-18*01 (2) >3'_IGHJ6*01	2744	V2-17_IGLJ2*01	852	1457
2834	VH3-23_IGHD5-24*01>1'_IGHJ6*01	2745	V2-17_IGLJ2*01	852	1457
2835	VH3-23_IGHD5-24*01>3'_IGHJ6*01	2746	V2-17_IGLJ2*01	852	1457
2836	VH3-23_IGHD6-6*01>1'_IGHJ6*01	2747	V2-17_IGLJ2*01	852	1457
2837	VH3-23_IGHD6-6*01>2'_IGHJ6*01	2748	V2-17_IGLJ2*01	852	1457
2838	VH3-23_IGHD6-6*01>3'_IGHJ6*01	2749	V2-17_IGLJ2*01	852	1457
2839	VH3-23_IGHD1-1*01>1_IGHJ6*01	2645	V2-6_IGLJ4*01	854	1459
2840	VH3-23_IGHD1-1*01>2_IGHJ6*01	2646	V2-6_IGLJ4*01	854	1459
2841	VH3-23_IGHD1-1*01>3_IGHJ6*01	2647	V2-6_IGLJ4*01	854	1459
2842	VH3-23_IGHD1-7*01>1_IGHJ6*01	2648	V2-6_IGLJ4*01	854	1459
2843	VH3-23_IGHD1-7*01>3_IGHJ6*01	2649	V2-6_IGLJ4*01	854	1459
2844	VH3-23_IGHD1-14*01>1_IGHJ6*01	2650	V2-6_IGLJ4*01	854	1459
2845	VH3-23_IGHD1-14*01>3_IGHJ6*01	2651	V2-6_IGLJ4*01	854	1459
2846	VH3-23_IGHD1-20*01>1_IGHJ6*01	2652	V2-6_IGLJ4*01	854	1459
2847	VH3-23_IGHD1-20*01>3_IGHJ6*01	2653	V2-6_IGLJ4*01	854	1459
2848	VH3-23_IGHD1-26*01>1_IGHJ6*01	2654	V2-6_IGLJ4*01	854	1459
2849	VH3-23_IGHD1-26*01>3_IGHJ6*01	2655	V2-6_IGLJ4*01	854	1459
2850	VH3-23_IGHD2-2*01>2_IGHJ6*01	2656	V2-6_IGLJ4*01	854	1459
2851	VH3-23_IGHD2-2*01>3_IGHJ6*01	2657	V2-6_IGLJ4*01	854	1459
2852	VH3-23_IGHD2-8*01>2_IGHJ6*01	2658	V2-6_IGLJ4*01	854	1459
2853	VH3-23_IGHD2-8*01>3_IGHJ6*01	2659	V2-6_IGLJ4*01	854	1459
2854	VH3-23_IGHD2-15*01>2_IGHJ6*01	2660	V2-6_IGLJ4*01	854	1459
2855	VH3-23_IGHD2-15*01>3_IGHJ6*01	2661	V2-6_IGLJ4*01	854	1459
2856	VH3-23_IGHD2-21*01>2_IGHJ6*01	2662	V2-6_IGLJ4*01	854	1459
2857	VH3-23_IGHD2-21*01>3_IGHJ6*01	2663	V2-6_IGLJ4*01	854	1459
2858	VH3-23_IGHD3-3*01>1_IGHJ6*01	2664	V2-6_IGLJ4*01	854	1459
2859	VH3-23_IGHD3-3*01>2_IGHJ6*01	2665	V2-6_IGLJ4*01	854	1459
2860	VH3-23_IGHD3-3*01>3_IGHJ6*01	2666	V2-6_IGLJ4*01	854	1459
2861	VH3-23_IGHD3-9*01>2_IGHJ6*01	2667	V2-6_IGLJ4*01	854	1459
2862	VH3-23_IGHD3-10*01>2_IGHJ6*01	2668	V2-6_IGLJ4*01	854	1459
2863	VH3-23_IGHD3-10*01>3_IGHJ6*01	2669	V2-6_IGLJ4*01	854	1459
2864	VH3-23_IGHD3-16*01>2_IGHJ6*01	2670	V2-6_IGLJ4*01	854	1459
2865	VH3-23_IGHD3-16*01>3_IGHJ6*01	2671	V2-6_IGLJ4*01	854	1459

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
2866	VH3-23_IGHD3-22*01>2_IGHJ6*01	2672	V2-6_IGLJ4*01	854	1459
2867	VH3-23_IGHD3-22*01>3_IGHJ6*01	2673	V2-6_IGLJ4*01	854	1459
2868	VH3-23_IGHD4-4*01 (1) >2_IGHJ6*01	2674	V2-6_IGLJ4*01	854	1459
2869	VH3-23_IGHD4-4*01 (1) >3_IGHJ6*01	2675	V2-6_IGLJ4*01	854	1459
2870	VH3-23_IGHD4-11*01 (1) >2_IGHJ6*01	2676	V2-6_IGLJ4*01	854	1459
2871	VH3-23_IGHD4-11*01 (1) >3_IGHJ6*01	2677	V2-6_IGLJ4*01	854	1459
2872	VH3-23_IGHD4-17*01>2_IGHJ6*01	2678	V2-6_IGLJ4*01	854	1459
2873	VH3-23_IGHD4-17*01>3_IGHJ6*01	2679	V2-6_IGLJ4*01	854	1459
2874	VH3-23_IGHD4-23*01>2_IGHJ6*01	2680	V2-6_IGLJ4*01	854	1459
2875	VH3-23_IGHD4-23*01>3_IGHJ6*01	2681	V2-6_IGLJ4*01	854	1459
2876	VH3-23_IGHD5-5*01 (2) >1_IGHJ6*01	2682	V2-6_IGLJ4*01	854	1459
2877	VH3-23_IGHD5-5*01 (2) >2_IGHJ6*01	2683	V2-6_IGLJ4*01	854	1459
2878	VH3-23_IGHD5-5*01 (2) >3_IGHJ6*01	2684	V2-6_IGLJ4*01	854	1459
2879	VH3-23_IGHD5-12*01>1_IGHJ6*01	2685	V2-6_IGLJ4*01	854	1459
2880	VH3-23_IGHD5-12*01>3_IGHJ6*01	2686	V2-6_IGLJ4*01	854	1459
2881	VH3-23_IGHD5-18*01 (2) >1_IGHJ6*01	2687	V2-6_IGLJ4*01	854	1459
2882	VH3-23_IGHD5-18*01 (2) >2_IGHJ6*01	2688	V2-6_IGLJ4*01	854	1459
2883	VH3-23_IGHD5-18*01 (2) >3_IGHJ6*01	2689	V2-6_IGLJ4*01	854	1459
2884	VH3-23_IGHD5-24*01>1_IGHJ6*01	2690	V2-6_IGLJ4*01	854	1459
2885	VH3-23_IGHD5-24*01>3_IGHJ6*01	2691	V2-6_IGLJ4*01	854	1459
2886	VH3-23_IGHD6-6*01>1_IGHJ6*01	2692	V2-6_IGLJ4*01	854	1459
2887	VH3-23_IGHD1-1*01>1'_IGHJ6*01	2702	V2-6_IGLJ4*01	854	1459
2888	VH3-23_IGHD1-1*01>2'_IGHJ6*01	2703	V2-6_IGLJ4*01	854	1459
2889	VH3-23_IGHD1-1*01>3'_IGHJ6*01	2704	V2-6_IGLJ4*01	854	1459
2890	VH3-23_IGHD1-7*01>1'_IGHJ6*01	2705	V2-6_IGLJ4*01	854	1459
2891	VH3-23_IGHD1-7*01>3'_IGHJ6*01	2706	V2-6_IGLJ4*01	854	1459
2892	VH3-23_IGHD1-14*01>1'_IGHJ6*01	2707	V2-6_IGLJ4*01	854	1459
2893	VH3-23_IGHD1-14*01>2'_IGHJ6*01	2708	V2-6_IGLJ4*01	854	1459
2894	VH3-23_IGHD1-14*01>3'_IGHJ6*01	2709	V2-6_IGLJ4*01	854	1459
2895	VH3-23_IGHD1-20*01>1'_IGHJ6*01	2710	V2-6_IGLJ4*01	854	1459
2896	VH3-23_IGHD1-20*01>2'_IGHJ6*01	2711	V2-6_IGLJ4*01	854	1459
2897	VH3-23_IGHD1-20*01>3'_IGHJ6*01	2712	V2-6_IGLJ4*01	854	1459
2898	VH3-23_IGHD1-26*01>1'_IGHJ6*01	2713	V2-6_IGLJ4*01	854	1459
2899	VH3-23_IGHD1-26*01>1_IGHJ6*01_B	2714	V2-6_IGLJ4*01	854	1459
2900	VH3-23_IGHD2-2*01>2_IGHJ6*01_B	2715	V2-6_IGLJ4*01	854	1459
2901	VH3-23_IGHD2-2*01>3'_IGHJ6*01	2716	V2-6_IGLJ4*01	854	1459
2902	VH3-23_IGHD2-8*01>1'_IGHJ6*01	2717	V2-6_IGLJ4*01	854	1459
2903	VH3-23_IGHD2-15*01>1'_IGHJ6*01	2718	V2-6_IGLJ4*01	854	1459
2904	VH3-23_IGHD2-15*01>3'_IGHJ6*01	2719	V2-6_IGLJ4*01	854	1459
2905	VH3-23_IGHD2-21*01>1'_IGHJ6*01	2720	V2-6_IGLJ4*01	854	1459
2906	VH3-23_IGHD2-21*01>3'_IGHJ6*01	2721	V2-6_IGLJ4*01	854	1459
2907	VH3-23_IGHD3-3*01>1'_IGHJ6*01	2722	V2-6_IGLJ4*01	854	1459
2908	VH3-23_IGHD3-3*01>3'_IGHJ6*01	2723	V2-6_IGLJ4*01	854	1459
2909	VH3-23_IGHD3-9*01>1'_IGHJ6*01	2724	V2-6_IGLJ4*01	854	1459

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
2910	VH3-23_IGHD3-9*01>3'_IGHJ6*01	2725	V2-6_IGLJ4*01	854	1459
2911	VH3-23_IGHD3-10*01>1'_IGHJ6*01	2726	V2-6_IGLJ4*01	854	1459
2912	VH3-23_IGHD3-10*01>3'_IGHJ6*01	2727	V2-6_IGLJ4*01	854	1459
2913	VH3-23_IGHD3-16*01>1'_IGHJ6*01	2728	V2-6_IGLJ4*01	854	1459
2914	VH3-23_IGHD3-16*01>3'_IGHJ6*01	2729	V2-6_IGLJ4*01	854	1459
2915	VH3-23_IGHD3-22*01>1'_IGHJ6*01	2730	V2-6_IGLJ4*01	854	1459
2916	VH3-23_IGHD4-4*01 (1) >1'_IGHJ6*01	2731	V2-6_IGLJ4*01	854	1459
2917	VH3-23_IGHD4-4*01 (1) >3'_IGHJ6*01	2732	V2-6_IGLJ4*01	854	1459
2918	VH3-23_IGHD4-11*01 (1) >1'_IGHJ6*01	2733	V2-6_IGLJ4*01	854	1459
2919	VH3-23_IGHD4-11*01 (1) >3'_IGHJ6*01	2734	V2-6_IGLJ4*01	854	1459
2920	VH3-23_IGHD4-17*01>1'_IGHJ6*01	2735	V2-6_IGLJ4*01	854	1459
2921	VH3-23_IGHD4-17*01>3'_IGHJ6*01	2736	V2-6_IGLJ4*01	854	1459
2922	VH3-23_IGHD4-23*01>1'_IGHJ6*01	2737	V2-6_IGLJ4*01	854	1459
2923	VH3-23_IGHD4-23*01>3'_IGHJ6*01	2738	V2-6_IGLJ4*01	854	1459
2924	VH3-23_IGHD5-5*01 (2) >1'_IGHJ6*01	2739	V2-6_IGLJ4*01	854	1459
2925	VH3-23_IGHD5-5*01 (2) >3'_IGHJ6*01	2740	V2-6_IGLJ4*01	854	1459
2926	VH3-23_IGHD5-12*01>1'_IGHJ6*01	2741	V2-6_IGLJ4*01	854	1459
2927	VH3-23_IGHD5-12*01>3'_IGHJ6*01	2742	V2-6_IGLJ4*01	854	1459
2928	VH3-23_IGHD5-18*01 (2) >1'_IGHJ6*01	2743	V2-6_IGLJ4*01	854	1459
2929	VH3-23_IGHD5-18*01 (2) >3'_IGHJ6*01	2744	V2-6_IGLJ4*01	854	1459
2930	VH3-23_IGHD5-24*01>1'_IGHJ6*01	2745	V2-6_IGLJ4*01	854	1459
2931	VH3-23_IGHD5-24*01>3'_IGHJ6*01	2746	V2-6_IGLJ4*01	854	1459
2932	VH3-23_IGHD6-6*01>1'_IGHJ6*01	2747	V2-6_IGLJ4*01	854	1459
2933	VH3-23_IGHD6-6*01>2'_IGHJ6*01	2748	V2-6_IGLJ4*01	854	1459
2934	VH3-23_IGHD6-6*01>3'_IGHJ6*01	2749	V2-6_IGLJ4*01	854	1459
2935	VH3-23_IGHD1-1*01>1_IGHJ6*01	2645	V2-7_IGLJ2*01	855	1460
2936	VH3-23_IGHD1-1*01>2_IGHJ6*01	2646	V2-7_IGLJ2*01	855	1460
2937	VH3-23_IGHD1-1*01>3_IGHJ6*01	2647	V2-7_IGLJ2*01	855	1460
2938	VH3-23_IGHD1-7*01>1_IGHJ6*01	2648	V2-7_IGLJ2*01	855	1460
2939	VH3-23_IGHD1-7*01>3_IGHJ6*01	2649	V2-7_IGLJ2*01	855	1460
2940	VH3-23_IGHD1-14*01>1_IGHJ6*01	2650	V2-7_IGLJ2*01	855	1460
2941	VH3-23_IGHD1-14*01>3_IGHJ6*01	2651	V2-7_IGLJ2*01	855	1460
2942	VH3-23_IGHD1-20*01>1_IGHJ6*01	2652	V2-7_IGLJ2*01	855	1460
2943	VH3-23_IGHD1-20*01>3_IGHJ6*01	2653	V2-7_IGLJ2*01	855	1460
2944	VH3-23_IGHD1-26*01>1_IGHJ6*01	2654	V2-7_IGLJ2*01	855	1460
2945	VH3-23_IGHD1-26*01>3_IGHJ6*01	2655	V2-7_IGLJ2*01	855	1460
2946	VH3-23_IGHD2-2*01>2_IGHJ6*01	2656	V2-7_IGLJ2*01	855	1460
2947	VH3-23_IGHD2-2*01>3_IGHJ6*01	2657	V2-7_IGLJ2*01	855	1460
2948	VH3-23_IGHD2-8*01>2_IGHJ6*01	2658	V2-7_IGLJ2*01	855	1460
2949	VH3-23_IGHD2-8*01>3_IGHJ6*01	2659	V2-7_IGLJ2*01	855	1460
2950	VH3-23_IGHD2-15*01>2_IGHJ6*01	2660	V2-7_IGLJ2*01	855	1460
2951	VH3-23_IGHD2-15*01>3_IGHJ6*01	2661	V2-7_IGLJ2*01	855	1460
2952	VH3-23_IGHD2-21*01>2_IGHJ6*01	2662	V2-7_IGLJ2*01	855	1460
2953	VH3-23_IGHD2-21*01>3_IGHJ6*01	2663	V2-7_IGLJ2*01	855	1460

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
2954	VH3-23_IGHD3-3*01>1_IGHJ6*01	2664	V2-7_IGLJ2*01	855	1460
2955	VH3-23_IGHD3-3*01>2_IGHJ6*01	2665	V2-7_IGLJ2*01	855	1460
2956	VH3-23_IGHD3-3*01>3_IGHJ6*01	2666	V2-7_IGLJ2*01	855	1460
2957	VH3-23_IGHD3-9*01>2_IGHJ6*01	2667	V2-7_IGLJ2*01	855	1460
2958	VH3-23_IGHD3-10*01>2_IGHJ6*01	2668	V2-7_IGLJ2*01	855	1460
2959	VH3-23_IGHD3-10*01>3_IGHJ6*01	2669	V2-7_IGLJ2*01	855	1460
2960	VH3-23_IGHD3-16*01>2_IGHJ6*01	2670	V2-7_IGLJ2*01	855	1460
2961	VH3-23_IGHD3-16*01>3_IGHJ6*01	2671	V2-7_IGLJ2*01	855	1460
2962	VH3-23_IGHD3-22*01>2_IGHJ6*01	2672	V2-7_IGLJ2*01	855	1460
2963	VH3-23_IGHD3-22*01>3_IGHJ6*01	2673	V2-7_IGLJ2*01	855	1460
2964	VH3-23_IGHD4-4*01 (1) >2_IGHJ6*01	2674	V2-7_IGLJ2*01	855	1460
2965	VH3-23_IGHD4-4*01 (1) >3_IGHJ6*01	2675	V2-7_IGLJ2*01	855	1460
2966	VH3-23_IGHD4-11*01 (1) >2_IGHJ6*01	2676	V2-7_IGLJ2*01	855	1460
2967	VH3-23_IGHD4-11*01 (1) >3_IGHJ6*01	2677	V2-7_IGLJ2*01	855	1460
2968	VH3-23_IGHD4-17*01>2_IGHJ6*01	2678	V2-7_IGLJ2*01	855	1460
2969	VH3-23_IGHD4-17*01>3_IGHJ6*01	2679	V2-7_IGLJ2*01	855	1460
2970	VH3-23_IGHD4-23*01>2_IGHJ6*01	2680	V2-7_IGLJ2*01	855	1460
2971	VH3-23_IGHD4-23*01>3_IGHJ6*01	2681	V2-7_IGLJ2*01	855	1460
2972	VH3-23_IGHD5-5*01 (2) >1_IGHJ6*01	2682	V2-7_IGLJ2*01	855	1460
2973	VH3-23_IGHD5-5*01 (2) >2_IGHJ6*01	2683	V2-7_IGLJ2*01	855	1460
2974	VH3-23_IGHD5-5*01 (2) >3_IGHJ6*01	2684	V2-7_IGLJ2*01	855	1460
2975	VH3-23_IGHD5-12*01>1_IGHJ6*01	2685	V2-7_IGLJ2*01	855	1460
2976	VH3-23_IGHD5-12*01>3_IGHJ6*01	2686	V2-7_IGLJ2*01	855	1460
2977	VH3-23_IGHD5-18*01 (2) >1_IGHJ6*01	2687	V2-7_IGLJ2*01	855	1460
2978	VH3-23_IGHD5-18*01 (2) >2_IGHJ6*01	2688	V2-7_IGLJ2*01	855	1460
2979	VH3-23_IGHD5-18*01 (2) >3_IGHJ6*01	2689	V2-7_IGLJ2*01	855	1460
2980	VH3-23_IGHD5-24*01>1_IGHJ6*01	2690	V2-7_IGLJ2*01	855	1460
2981	VH3-23_IGHD5-24*01>3_IGHJ6*01	2691	V2-7_IGLJ2*01	855	1460
2982	VH3-23_IGHD6-6*01>1_IGHJ6*01	2692	V2-7_IGLJ2*01	855	1460
2983	VH3-23_IGHD1-1*01>1'_IGHJ6*01	2702	V2-7_IGLJ2*01	855	1460
2984	VH3-23_IGHD1-1*01>2'_IGHJ6*01	2703	V2-7_IGLJ2*01	855	1460
2985	VH3-23_IGHD1-1*01>3'_IGHJ6*01	2704	V2-7_IGLJ2*01	855	1460
2986	VH3-23_IGHD1-7*01>1'_IGHJ6*01	2705	V2-7_IGLJ2*01	855	1460
2987	VH3-23_IGHD1-7*01>3'_IGHJ6*01	2706	V2-7_IGLJ2*01	855	1460
2988	VH3-23_IGHD1-14*01>1'_IGHJ6*01	2707	V2-7_IGLJ2*01	855	1460
2989	VH3-23_IGHD1-14*01>2'_IGHJ6*01	2708	V2-7_IGLJ2*01	855	1460
2990	VH3-23_IGHD1-14*01>3'_IGHJ6*01	2709	V2-7_IGLJ2*01	855	1460
2991	VH3-23_IGHD1-20*01>1'_IGHJ6*01	2710	V2-7_IGLJ2*01	855	1460
2992	VH3-23_IGHD1-20*01>2'_IGHJ6*01	2711	V2-7_IGLJ2*01	855	1460
2993	VH3-23_IGHD1-20*01>3'_IGHJ6*01	2712	V2-7_IGLJ2*01	855	1460
2994	VH3-23_IGHD1-26*01>1'_IGHJ6*01	2713	V2-7_IGLJ2*01	855	1460
2995	VH3-23_IGHD1-26*01>1_IGHJ6*01_B	2714	V2-7_IGLJ2*01	855	1460
2996	VH3-23_IGHD2-2*01>2_IGHJ6*01_B	2715	V2-7_IGLJ2*01	855	1460
2997	VH3-23_IGHD2-2*01>3'_IGHJ6*01	2716	V2-7_IGLJ2*01	855	1460

TABLE 17A: Exemplary Nucleic Acid Paired Library					
	HEAVY CHAIN	RS	LIGHT CHAIN	RS	NO RS
2998	VH3-23_IGHD2-8*01>1'_IGHJ6*01	2717	V2-7_IGLJ2*01	855	1460
2999	VH3-23_IGHD2-15*01>1'_IGHJ6*01	2718	V2-7_IGLJ2*01	855	1460
3000	VH3-23_IGHD2-15*01>3'_IGHJ6*01	2719	V2-7_IGLJ2*01	855	1460
3001	VH3-23_IGHD2-21*01>1'_IGHJ6*01	2720	V2-7_IGLJ2*01	855	1460
3002	VH3-23_IGHD2-21*01>3'_IGHJ6*01	2721	V2-7_IGLJ2*01	855	1460
3003	VH3-23_IGHD3-3*01>1'_IGHJ6*01	2722	V2-7_IGLJ2*01	855	1460
3004	VH3-23_IGHD3-3*01>3'_IGHJ6*01	2723	V2-7_IGLJ2*01	855	1460
3005	VH3-23_IGHD3-9*01>1'_IGHJ6*01	2724	V2-7_IGLJ2*01	855	1460
3006	VH3-23_IGHD3-9*01>3'_IGHJ6*01	2725	V2-7_IGLJ2*01	855	1460
3007	VH3-23_IGHD3-10*01>1'_IGHJ6*01	2726	V2-7_IGLJ2*01	855	1460
3008	VH3-23_IGHD3-10*01>3'_IGHJ6*01	2727	V2-7_IGLJ2*01	855	1460
3009	VH3-23_IGHD3-16*01>1'_IGHJ6*01	2728	V2-7_IGLJ2*01	855	1460
3010	VH3-23_IGHD3-16*01>3'_IGHJ6*01	2729	V2-7_IGLJ2*01	855	1460
3011	VH3-23_IGHD3-22*01>1'_IGHJ6*01	2730	V2-7_IGLJ2*01	855	1460
3012	VH3-23_IGHD4-4*01 (1) >1'_IGHJ6*01	2731	V2-7_IGLJ2*01	855	1460
3013	VH3-23_IGHD4-4*01 (1) >3'_IGHJ6*01	2732	V2-7_IGLJ2*01	855	1460
3014	VH3-23_IGHD4-11*01 (1) >1'_IGHJ6*01	2733	V2-7_IGLJ2*01	855	1460
3015	VH3-23_IGHD4-11*01 (1) >3'_IGHJ6*01	2734	V2-7_IGLJ2*01	855	1460
3016	VH3-23_IGHD4-17*01>1'_IGHJ6*01	2735	V2-7_IGLJ2*01	855	1460
3017	VH3-23_IGHD4-17*01>3'_IGHJ6*01	2736	V2-7_IGLJ2*01	855	1460
3018	VH3-23_IGHD4-23*01>1'_IGHJ6*01	2737	V2-7_IGLJ2*01	855	1460
3019	VH3-23_IGHD4-23*01>3'_IGHJ6*01	2738	V2-7_IGLJ2*01	855	1460
3020	VH3-23_IGHD5-5*01 (2) >1'_IGHJ6*01	2739	V2-7_IGLJ2*01	855	1460
3021	VH3-23_IGHD5-5*01 (2) >3'_IGHJ6*01	2740	V2-7_IGLJ2*01	855	1460
3022	VH3-23_IGHD5-12*01>1'_IGHJ6*01	2741	V2-7_IGLJ2*01	855	1460
3023	VH3-23_IGHD5-12*01>3'_IGHJ6*01	2742	V2-7_IGLJ2*01	855	1460
3024	VH3-23_IGHD5-18*01 (2) >1'_IGHJ6*01	2743	V2-7_IGLJ2*01	855	1460
3025	VH3-23_IGHD5-18*01 (2) >3'_IGHJ6*01	2744	V2-7_IGLJ2*01	855	1460
3026	VH3-23_IGHD5-24*01>1'_IGHJ6*01	2745	V2-7_IGLJ2*01	855	1460
3027	VH3-23_IGHD5-24*01>3'_IGHJ6*01	2746	V2-7_IGLJ2*01	855	1460
3028	VH3-23_IGHD6-6*01>1'_IGHJ6*01	2747	V2-7_IGLJ2*01	855	1460
3029	VH3-23_IGHD6-6*01>2'_IGHJ6*01	2748	V2-7_IGLJ2*01	855	1460
3030	VH3-23_IGHD6-6*01>3'_IGHJ6*01	2749	V2-7_IGLJ2*01	855	1460

4. Antibody Libraries

Provided herein are antibody libraries containing antibodies or portions thereof minimally containing a VH chain and a VL chain or a portion thereof containing a sufficient antigen binding site. The VH chain or portion thereof of the antibody members in the libraries provided herein are encoded by any of the nucleic acid members of the library set forth in Section E.1 above. The VL chain or portion thereof of the antibody members in the libraries provided herein are encoded by any of the nucleic acid members set forth in Section

E.2 above. Thus, each antibody member of the library is derived in full or in part from germline segment sequences and/or are derived from modified sequences thereof. In some examples, the libraries are provided as addressed libraries.

In addition, each antibody in the library is productive and functional by virtue of containing a sufficient antigen binding site. The antibodies in the library are different, and when provided in an addressed format, each locus of the library contains a different antibody from all other loci in the library. Thus, the libraries provided herein exhibit high antibody diversity. The antibody libraries provided herein contain as few as 10^2 different members and typically contain about or 10^3, 10^4, 2×10^4, 3×10^4, 4×10^4, 5×10^4, 6×10^4, 7×10^4, 8×10^4, 9×10^4, 10^5 and more unique members, including about or 10^6, 10^7,10^8, 10^9 and more unique members. The antibody libraries provided herein can be produced by the methods herein, whereby the natural recombination process and natural structural diversity of the antibody repertoire is mimicked.

Besides containing a VH chain and a VL chain, or a portion thereof containing a sufficient antigen-binding site, the resulting antibodies in the library provided herein can contain all or a portion of a constant region. For example, the antibodies can contain one or more of a C_{H1}, C_{H2}, C_{H3} or C_L portion. Generally, the antibodies or portions thereof contain a C_{H1} portion. The resulting antibodies or portions thereof include, but are not limited to a full-length antibody, Fab, Fab', $F(ab')_2$, single-chain Fvs (scFv), Fv, dsFv, diabody, Fd and Fd' fragments. Exemplary addressed antibody libraries provided herein are Fab libraries.

The number of different members in the antibody libraries provided herein can be restricted such that each member of the library is selected based on sequence similarities or differences or based on shared characteristics (e.g., a V region family, CDR3 length or composition or other biochemical attribute). For example, members of the library can be selected so that individual encoding germline segments of the VL or VH chains of the resulting antibodies have shared characteristics (e.g. are of the same subgroup or gene family) or otherwise contain similar or different sequence identity. In another example, the members of the library can be selected based on the sequence diversity of the VH or VL chains of the resulting antibody members. The antibody members of the library can be selected to be diverse in the represented sequences or to be similar. Thus, in some instances, library members represent a group of highly diverse antibodies. In other instances, library members represent a group similar, non-diverse antibodies. For example, library members can have 40%, 50%, 60%, 70%, 80%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% sequence similarity of the VH or VL to all other members in the library. The choice of

antibody library is a function of the application and is within the level of one of skill in the art.

In some examples, the addressed libraries provided herein are human naïve libraries. That means that every member of the library is derived completely from human germline segment sequences. For example, the VH chain of each antibody member is encoded by a nucleic acid molecule made up of a combination of a V_H, D_H and J_H germline segment, for example, any set forth in Table 3 above, or a subset thereof, such that the resulting nucleic acid molecule has a sequence where the V_H segment is 5' to the D_H segment which is 5' to the J_H segment. The VL chain of each antibody member is encoded by a combination of a V_κ and J_κ germline segments and/or V_λ and J_λ germline segments, for example, any set forth in Tables 3-4 above, or a subset thereof, such that the resulting nucleic acid molecule has a sequence where the V_L segment (V_κ or V_λ) is 5' to the J_L segment (J_κ or J_λ). It is understood that the library is considered to be naïve and derived from germline even though, in practicing the method herein, the joint regions of the segments are altered to render the resulting encoding nucleic acid molecules in frame. Such alterations, however, are minor and variously include insertion or deletion generally of only a single nucleotide of a germline segment. In addition, other modification made to the recombined nucleic acid sequence by virtue of practice of the method herein, such as removal of stop codons and restriction enzyme site sequences, also result in naïve antibodies. Naïve antibody libraries provided herein can include the entire repertoire of naïve antibodies, or a subset thereof. For example, a naïve library provided herein can include 10^3, 10^4, 2×10^4, 3×10^4 4×10^4, 5×10^4, 6×10^4, 4×10^4, 7×10^4, 8×10^4, 9×10^4, 10^5 and more unique members, including about or 10^6, 10^7 or more members.

In particular examples, the VH chain of members of the antibody library is encoded by a sequence of nucleotides made up entirely of a V_H and a J_H germline segment, and also any sequence of nucleotides between the V_H and J_H germline segment. The V_H segment is 5' to the random sequence of nucleotides which is 5' to the J_H segment in the encoding nucleic acid molecule. Thus, the resulting antibody members of the library contain a random sequence of amino acids in the region that includes the central portion of the CDRH3, which is largely responsible for the antigen specificity of the resulting antibody. The sequence of nucleotides can be any random sequence of nucleotides. In some instances, the sequence of nucleotides is a sequence that encodes a peptide mimetic against any desired target, for example, a cell surface receptor. Exemplary peptide mimetics are set forth in Table 16. In other examples, the random sequence of nucleotides is a D_H germline segment, or modified

form thereof. Generally, the sequence of nucleotides is or is about 5, 10, 15, 20, 25, 30, 40, 50, 60, 70, 80, 90 or more nucleotides in length.

Also provided herein are antibody libraries where the antibodies in the libraries are derived at least in part from modified germline segment sequences. In some examples, all encoding germline segments are modified, for example, by random mutation. In other examples, particular regions of germline segments are targeted for modification. For example, the modified germline segment sequences can include modifications, such as by amino acid mutation, of one or more CDR. In particular, resulting antibody members of the libraries provided herein can contain modification of CDR3, such as of CDRH3. Thus, the resulting members of the library can contain one or more amino acid replacement of a CDR as compared to a naïve antibody.

In some examples, the members of the antibody libraries provided herein can be directed toward a desired target or function by incorporation of sequences into the variable regions of a naive antibody that correspond to a polynucleotide target of interest. Thus, except for the incorporated sequence, which is added by replacement or insertion into the antibody sequence, the remaining antibody represents germline segment sequences. These incorporated sequences include, but are not limited to, peptides as well as portions of monoclonal antibodies.

For example, the antibody can contain a directed peptide that acts as a mimetic against a particular target. Generally, such antibodies act as agonists toward the target, but in some instances, can be antagonists. The peptides can be included in any region of the antibody, but generally are included in the variable region, and more generally in one or more of the CDR regions. In particular, directed peptides are included in the CDR3 region of the antibody. Each member antibody member of the library can be modified with the same directed peptide and/or with different directed peptides.

In related examples, the antibody can contain a sequence portion from a known monoclonal antibodies. The portion can include a portion corresponding to one or more CDRs of a known monoclonal antibody. In other cases, antibodies in the addressed library can contain entire variable region (for example, VL or VH) of a monoclonal antibody. For example, antibodies in the library can contain a VH or VL of a known monoclonal antibody, which can be combined with a VL or VH derived from germline segments as described herein. Exemplary of such an antibody library is one where one or more of the antibody members contain a VH or VL chain from any known monoclonal antibody set forth in Table 9 above.

The antibody libraries of provided herein can include members that represent one, some or all of the above examples.

In the libraries provided herein, the individual VH and VL chains or portions thereof can be the same of different from the VH and VL chains of other antibodies in the library. It is the combination of the VH and VL chain that renders each antibody in the library different, for example, each addressed antibody at a locus. Thus, for example, libraries provided herein can all contain a common VH chain, but can each contain a different VL chain. Thus, the resulting antibody members of the library each contain a different combination of VH and VL chain.

An antibody library provided herein can include a VH encoded from any of nucleic acid sequences SEQ ID NOS: 454-805 (each encoding a VH chain), and a VL chain encoded by any of nucleic acid molecule set forth in any of SEQ ID NOS: 806-815, 817, 819-834, and 836-867 (each encoding a VL chain), or sequences thereof that do not contain heterologous sequence for restriction sites at the 3' and 5 ' ends, and subsets thereof. An antibody library provided herein also can include a VH encoded from any of nucleic acid sequences SEQ ID NOS: 2070-2759 (each encoding a VH chain), and a VL chain encoded by any of nucleic acid molecule set forth in any of SEQ ID NOS: 806-815, 817, 819-834, and 836-867 (each encoding a VL chain), or sequences thereof not do not contain heterologous sequence for restriction sites at the 3' and 5 ' ends. Any combination of VH and VL from any of the above recombined nucleic acids provided herein can be paired to generate an antibody library. The components of the library, the size of the library and the type of library (e.g. Fab, full-length antibody , etc) all can be varied

Exemplary of such an antibody library provided herein incudes a VH and a VL encoded by a sequence of nucleic acids set forth in Table 17. An additional exemplary antibody library includes a subset of members set forth in Table 17, including a VH and a VL chain encoded from nucleic acid sequences set forth in Table 22 below. For example, in such an exemplary library any of the VH chain sequences set forth in any of SEQ ID NOS: 1475-1826 is paired with any of the VL light chain sequences set forth in SEQ ID NOS:1827-1838, 1840-1855, 1857-1888. The resulting library, when expressed with a CH as exemplified in Example 9, is a Fab library. By virtue of the pairing of VH and VL chain the resulting library can contain at or about $2.1.0x10^5$ or more members, or a subset thereof. Each member pair is encoded by germline segments and represents a naïve antibody.

Exemplary of such an antibody library provided herein incudes a VH and a VL encoded by a sequence of nucleic acids set forth in 17.A above.

5. Addressable Formats

The libraries provided herein are provided as addressed libraries such that each loci is a distinct address containing a different member of the library compared to all other loci of the library, and each can be identified by virtue of its address. For example, members at a loci can be identified by prior recording of their distinct location or by an identifiable tag. Where the library is a nucleic acid library, each loci of the library contains a nucleic acid molecule that is different from all other nucleic acid molecules at other loci in the library. Where the library is an antibody library, each loci of the library contains an antibody or portion thereof that is different from all other antibodies or portion thereof at other loci in the library.

The libraries provided herein can be presented in any addressable format known to one of skill in the art. Addressing can be effected by position on a surface or other physical locus or can be otherwise identifiable and/or sortable by other identifiers, such as a tag encoded with a bar code or other symbology, a chemical tag, an electronic, such RF tag, a color-coded tag or other such identifier. One of skill in the art is familiar with various addressable format. Exemplary of such formats is as an array. The library members can be provided on or in the array by immobilization or attachment, or can be provided in solution.

Any nucleic acid molecule or antibody provided herein can be provided in overlapping areas or at random locations on an array, such as a multiwell plate. Alternatively the library members can be provided in spatial array, such that each nucleic acid molecule or antibody is provided in a distinct region of the array which does not overlap with the any other region containing any other antibody or nucleic acid molecules. Any addressable array technology known in the art can be employed with the antibodies.

a. Multiwell Plate

Nucleic acid molecules or antibodies can be spatially arrayed in multiwell plates, such that each individual locus of the plate corresponds to one individual antibody. Multiwell plates can include, but are not limited to, 12-well, 24-well, 48-well, 96-well plates, 384-well plates, and 1536-well plates. In this instance, the identity of each member in each well is known. The members can be attached to the support or provided in solution. For example, one advantage of this technique is that antibodies are presented in solution and are therefore fully folded and functional thereby eliminating the loss of activity observed when proteins are immobilized on filters, chip surfaces or slides. In addition, in the case of antibodies, the antibodies can be screened for any desired activity, including but not limited to binding, cytotoxicity, differentiation or proliferation of cells, and alteration of gene expression. Since

the identity of each antibody is known, information on structure activity relationships (SAR) is immediately available. Finally, pharmacokinetics and/or dose response experiments can be performed during screening or immediately following identification of a "hit" or lead compound.

In another instance, nucleic acid molecule and antibody members can be spatially arrayed in multiwell plates, such that each individual locus of the plate corresponds to a group of members. In this instance, the identity of every member within the group in any particular well is known. Groups of members can contain 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100 or more antibodies or nucleic acid molecules. For example, antibodies or nucleic acid molecules can be grouped randomly or by any desired characteristic, such as belonging to the same V-region family, containing similar CDR3 region amino acid composition or length, or any other biochemical attributes. For the case of antibodies, the group of addressed antibodies can be screened for any desired activity, including but not limited to binding, cytotoxicity, differentiation or proliferation of cells, and alteration of gene expression. Screening groups of libraries allows for screening a greater number of library members at any given time thereby covering a larger part of the available antibody diversity. Furthermore, following the identification of a "hit" or lead group, since the identity of every antibody within a group is known and the antibodies are all readily available individually, individual antibodies can be immediately screened to identify "active" library members within the group.

ii. Solid Support

Nucleic acid and antibody arrays include those in which members are immobilized on a solid support, such as in a microarray. For example, solid supports for attachment or immobilization include, but are not limited to, blotting on filters, on chip surfaces, or on cellulose and by attachment to slides using affinity tags. In some examples, cells expressing variant polypeptides can be naturally adsorbed to a bead, such that a population of beads contains a single cell per bead (Freeman *et al.* Biotechnol. Bioeng. (2004) 86:196-200). Following immobilization to a glass support, microcolonies can be grown and screened with a chromogenic or fluorogenic substrate. See, e.g., U.S. Pat. Nos. 6,372,483, 6,352,842, 6,346,416 and 6,242,266.

For example, it is contemplated herein that antibody members of the libraries can be immobilized on a chip. Exemplary of chips include those used for BIAcore. Determining the ability of the protein to bind to a target molecule can be accomplished, e.g., using a technology such as real-time Biomolecular Interaction Analysis (BIA). Sjolander, S. and

Urbaniczky, C. (1991) *Anal. Chem.* 63:2338-2345 and Szabo *et al.* (1995) *Curr. Opin. Struct. Biol.* 5:699-705. Biacore is a method for measuring protein-protein interaction and binding affinity. The technology is based on surface plasmon resonance (SPR), an optical phenomenon that enables detection of unlabeled interactants in real time (Welford K. 1991, Opt. Quant. Elect. 23:1; Morton and Myszka, 1998, Methods in Enzymology 295: 268). The SPR-based biosensors can be used to monitor biomolecular interactions in real time to determine active concentration, screening and characterization in terms of both affinity and kinetics. BIAcore analysis conveniently generates association rate constants, dissociation rate constants, equilibrium dissociation constants, and affinity constants.

The methodology relies on immobilization of ligands onto the surface of a sensor chip consisting of a glass substrate having a gold film covered by a monolayer of a long hydroxyalkyl thiol to which is covalently attached a thin layer of carboxymethylated dextran. The immobilization procedure is performed with the sensor chip in place in the instrument and is continuously monitored by the SPR detector. An unknown sample or ligate solution is introduced into the apparatus to contact the immobilized ligand. The interaction between ligand and ligate is observed directly by surface plasmon resonance techniques and the measurements recorded on a computer via a program such as Bialogue [Pharmacia].

6. Other Display Methods

The libraries also can be provided in other non-addressable formats. Exemplary of such other non-addressable formats include by display, in particular, any display format that facilitates screening of the members of the libraries for an activity or activities. Generally, such formats are used for the antibody libraries, but if desired can also be provided for the nucleic acid or vector libraries. Typically libraries are screened using a display technique, such that there is a physical link between individual molecules of the library (phenotype) and the genetic information encoding them (genotype). These methods include, but are not limited to, cell display, phage display, mRNA display, ribosome display and DNA display.

a. Cell Display

Antibody libraries for screening can be expressed on the surfaces of cells, including bacteria *E. coli*, yeast *S. cerevisiae,* and mammalian cells, by fusing them with a protein that is expressed on the surface of the cell. Cell display is a technology used to screen antibody libraries wherein immobilization of the target antigen is unnecessary. Instead a technique, such as fluorescence-activated cell sorting (FACS), can be used to identify desired antibodies. FACS permits the separation of subpopulations of cells on the basis of their light scatter properties as they pass through a laser beam. See e.g. United States Published Patent

Application Nos. US 2003/0100023 and US 2003/0036092. Single chain antibodies can be expressed on the external surface of *E. coli* by fusing them to a protein previously shown to direct heterologous proteins to the bacterial surface (Francisco *et al.*, (1993) *Proc. Natl. Acad. Sci., USA*, 90:10444-10448). Single chain and Fab antibodies can be displayed on the surface of a yeast cell, and homologous recombination in yeast can be exploited to generate libraries of transformants (see e.g. Kieke *et al.*, (1997) *Prot. Eng.*, 10:1303-1310; Weaver-Feldhaus *et al.*, (2004) *FEBS Lett.*, 564:24-34; and Swers *et al.*, (2004) *Nucleic Acids Res.*, 32:e36). Mammalian cell display has been utilized to screen scFv libraries as well as IgGs (Ho *et al.*, (2005) *J. Biol. Chem.*, 280:07-617).

b. Phage Display

Phage display is a widely used method for screening antibody libraries for their ability to bind to a particular antigen. Phage display is a cell based method in which proteins or peptides are expressed individually on the surface of phage as fusions to a coat protein, while the same phage particle carries the DNA encoding the protein or peptide (Smith, G. P. (1985) *Science* 228:1315-1317). Selection of the phage is achieved through a specific binding reaction involving recognition of the protein or peptide, enabling the particular phage to be isolated and cloned and the DNA for the protein or peptide to be recovered and propagated or expressed. Use of phage display is rapid and facile due to its reliance upon *E. coli* for amplification and propagation. Typical use involves panning phage libraries against an immobilized antigen.

c. mRNA Display and Ribosome Display

The use of mRNA display and ribosome display allow for totally *in vitro* construction of antibody libraries. mRNA display is a method of displaying proteins or peptides in which the nascent protein is caused to bind covalently to its mRNA through a puromycin link (Roberts *et al.* (1997) *Proc. Natl. Acad. Sci, U.S.A.* 64:12297-12302). Puromycin acts as a mimic of aminacyl tRNA, enters the ribosome A site, and the nascent protein is bound covalently to it by the peptidyl-transferase activity of the ribosome. Selection is carried out on these protein-mRNA fusions after dissociation of the ribosome. Alternatively, ribosome display is a method of displaying proteins or peptides in nascent form on the surface of ribosomes, such that a stable complex with the encoding mRNA is formed; the complexes are selected with a ligand for the protein or peptide and the genetic information is obtained by reverse transcription of the isolated mRNA (see e.g. United States Patent Nos. US 5,643,768 and US 5,658,754). Selection techniques are similar to that of phage display wherein an ribosome display libraries are panned against an immobilized antigen.

d. DNA Display

In DNA display the DNA encoding the peptide is linked to the peptide. In non-covalent DNA display, the DNA-protein linkage is promoted by the recognition of the bacterial RepA protein as well as its own origin of replication sequence integrated into the template DNA (Odegrip *et al.* (2004) *Proc. Natl. Acad. Sci, U.S.A.* 101:2806-2810). Alternatively, a biotin-streptavidin interaction can be utilized. In covalent DNA display a bacteriophage P2 protein genetically fused to an antibody fragment binds to its own DNA sequence (Reiersen *et al.* (2005) *Nucl. Acids Res.* 33:e10). Alternatively, the DNA and the peptide can be compartmentalized, such as in an oil-in-water emulsion. Selection techniques are similar to that of phage display wherein DNA display libraries are panned against an immobilized antigen. See e.g. International Patent Publication No. WO 98/037186.

F. Methods of Production of Antibodies

Nucleic acid molecules and antibody members of the libraries provided herein can be made by any method known to one of skill in the art. Such procedures are routine and are well known to the skill artisan. They include routine molecular biology techniques including gene synthesis, PCR, ligation, cloning, transfection and purification techniques. A description of such procedures is provided below.

For example, nucleic acid sequences can be constructed using gene synthesis techniques as discussed herein above. Gene synthesis or routine molecular biology techniques also can be used to effect insertion, deletion, addition or replacement of nucleotides. For example, additional nucleotide sequences can be joined to a nucleic acid sequence. In one example linker sequences can be added, such as sequences containing restriction endonuclease sites for the purpose of cloning the synthetic gene into a vector, for example, a protein expression vector or a vector designed for the amplification of the antibody constant region coding DNA sequences. Furthermore, additional nucleotide sequences specifying functional DNA elements can be operatively linked to a recombined germline encoding nucleic acid molecule. Examples of such sequences include, but are not limited to, promoter sequences designed to facilitate intracellular protein expression, and leader peptide sequences designed to facilitate protein secretion. Additional nucleotide sequences such as sequences specifying protein binding regions also can be linked to nucleic acid sequences. Such regions include, but are not limited to, sequences to facilitate uptake of recombined antibodies or fragments thereof into specific target cells, or otherwise enhance the pharmacokinetics of the synthetic gene.

Nucleic acid sequences can be further engineered as described herein, such as by mutagenesis, to generate mutant antibodies. Mutagenesis can be effected entirely through gene synthesis. For example, nucleic acid molecules can be designed manually or *in silico* for synthesis to encode mutant antibodies. The benefit of using gene synthesis methods is that the mutations can be effected so that the resulting nucleic acid molecules are in-frame and are "productive" as discussed herein above. Other methods of synthesis exist where randomization can be achieved during the gene synthesis. For example, a protocol has been developed by which synthesis of an oligonucleotide is "doped" with non-native phosphoramidites, resulting in randomization of the gene section targeted for random mutagenesis (Wang and Hoover (1997) J. Bacteriol., 179:5812-9). This method allows control of position selection while retaining a random substitution rate. Alternatively, mutagenesis can be effected through other molecular biology techniques. Generally, site-directed mutagenesis strategies can be employed.

Other current methods can be used to create mutant antibody libraries from a template nucleic acid molecule or molecules, such as a germline recombined nucleic acid molecule encoding a naïve antibody. Such methods include, but are not limited to, error-prone polymerase chain reaction (Caldwell and Joyce (1992); Gram *et al.* (1992) Proc. Natl. Acad. Sci., 89:3576-80); cassette mutagenesis in which the specific region to be optimized is replaced with a synthetically mutagenized oligonucleotide (Stemmer and Morris (1992) Biotechniques, 13:214-20); Arkin and Youvan (1992) Proc. Natl. Acad. Sci., 89:7811-7815; Oliphant *et al.* (1986) Gene, 44:177-83; Hermes *et al.* (1990) Proc. Natl. Acad. Sci, 87:696-700); the use of mutator strains of hosts cells to add mutational frequency (Greener *et al.* (1997) Mol. Biotechnol., 7:189-95); DNA shuffling (Crameri *et al.* (1998) Nature, 391:288-291; U.S. Patent No. 6,177,263; U.S. Patent No. 5,965,408; Ostermeier *et al.* (1999) Nat. Biotechnol., 17:1205-1209); and other random mutagenesis methods.

1. Vectors

Provided herein are vectors that contain nucleic acid encoding the recombined antibodies or portions thereof. The nucleic acids encoding antibody polypeptides are typically cloned into a intermediate vector before transformation into prokaryotic or eukaryotic cells. Choice of vector can depend on the desired application. For example, after insertion of the nucleic acid, the vectors typically are used to transform host cells, for example, to amplify the recombined antibody genes for replication and/or expression thereof. In such examples, a vector suitable for high level expression is used. In other cases, a vector

is chosen that is compatible with display of the expressed polypeptide on the surface of the cell.

Many expression vectors are available and known to those of skill in the art for the expression of recombined antibodies or portions thereof. The choice of an expression vector is influenced by the choice of host expression system. Such selection is well within the level of skill of the skilled artisan. In general, expression vectors can include transcriptional promoters and optionally enhancers, translational signals, and transcriptional and translational termination signals. Expression vectors that are used for stable transformation typically have a selectable marker which allows selection and maintenance of the transformed cells. In some cases, an origin of replication can be used to amplify the copy number of the vectors in the cells. Vectors also generally can contain additional nucleotide sequences operably linked to the ligated nucleic acid molecule (e.g. His tag, Flag tag). For purposes herein, vectors generally include sequences encoding the constant region. Thus, recombined antibodies or portions thereof also can be expressed as protein fusions. For example, a fusion can be generated to add additional functionality to a polypeptide. Examples of fusion proteins include, but are not limited to, fusions of a signal sequence, an epitope tag such as for localization, e.g. a his_6 tag or a myc tag, or a tag for purification, for example, a GST fusion, and a sequence for directing protein secretion and/or membrane association.

For example, expression of the proteins can be controlled by any promoter/enhancer known in the art. Suitable bacterial promoters are well known in the art and described herein below. Other suitable promoters for mammalian cells, yeast cells and insect cells are well known in the art and some are exemplified below. Selection of the promoter used to direct expression of a heterologous nucleic acid depends on the particular application. Promoters which can be used include but are not limited to eukaryotic expression vectors containing the SV40 early promoter (Bernoist and Chambon, *Nature 290*:304-310 (1981)), the promoter contained in the 3' long terminal repeat of Rous sarcoma virus (Yamamoto *et al. Cell 22*:787-797 (1980)), the herpes thymidine kinase promoter (Wagner *et al.*, *Proc. Natl. Acad. Sci. USA 78*:1441-1445 (1981)), the regulatory sequences of the metallothionein gene (Brinster *et al.*, *Nature 296*:39-42 (1982)); prokaryotic expression vectors such as the β-lactamase promoter (Jay *et al.*, (1981) *Proc. Natl. Acad. Sci. USA 78*:5543) or the *tac* promoter (DeBoer *et al.*, *Proc. Natl. Acad. Sci. USA 80*:21-25 (1983)); see also "Useful Proteins from Recombinant Bacteria": in Scientific American *242*:79-94 (1980)); plant expression vectors containing the nopaline synthetase promoter (Herrara-Estrella *et al.*, *Nature 303*:209-213 (1984)) or the cauliflower mosaic virus 35S RNA promoter (Gardner *et al.*, *Nucleic Acids Res. 9*:2871

(1981)), and the promoter of the photosynthetic enzyme ribulose bisphosphate carboxylase (Herrera-Estrella *et al.*, *Nature 310*:115-120 (1984)); promoter elements from yeast and other fungi such as the Gal4 promoter, the alcohol dehydrogenase promoter, the phosphoglycerol kinase promoter, the alkaline phosphatase promoter, and the following animal transcriptional control regions that exhibit tissue specificity and have been used in transgenic animals: elastase I gene control region which is active in pancreatic acinar cells (Swift *et al.*, *Cell 38*:639-646 (1984); Ornitz *et al.*, *Cold Spring Harbor Symp. Quant. Biol. 50*:399-409 (1986); MacDonald, *Hepatology 7*:425-515 (1987)); insulin gene control region which is active in pancreatic beta cells (Hanahan *et al.*, *Nature 315*:115-122 (1985)), immunoglobulin gene control region which is active in lymphoid cells (Grosschedl *et al.*, *Cell 38*:647-658 (1984); Adams *et al.*, *Nature 318*:533-538 (1985); Alexander *et al.*, *Mol. Cell Biol. 7*:1436-1444 (1987)), mouse mammary tumor virus control region which is active in testicular, breast, lymphoid and mast cells (Leder *et al.*, *Cell 45*:485-495 (1986)), albumin gene control region which is active in liver (Pinckert *et al.*, *Genes and Devel. 1*:268-276 (1987)), alpha-fetoprotein gene control region which is active in liver (Krumlauf *et al.*, *Mol. Cell. Biol. 5*:1639-1648 (1985); Hammer *et al.*, *Science 235*:53-58 1987)), alpha-1 antitrypsin gene control region which is active in liver (Kelsey *et al.*, *Genes and Devel. 1*:161-171 (1987)), beta globin gene control region which is active in myeloid cells (Magram *et al.*, *Nature 315*:338-340 (1985); Kollias *et al.*, *Cell 46*:89-94 (1986)), myelin basic protein gene control region which is active in oligodendrocyte cells of the brain (Readhead *et al.*, *Cell 48*:703-712 (1987)), myosin light chain-2 gene control region which is active in skeletal muscle (Shani, *Nature 314*:283-286 (1985)), and gonadotrophic releasing hormone gene control region which is active in gonadotrophs of the hypothalamus (Mason *et al.*, *Science 234*:1372-1378 (1986)).

In addition to the promoter, the expression vector typically contains a transcription unit or expression cassette that contains all the additional elements required for the expression of the antibody, or portion thereof, in host cells. A typical expression cassette contains a promoter operably linked to the nucleic acid sequence encoding the germline antibody chain and signals required for efficient polyadenylation of the transcript, ribosome binding sites and translation termination. Additional elements of the cassette can include enhancers. In addition, the cassette typically contains a transcription termination region downstream of the structural gene to provide for efficient termination. The termination region can be obtained from the same gene as the promoter sequence or can be obtained from different genes.

Some expression systems have markers that provide gene amplification such as thymidine kinase and dihydrofolate reductase. Alternatively, high yield expression systems

not involving gene amplification are also suitable, such as using a baculovirus vector in insect cells, with a nucleic acid sequence encoding a germline antibody chain under the direction of the polyhedron promoter or other strong baculovirus promoter.

For purposes herein, vectors are provided that contain a sequence of nucleotides that encodes a constant region of an antibody operably linked to the nucleic acid sequence encoding the recombined variable region of the antibody. The vector can include the sequence for one or all of a CH1, CH2, CH3 or CH4 and/or CL. Generally, such as for expression of Fabs, the vector contains the sequence for a CH1 or CL. Exemplary of such vectors containing a heavy chain constant region gene (e.g. CH1) are plasmids A and D, described herein. Exemplary of such vectors containing a light chain constant region genes are plasmids C and E, described herein.

Exemplary expression vectors include any mammalian expression vector such as, for example, pCMV. For bacterial expression, such vectors include pBR322, pUC, pSKF, pET23D, and fusion vectors such as MBP, GST and LacZ. Exemplary of such a vector are bacterial expression vectors such as, for example, plasmid A, plasmid C, plasmid D and plasmid E, described herein. Other eukaryotic vectors, for example any containing regulatory elements from eukaryotic viruses can be used as eukaryotic expression vectors. These include, for example, SV40 vectors, papilloma virus vectors, and vectors derived from Epstein-Bar virus. Other exemplary eukaryotic vectors include pMSG, pAV009/A+, pMT010/A+, pMAMneo-5, baculovirus pDSCE, and any other vector allowing expression of proteins under the direction of the CMV promoter, SV40 early promoter, SV40 late promoter, metallothionein promoter, murine mammary tumor virus promoter, Rous sarcoma virus promoter, polyhedron promoter, or other promoters shown effective for expression in eukaryotes.

Exemplary plasmid vectors for transformation of *E. coli* cells, include, for example, the ColE1 replication vectors described herein. Several features common to all these vectors include (a) a pBAD inducible promoter; (b) an AraC gene, which controls the pBAD promoter; (c) a synthetic ribosomal binding site (RBS) for efficient translation; (d) a ColE1 origin of replication, allowing for high copy expression; (e) a STII leader sequence, allowing for expressed proteins to be translocated to the periplasm; (f) a f1 origin of replication; and (g) a gene for conferring antibiotic resistance. Such plasmids include plasmid A (Figure 3), plasmid C (Figure 5), plasmid D (Figure 4) and plasmid E (Figure 6). Plasmid A and Plasmid D are utilized for expression of heavy chain antibody genes in as they contain a gene for the heavy chain constant region (CH1) operably linked to the inserted gene for the heavy chain

variable region. The vectors contain NheI and NcoI restriction sites to allow for cloning of the recombined antibody genes described herein. Both vectors contain a pUC origin of replication, a ColE1 type origin of replication, and an aminoglycoside phosphotransferase gene conferring kanamycin resistance. Plasmid A contains a $(His)_6$ Tag and a Flag Tag for protein purification. Plasmid D contains both a $(His)_6$ Tag and a Flag Tag, and an additional LPETG tag, which allows for covalent attachment of the resulting protein using a sortase. Plasmid C and Plasmid E are utilized for expression of light chain antibody genes in as they contain a gene for the light chain constant region (CL) operably linked to the inserted gene for the light chain variable region. Plasmid C is specific for kappa light chains and contains BseWI and NcoI restriction sites to allow for cloning of the recombined antibody genes described herein. Plasmid E is specific for lambda light chains and contains AcrII and NcoI restriction sites to allow for cloning of the recombined antibody genes described herein. Both vectors contain a 3.3 origin of replication, a ColE1 type origin of replication, and a gene conferring chloramphenicol resistance. The vectors described above are designed to be utilized in a dual vector system, in which a light chain vector and a heavy chain vector are co-transformed. Thus, they contain two different but compatible ColE1 origins of replication utilized, one for heavy chains and one light chain. This allows for efficient expression of both chains of the antibody when the vectors are co-transformed and expressed.

Any methods known to those of skill in the art for the insertion of DNA fragments into a vector can be used to construct expression vectors containing a nucleic acid encoding an antibody chain. These methods can include *in vitro* recombinant DNA and synthetic techniques and *in vivo* recombinants (genetic recombination). The insertion into a cloning vector can, for example, be accomplished by ligating the DNA fragment into a cloning vector which has complementary cohesive termini. If the complementary restriction sites used to fragment the DNA are not present in the cloning vector, the ends of the DNA molecules can be enzymatically modified. Alternatively, any site desired can be produced by ligating nucleotide sequences (linkers) onto the DNA termini; these ligated linkers can contain specific chemically synthesized nucleic acids encoding restriction endonuclease recognition sequences.

2. Cells and Expression Systems

Cells containing the vectors also are provided. Generally, any cell type that can be engineered to express heterologous DNA and has a secretory pathway is suitable. Expression hosts include prokaryotic and eukaryotic organisms such as bacterial cells (e.g. *E. coli*), yeast cells, fungal cells, Archea, plant cells, insect cells and animal cells including human cells.

Expression hosts can differ in their protein production levels as well as the types of post-translational modifications that are present on the expressed proteins. Further, the choice of expression host is often related to the choice of vector and transcription and translation elements used. For example, the choice of expression host is often, but not always, dependent on the choice of precursor sequence utilized. For example, many heterologous signal sequences can only be expressed in a host cell of the same species (i.e., an insect cell signal sequence is optimally expressed in an insect cell). In contrast, other signal sequences can be used in heterologous hosts such as, for example, the human serum albumin (hHSA) signal sequence which works well in yeast, insect, or mammalian host cells and the tissue plasminogen activator pre/pro sequence which has been demonstrated to be functional in insect and mammalian cells (Tan *et al.*, (2002) *Protein Eng.* 15:337). The choice of expression host can be made based on these and other factors, such as regulatory and safety considerations, production costs and the need and methods for purification. Thus, the vector system must be compatible with the host cell used.

Expression in eukaryotic hosts can include expression in yeasts such as *Saccharomyces cerevisiae* and *Pichia pastoris*, insect cells such as *Drosophila* cells and *lepidopteran* cells, plants and plant cells such as tobacco, corn, rice, algae, and lemna. Eukaryotic cells for expression also include mammalian cells lines such as Chinese hamster ovary (CHO) cells or baby hamster kidney (BHK) cells. Eukaryotic expression hosts also include production in transgenic animals, for example, including production in serum, milk and eggs.

Recombinant molecules can be introduced into host cells via, for example, transformation, transfection, infection, electroporation and sonoporation, so that many copies of the gene sequence are generated. Generally, standard transfection methods are used to produce bacterial, mammalian, yeast, or insect cell lines that express large quantity of antibody chains, which is then purified using standard techniques (see e.g., Colley *et al.* (1989) J. Biol. Chem., 264:17619-17622; Guide to Protein Purification, in Methods in Enzymology, vol. 182 (Deutscher, ed.), 1990). Transformation of eukaryotic and prokaryotic cells are performed according to standard techniques (see, e.g., Morrison (1977) J. Bact. 132:349-351; Clark-Curtiss and Curtiss (1983) Methods in Enzymology, 101, 347-362). For example, any of the well-known procedures for introducing foreign nucleotide sequences into host cells can be used. These include the use of calcium phosphate transfection, polybrene, protoplast fusion, electroporation, biolistics, liposomes, microinjection, plasma vectors, viral vectors and any other the other well known methods for introducing cloned genomic DNA,

cDNA, synthetic DNA or other foreign genetic material into a host cell. Generally, for purposes herein, host cells are transfected with a first vector encoding at least a VH chain and a second vector encoding at least a VL chain. Thus, it is only necessary that the particular genetic engineering procedure used be capable of successfully introducing at least both genes into the host cell capable of expressing germline, or modified form thereof, antibody polypeptide.

Transformation of host cells with recombinant DNA molecules that incorporate the isolated recombined variable region gene, cDNA, or synthesized DNA sequence enables generation of multiple copies of the gene. Thus, the gene can be obtained in large quantities by growing transformants, isolating the recombinant DNA molecules from the transformants and, when necessary, retrieving the inserted gene from the isolated recombinant DNA. Generally, After the expression vector is introduced into the cells, the transfected cells are cultured under conditions favoring expression of the germline chain, which is recovered from the culture using standard purification techniques identified below.

Antibodies and portions thereof can be produced using a high throughput approach by any methods known in the art for protein production including *in vitro* and *in vivo* methods such as, for example, the introduction of nucleic acid molecules encoding recombined antibodies or portions thereof into a host cell or host animal and expression from nucleic acid molecules encoding recombined antibodies *in vitro*. Prokaryotes, especially *E. coli*, provide a system for producing large amounts of recombined antibodies or portions thereof, and are particularly desired in applications of high-throughput expression and purification of proteins. Transformation of *E. coli* is a simple and rapid technique well known to those of skill in the art. *E. coli* host strains for high throughput expression include, but are not limited to, BL21 (EMD Biosciences) and LMG194 (ATCC). Exemplary of such an *E. coli* host strain is BL21. Vectors for high throughput expression include, but are not limited to, pBR322 and pUC vectors. Exemplary of such vectors are the vectors described herein, including plasmid A, plasmid C, plasmid D and plasmid E. Automation of expression and purification can facilitate high-throughput expression. For example, use of a Piccolo™ system , a fully automatic system that combines cell culture with automated harvesting, lysing and purification units, or other similar robotic system can be employed.

a. Prokaryotic Expression

Prokaryotes, especially *E. coli*, provide a system for producing large amounts of recombined antibodies or portions thereof. Transformation of *E. coli* is a simple and rapid technique well known to those of skill in the art. Expression vectors for *E. coli* can contain

inducible promoters that are useful for inducing high levels of protein expression and for expressing proteins that exhibit some toxicity to the host cells. Examples of inducible promoters include the lac promoter, the trp promoter, the hybrid tac promoter, the T7 and SP6 RNA promoters and the temperature regulated λP_L promoter.

Recombined antibodies or portions thereof can be expressed in the cytoplasmic environment of *E. coli*. The cytoplasm is a reducing environment and for some molecules, this can result in the formation of insoluble inclusion bodies. Reducing agents such as dithiothreitol and β-mercaptoethanol and denaturants (e.g., such as guanidine-HCl and urea) can be used to resolubilize the proteins. An exemplary alternative approach is the expression of recombined antibodies or fragments thereof in the periplasmic space of bacteria which provides an oxidizing environment and chaperonin-like and disulfide isomerases leading to the production of soluble protein. Typically, a leader sequence is fused to the protein to be expressed which directs the protein to the periplasm. The leader is then removed by signal peptidases inside the periplasm. There are three major pathways to translocate expressed proteins into the periplasm, namely the Sec pathway, the SRP pathway and the TAT pathway. Examples of periplasmic-targeting leader sequences include the pelB leader from the pectate lyase gene, the StII leader sequence, and the DsbA leader sequence. An exemplary leader sequence is a DsbA leader sequence. In some cases, periplasmic expression allows leakage of the expressed protein into the culture medium. The secretion of proteins allows quick and simple purification from the culture supernatant. Proteins that are not secreted can be obtained from the periplasm by osmotic lysis. Similar to cytoplasmic expression, in some cases proteins can become insoluble and denaturants and reducing agents can be used to facilitate solubilization and refolding. Temperature of induction and growth also can influence expression levels and solubility. Typically, temperatures between 25 °C and 37 °C are used. Mutations also can be used to increase solubility of expressed proteins. Typically, bacteria produce aglycosylated proteins. Thus, if proteins require glycosylation for function, glycosylation can be added *in vitro* after purification from host cells.

b. Yeast

Yeasts such as *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, *Yarrowia lipolytica*, *Kluyveromyces lactis,* and *Pichia pastoris* are useful expression hosts for recombined antibodies or portions thereof. Yeast can be transformed with episomal replicating vectors or by stable chromosomal integration by homologous recombination. Typically, inducible promoters are used to regulate gene expression. Examples of such promoters include AOX1, GAL1, GAL7, and GAL5 and metallothionein promoters such as

CUP1. Expression vectors often include a selectable marker such as LEU2, TRP1, HIS3, and URA3 for selection and maintenance of the transformed DNA. Proteins expressed in yeast are often soluble. Co-expression with chaperonins such as Bip and protein disulfide isomerase can improve expression levels and solubility. Additionally, proteins expressed in yeast can be directed for secretion using secretion signal peptide fusions such as the yeast mating type alpha-factor secretion signal from Saccharomyces cerevisae and fusions with yeast cell surface proteins such as the Aga2p mating adhesion receptor or the *Arxula adeninivorans* glucoamylase. A protease cleavage site such as for the Kex-2 protease, can be engineered to remove the fused sequences from the expressed polypeptides as they exit the secretion pathway. Yeast also is capable of glycosylation at Asn-X-Ser/Thr motifs.

c. Insects

Insect cells, particularly using baculovirus expression, are useful for expressing antibodies or portions thereof. Insect cells express high levels of protein and are capable of most of the post-translational modifications used by higher eukaryotes. Baculovirus have a restrictive host range which improves the safety and reduces regulatory concerns of eukaryotic expression. Typical expression vectors use a promoter for high level expression such as the polyhedrin promoter and p10 promoter of baculovirus. Commonly used baculovirus systems include the baculoviruses such as *Autographa californica* nuclear polyhedrosis virus (AcNPV), and the *Bombyx mori* nuclear polyhedrosis virus (BmNPV) and an insect cell line such as Sf9 derived from *Spodoptera frugiperda* and TN derived from *Trichoplusia ni.* For high-level expression, the nucleotide sequence of the molecule to be expressed is fused immediately downstream of the polyhedrin initiation codon of the virus. To generate baculovirus recombinants capable of expressing human antibodies, a dual-expression transfer, such as pAcUW51 (PharMingen) is utilized. Mammalian secretion signals are accurately processed in insect cells and can be used to secrete the expressed protein into the culture medium

An alternative expression system in insect cells is the use of stably transformed cells. Cell lines such as Sf9 derived cells from *Spodoptera frugiperda* and TN derived cells from *Trichoplusia ni* can be used for expression. The baculovirus immediate early gene promoter IE1 can be used to induce consistent levels of expression. Typical expression vectors include the pIE1-3 and pI31-4 transfer vectors (Novagen). Expression vectors are typically maintained by the use of selectable markers such as neomycin and hygromycin.

d. Mammalian Cells

Mammalian expression systems can be used to express antibodies or portions thereof. Expression constructs can be transferred to mammalian cells by viral infection such as adenovirus or by direct DNA transfer such as liposomes, calcium phosphate, DEAE-dextran and by physical means such as electroporation and microinjection. Expression vectors for mammalian cells typically include an mRNA cap site, a TATA box, a translational initiation sequence (Kozak consensus sequence) and polyadenylation elements. Such vectors often include transcriptional promoter-enhancers for high-level expression, for example the SV40 promoter-enhancer, the human cytomegalovirus (CMV) promoter and the long terminal repeat of Rous sarcoma virus (RSV). These promoter-enhancers are active in many cell types. Tissue and cell-type promoters and enhancer regions also can be used for expression. Exemplary promoter/enhancer regions include, but are not limited to, those from genes such as elastase I, insulin, immunoglobulin, mouse mammary tumor virus, albumin, alpha fetoprotein, alpha 1 antitrypsin, beta globin, myelin basic protein, myosin light chain 2, and gonadotropic releasing hormone gene control. Selectable markers can be used to select for and maintain cells with the expression construct. Examples of selectable marker genes include, but are not limited to, hygromycin B phosphotransferase, adenosine deaminase, xanthine-guanine phosphoribosyl transferase, aminoglycoside phosphotransferase, dihydrofolate reductase and thymidine kinase. Antibodies are typically produced using a NEO^R/G418 system, a dihydrofolate reductase (DHFR) system or a glutamine synthetase (GS) system. The GS system uses joint expression vectors, such as pEE12/pEE6, to express both heavy chain and light chain. Fusion with cell surface signaling molecules such as TCR-ζ and $Fc_\varepsilon RI$-γ can direct expression of the proteins in an active state on the cell surface.

Many cell lines are available for mammalian expression including mouse, rat human, monkey, chicken and hamster cells. Exemplary cell lines include but are not limited to CHO, Balb/3T3, HeLa, MT2, mouse NS0 (nonsecreting) and other myeloma cell lines, hybridoma and heterohybridoma cell lines, lymphocytes, fibroblasts, Sp2/0, COS, NIH3T3, HEK293, 293S, 2B8, and HKB cells. Cell lines also are available adapted to serum-free media which facilitates purification of secreted proteins from the cell culture media. One such example is the serum free EBNA-1 cell line (Pham *et al.*, (2003) *Biotechnol. Bioeng. 84*:332-42.)

e. Plants

Transgenic plant cells and plants can be used to express proteins such as any antibody or portion thereof described herein. Expression constructs are typically transferred to plants using direct DNA transfer such as microprojectile bombardment and PEG-mediated transfer into protoplasts, and with agrobacterium-mediated transformation. Expression vectors can

include promoter and enhancer sequences, transcriptional termination elements and translational control elements. Expression vectors and transformation techniques are usually divided between dicot hosts, such as *Arabidopsis* and tobacco, and monocot hosts, such as corn and rice. Examples of plant promoters used for expression include the cauliflower mosaic virus CaMV 35S promoter, the nopaline synthase promoter, the ribose bisphosphate carboxylase promoter and the maize ubiquitin-1 (*ubi*-1) promoter promoters. Selectable markers such as hygromycin, phosphomannose isomerase and neomycin phosphotransferase are often used to facilitate selection and maintenance of transformed cells. Transformed plant cells can be maintained in culture as cells, aggregates (callus tissue) or regenerated into whole plants. Transgenic plant cells also can include algae engineered to produce proteases or modified proteases (see for example, Mayfield *et al.* (2003) *PNAS 100*:438-442). Because plants have different glycosylation patterns than mammalian cells, this can influence the choice of protein produced in these hosts.

3. Purification

Antibodies and portions thereof are purified by any procedure known to one of skill in the art. The recombined germline antibodies can be purified to substantial purity using standard protein purification techniques known in the art including but not limited to, SDS-PAGE, size fraction and size exclusion chromatography, ammonium sulfate precipitation, chelate chromatography, ionic exchange chromatography or column chromatography. For example, antibodies can be purified by column chromatography. Exemplary of a method to purify antibodies is by using column chromatography, wherein a solid support column material is linked to Protein G, a cell surface-associated protein from *Streptococcus*, that binds immunoglobulins with high affinity. The antibodies can be purified to 60%, 70%, 80% purity and typically at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% purity. Purity can be assessed by standard methods such as by SDS-PAGE and coomassie staining.

Methods for purification of recombined antibodies or portions thereof from host cells depend on the chosen host cells and expression systems. For secreted molecules, proteins are generally purified from the culture media after removing the cells. For intracellular expression, cells can be lysed and the proteins purified from the extract. When transgenic organisms such as transgenic plants and animals are used for expression, tissues or organs can be used as starting material to make a lysed cell extract. Additionally, transgenic animal production can include the production of polypeptides in milk or eggs, which can be collected, and if necessary further the proteins can be extracted and further purified using standard methods in the art.

When antibodies are expressed by transformed bacteria in large amounts, typically after promoter induction, although expression can be constitutive, the polypeptides can form insoluble aggregates. There are several protocols that are suitable for purification of polypeptide inclusion bodies known to one of skill in the art. Numerous variations will be apparent to those of skill in the art.

For example, in one method, the cell suspension is generally centrifuged and the pellet containing the inclusion bodies resuspended in buffer which does not dissolve but washes the inclusion bodies, e.g., 20 mM Tris-HCL (pH 7.2), 1 mM EDTA, 150 mM NaCl and 2% Triton-X 100, a non-ionic detergent. It can be necessary to repeat the wash step to remove as much cellular debris as possible. The remaining pellet of inclusion bodies can be resuspended in an appropriate buffer (e.g., 20 mM sodium phosphate, pH 6.8, 150 mM NaCl). Other appropriate buffers are apparent to those of skill in the art.

Alternatively, antibodies can be purified from bacteria periplasm. Where the polypeptide is exported into the periplasm of the bacteria, the periplasmic fraction of the bacteria can be isolated by cold osmotic shock in addition to other methods known to those of skill in the art. For example, in one method, to isolate recombinant polypeptides from the periplasm, the bacterial cells are centrifuged to form a pellet. The pellet is resuspended in a buffer containing 20% sucrose. To lyse the cells, the bacteria are centrifuged and the pellet is resuspended in ice-cold 5 mM $MgSO_4$ and kept in an ice bath for approximately 10 minutes. The cell suspension is centrifuged and the supernatant decanted and saved. The recombinant polypeptides present in the supernatant can be separated from the host proteins by standard separation techniques well known to those of skill in the art. These methods include, but are not limited to, the following steps: solubility fractionation, size differential filtration, and column chromatography.

G. Applications and uses of the libraries

Provided herein are methods of using the antibody libraries provided herein for screening to identify or select an antibody or antibodies that alter or modulate (increase or decrease) an activity of a target. As discussed above, the antibody libraries provided herein contain members 1) that are each different from all other members in the library; and 2) that are each productive and functional. By virtue of these characteristics the libaries are both diverse and robust in their screening capabilties. For example, using the libraries provided herein, it is possible to screen a small library (e.g. containing 1000 or fewer members) and identify antibodies having desired functions or activities. This is exemplified in Example 13

where a library of only 960 members was used in a screening assay for binding to various targets, resulting in the identification of several high affinity (nanomolar affinity) antibodies.

In the method of screening herein, any desired activity can be assayed for, including but not limited to binding, cytotoxicity, differentiation or proliferation of cells, cell migration, apoptosis, angiogenesis and alteration of gene expression. For example, the resulting libraries can be screened for the discovery of agonist or antagonist antibodies against therapeutic targets, such as, for example, targets involved in cell proliferation and differentiation, cell migration, apoptosis and angiogeneis. Such targets include, but not limited to, growth factors, cytokines, lymphocytic antigens, other cellular activators and receptors thereof.

In other examples, the libraries can be screened using "blind"functional screens to measure an observable biological processes of interest without requiring specific knowledge of the target in advance. Any Hit that is identified in such screeing assays, for example by virtue of a strong functional activity, can be further analyzed to identify the specific target. The "blind" assay approach can be applied to any observable biological outcome. For example, apoptosis of B-cells can be readily assayed, and a screen for increased B-cell apoptosis can yield antibody Hits that promote B-cell killing. Such antibodies can bind known B-cell surface-proteins like CD-20, or bind a novel target. In another example, the increased (or decreased) secretion of specific cytokines, for example interferon alpha, from a population of cells such as bone marrow cells can be assayed by ELISA, allowing screening for antibodies which modify the secretion of these proteins. No *a priori* knowledge of the mechanism that achieves the screened outcome is necessary, and the specific antibody target can later be pursued if the effect is strong. The blind functional assays can also be merged with high-content screening approaches to find antibodies that induce morphological changes in a certain cell type or promote cell differentiation in a progenitor cell population.

The methods of screening provided herein involve contacting each member of an antibody library provided herein with a target protein, peptide or antigen or cell expressing a target protein, peptide or antigen or simply a cell population and identifying antibody members that modulate (increase or decrease) the activity of the target protein or cell. For example, the members of the library can be contacted to identify antibodes that bind to the target protein. In another example, antibodies can be screened for modulation of a functional activity of a target. Functional assays permit identification of agonist and antagonist antibodies. It is contemplated herein that this screening assay is particularly useful against membrane-bound proteins, such as receptor targets and other signaling molecules.

The antibody libraries provided herein can be presented in a format that permits screening, such as, for example, as addressable libraries, including spatial arrays; and cell display libraries, including yeast display and mammalian display, phage display, mRNA display, including ribosome display, and DNA display. For example, screening is performed on addressable antibody libraries, such as a spatial arrayed library, whereby each antibody member at a locus (e.g. well) is separately contacted and screened against a target protein or proteins from all other members in the library. Thus, upon identification of a "HIT" the identity of the antibody member is immediately known from its location in the array without any requirement for further enrichment, amplification or sequencing thereof. Library screening can be high-throughput by screening hundreds to thousands or more antibodies in the same screening assay.

Any technique known to one of skill in the art can be used for antibody screening herein to identify antibody members having a desired activity. For a typical high-throughput screen, sets of microtiter plates are generated, whereby each well in the microplate contains a different library member. For example, plates can be created where every well of a plate contains an antibody containing the same antibody heavy chain, but each well contains a different light chain such that the paired antibody (heavy and light chain) in each well is different from the antibody in all other wells of the plate. All wells are then loaded with the constant components necessary for performing the screening assay (for example, target protein or cell expressing a target protein, buffer, assay reagent), incubated for the appropriate time, and assayed for a readout of choice. This method can be used for screening for activities such as binding or other functional assays where reaction with a single purified target molecule or cell(s) is sufficient to give a readout.

For example, in such methods, a cell-based assay can be performed to effect activation of the target (e.g. in the presence of a ligand thereof) and activation (such as by assessing signaling, differentiation, proliferation, chemotaxis, apoptosis or other downstream process) is assessed in the presence of the antibody. Generally, the performance of such functional assays require the presence of soluble protein. Hence, it is an advantage of the antibody libraries provided herein that they permit screening in a soluble format. For example, the antibodies can be addressed, for example, in wells of a multiwall plate. Each antibody at each locus is different. Thus, upon assessing activity the identity of a "Hit" can be immediately determined.

Following an initial round of screening, identified "HITS" can be further optimized by iterative screening and/or by directed evolution methods. For example, following

identification of a "Hit" 'focused' libraries can be created using information gained from the primary screening libraries. Focused libraries represent substructures of the original primary library because they are created from germline segment components that are related to those of the "Hit." They can allow one to refine the properties of a selected "Hit", such as by increasing its affinity of binding or associated functional activity.

The identity of the antibody is known by virtue of its address. Once identified, the antibody Hits can be generated as a full-length IgG or as Fab, Fab', Fab'-SH and $F(ab')_2$ fragments. The antibody or fragments thereof can be created by traditional means, such as using recombinant techniques and enzymatic digestion. Antibodies or fragments thereof can be chimeric or humanized. The antibodies or fragments thereof can be used for diagnostic and therapeutic purposes as set forth below.

1. Binding Assays

The antibody libraries provided herein can be screened for their ability to bind a selected target by any method known to one of skill in the art. Exemplary target antigens are described below. Binding assays can be performed in solution, suspension or on a solid support. For example, target antigens can be immobilized to a solid support (e.g. a carbon or plastic surface or chip) and contacted with antibody. Unbound antibody or target protein can be washed away and bound complexes can then be detected. Binding assays can be performed under conditions to reduce nonspecific binding, such as by using a high ionic strength buffer (e.g. 0.3-0.4 M NaCl) with nonionic detergent (e.g. 0.1% Triton X-100 or Tween 20) and/or blocking proteins (e.g. bovine serum albumin or gelatin). Negative controls also can be including in such assays as a measure of background binding. Binding affinities can be determined using Scatchard analysis (Munson *et al.*, *Anal. Biochem.*, 107:220 (1980)), BIACore or other methods known to one of skill in the art.

Exemplary binding assays include, but are not limited to immunoassays such as competitive and non-competitive assay systems using techniques such as western blots, radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, Meso Scale Discovery (MSD, Gaithersburg, Maryland), immunoprecipitation assays, ELISPOT, precipitin reactions, gel diffusion precipitin reactions, immunodiffusion assays, agglutination assays, complement-fixation assays, immunoradiometric assays, fluorescent immunoassays, and protein A immunoassays. Such assays are routine and well known in the art (see, e.g., Ausubel *et al.*, eds, 1994, Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York, which is incorporated by reference herein in its entirety). Other assay formats include liposome immunoassays (LIA), which use liposomes

designed to bind specific molecules (e.g., antibodies) and release encapsulated reagents or markers. The released chemicals are then detected according to standard techniques (see Monroe *et al.*, (1986) *Amer. Clin. Prod. Rev.* 5:34-41).

Generally, binding is detected using a detectable moiety or label (e.g. an enzyme, a radionuclide, a fluorescent probe, electrochemiluminescent label, or a color dye) typically attached to the target or, if desired, directly to the antibody members in the library. Alternatively, binding can be detected by a further third reagent that itself is labeled or detectable. For example, detection of an antibody bound to a target protein can be achieved using a labeled capture molecule in a sandwich assay format. Other proteins capable of specifically binding immunoglobulin constant regions, such as protein A or protein G also can be used as the label agent. These proteins exhibit a strong non-immunogenic reactivity with immunoglobulin constant regions from a variety of species (see, e.g., Kronval *et al.*, (1973) *J. Immunol.* 111:1401-1406; Akerstrom *et al.*, (1985) *J. Immunol.* 135:2589-2542). The detction agent can be modified with a detectable moiety, such as biotin, to which another molecule can specifically bind, such as streptavidin. A variety of detectable moieties are well known to those skilled in the art.

The choice of label or detectable group used in the assay is not critical, as long as it does not significantly interfere with the specific binding of the antibody used in the assay. Generally, the choice depends on sensitivity required, ease of conjugation with the compound, stability requirements, available instrumentation, and disposal provisions. One of skill in the art is familiar with labels and can identify a detectable label suitable for and compatible with the assay employed.

The detectable group can be any material having a detectable physical or chemical property. Such detectable labels have been well-developed in the field of immunoassays and, in general, most any label useful in such methods can be applied to the present invention. Thus, a label is any composition detectable by spectroscopic, photochemical, biochemical, immunochemical, electrical, optical or chemical means. Useful labels in the present invention include magnetic beads (e.g., DYNABEADS™), fluorescent dyes (e.g., fluorescein isothiocyanate, Texas red, rhodamine, and the like), radiolabels (e.g., 3H, 125I, 35S, 14C, or 32P), enzymes (e.g., horse radish peroxidase, alkaline phosphatase and others commonly used in an ELISA), chemiluminescent labels (luciferin and 2,3-dihydrophtahlazinediones, e.g., luminol), and colorimetric labels such as colloidal gold or colored glass or plastic beads (e.g., polystyrene, polypropylene, latex, etc.). For a review of various labeling or signal producing systems that can be used, see e.g. United States Patent No. 4,391,904.

Means of detecting labels are well known to those of skill in the art. Thus, for example, where the label is a radioactive label, means for detection include a scintillation counter or photographic film as in autoradiography. Where the label is a fluorescent label, it can be detected by exciting the fluorochrome with the appropriate wavelength of light and detecting the resulting fluorescence. The fluorescence can be detected visually, by the use of electronic detectors such as charge coupled devices (CCDs) or photomultipliers and the like. Similarly, enzymatic labels can be detected by providing the appropriate substrates for the enzyme and detecting the resulting reaction product. Finally simple colorimetric labels can be detected simply by observing the color associated with the label.

Some assay formats do not require the use of labeled components. For instance, agglutination assays can be used to detect the presence of the target antibodies. In this case, antigen-coated particles are agglutinated by samples containing the target antibodies. In this format, none of the components need be labeled and the presence of the target antibody is detected by simple visual inspection.

Alternatively, the antibody libraries provided herein can be screened for their ability to bind to cells, using whole cell panning, with or without subtractive panning. Screening can be done against live cells or against intact, mildly fixed target cells. Methods for whole cell panning have been described previously (see e.g. Siegel *et al.* (1997) *J. Immunol. Methods* 206:73-85 incorporated herein by reference). Other techniques for screening which can be applied include fluorescent activated cell sorting (FACs).

For high-throughput screening, assays can be multiplexed. Thus, the binding affinities of antibodies to a number of different target proteins can be determined at once. In one example, different target proteins can be separately labeled with different detectable moieities. For example, different antigens can be coupled to color-coded beads (Schwenk *et al.* (2007) Mol. Cell. Prot., 6:125-132). In another example, multi-spot plates can be used that permit assay multiplexing by absorption of of up to 100 proteins in a locus of the plate (e.g. using Multi-Array or Multi-Spot plates from Meso Scale Discovery; MSD, Gaithersburg, MD). In such an example, addressed antibody libraries provided herein can be screened by addition of a different antibody member to each well of a multi-spot plate. The assay readily permits the screening of thousands of antibodies at once against numerous target proteins. This is exemplified herein in Example 13.

In the methods of screening herein, the binding affinity of the antibodies is determined to identify or select antibodies that have high affinity for a target protein. Typically, antibodies are selected or identified that have a binding affinity that is or is about

10^{-6}M, 10^{-7}M, 10^{-8}M, 10^{-9}M, 10^{-10}M, 10^{-11}M, 10^{-12}M or lower. Generally, antibodies are screened until antibodies are identified having nanomolar or sub-nanomolar binding affinity. A "Hit" identified in a first round of screening that does not have the desired binding affinity can be optimized by iterative screening and/or directed evolution methods and further screened for binding to a target antigen to identify an antibody that has a high binding affinity.

Any method known to one of skill in the art can be used to measure the binding affinity of an antibody. For example, the binding properties of an antibody can be assessed by performing a saturation binding assay, for example, a saturation ELISA, whereby binding to a target protein is assessed with increasing amounts of antibody. In such experiments, it is possible to assess whether the binding is dose-dependent and/or saturable. In addition, the binding affinity can be extrapolated from the 50% binding signal. Typically, apparent binding affinity is measured in terms of its association constant (Ka) or dissociation constant (Kd) and determined using Scatchard analysis (Munson *et al.*, *Anal. Biochem.*, 107:220 (1980). For example, binding affinity to a target protein can be assessed in a competition binding assay in where increasing concentrations of unlabeled protein is added, such as by radioimmunoassay (RIA) or ELISA. Binding affinity also can be analyzed using BIAcore kinetic analysis. This involves analyzing the binding and dissociation of an antibody member from chips containing immobilized target proteins on their surface. The Biacore evaluation software generates the values of Ka and Kd by fitting the data to interaction models. It is understood that the binding affinity of an antibody can vary depending on the assay and conditions employed, although all assays for binding affinity provide a rough approximation. By performing various assays under various conditions it is possible to estimate the binding affinity of an antibody.

In addition, binding affinities can differ depending on the structure of an antibody. For example, generally a bivalent antibody, for example a bivalent F(ab')2 fragment or full-length IgG, has a better binding affinity then a monovalent Fab antibody. Hence, it is understood that where a Fab has a specified binding affinity for a particular target, it is excepted that the binding affinity is even greater for a full-lenth IgG that is bivalent.

2. Functional Activity

The antibody libraries provided herein can be screened for their ability to modulate the functional activity of a target by any method known to one of skill in the art. Assays can be designed to identify antibodies capable of binding and/or modulating cell surface receptors. Such antibodies can either be agonists, mimicking the normal effects of receptor

binding, or antagonists, inhibiting the normal effects of receptor binding. Of particular interest is the identification of agents which bind to the receptors and modulate intracellular signalling.

In some example, such assays are cell-based assays. Generally, assays are performed using cell lines known to express the target of interest. Such cells are known to one of skill in the art. For example, one can consult the ATCC Catalog (atcc.org) to identify cell lines. Also, if a particular cell type is desired, the means for obtaining such cells, and/or their instantly available source is known to those in the art. An analysis of the scientific literature can readily reveal appropriate choice of cells expressing any desired target. Table 18 lists exemplary cells lines that express targets of interest that can be screened in functional activities herein against antibody libraries provided herein.

Table 18. Cell lines expressing targets

Target	Cell Lines	References
GP IIb/IIIa	MEG-01 chronic myelogenous leukemia megakaryoblast cells (ATCC CRL-2021); UT-7 human leukemia cell ine	Ogura *et al.* Establishment of a novel human megakaryoblastic leukemia cell line, MEG- 01, with positive Philadelphia chromosome. Blood 66: 1384-1392, 1985; Komatsu *et al.* Establishment and Characterization of a Human Leukemic Cell Line with Megakaryocytic Features: Dependency on Granulocyte-Macrophage Colony-stimulating Factor, Interleukin 3, or Erythropoietin for Growth and Survival. Cancer Research 51:341-348 (1991)
GM-CSF-R	VA-ES-BJ epitheloid sarcoma cells (ATCC CRL-2138); TF1-HaRas; TF1-vRaf; TF1-vSrc; HL-60 (ATCC CCL-240); U-937 (ATCC CRL-1593.2); ML-2	Int J Oncol 1995;7:51-56; Ali Habib *et al.* A urokinase-activated recombinant diphtheria toxin targeting the granulocyte-macrophage colony-stimulating factor receptor is selectively cytotoxic to human acute myeloid leukemia blasts. Blood 104(7):2143-2148 (2004); Kiser *et al.* Oncogene-dependent engraftment of human myeloid leukemia cells in immunosuppressed mice. Leukemia 15(5):814-818 (2001)
VEGFA	Human A673 rhabdomyosarcoma cells (ATCC CRL-1598); Breast carcinoma MDA-MB-435 cells (ATCC); Bovine adrenal cortex-derived capillary endothelial cells	Gerber *et al.* Complete inhibition of rhabdomyosarcoma xenograft growth and neovascularization requires blockade of both tumor and host vascular endothelial growth factor. Cancer Res. 60(22):6253-8 (2000); Presta *et al.* Humanization of an anti-vascular endothelial growth factor monoclonal antibody for the therapy of solid tumors and other disorders. Cancer Research, 57(20):4593-4599 (1997)
CD3 `	Jurkat E6.1 Human leukemic T cell lymphoblast (Sigma Aldrich 88042803)	Buhler *et al.* A bispecific diabody directed against prostate-specific membrane antigen and CD3 induces T-cell mediated lysis of prostate cancer cells. Cancer Immunol Immunother. 57(1):43-52 (2008)
EGFR	DiFi human colorectal carcinoma cells; A431 cells (ATCC CRL-1555); Caco-2 colorectal	Olive *et al.* Characterization of the DiFi rectal carcinoma cell line derived from a familial adenomatous polyposis patient. In Vitro Cell Dev Biol. 29A(3 Pt 1):239-248 (1993); Wu *et al.* Apoptosis induced by an anti-epidermal growth factor receptor monoclonal antibody in a human colorectal

	adenocarcinoma cells (ATCC HTB-37); HRT-18 colorectal adenocarcinoma cells (ATCC CCL-244); HT-29 colorectal adenocarcinoma cells (ATCC HTB-38)	carcinoma cell line and its delay by insulin. Clin. Invest. 95(4): 1897-1905 (1995)
EPO receptor	A2780 ovarian cancer cells; UT-7 human leukemia cell ine	Jeong *et al.* Characterization of erythropoietin receptor and erythropoietin expression and function in human ovarian cancer cells. Int J Cancer. 122(2):274-280 (2008); Elliott *et al.* Activation of the Erythropoietin (EPO) Receptor by Bivalent Anti-EPO Receptor Antibodies. J Biol Chem. 271(40):24691-24697 (1996)
Her2/Neu receptor	BT-474 ductal carcinoma breast cancer cell (ATCC HTB-20); SK-BR-3 adenocarcinoma breast cancer cell (ATCC HTB-30); MDA-MB-453 metastatic carcinoma cell line (ATCC HTB-131)	Le *et al.* Roles of human epidermal growth factor receptor 2, c-jun NH2-terminal kinase, phosphoinositide 3-kinase, and p70 S6 kinase pathways in regulation of cyclin G2 expression in human breast cancer cells. Mol Cancer Ther. 6(11):2843-2857 (2007)
cMet	H1993 lung adenocarcinoma cells (ATCC CRL-5909); H1838 lung adenocarcinoma cells (ATCC CRL-5899); SW 900 lung squamous cell carcinoma cells (ATCC HTB-59); H358 lung bronchioalveolar carcinoma cells (ATCC CRL-5807); SK-Lu-1 lung adenocarcinoma cells (ATCC HTB-57); H441 Non-small cell lung cancer cells (ATCC HTB-174)	Ma *et al.* Functional expression and mutations of c-Met and its therapeutic inhibition with SU11274 and small interfering RNA in non-small cell lung cancer. Cancer Res. 65(4):1479-1488 (2005); Ma *et al.* A selective small molecule c-MET Inhibitor, PHA665752, cooperates with rapamycin. Clin Cancer Res 11(6):2312-2319 (2005)
CD20	Ramos Burkitt's lymphoma B cells (ATCC CRL-1596); Raji Burkitt's lymphoma B cells (ATCC CCL-86): Daudi Burkitt's lymphoma B cells (ATCC CCL-213); 2F7 Burkitt's lymphoma B cells	Jazirehi *et al.* Rituximab (anti-CD20) selectively modifies Bcl-xL and apoptosis protease activating factor-1 (Apaf-1) expression and sensitizes human non-Hodgkin's lymphoma B cell lines to paclitaxel-induced apoptosis. Mol Cancer Ther. 2(11):1183-1193 (2003)

In addition, cells lines expressing a target of interest can be generated by transient or stable transfection with an expression vector expressing a target of interest. Methods of transfection and expression are known to those of skill in the art (see e.g., Kaufman R.J. (1990) Methods in Enzymology 185:537-566; Kaufman *et al.* (1990) Methods in Enzymology 185:537-566). In addition, any primary cell or cell line can be assessed for expression of a particular target (e.g. cell surface marker). Cell surface markers can be assayed using fluorescently labeled antibodies and FACS. Suitable cell lines include A549 (lung), HeLa , Jurkat, BJAB, Colo205, H1299 , MCF7, MDA-MB-231, PC3, HUMEC, HUVEC, and PrEC.

Any suitable functional effect can be measured, as described herein. For example, cellular morphology (e.g., cell volume, nuclear volume, cell perimeter, and nuclear perimeter), ligand binding, substrate binding, nuclease activity, apoptosis, chemotaxis or cell migrations, cell surface marker expression, cellular proliferation, GFP positivity and dye dilution assays (e.g., cell tracker assays with dyes that bind to cell membranes), DNA synthesis assays (e.g., 3H-thymidine and fluorescent DNA-binding dyes such as BrdU or Hoechst dye with FACS analysis) and nuclear foci assays, are all suitable assays to identify potential modulators using a cell based system. Other functional activities that can be measured include, but are not limited to, ligand binding, substrate binding, endonuclease and/or exonuclease activity, transcriptional changes to both known and uncharacterized genetic markers (e.g., northern blots), changes in cell metabolism, changes related to cellular proliferation, cell surface marker expression, DNA synthesis, marker and dye dilution assays (e.g., GFP and cell tracker assays), contact inhibition, tumor growth in nude mice, and others.

For example, antibodies or portions thereof in the libraries provided herein can be assessed for their modulation of one or more phenotypes of a cell known to express a target protein. Phenotypic assays, kits and reagents for their use are well known to those skilled in the art and are herein used to screen antibody libraries. Representative phenotypic assays, which can be purchased from any one of several commercial vendors, include those for determining cell viability, cytotoxicity, proliferation or cell survival (Molecular Probes, Eugene, Oregon; PerkinElmer, Boston, Mass.), protein-based assays including enzymatic assays (Panvera, LLC, Madison, Wis.; BD Biosciences, Franklin Lakes, N.J.; Oncogene Research Products, San Diego, Calif.), cell regulation, signal transduction, inflammation, oxidative processes and apoptosis (Assay Designs Inc., Ann Arbor, Mich.), triglyceride accumulation (Sigma-Aldrich, St. Louis, Mo.), angiogenesis assays, tube formation assays, cytokine and hormone assays and metabolic assays (Chemicon International Inc., Temecula, Calif.; Amersham Biosciences, Piscataway, N.J.).

Cells determined to be appropriate for a particular phenotypic assay (i.e., A549, HeLa, Jurkat, BJAB, Colo205, H1299, MCF7, MDA-MB-231, PC3, HUMEC, HUVEC, and PrEC and any others known to express the target of interest) are treated with antibodies as well as control compounds. If necessary, a ligand for the receptor target is included so that activation of the receptor is effected. At the end of the treatment period, treated and untreated cells are analyzed by one or more methods specific for the assay to determine phenotypic outcomes and endpoints.

Phenotypic endpoints include changes in cell morphology over time or treatment dose as well as changes in levels of cellular components such as proteins, lipids, nucleic acids, hormones, saccharides or metals. Measurements of cellular status which include pH, stage of the cell cycle, intake or excretion of biological indicators by the cell, are also endpoints of interest.

The assays can be performed to assess the direct effects of an antibody on a target protein. For example, if the target protein is a cell surface receptor, an antibody can be added to assess whether the target protein directly modulates, such as by stimulation, the activity or function of the receptor. In such instances, the antibody is deemed an agonist antibody. In other examples, if the target protein is a cell surface receptor, the activity of the receptor can be stimulated in the presence of a ligand or other stimulating agent in the presence or absence of the antibody to determine if the antibody modulates (e.g. inhibits) the actions of the antibody. For example, the antibody can act by blocking the ability of the ligand to interact with the receptor and/or otherwise induce a negative stimulatory signal. In such instances, the antibody is deemed to be an antagonist of the receptor. Thus, the methods of screening herein by functional activity permits identification of agonist and antagonist antibodies.

a. Differentiation

Cellular differentiation can be analyzed using any assay that allows a detection of a physical, chemical or phenotypic change. Various assays are used to quantitatively determine cellular proliferation and activation in response to an external stimuli. Cell proliferation assays are used to quantitatively determine cellular proliferation by incorporating a reagent into the DNA of newly synthesized cells upon cell division. Such reagents include, but are not limited to ^{3}H-thymidine, 5-bromo-2′-deoxyuridine (BrdU) and fluorescent Hoechst dyes. Cell viability assays are used to determine the number of healthy cells in a sample by staining cells with a dye and measuring how many cells uptake the dye based on the fact that living cells will exclude the dye. Such dyes include but are not limited to 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT), 2,3-Bis(2-methoxy-4-nitro-5-sulfophenyl)-2H-

tetrazolium-5-carboxanilide inner salt (XTT), and 4-[3-(4-iodophenyl)-2-(4-nitrophenyl)-2H-5-tetrazolio]-1,3-benzene disulfonate (WST-1). Uptake of the reagent is measured either colorimetrically using a spectrophotometer or by measuring radiation with a scintillation counter. Details of these methods are well-known to one skilled in the art. For example, Example 12 exemplifies an MTT proliferation assay to assess cell proliferation.

Fluorescent dyes are commonly used for the detection of live cells and key functional activities in a variety of cell-based assays. There are several non-radioactive, fluorescence-based assays that are not dependent on cellular metabolism. The fluorescent dye binds nucleic acids and the fluorescence can then be measured quantitatively or qualitatively. Such dyes include, but are not limited to, propidium iodide and Hoechst 33342. The cell number can then be quantitated based on the fluorescence. DNA content can also be quantitated using the tools available in the imaging instruments. Details of these methods are well known to one skilled in the art.

The degree of invasiveness into Matrigel or some other extracellular matrix constituent can be used as an assay to identify antibodies that are capable of inhibiting abnormal cell proliferation and tumor growth. Tumor cells exhibit a good correlation between malignancy and invasiveness of cells into Matrigel or some other extracellular matrix constituent. In this assay, tumorigenic cells are typically used as host cells. Therefore, antibodies can be identified by measuring changes in the level of invasiveness between the host cells before and after the introduction of potential modulators.

Briefly, the level of invasion of host cells can be measured by using filters coated with Matrigel or some other extracellular matrix constituent. Penetration into the gel, or through to the distal side of the filter, is rated as invasiveness, and rated histologically by number of cells and distance moved, or by prelabeling the cells with 125I and counting the radioactivity on the distal side of the filter or bottom of the dish. (see, e.g., Freshney, Culture of Animal Cells a Manual of Basic Technique, 3rd ed., Wiley-Liss, New York (1994), herein incorporated by reference).

b. Alteration of Gene Expression

Detection of binding and/or modulation of a target by an antibody can be accomplished by detecting a biological response, such as, for example, measuring Ca^{2+} ion flux, cAMP, IP3 , PIP3 or transcription of reporter genes. Analysis of the genotype of the cell (measurement of the expression of one or more of the genes of the cell using a reporter gene assay) after treatment is also used as an indicator of the efficacy or potency of the antibody.

Hallmark genes, or those genes suspected to be associated with a signal transduction pathway are measured in both treated and untreated cells.

Assays can be performed that measure the activation of a reporter gene. Suitable reporter genes include endogenous genes as well as exogenous genes that are introduced into a cell by any of the standard methods familiar to the skilled artisan, such as transfection, electroporation, lipofection and viral infection. For example, cells expressing a recombinant receptor can be transfected with a reporter gene (e.g., chloramphenicol acetyltransferase, firefly luciferase, bacterial luciferase, β-galactosidase and alkaline phosphatase) operably linked to a response element. The cells are then incubated with antibodies and the expression of the reporter gene is compared to expression in control cells that do not express the recombinant receptor but that are essentially identical in other respects. A statistically significant change in reporter gene expression in the receptor-expressing cells is indicative of a test compound that interacts with the receptor. Furthermore, the protein of interest can be used as an indirect reporter via attachment to a second reporter such as red or green fluorescent protein (see, e.g., Mistili & Spector, (1997) *Nature Biotechnology* 15:961-964).

The reporter construct is typically transfected into a cell. After treatment with a potential modulator, the amount of reporter gene transcription, translation, or activity is measured according to standard techniques known to those of skill in the art. The use of a reporter gene assay using luciferase to measure activiation of STAT5 directly or by induction of cyclin-D promoter is exemplified in Example 12.

c. Cytotoxicity Activity

Antibodies can be screened for their ability to directly induce apoptosis or programmed cell death or to indirectly induce apoptosis by blocking growth factor receptors, thereby effectively arresting proliferation. Antibodies also bind complement, leading to direct cell toxicity, known as complement dependent cytotoxicity (CDC). Thus, assays can be performed to assess complement-dependent cytotoxicity.

A variety of assays to assess apoptosis are known to one of skill in the art. For example, apoptosis assays include those that assay for the activation of a caspase, which are enzymes involved in apoptosis. Caspase assays are based on teh measurement of zymogen processing to an active enzyme and proteolytic activity. A number of commercial kits and reagents are available to assess apoptosis based on caspase function including, but not limited to, PhiPhiLux (OncoImmunin, Inc.), Caspase 3 activity assay (Roche Applied science), Homogenous Caspase assay (Roche Applied Science), Caspase-Glo Assays (Promega), Apo-ONE Homogeneous Caspase-3/7 Assay (Promega), CaspACE Assay System Colorimetric or

Fluormetric (Promega), EnzChek Caspase-3 Assay Kit (Invitrogen), Imag-iT LIVE green Caspase-3 and 7 Detection Kit (Invitrogen), Active Caspase-3 Detection Kits (Stratagene), Caspase-mediated Apoptosis Products (BioVision) and CasPASE Apoptosis Assay Kit (Genotech). Example 11 exemplifies a assaying for apoptosis using a caspase assay.

Assays for apoptosis include TUNEL and DNA fragmentation assays that measure the activation of nucleases and subsequent cleavage of DNA into 180 to 200 base pair increments. Such assays and kits are commercially available and include, but are not limited to, Apoptotic DNA Ladder Kit (Roche Applied Science), Cellular DNA Fragmentation ELISA (Roche Applied Science), Cell Death Detection ELISAPLUS (Roche Applied Science), In Situ Cell Death Detection Kit (Roche Applied Science), DeadEnd Fluorometirc or Colorimetric TUNEL System (Promega), APO-BrdU TUNEL Assay Kit (Invitrogen), and TUNEL Apoptosis Detection Kit (Upstate).

Other assays to assess apoptosis include, for example, cell permeability assays that evaluate the loss of membrane integrity. For example, to determine whether the antibody is able to induce cell death, loss of membrane integrity as evaluated by uptake of propidium iodide (PI), trypan blue, or 7-aminoactinomycin D (7AAD) can be assessed relative to untreated cells. In addition, commercial kits such as APOPercentage Assay (Biocolor Assays) can be used to measure apoptosis. Annexin V assays also can be employed. Annexin V binds to phosphatidylserine, which is normally found on the inner surface of the cytoplasmic membrane. During apoptosis, phosphatidylserine is translocated to the otuer surface and can be detected by Annexin V. For example, standard binding assays using a fluorescent labeled Annexin V can be used (e.g. Annexin V, Alex Fluor 350 Conjugate from Invitrogen). Apoptosis also can be measured by assessing the presence of other markers of apoptosis, assessing protein cleavage, and/or by mitochondrial and ATP/ADP assays. Such assays are routine and known to one of skill in the art.

For example, apoptosis analysis can be used as an assay to identify functional antibodies using cell lines, such as RKO or HCT116, or other cells expressing a target protein of interest. The cells can be co-transfected with a construct containing a marker gene, such as a gene that encodes green fluorescent protein, or a cell tracker dye. The apoptotic change can be determined using methods known in the art, such as DAPI staining and TUNEL assay using fluorescent microscope. For TUNEL assay, commercially available kit can be used (e.g., Fluorescein FragEL DNA Fragmentation Detection Kit (Oncogene Research Products, Cat.# QIA39) and Tetramethyl-rhodamine-5-dUTP (Roche, Cat. # 1534 378)). Cells contacted with an antibody can exhibit, e.g., an increased apoptosis compared to control.

Cell death *in vitro* can be determined in the absence of complement and immune effector cells to distinguish cell death induced by antibody dependent cellular cytotoxicity (ADCC) or complement dependent cytotoxicity (CDC). Thus, the assay for cell death can be performed using heat inactivated serum (i.e. in the absence of complement) and in the absence of immune effector cells.

3. Targets

In the screening methods provided herein, the antibodies are screened for any activity, such as binding or other functional activity, against a target. The activity can be an agonist or antagonist activity of the target. The screening assays can be designed based on any contemplated target. Exemplary of such targets include membrane-bound proteins, receptors and ligands thereof; ion channels; G-protein coupled receptors; novel epitopes; and non-protein antigens. Any activity can be assessed and is a function of the target of interest. One of skill in the art is familiar with the activities of various targets, and can choose a screening assay based on such known activities. Many of these activities for exemplary targets are exemplified herein below. Binding activity can be assessed for all targets.

Membrane-bound proteins, receptors and ligands thereof

Exemplary targets are membrane-bound proteins, receptors and ligands thereof that can play important roles in, among other things, the formation, differentiation and maintenance of multicellular organisms. Identifying antibodies that interfere with these functions is contemplated. For example, the fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. These secreted polypeptides or signaling molecules normally pass through the cellular secretory pathway to reach their site of action in the extracellular environment. Thus, identification of antibodies against any one or more of such targets (receptor or ligand) can modulate a pathway important in a disease, thereby modulating the disease and ameliorating symptoms thereof.

Such membrane-bound proteins and cell receptors include, but are not limited to, cytokine receptors, receptor kinases, receptor phosphatases, receptors involved in cell-cell interactions, and cellular adhesin molecules like cadherins and integrins, and ligands of any such receptors. Exemplary of such targets include, membrane bound receptors, such as cell

surface receptors, including, but are not limited to, a VEGFR-1, VEGFR-2, VEGFR-3 (vascular endothelial growth factor receptors 1, 2, and 4), a epidermal growth factor receptor (EGFR), ErbB-2, ErbB-b3, IGF-R1, C-Met (also known as hepatocyte growth factor receptor; HGFR), DLL4, DDR1 (discoidin domain receptor), KIT (recetpr for c-kit), FGFR1, FGFR2, FGFR4 (fibroblast growth factor receptors 1, 2, and 4), RON (recepteur d'origine nantais; also known as macrophage stimulating 1 receptor), TEK (endothelial-specific receptor tyrosine kinase), TIE (tyrosine kinase with immunoglobulin and epimermal growth factor homology domains receptor), CSF1R (colngly stimulating factor 1 receptor), PDGFRB (platelet-derived growth factor receptor B), EPHA1, EPHA2, EPHB1 (erythropoietin-producing hepatocellular receptor A1, A2 and B1), TNF-R1, TNF-R2, HVEM, LT-βR, CD20, CD3, CD25, NOTCH, G-CSF-R, GM-CSF-R and EPO-R. Other targets include membrane-bound proteins such as selected from among a cadherin, integrin, CD52 or CD44. Exemplary ligands that can be targets of the screening methods herein, include, but are not limited to, VEGF-A, VEGF-B, VEGF-C, VEGF-D, PIGF, EGF, HGF, TNF-α, LIGHT, BTLA, lymphotoxin (LT), IgE, G-CSF, GM-CSF and EPO.

One of skill in the art is familiar with the activity and functions of various target proteins. Thus, screening assays (e.g. binding or functional assays), such as any described above, for example, binding, proliferation or apoptosis assays, can be chosen to screen antibody libraries herein. Table 18A provides a summary of the activities and known function of exemplary target proteins, and exemplary assays that can be employed to screen such target proteins. In another example, antibodies or fragments thereof can be screened for binding affinity for a target protein. Binding can be to a known epitope in a target protein or to a novel epitope, which can be identified as described herein below. Table 18B provides examples of known epitopes for exemplary target proteins recognized by therapeutic antibodies. The sections that follow also further exemplify the activity and function of target proteins, including exemplary screening assays and antibodies identified thereby. It is understood that similar assays can be employed against any target protein of interest to identify antibodies that exhibit high affinity to the target protein and/or otherwise modulate the activity of a target protein.

TABLE 18A: TARGET PROTEINS

Target	SEQ ID NO	Screening Assay	Functions/Activity	Existing Antibody Drugs
CD20	2011	Apoptosis of B cell lymphoma cell lines expressing CD20 on the surface	B-cell lymphoma	Rituxan

HER2/ Neu receptor	1999	Binding to HER2/Neu receptor and inhibition of cancer cell growth	Breast cancer	Herceptin
VEGFA	2012	Binding	Colorectal cancer, non-small lung cancer. Neovascular age-related macular degeneration	Avastin, Lucentis
EGFR	2000	Binding	Colorectal, head and neck, metastatic cancers	Erbitux, Vectibix
CD52	2013	Binding to CD52 on T and B cells	B-cell chronic lymphocytic leukemia	Campath
TNFα	2014	Binding to TNFα blocks its interaction with p55 and p75 receptors, reducing the level of inflammation markers, CRP, ESR, IL6	Rheumatoid arthritis	Humira, Remicade
CD25	2015	Binding to CD25 (IL2 receptor) inhibits lymphocyte activation	Prophylaxis against allograft rejection	Simulect, Zenapax
CD3	2016 (delta) 2017 (gamma) 2018 (zeta) 2019 (epsilon)	Binding blocks T cell function	Allograft rejection, acute renal and hepatic	Orthoclone
IgE	2020 (constant) 2021 (FcER1) 2022 (FcERII)	Binding to high affinity IgE reduces activation of mast cells, basophils and release of inflammatory mediators	Asthma	Xolair
IIb/IIIa integrin receptor	2023 (IIIa) 2024 (IIb)	Binding to the receptor inhibits platelet aggregation	Prevention of cardiac ischaemia	ReoPro
EPO-R	2009	EPO binding activates STAT and stimulates erythropoiesis	Anaemia	Epogen
G-CSF receptor	2025	G-CSF binding stimulates neutrophill proliferation	Neutropaenia	Neupogen, Neulasta
GM-CSF receptor	2026	GM-CSF binding stiumulates proliferation and differentiation of neutrophils, eosinophils and monocytes	Leukopaenia	Lukine

TABLE 18B: Epitopes			
TARGET	ANTIBODY	AMINO ACID SEQUENCE	SEQ ID NO
DLL4	YW26.82	ECIPHNGCRHGTCSTPWQCTCDEGWGG LFCD (252-282)	2029
EpoR	Mab 71 and Mab 73	PGNYSFSYQLEDEPWKLCRLHQAPTAR GAV (49-78	2030
ErbB2	7C2 and 7F3	STQVCTGTDMKLRLPASPETHLDMLRH LYQGC (22-53)	2031
	4D5	LPCHPECQPQNGSVTCFGPEADQCVACA HYKDPPFCVARCPSGVKPDLSYMPIWKF PDEEGACQP (561-625)	2032
	3H4	VEECRVLQGLPREYVNARHCLPCHPEC QPQNGSVTCFGPEADQCVACAHYKDPP FCVAR (541-599)	2033
Her2/Neu	Herceptin	PEADQ(557-561)+DPPF(570-	2034

		573)+KFPDEEGACQP(593-603)	
	C24 (Pertuzumab)	Q156+H245+YF(252,257)+T268+DVGSCT PLH(285-290,294-296)+K311	2035
EGFR	IMC-C225 (Erbitux)	R353+Q384+QHFVS(408-409,412,417-418)+ISK(438,440,443)+KIISN(465-468,473)	2036
	EGFR antibody [1i8k]	KK(293-294)+G+NYVVTD(298-303)	2037
VEGFA	Fab12 (Avastin)	[fy(17,21)] + [yk(45,48)+qiMRIkhqGQhiGEM(79-84,86-94)]	2038
	G6	[FMYQY(17,18,21,22,25) +Del(63,64,66)+cp(104,106)] + [k48+mIHqgQhI(81,83,86-91)]	2039
	B20-4	[kFMDYqRYCH(16-19,21-23,25-27) +cndl(61-63,66)+nkec(100,101,103,104)] + [e30+k48+qmiQi(79,81,83,89,91)]	2040
	Fab 12 variant Y0317	Y(71)+K(74)+QIMRIK(105-110) +HQGQHIGEM(112-120)+F(43)+Y(47)	2041
	Fab 12 variant Y0317	F(43)+Y(47)+Y(71)+K(74)+QIMRIK(105-110) +HQGQHIGEM(112-120)	2042
CD52	Campath	G+TSSPSA(32-37)+D	2043
CD20	C2h7	EPANPSEK 168-175	2044
	C2b8 (Rituxan)	I(164)+NCEPANPSE(166-174)	2045
	C2b8 (Rituxan)	IYNCEPANP(164-172)+K(175)	2046
CD40	5c8	EASS(129-132)+EKGYY(142-146) +C178+C218+SQVSHG(245-250)	2047
CD41 (GPIIb)	10E5	RNVGSQ(77-82) +N149+N158+SRLWH(206,208,213-215)	2048
TPO	TN1	ETKAQ(57-61) +RGALQSLLGTQLPPQ(98,102-115)	2049

i. Notch and Notch ligands

a) Notch Proteins

The Notch proteins (Notch1, set forth in SEQ ID NO:2002; Notch 2, set forth in SEQ ID NO:2003; Notch 3, set forth in SEQ ID NO: 2004; and Notch 4 set forth in SEQ ID NO:2005) are single-pass transmembrane receptor proteins that play a crucial role in cell-to-cell communication. Cell surface receptors in the Notch family are expressed on numerous types of cells, including many types of stem cells and undifferentiated progenitor cells, either in the embryo or in self-renewing tissues after birth, see e.g. Artavanis-Tsakonas, *et al.*, (1995) *Science* 268:225-32. For example, human primary macophages express all Notch receptors, with Notch 3 being selectively increased during macrophage differentiation (see e.g., Fung *et al.* (2007) Circulation, 115: 2948-2956). Notch 4 also is expressed specifically

in endothelial cells and plays a role in angiogenesis. Notch also is expressed on lymphocytes where Notch signaling participates in lymphocyte development, maturation, activation and transformation.

There are five Notch ligands, designated Delta Like-1 (DLL-1), Delta Like-3 (DLL-3), Delta Like-4 (DLL-4), Jagged-1 and Jagged-2. When Notch is activated by a ligand, its intracellular domain is proteolytically cleaved and transported to the nucleus, along with CSL (CBF-1/Su(H)/Lag-1/RBP-J_K) transcription factor to activate transcription of downstream effectors. The resulting effector can repress the transcriptional activity of other genes encoding transcription factors for entry into terminal differentiation.

The Notch Signaling Pathway (NSP) is involved in many cellular processes, such as differentiation, cell fate decisions, maintenance of stem cells, cell motility, proliferation, and apoptosis in various cell types during development and tissue homeostasis. Notch signalling is dysregulated in many cancers, and faulty Notch signalling is implicated in many diseases including T-ALL (T-cell acute lymphoblastic leukemia), CADASIL, (Cerebral Autosomal Dominant Arteriopathy with Sub-cortical Infarcts and Leukoencephalopathy), Multiple Sclerosis (MS), Tetralogy of Fallot, Alagille Syndrome, multiple myeloma and other disease states thereby making Notch an important target in protein therapeuics (see e.g. United States Patent No. 6,083,904).

Antibody libraries provided herein can be screened for modulation of an acitivity by assaying for binding to a Notch receptor and/or assaying for a functional activity, for example, proliferation, cell motility or apoptosis of cells known to express a Notch receptor. Example 13 exemplifies a binding assay to screen antibody libraries provided herein to select or identify antibodies that bind to Notch-1. Assays also include signal transduction assays such as by using an RBP-Jκ/CBF-1 luciferase reporter assay (Fung *et al.* (2007) Circulation, 115: 2948-2956.) Assays can be performed in the presence or absence of a Notch ligand, for example, by coincubation of cells that express DLL4 (see e.g., Fung *et al.* (2007) Circulation, 115: 2948-2956) or by immobilization of a ligand (see e.g., Lefort *et al.* (2003) Experimental Hematology, 34:1720-1729). For example, as described in Fung *et al.*, cells can be stably transfected with a construct expressing DLL4, and can be overlaid on human primary macrophages that express Notch and assayed in the presence of antibody library members.

The antibodies or portions thereof identified from the libraries provided herein that modulate an activity of a Notch receptor (Notch 1, Notch 2, Notch 3 and/or Notch 4) can be used for the treatment or prevention of a disease associated with expression and/or activity of Notch. The antibodies can be used as agonist antibodies or antagonist antibodies in such

treatments. For example, agonist antibodies to Notch can be used to inhibit or decrease cancer cell growth or proliferation, such as in the treatment of various cancers including, but not limited to, prostate disorders and leukemia (see e.g., US6689744).

Antagonist antibodies provided herein also can be used in the treatment of a T-cell acute lymphoblastic leukemia; lymphoma; liver disease involving aberrant bascularization; diabetes; ovarian cancer; diseases involving vascular cell fate; rheumatoid arthritis; pancreatic cancer; non-small cell lung carcinoma; plasma cell neoplasmas such as multiple myeloma, plasma cell leukemia and extramedullary plasmacytoma; and neuroblastoma; and in treatment of plasma cell disorders such as multiple myeloma; angiogenesis; cancers such as sarcomas and carcinomas including but not limited to, breast cancer, colorectal cancer, lung cancer, pancreatic cancer, prostate cancer, liver cancer, ovarian cancer, head and neck cancer, skin cancer, brain cancer or blood cancer (see e.g., US20080226621, WO2008/091641, WO2005/054434). Notch signaling is associated in the development of skin, blood vessels and fat, and activated receptor can transform mammary epithelium. Hence, antagonist antibodies to Notch can be used in the treatment of breast tumors (see e.g. US20080206753).

Provided herein are antibodies that modulate the activity of Notch-1 and therefore can be used in the treatment of diseases or conditions associated with expression or activity of Notch-1. Such antibodies include those that have a VH chain and a VL chain encoded by a sequence of nucleotides compiled from germline segments, or any antibodies optimized therefrom. Exemplary of such antibodies are Fab antibodies. The antibodies further can contain a constant region. The antibodies include those that have a binding affinity for Notch-1 that is or is about 10^{-6} M, 10^{-7} M, 10^{-8} M, 10^{-9} M, 10^{-10} M, 10^{-11} M, 10^{-12} M or lower, in particular any that have a nanomolar or sub-nanomolar binding affinity.

Anti-Notch-1 antibodies provided herein include antibodies having at least one CDR that is a CDRH1, CDRH2, CDRH3, CDRL1, CDRL2 and/or CDRL3. For example, a CDRH1 is GYTFTSYYMH (amino acids 26-35 of SEQ ID NO:1512); a CDRH2 is IINPSGGSTSYAQKFQG (amino acids 50-66 of SEQ ID NO:1512); a CDRH3 is EGYSSSWYDYFDY (amino acids 99-111 of SEQ ID NO:1512); a CDRH3 is EYYYGSGSYYNDYFDY (amino acids 99-114 of SEQ ID NO:1509); a CDRL1 is RASQSVSSNLA (amino acids 24-34 of SEQ ID NO:1843); a CDRL1 is RASQSVSSSYLA (amino acids 24-35 of SEQ ID NO:1833); a CDRL1 is RASQSISSWLA (amino acids 24-34 of SEQ ID NO:1841); a CDRL2 is GASTRAT (amino acids 50-56 of SEQ ID NO:1843); a CDRL2 is GASSRAT (amino acids 51-57 of SEQ ID NO:1833); a CDRL2 is DASSLES (amino acids 50-56 of SEQ ID NO:1841); a CDRL3 is QQYNNWPPWT (amino acids 8-98

of SEQ ID NO:1843); a CDRL3 is QQYGSSPPWT (amino acids 90-99 of SEQ ID NO:1833); and a CDRL3 is QQYNSYSPWT (amino acids 89-98 of SEQ ID NO:1841). Also provided herein is a CDR that exhibits 60 %, 65 %, 70 %, 80 %, 90 %, 91 %, 92 %, 93 %, 94 %, 95 %, 96 %, 97 %, 98 %, 99 % or more sequence identity to any of the above CDRs.

For example, antibodies that modulate an activity of Notch-1 include any that contain a VH chain encoded by a sequence of nucleotides containing germline components compiled from a V_H germline segment that is an IGHV1 (e.g. any set forth in any of SEQ ID NOS:1-43); a D_H germline segment that is an IGHD6 (e.g. any set forth in SEQ ID NOS: 268-271) or an IGHD3 (e.g. any set forth in SEQ ID NOS: 252-259); and a J_H germline segment that is an IGHJ4 (e.g. set forth in SEQ ID NO: 278 or 279). Such antibodies also include any that contain a VL chain encoded by a sequence of nucleotides containing germline components compiled from a Vκ germline segment that is an IGKV1 (set forth in any of SEQ ID NOS: 286-316) or an IGKV3 (e.g. any set forth in any of SEQ ID NOS:332-350); and a Jκ germline segment that is an IGKJ1 (e.g. set forth in SEQ ID NO: 356). Such antibodies also include any that are encoded by a sequence of nucleotides containing germline segments that are variants of any of the above germline segments, for example due to conservative mutations or other mutations, so long as the resulting antibody is a functional and productive antibody and binds to Notch-1 and/or modulates a functional activity.

Exemplary of antibodies against Notch-1 include an antibody where the VH chain is encoded by a sequence of nucleotides compiled from a V_H germline segment that is a IGHV1-46 (e.g. an IGHV1-46*01, IGHV1-46*02, or an IGHV1-46*03); a D_H germline segment that is an IGHD3-10 (e.g. IGHD3-10*01, IGHD3-10*02) or an IGHD6-13 (e.g. IGHD6-13*01); and a JH germline segment that is an IGHJ4 (e.g. IGHJ4*01, IGHJ4*02, IGHJ4*03). The VL chain is encoded by a sequence of nucleotides compiled from a Vκ germline segment that is an IGKV3-15 (e.g. IGKV3-15*01), IGKV3-20 (e.g. IGKV3-20*01, IGKV3-20*02) or an IGKV1-5 (e.g. IGKV1-5*01, IGKV1-5*02, IGKV1-5*03); and a Jκ germline segment that is a IGKJ1*01. Exemplary antibodies provided herein that modulate an activity of Notch-1 are set forth in Table 18C.

TABLE 18C: Anti-Notch-1 Antibodies

Heavy Chain Germline Segments	SEQ ID NO		Light Chain Germline Segments	SEQ ID NO	
	nucleotide	Amino acid		nucleotide	Amino acid
IGHV1-46*01; IGHD6-13*01; IGHJ4*01	1096	1512	IGKV3-15*01; IGKJ1*01	1427	1843
IGHV1-46*01;	1096	1512	IGKV3-20*01;	1417	1833

IGHD6-13*01; IGHJ4*01			IGKJ1*01		
IGHV1-46*01; IGHD3-10*01; IGHJ4*01	1093	1509	IGKV1-5*01; IGKJ1*01	1425	1841

b) DLL4

DLL4 (set forth in SEQ ID NO:2010) is a transmembrane protein ligand for Notch transmembrane receptors. It is expressed widely in a variety of tissues, but its expression is predominantly localized to the vasculature. DLL4 activiates Notch-1 and Notch-4 receptors. It is required for normal vascular development and is expressed on tumor vessels. It is upregulated in blood vessels during tumor angiogenesis and expression is dependent on VEGF signaling. DLL4 expression on angiogenic endothelial cells acts as a negative regulator of vascular growth by acting to allow angiogenesis to productively proceed (Ridgway *et al.* (2006) Nature, 444:1083; Noguera-Troise *et al.* (2006) Nature, 444:1032). It acts to inhibit endothelial cell proliferation. Blockage of DLL4, however, is associated with increased angiogenesis characterized by sprouting and branching of blood vessels, but a decrease in vessel function, thereby resulting in decreased tumor growth (Ridgway *et al.* (2006) Nature, 444:1083; Noguera-Troise *et al.* (2006) Nature, 444:1032). Thus, DLL4 function is associated with an uncoupling of tumor growth from tumor vascular density. DLL4 also is expressed on activated macrophages exposed to proinflammatory stimuli such as lipopolysaccharide, interleukin-1β, Toll-like receptor 4 ligands and other proinflammatory stimuli and it's signaling through the Notch pathway plays a role in inflammatory states characterized by macrophage activation (Fung *et al.* (2007) Circulation, 115: 2948-2956).

Antibody libraries provided herein can be screened for modulation of an acitivity by assaying for binding to DLL4 and/or assaying for a functional activity. Example 13 exemplifies a binding assay to screen antibody libraries provided herein to select or identify antibodies that bind to DLL4. Assays also include binding assasys to assess the inhibition of DLL4-Notch interaction in the presence of an anti-DLL4 antibody. Such assays can be used to identify anagonist antibodies. This is exemplified in Example 17. Assays for functional activity include those that assess activation of Notch signaling by DLL4 by assaying for signal transduction and/or down stream functional activities such as are descrbed above. Activiation of Notch can be achieved, for example, by coincubation with cells that express DLL4 and/or immobilization of DLL4, and assays performed in the presence of antibody members. In such assays, for example, the effects of antibodies on endothelial cell proliferation (e.g. HUVECs) induced by DLL4 can be assessed (see e.g., Ridgway *et al.*

(2006) Nature, 444:1083). In some examples, antibodies can be used to assess effects on cell differentiation of a cell expressing Notch. The cells can be co-cultured with cells expressing a ligand for Notch, for example, DLL4 or Jag1. To identify antibodies that promote differentiation (i.e. interfere with Notch activation), antibodies can be added to the assay. An exemplary assay is set forth in Example 18.

Hence, the antibodies identified from the libraries provided herein or the antibodies provided herein bind (such as specifically bind) DLL4, and in some embodiments, can modulate one or more aspects of DLL4-associated effects, including but not limited to any one or more of reduction or blocking of Notch receptor activation, reduction or blocking of Notch receptor downstream molecular signaling, disruption or blocking of Notch receptor binding to DLL4, and/or promotion of endothelial cell proliferation, and/or inhibition of endothelial cell differentiation, and/or inhibition of arterial differentiation, and/or inhibition of tumor vascular perfusion, and/or treatment and/or prevention of a tumor, cell proliferative disorder or a cancer; and/or treatment or prevention of a disorder associated with DLL4 expression and/or activity and/or treatment or prevention of a disorder associated with Notch receptor expression and/or activity. In some embodiments, the antibody specifically binds to DLL4. In some embodiments, the antibody specifically binds to the DLL4 extracellular domain (ECD). In some embodiments, an antibody reduces, inhibits, and/or blocks DLL4 activity in vivo and/or in vitro. In some embodiments, the antibody competes for binding with DLL4-ligand (reduces and/or blocks Notch receptor binding to DLL4).

The antibodies or portions thereof identified from the libraries provided herein that modulate an activity of DLL4 can be used for the treatment or prevention of disease states associated with expression and/or activity of DLL4, such as increased expression and/or activity or undesired expression and/or activity (see e.g., U.S. Published Application Serial No. US20080175847 and International Published PCT Appl. No. WO2008060705, WO2008091222). Treatment includes neoplastic and non-neoplastic disorders. For example, the antibodies or portions thereof can be used to treat a tumor, a cancer (e.g. colon cancer, lung cancer or breast cancer) and/or a cell proliferative disorder and/or conditions associated with angiogenesis (e.g. intraocular neovascular disease). In particular, the antibodies or portions thereof can be used in combination with anti-VEGF therapies and/or in treatments that are resistant to anti-VEGF treatment.

Angiogenesis is implicated in the pathogenesis of a variety of disorders. These include solid tumors and metastasis, atherosclerosis, retrolental fibroplasia, hemangiomas, chronic inflammation, intraocular neovascular diseases such as proliferative retinopathies,

e.g., diabetic retinopathy, age-related macular degeneration (AMD), neovascular glaucoma, immune rejection of transplanted corneal tissue and other tissues, rheumatoid arthritis, and psoriasis. Folkman et al., *J. Biol. Chem.* 267:10931-34 (1992); Klagsbrun et al., *Annu. Rev. Physiol.* 53:217-39 (1991); and Garner A., "Vascular diseases," In: Pathobiology of Ocular Disease. A Dynamic Approach, Garner A., Klintworth G K, eds., 2nd Edition (Marcel Dekker, NY, 1994), pp 1625-1710.

In the case of tumor growth, angiogenesis appears to be crucial for the transition from hyperplasia to neoplasia, and for providing nourishment for the growth and metastasis of the tumor. Folkman et al., *Nature* 339:58 (1989). The neovascularization allows the tumor cells to acquire a growth advantage and proliferative autonomy compared to the normal cells. A tumor usually begins as a single aberrant cell which can proliferate only to a size of a few cubic millimeters due to the distance from available capillary beds, and it can stay 'dormant' without further growth and dissemination for a long period of time. Some tumor cells then switch to the angiogenic phenotype to activate endothelial cells, which proliferate and mature into new capillary blood vessels. These newly formed blood vessels not only allow for continued growth of the primary tumor, but also for the dissemination and recolonization of metastatic tumor cells. Accordingly, a correlation has been observed between density of microvessels in tumor sections and patient survival in breast cancer as well as in several other tumors. Weidner et al., *N. Engl. J. Med.* 324:1-6 (1991); Horak et al., *Lancet* 340:1120-24 (1992); Macchiarini et al., *Lancet* 340:145-46 (1992). The precise mechanisms that control the angiogenic switch is not well understood, but it is believed that neovascularization of tumor mass results from the net balance of a multitude of angiogenesis stimulators and inhibitors (Folkman, *Nat. Med.* 1(1):27-31 (1995)).

In addition, antibodies or portions thereof can be used to treat non-neoplastic disorders including, but not limited to, undesired or aberrant hypertrophy, arthritis, rheumatoid arthritis (RA), psoriasis, psoriatic plaques, sarcoidosis, atherosclerosis, atherosclerotic plaques, edema from myocardial infarction, diabetic and other proliferative retinopathies including retinopathy of prematurity, retrolental fibroplasia, neovascular glaucoma, age-related macular degeneration, diabetic macular edema, corneal neovascularization, corneal graft neovascularization, corneal graft rejection, retinal/choroidal neovascularization, neovascularization of the angle (rubeosis), ocular neovascular disease, vascular restenosis, arteriovenous malformations (AVM), meningioma, hemangioma, angiofibroma, thyroid hyperplasias (including Grave's disease), corneal and other tissue transplantation, chronic inflammation, lung inflammation, acute lung injury/ARDS, sepsis,

primary pulmonary hypertension, malignant pulmonary effusions, cerebral edema (e.g., associated with acute stroke/closed head injury/trauma), synovial inflammation, pannus formation in RA, myositis ossificans, hypertropic bone formation, osteoarthritis (OA), refractory ascites, polycystic ovarian disease, endometriosis, 3rd spacing of fluid diseases (pancreatitis, compartment syndrome, burns, bowel disease), uterine fibroids, premature labor, chronic inflammation such as IBD (Crohn's disease and ulcerative colitis), renal allograft rejection, inflammatory bowel disease, nephrotic syndrome, undesired or aberrant tissue mass growth (non-cancer), obesity, adipose tissue mass growth, hemophilic joints, hypertrophic scars, inhibition of hair growth, Osier-Weber syndrome, pyogenic granuloma retrolental fibroplasias, scleroderma, trachoma, vascular adhesions, synovitis, dermatitis, preeclampsia, ascites, pericardial effusion (such as that associated with pericarditis), and pleural effusion.

Provided herein are antibodies that modulate the activity of DLL4 and therefore can be used in the treatment of diseases or conditions associated with expression or activity of DLL4. Such antibodies include those that have a VH chain and a VL chain encoded by a sequence of nucleotides compiled from germline segments, or any antibodies optimized therefrom. Exemplary of such antibodies are Fab antibodies. The antibodies further can contain a constant region. The antibodies include those that have a binding affinity for DLL4 that is or is about 10^{-6} M, 10^{-7} M, 10^{-8} M, 10^{-9} M, 10^{-10} M, 10^{-11} M, 10^{-12} M or lower, in particular any that have a nanomolar or sub-nanomolar binding affinity.

Anti-DLL4 antibodies provided herein include antibodies having at least one CDR that is a CDRH1, CDRH2, CDRH3, CDRL1, CDRL2 and/or CDRL3. For example, a CDRH1 is GYTFTSYYMH (amino acids 26-35 of SEQ ID NO:1513); a CDRH1 is GYSFTSYWIG (amino acids 26-35 of SEQ ID NO:1803); a CDRH1 is GDSVSSNSAAWN (amino acids 26-37 of SEQ ID NO:1812); a CDRH1 is GGSFSGYYWS (amino acids 26-35 of SEQ ID NO:1779); a CDRH1 is GYTFTSYAMH (amino acids 26-35 of SEQ ID NO:1494); a CDRH1 is GYTFTSYDIN (amino acids 26-35 of SEQ ID NO:1537); a CDRH1 is GGSISSGGYYWS (amino acids 26-37 of SEQ ID NO:1761); a CDRH2 is IINPSGGSTSYAQKFQG (amino acids 50-66 of SEQ ID NO:1513); a CDRH2 is IIYPGDSDTRYSPSFQG (amino acids 50-66 of SEQ ID NO:1803); a CDRH2 is RTYYRSKWYNDYAVSVKS (amino acids 52-69 of SEQ ID NO:1812); a CDRH2 is EINHSGSTNYNPSLKS (amino acids 50-65 of SEQ ID NO:1779); a CDRH2 is WSNAGNGNTKYSQEFQG (amino acids 50-66 of SEQ ID NO:1494); a CDRH2 is WMNPNSGNTGYAQKFQG (amino acids 50-66 of SEQ ID NO:1537); a CDRH2 is (amino

acids 52-67 of SEQ ID NO:1761); a CDRH3 is EEYSSSSAEYKQH (amino acids 99-111 of SEQ ID NO:1513); a CDRH3 is RGYSYGYDYFDY (amino acids 99-110 of SEQ ID NO:1803); a CDRH3 is EYYDFWSGYYTDYFD (amino acids 102-117 of SEQ ID NO:1812); a CDRH3 is EGYSSSWYDYFDY (amino acids 99-111 of SEQ ID NO:1512); a CDRH3 is ANWGDYFDY (amino acids 89-106 of SEQ ID NO:1779); a CDRH3 is ANWGYWYFDL (amino acids 99-108 of SEQ ID NO:1514); a CDRH3 is DDYGGNSDYFDY (amino acids 99-110 of SEQ ID NO:1494); a CDRH3 is EGYCSGGSCYSYWYFDL (amino acids 99-115 of SEQ ID NO:1508); a CDRH3 is EYYYGSGSYYNDYFDY (amino acids 99-114 of SEQ ID NO:1509); a CDRH3 is GGYCSSTSCYADYYYYYGMDV (amino acids 99-119 of SEQ ID NO:1537); a CDRH3 is EGYCSGGSCYSYWYFDL (amino acids 100-116 of SEQ ID NO:1761); a CDRL1 is RASQSVSSYLA (amino acids 24-34 of SEQ ID NO:1850); a CDRL1 is GLSSGSVSTSYYPS (amino acids 23-36 of SEQ ID NO:1881); a CDRL1 is TLRSGINLGSYRIF (amino acids 23-36 of SEQ ID NO:1884); a CDRL1 is RASQSVSSNLA (amino acids 24-34 of SEQ ID NO:1843); a CDRL1 isRASQGISSWLA (amino acids 24-34 of SEQ ID NO:1849); a CDRL1 is RASQSVSSSYLA (amino acids 24-35 of SEQ ID NO:1833); a CDRL1 is RASQSISSWLA (amino acids 24-34 of SEQ ID NO:1841); a CDRL1 is RSSQSLLDSDDGNTYLD (amino acids 24-40 of SEQ ID NO:1853); a CDRL1 is TGTSSDVGGYNYVS (amino acids 23-36 of SEQ ID NO:1864); a CDRL1 is TLSSDLSVGGKNMF (amino acids 23-36 of SEQ ID NO:1886); a CDRL2 is DASNRAT (amino acids 50-56 of SEQ ID NO:1850); a CDRL2 is STNTRSS (amino acids 52-58 of SEQ ID NO:1881); a CDRL2 is YYSDSSK (amino acids 52-58 of SEQ ID NO:1884); a CDRL2 is GASTRAT (amino acids 50-56 of SEQ ID NO:1843); a CDRL2 is AASSLQS (amino acids 50-56 of SEQ ID NO:1849); a CDRL2 is GASSRAT (amino acids 51-57 of SEQ ID NO:1833); a CDRL2 is DASSLES (amino acids 50-56 of SEQ ID NO:1841); a CDRL2 is TLSYRAS (amino acids 56-62 of SEQ ID NO:1853); a CDRL2 is EVSNRPS (amino acids 52-58 of SEQ ID NO:1864); a CDRL2 is HYSDSDK (amino acids 52-58 of SEQ ID NO:1886); a CDRL3 is QQRSNWPPWT (amino acids 89-98 of SEQ ID NO:1850); a CDRL3 is VLYMGSGISYV (amino acids 91-101 of SEQ ID NO:1881); a CDRL3 is MIWHSSASFV (amino acids 97-106 of SEQ ID NO:1884); a CDRL3 is QQYNNWPPWT (amino acids 89-98 of SEQ ID NO:1843); a CDRL3 is QQANSFPPWT (amino acids 89-98 of SEQ ID NO:1849); a CDRL3 is QQYGSSPPWT (amino acids 90-99 of SEQ ID NO:1833); a CDRL3 is QQYNSYSPWT (amino acids 89-98 of SEQ ID NO:1841); a CDRL3 is MQRIEFPSWT (amino acids 95-104 of SEQ ID NO:1853); a CDRL3

is SSYTSSSTLFV (amino acids 91-101 of SEQ ID NO:1864); and a CDRL3 is QVYESSANFV (amino acids 89-98 of SEQ ID NO:1886). Also provided herein is a CDR that exhibits 60 %, 65 %, 70 %, 80 %, 90 %, 91 %, 92 %, 93 %, 94 %, 95 %, 96 %, 97 %, 98 %, 99 % or more sequence identity to any of the above CDRs.

For example, antibodies that modulate an activity of DLL4 include any that contain a VH chain encoded by a sequence of nucleotides containing germline components compiled from a V_H germline segment that is an IGHV1 (e.g. any set forth in any of SEQ ID NOS:10-43), an IGHV4 (e.g. any set forth in SEQ ID NOS: 153-224), an IGHV5 (e.g. any set forth in SEQ ID NOS: 225-232) or an IGHV6 (e.g., any set forth in any of SEQ ID NOS: 233 or 234); a D_H germline segment that is an IGHD6 (e.g. any set forth in SEQ ID NOS: 268-271), an IGHD5 (e.g. any set forth in any of SEQ ID NOS: 264-267); an IGHD4 (e.g. any set forth in SEQ ID NOS: 260-263); an IGHD2 (e.g. any set forth in SEQ ID NOS: 244-251), an IGHD3 (e.g. any set forth in any of SEQ ID NOS: 252-259) an IGHD6 (e.g. any set forth in SEQ ID NO: 268-271), or an IGHD7 (e.g. set forth in SEQ ID NO:272); and a J_H germline segment that is an IGHJ1 (e.g., set forth in SEQ ID NO:273), an IGHJ2 (set forth in SEQ ID NO:274), an IGHJ4 (e.g. any set forth in any of SEQ ID NOS: 277-279), or an IGHJ6 (e.g. any set forth in SEQ ID NOS: 282-285). Such antibodies also include any that contain a VL chain encoded by a sequence of nucleotides containing germline components compiled from a Vκ germline segment that is an IGKV1 (e.g. any set forth in any of SEQ ID NOS: 286-316), an IGKV2 (e.g. any set forth in SEQ ID NOS: 317-331), or an IGKV3 (e.g. any set forth in any of SEQ ID NOS:332-350) and a Jκ germline segment that is an IGKJ1 (e.g. set forth in SEQ ID NO: 356); or from a V_λ germline segment that is an IGLV2 (e.g. any set forth in any of SEQ ID NOS:380-399), IGLV8 (e.g. any set forth in any of SEQ ID NOS: 436-438), IGLV11 (e.g. any set forth in any of SEQ ID NO: 379), or a IGLV5 (e.g. any set forth in any of SEQ ID NOS: 424-431) and a J_λ germline segment that is a IGLJ1 (e.g. set forth in SEQ ID NO:442) or an IGLJ4 (e.g. set forth in SEQ ID NO:446). Such antibodies also include any that are encoded by a sequence of nucleotides containing germline segments that are variants of any of the above germline segments, for example due to conservative mutations or other nucleotide mutations, so long as the resulting antibody is a functional and productive antibody and binds to DLL4 and/or modulates a functional activity.

Exemplary of antibodies against DLL4 include an antibody where the VH chain is encoded by a sequence of nucleotides compiled from a V_H germline segment that is an IGHV1-3 (e.g. IGHV1-3*01, IGHV1-3*02), an IGHV1-8*01, an IGHV1-46 (e.g. an IGHV1-46*01, IGHV1-46*02 or an IGHV1-46*03), an IGHV4-31 (e.g. IGHV4-31*01, IGHV4-

31*02, IGHV4-31*03, IGHV4-31*04, IGHV4-31*05, IGHV4-31*06, IGHV4-31*07, IGHV4-31*08, IGHV4-31*09, IGHV4-31*10), an IGHV4-34 (e.g. IGHV4-34*01, IGHV4-34*02, IGHV4-34*03, IGHV4-34*04, IGHV4-34*05, IGHV4-34*06, IGHV4-34*07, IGHV4-34*08, IGHV4-34*09, IGHV4-34*10, IGHV4-34*11, IGHV4-34*12, IGHV4-34*13), an IGHV5-51 (e.g., an IGHV1-5-51*01, IGHV1-5-51*02, IGHV1-5-51*03, IGHV1-5-51*04 or IGHV1-5-51*05) or is an IGHV6-1 (e.g. an IGHV6-1*01 or an IGHV6-1*02); a D_H germline segment that is an IGHD2-2 (e.g. IGHD2-2*01, IGHD2-2*02), an IGHD2-15*01, an IGHD4-23*01, an IGHD6-6 (e.g. IGHD6-6*01), an IGHD6-13*01, an IGHD5-18 (e.g. an IGHD5-18*01), an IGHD3-3 (e.g. an IGHD3-3*01 or IGHD3-3*02), an IGHD3-10 (e.g. IGHD3-10*01, IGHD3-10*02), or an IGHD7-27*01; and a J_H germline segment that is a IGHJ1*01, IGHJ2*01, IGHJ4*01, IGHJ4*02, IGHJ4*03, or an IGHJ6 (e.g. IGHJ6*01, IGHJ6*02, IGHJ6*03, IGHJ6*04). The VL chain is encoded by a sequence of nucleotides compiled from a Vκ germline segment that is an IGKV1-5 (e.g. IGKV1-5*01, IGKV1-5*02, IGKV1-5*03), an IGKV1-12 (e.g IGKV1-12*01, IGKV1-12*02), an IGKV2-D-40*01, an IGKV3-11 (e.g. IGKV3-11*01 or IGKV3-11*02), an IGKV3-15*01, an IGKV3-20 (e.g. IGKV3-20*01, IGKV3-20*02) and a Jκ germline segment that is a IGKJ1*01; or is compiled from a V_λ germline segment that is an IGLV2-14 (e.g. IGLV2-14*01, IGLV2-14*02, IGLV2-14*03, IGLV2-14*04), an IGLV8-61 (e.g. IGLV8-61*01, IGLV8-61*02 or IGLV8-61*03), an IGLV5 (e.g. IGLV5-48*01), or an IGLV11-55*01 and a J_λ germline segment that is a IGLJ1*01 or IGLJ4*01. Exemplary antibodies provided herein that modulate an activity of DLL4 are set forth in Table 18D.

TABLE 18D: Anti-DLL4 Antibodies

Heavy Chain Germline Segments	SEQ ID NO		Light Chain Germline Segments	SEQ ID NO	
	nucleotide	Amino acid		nucleotide	Amino acid
IGHV1-46*01; IGHD6-6*01; IGHJ1*01	1097	1513	IGKV3-11*01; IGKJ1*01	1434	1850
IGHV5-51*03; IGHD5-18*01>3; IGHJ4*01	1387	1803	IGLV8-61*01; IGLJ1*01	1465	1881
IGHV6-1*01; IGHD3-3*01; IGHJ4*01	1396	1812	IGLV5-48*01; IGLJ4*01	1468	1884
IGHV1-46*01; IGHD6-13*01; IGHJ4*01	1096	1512	IGKV3-15*01; IGKJ1*01	1427	1843
IGHV4-34*01; IGHD7-27*01;	1363	1779	IGKV1-12*01; IGKJ1*01	1433	1849

IGHJ4*01					
IGHV1-46*01; IGHD6-13*01; IGHJ4*01	1096	1512	IGKV3-20*01; IGKJ1*01	1417	1833
IGHV1-3*02; IGHD4-23*01; IGHJ4*01	1078	1494	IGKV1-5*01; IGKJ1*01	1425	1841
IGHV1-46*01; IGHD2-15*01; IGHJ2*01	1092	1508	IGKV1-5*01; IGKJ1*01	1425	1841
IGHV1-46*01; IGHD3-10*01; IGHJ4*01	1093	1509	IGKV1-5*01; IGKJ1*01	1425	1841
IGHV1-8*01; IGHD2-2*01; IGHJ6*01	1121	1537	IGKV1-5*01; IGKJ1*01	1425	1841
IGHV1-46*01; IGHD6-13*01; IGHJ4*01	1096	1512	IGKV2D-40*01; IGKJ1*01	1437	1853
IGHV4-34*01; IGHD7-27*01; IGHJ4*01	1363	1779	IGLV2-14*01; IGLJ4*01	1448	1864
IGHV4-31*02; IGHD2-15*01; IGHJ2*01	1345	1761	IGLV2-14*01; IGLJ4*01	1448	1864
IGHV4-34*01; IGHD7-27*01; IGHJ4*01	1363	1779	IGLV11-55*01; IGLJ4*01	1470	1886

Anti-DLL4 antibodies provided herein include antibodies that are optimized compared to any of the identified anti-DLL4 germline Hits. The antibodies include one or more mutations in the VH chain and/or one or more mutations in the VL chain compared to an identified germline Hit. For example, the antibodies can contain 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more amino acid replacements compared to the corresponding antibody germline Hit. The mutations can be in the VH chain, for example, in any one or more of the amino acid residues of a V_H, D_H or J_H region. Alternatively, or in addition, the mutations can be in the VL chain, for example, in any one or more of the amino acid residues of the V_L or J_L region. Optimized antibodies containing one or more mutations exhibit improved activity compared to the parent antibody (e.g. germline Hit not containing the modifications). The antibodies are optimized to exhibit an improved functional activity, either agonistic or antagonistic, against the DLL4 target protein. In other examples, the antibodies are optimized to exhibit an improved binding affinity for DLL4. Generally, an activity or binding affinity is increased by at or about 1.5-fold, 2-fold, 3-fold, 4-fold, 5-fold,

6-fold, 7-fold, 8-fold, 9-fold, 10-fold, 20-fold, 30-fold, 40-fold, 50-fold, 60-fold, 70-fold, 80-fold, 90-fold, 100-fold, 200-fold, 300-fold, 400-fold, 500-fold, 600-fold, 700-fold, 800-fold, 900-fold, 1000-fold or more compared to an activity or binding affininity of the parent antibody (e.g. germline Hit not containing the modification(s)). For example, as described in the Examples, optimized anti-DLL4 antibodies provided herein exhibit a binding affinity that is improved by at least 100-fold compared to the parent antibody. Such antibodies exhibit a nanomolar binding affinity.

For example, provided herein are optimized anti-DLL4 antibodies that contain one or more mutations in the VH chain of an anti-DLL4 Hit, for example, any set forth in any of SEQ ID NOS: 1494, 1508-1509, 1512-1513, 1537, 1761, 1779, 1803 and 1812. In one example, the one or more mutations include mutations in the D_H region. For example, an anti-DLL4 antibody provided herein can include a VH chain containing a germline segment compiled from a variant of a IGHD5-18*01 that encodes a D_H region that contains a mutation(s) at position G1 and/or G5 corresponding to amino acid residues set forth in SEQ ID NO:3736 (also corresponding to amino acid residues G100 and/or G104 set forth in the VH chain of the anti-DLL4 Hit set forth in SEQ ID NO: 1803). The mutation can be to any other amino acid residue, in particular, the mutation is a lysine (K), Arginine (R), threonine (T). Exemplary of such mutations are G1K, G1R, and/or G5T corresponding to amino acid replacements in the D_H region set forth in SEQ ID NO:3736 (also corresponding to amino acid replacements G100K, G100R, and/or G104T in the VH chain of the anti-DLL4 Hit set forth in SEQ ID NO:1803). In another example, an anti-DLL4 antibody provided herein can include a VH chain containing germline segments compiled from a variant of IGHD6-6*01 that encodes a D_H region that contains a mutations(s) at positions S3, S4 and/or S5 corresponding to amino acid residues set forth in SEQ ID NO:3737 (also corresponding to amino acid residues S102, S103 and/or S104 in the VH chain of the anti-DLL4 Hit set forth in SEQ ID NO: 1513. The mutation can be to any other amino acid residue, in particular, the mutation is a alanine (A), proline (P) or phenylalanine (F). Exemplary of such mutations are S3A, S4P, S5F and/or S5A corresponding to amino acid replacements in the D_H region set forth in SEQ ID NO:3737 (also corresponding to amino acid replacements S102A, S103P, S104F and S104A in the VH chain of the anti-DLL4 Hit set forth in SEQ ID NO:1513. Table 18E lists exemplary anti-DLL4 antibody variants containing one or more mutations in the D_H region of the VH chain of anti-DLL4 Hits.

Also provided herein are optimized anti-DLL4 antibodies containing one or more mutations in the J_H region of the VH chain of an anti-DLL4 hit. For example, an anti-DLL4

antibody provided herein can include a VH chain containing a germline segment compiled from a variant of an IGHJ1*01 that encodes a J_H region that contains a mutation at position H6 corresponding to amino acid residue set forth in SEQ ID NO:3738 (also corresponding to amino acid residue H111 in the VH chain of the anti-DLL4 Hit set forth in SEQ ID NO:1513). The mutation can be to any other amino acid residue, in particular, the mutation is a phenylalanine (F) or a tyrosine (Y). Exemplary of such mutations are H6F and H6Y corresponding to amino acid replacements in the J_H region set forth in SEQ ID NO:3738 (also corresponding to amino acid replacements H111F and H111Y in the J_H region of the VH chain of the anti-DLL4 Hit set forth in SEQ ID NO:1513). Table 18E lists exemplary anti-DLL4 antibody variants containing one or more mutations in the J_H region of the VH chain of anti-DLL4 Hits.

Optimized anti-DLL4 antibodies provided herein also can contain one or more amino acid mutations in the VL chain. For example, provided herein are optimized anti-DLL4 antibodies containing one or more mutation in the Vκ region of the VL chain of an anti-DLL4 hit. For example, an anti-DLL4 antibody provided herein can include a VL chain containing a germline segment compiled from a variant of an IGKV3-11 (e.g. IGKV3-11*01 or IGKV3-11*02) that encodes a Vκ region that contains a mutation at position S28, S30 and/or S31 corresponding to amino acid residues set forth in SEQ ID NO:3739 (also corresponding to amino acid resdues S28, S30 and/or S31 in the VL chain of the anti-DLL4 Hit set forth in SEQ ID NO:1850). The mutation can be to any other amino acid residue, in particular, the mutation is a proline (P), asparagine (N), or lysine (K). Exemplary of such mutations are S28P, S30N and/or S31K corresponding to amino acid replacements in the Vκ region set forth in SEQ ID NO:3739 (also corresponding to amino acid replacements S28P, S30N and/or S31K in the Vκ region of the VL chain of the anti-DLL4 Hit set forth in SEQ ID NO:1850). Table 18E lists exemplary anti-DLL4 antibody variants containing one or more mutations in the Vκ region of the VL chain of anti-DLL4 Hits.

TABLE 18E: Anti-DLL4 antibody variants							
Parent anti-DLL4 VH chain Hit	**Muta-tion(s)**	**SEQ ID NO**		**Parent anti DLL4 VL chain Hit**	**Muta-tion(s)**	**SEQ ID NO**	
		Nucle-otide	**Amino acid**			**Nucleo-tide**	**Amino acid**
IGHV5-51*03; IGHD5-18*01>3; IGHJ4*01	G100K	3741	3720	IGLV8-61*01; IGLJ1*01	n/a	1465	1881
IGHV5-51*03; IGHD5-18*01>3; IGHJ4*01	G100R	3742	3721	IGLV8-61*01; IGLJ1*01	n/a	1465	1881
IGHV5-51*03; IGHD5-18*01>3; IGHJ4*01	G104T	3745	3724	IGLV8-61*01; IGLJ1*01	n/a	1465	1881
IGHV5-51*03; IGHD5-18*01>3; IGHJ4*01	G100K/ G104T	3749	3728	IGLV8-61*01; IGLJ1*01	n/a	1465	1881
IGHV1-46*01; IGHD6-6*01; IGHJ1*01	S104F	3743	3722	IGKV3-11*01; IGKJ1*01	n/a	1434	1850
IGHV1-46*01; IGHD6-6*01; IGHJ1*01	S104A	3744	3723	IGKV3-11*01; IGKJ1*01	n/a	1434	1850
IGHV1-46*01; IGHD6-6*01; IGHJ1*01	S103P	3746	3725	IGKV3-11*01; IGKJ1*01	n/a	1434	1850
IGHV1-46*01; IGHD6-6*01; IGHJ1*01	S102A	3747	3726	IGKV3-11*01; IGKJ1*01	n/a	1434	1850
IGHV1-46*01; IGHD6-6*01;	S102A/ S103P/ S104F	3748	3727	IGKV3-11*01; IGKJ1*01	n/a	1434	1850

IGHJ1*01							
IGHV1-46*01; IGHD6-6*01; IGHJ1*01	S102A/ S103P/ S104F/ H111F	3750	3729	IGKV3-11*01; IGKJ1*01	n/a	1434	1850
IGHV1-46*01; IGHD6-6*01; IGHJ1*01	S102A/ S103P/ S104F/ H111Y	3751	3730	IGKV3-11*01; IGKJ1*01	n/a	1434	1850
IGHV1-46*01; IGHD6-6*01; IGHJ1*01	S102A/ S103P/ S104Y/ H111Y	3752	3731	IGKV3-11*01; IGKJ1*01	n/a	1434	1850
IGHV1-46*01; IGHD6-6*01; IGHJ1*01	S102A/ S103P/ S104F	3748	3727	IGKV3-11*01; IGKJ1*01	S28P	3753	3735
IGHV1-46*01; IGHD6-6*01; IGHJ1*01	S102A/ S103P/ S104F	3748	3727	IGKV3-11*01; IGKJ1*01	S30N	3754	3733
IGHV1-46*01; IGHD6-6*01; IGHJ1*01	S102A/ S103P/ S104F	3748	3727	IGKV3-11*01; IGKJ1*01	S31K	3755	3734

ii. ErbB family

Group I receptor tyrosine kinases, including EGFR (ErbB-1), HER2/c-neu (ErbB-2), Her 3 (ErbB-3) and Her 4 (ErbB-4), are widely expressed in epithelial, mesenchymal, and neuronal tissues and play fundamental roles in proliferation and differentiation. They are activated by a family of ligands that variously bind to the receptors. For example, epidermal growth factor (EGF), transforming growth factor alpha (TGF-alpha) and amphiregulin bind to ErbB1, but not to other receptors. The neuregulins bind to ErbB3 and ErbB4. Finally, b-cellulin (BTC), heparin-binding EGF and epiregulin bind to ErbB1 and ErbB4. ErbB2 has no characterized ligand, but can be activated by homodimerization in trans by heterodimerization with another ErbB family member.

a) Epidermal Growth Factor Receptor (EGFR)

The epidermal growth factor receptor (EGFR; ErbB-1; HER1 in humans; set forth in SEQ ID NO:2000) is a cell-surface receptor for members of the epidermal growth factor family (EGF-family) of extracellular protein ligands. Upon binding by the ligand epidermal growth factor (EGF), EGFR dimerizes stimulating its intrinsic intracellular protein-tyrosine kinase activity. This autophosphorylation elicits downstream activation and signaling by several other proteins that associate with the phosphorylated tyrosines through their own phosphotyrosine-binding SH2 domains. These downstream signaling proteins initiate several signal transduction cascades, including MAPK, Akt and JNK pathways, leading to DNA synthesis and cell proliferation. Such proteins modulate phenotypes such as cell migration, adhesion, and proliferation. Therefore, mutations affecting EGFR expression or activity can result in cancer

Upregulation of EGFR is associated with poor cancer prognosis. ERBITUX® (cetuximab) is a chimeric monoclonal antibody approved for the treatment of colorectal and/or head and neck cancers. ERBITUX® binds the EGFR and thereby prevents intracellular signaling associated with DNA synthesis and cell proliferation. VECTIBIX® (panitumumab) is a fully human monoclonal antibody approved for the treatment of EGFR-expressing, metastatic colorectal carcinoma. Both ERBITUX® and VECTIBIX® can be used alone or in conjuction with a chemotherapeutic agent.

Antibody libraries provided herein can be screened for modulation of an acitivity by assaying for binding to EGFR and/or assaying for a functional activity, for example, signal transduction, cell migration, adhesion, and proliferation. Functional assays can be performed in the presence or absence of the EGF ligand. Example 13 exemplifies a binding assay to screen antibody libraries provided herein to select or identify antibodies that bind to EGFR.

The antibodies or portions thereof identified from the libraries provided herein that modulate an activity of EGFR can be used for the treatment or prevention of disease states associated with expression and/or activity of EGFR. For example, the antibodies or portions thereof can be used in the treatment of cancers including, but not limited to, glioblastoma, head and neck cancer, pancreatic cancer, colorectal cancer, lung cancer, cancer of the nervous system, gastrointestinal cancer, prostate cancer, ovarian cancer, breast cancer, kidney cancer, retina cancer, skin cancer, liver cancer, genital-urinary cancer, bladder cancer, or a lung cancer such as a lun adenocarcinoma, lung squamous cell carcinoma or non-small cell lung cancer.

Provided herein are antibodies that modulate the activity of EGFR and therefore can be used in the treatment of diseases or conditions associated with expression or activity of

EGFR. Such antibodies include those that have a VH chain and a VL chain encoded by a sequence of nucleotides compiled from germline segments, or any antibodies optimized therefrom. Exemplary of such antibodies are Fab antibodies. The antibodies further can contain a constant region. The antibodies include those that have a binding affinity for EGFR that is or is about 10^{-6} M, 10^{-7} M, 10^{-8} M, 10^{-9} M, 10^{-10} M, 10^{-11} M, 10^{-12} M or lower, in particular any that have a nanomolar or sub-nanomolar binding affinity.

Anti-EGFR antibodies provided herein include antibodies having at least one CDR that is a CDRH1, CDRH2, CDRH3, CDRL1, CDRL2 and/or CDRL3. For example, a CDRH1 is GYTFTSYYMH (amino acids 26-35 of SEQ ID NO:1508); a CDRH2 is IINPSGGSTSYAQKFQG (amino acids 50-66 of SEQ ID NO:1508); a CDRH3 is EGYCSGGSCYSYWYFDL (amino acids 99-115 of SEQ ID NO:1508); a CDRH3 is EGYSSSWYDYFDY (amino acids 99-111 of SEQ ID NO:1512); a CDRL1 is RASQSVSSNLA (amino acids 24-34 of SEQ ID NO:1843); a CDRL1 is RASQSISSWLA (amino acids 24-34 of SEQ ID NO:1841); a CDRL2 is GASTRAT (amino acids 50-56 of SEQ ID NO:1843); a CDRL2 is DASSLES (amino acids 50-56 of SEQ ID NO:1841); a CDRL3 is QQYNNWPPWT (amino acids 89-98 of SEQ ID NO:1843); and a CDRL3 is QQYNSYSPWT (amino acids 89-98 of SEQ ID NO:1841). Also provided herein is a CDR that exhibits 60 %, 65 %, 70 %, 80 %, 90 %, 91 %, 92 %, 93 %, 94 %, 95 %, 96 %, 97 %, 98 %, 99 % or more sequence identity to any of the above CDRs.

For example, antibodies that modulate an activity of EGFR include any that contain a VH chain encoded by a sequence of nucleotides containing germline components compiled from a V_H germline segment that is an IGHV1 (e.g. any set forth in any of SEQ ID NOS:1-43); a D_H germline segment that is an IGHD6 (e.g. any set forth in SEQ ID NOS: 268-271) or an IGHD2 (e.g. any set forth in SEQ ID NOS: 244-251); and a J_H germline segment that is an IGHJ2 (e.g., set forth in SEQ ID NO:274) or an IGHJ4 (e.g. set forth in SEQ ID NO: 278 or 279). Such antibodies also include any that contain a VL chain encoded by a sequence of nucleotides containing germline components compiled from a Vκ germline segment that is an IGKV1 (set forth in any of SEQ ID NOS: 286-316) or an IGKV3 (e.g. any set forth in any of SEQ ID NOS:332-350); and a Jκ germline segment that is an IGKJ1 (e.g. set forth in SEQ ID NO: 356). Such antibodies also include any that are encoded by a sequence of nucleotides containing germline segments that are variants of any of the above germline segments, for example due to conservative mutations or other mutations, so long as the resulting antibody is a functional and productive antibody and binds to EGFR and/or modulates a functional activity.

Exemplary of antibodies against EGFR include an antibody where the VH chain is encoded by a sequence of nucleotides compiled from a V_H germline segment that is a IGHV1-46 (e.g. an IGHV1-46*01, IGHV1-46*01, or an IGHV1-46*03); a D_H germline segment that is an IGHD2-15 (e.g. IGHD2-15*01) or an IGHD6-13 (e.g. IGHD6-13*01); and a JH germline segment that is an IGHJ2*01 or an IGHJ4 (e.g. IGHJ4*01, IGHJ4*02, IGHJ4*03). The VL chain is encoded by a sequence of nucleotides compiled from a Vκ germline segment that is an IGKV1-5 (e.g. IGKV1-5*01, IGKV1-5*02, IGKV1-5*03) or an IGKV3-15(e.g. IGHV3-15*01); and a Jκ germline segment that is a IGKJ1*01. Exemplary antibodies provided herein that modulate an activity of EGFR are set forth in Table 18F.

TABLE 18F: Anti-EGFR Antibodies

Heavy Chain Germline Segments	SEQ ID NO		Light Chain Germline Segments	SEQ ID NO	
	nucleotide	Amino acid		nucleotide	Amino acid
IGHV1-46*01; IGHD2-15*01; IGHJ2*01	1092	1508	IGKV3-15*01; IGKJ1*01	1427	1841
IGHV1-46*01; IGHD6-13*01; IGHJ4*01	1096	1512	IGKV3-15*01; IGKJ1*01	1427	1841
IGHV1-46*01; IGHD2-15*01; IGHJ2*01	1092	1508	IGKV1-5*01; IGKJ1*01	1425	1843

b) Human Epidermal Growth Factor Receptor 2 (HER2/neu)

HER2/neu (ErbB-2; set forth in SEQ ID NO: 1999) is a cell membrane surface-bound receptor tyrosine kinase normally involved in the signal transduction pathways leading to cell growth and differentiation. ErbB-2 is thought to be an orphan receptor, with none of the EGF family of ligands able to activate it. However, ErbB receptors dimerize on ligand binding, and ErbB-2 is the preferential dimerization partner of other members of the ErbB family. ErbB2 activation leads to kinase activation and cell proliferation. ErbB-2 is notable for its role in the pathogenesis of breast cancer and therefore as a target for treatment. In fact, ErbB-2 protein overexpression is observed in 25-30% of primary breast cancers. HERCEPTIN® (trastuzumab) is a recombinant DNA-derived humanized monoclonal antibody, used to treat breast cancer, that selectively binds to the extracellular domain of ErbB-2 Thus, ErbB-2is an attractive target for additional protein therapeutics. See e.g. Carter *et al.*, (1992) *Proc. Natl. Acad. Sci. USA,* 89:4285-4289; and United States Patent No. 5,725,856.

Antibody libraries provided herein can be screened for modulation of an acitivity by assaying for binding to ErbB-2 and/or assaying for a functional activity, for example, signal transduction, cell migration, adhesion, and proliferation. For example, cells that are known to express ErbB-2 can be assessed for proliferation in the presence or absence of an antibody or portion thereof. Alternatively, reporter system assays can be constructed, whereby the expression of a reporter protein, such as luciferase, is dependent on the activiation of ErbB2 (see e.g. Ueda *et al.* (2004) J Biol. Chem., 279:24505-24513). Assays can be peformed in the presence of EGF, TGF or other ErbB lignads that are ligands for ErbB-2 binding partners. Example 13 exemplifies a binding assay to screen antibody libraries provided herein to select or identify antibodies that bind to ErbB-2.

The antibodies or portions thereof identified from the libraries provided herein that modulate an activity of ErbB-2 can be used for the treatment or prevention of disease states associated with expression and/or activity of ErbB-2. For example, the antibodies or portions thereof can be used in the treatment of proliferative diseases such as cancers, including, but not limited to, breast cancer, ovarian cancer, colon cancer, lung cancer and prostate cancer.

Provided herein are antibodies that modulate the activity of ErbB-2 and therefore can be used in the treatment of diseases or conditions associated with expression or activity of ErbB-2. Such antibodies include those that have a VH chain and a VL chain encoded by a sequence of nucleotides compiled from germline segments, or any antibodies optimized therefrom. Exemplary of such antibodies are Fab antibodies. The antibodies further can contain a constant region. The antibodies include those that have a binding affinity for ErbB-2 that is or is about 10^{-6} M, 10^{-7} M, 10^{-8}M, 10^{-9} M, 10^{-10} M, 10^{-11} M, 10^{-12} M or lower, in particular any that have a nanomolar or sub-nanomolar binding affinity.

Anti-ErbB-2 antibodies provided herein include antibodies having at least one CDR that is a CDRH1, CDRH2, CDRH3, CDRL1, CDRL2 and/or CDRL3. For example, a CDRH1 is GGSISSGGYYWS (amino acids 26-37 of SEQ ID NO:1760); a CDRH1 is GYTFTSYYMH (amino acids 26-35 of SEQ ID NO:1512); a CDRH1 is GFSLSTSGVGVG (amino acids 26-37 of SEQ ID NO:1559); a CDRH1 is GGTFSSYAIS (amino acids 26-35 of SEQ ID NO:1522); a CDRH2 is YIYYSGSTYYNPSLKS (amino acids 52-67 of SEQ ID NO:1760); a CDRH2 is IINPSGGSTSYAQKFQG (amino acids 50-66 of SEQ ID NO:1512); a CDRH2 is LIYWNDDKRYSPSLKS (amino acids 52-67 of SEQ ID NO:1559); a CDRH2 is GIIPIFGTANYAQKFQG (amino acids 50-66 of SEQ ID NO:1522); a CDRH3 is EGYSSSWYDYFDY (amino acids 100-112 of SEQ ID NO:1760); a CDRH3 is

GYSGSYYYWYFDL (amino acids 99-111 of SEQ ID NO:1512); a CDRH3 is EEYSSSSAEYKQH (amino acids 99-111 of SEQ ID NO:1513); a CDRH3 is RPNWGYWYFDL (amino acids 100-110 of SEQ ID NO:1559); a CDRH3 is GYNWNDDYYYYYGMDV (amino acids 99-114 of SEQ ID NO:1522); a CDRL1 is RASQSVSSSYLA (amino acids 24-35 of SEQ ID NO:1833); a CDRL1 is KSSQSVLYSSNNKNYLA (amino acids 24-40 of SEQ ID NO:1838); a CDRL1 is RASQSVSSNLA (amino acids 24-34 of SEQ ID NO:1843); a CDRL1 is RSSQSLVYSDGNTYLN (amino acids 24-39 of SEQ ID NO:1828); a CDRL2 is GASSRAT (amino acids 51-57 of SEQ ID NO:1833); a CDRL2 is WASTRES (amino acids 56-62 of SEQ ID NO:1838); a CDRL2 is GASTRAT (amino acids 50-56 of SEQ ID NO:1843); a CDRL2 is KVSNDRS (amino acids 55-61 of SEQ ID NO:1828); a CDRL3 is QQYGSSPPWT (amino acids 90-99 of SEQ ID NO:1833); a CDRL3 is QQYYSTPPWT (amino acids 95-104 of SEQ ID NO:1838); a CDRL3 is QQYNNWPPWT (amino acids 89-98 of SEQ ID NO:1843); and a CDRL3 is MQGTHWPPWT (amino acids 94-103 of SEQ ID NO:1828). Also provided herein is a CDR that exhibits 60 %, 65 %, 70 %, 80 %, 90 %, 91 %, 92 %, 93 %, 94 %, 95 %, 96 %, 97 %, 98 %, 99 % or more sequence identity to any of the above CDRs.

For example, antibodies that modulate an activity of ErbB-2 include any that contain a VH chain encoded by a sequence of nucleotides containing germline components compiled from a V_H germline segment that is an IGHV4 (e.g. any set forth in any of SEQ ID NOS:153-224), an IGHV1 (e.g. any set forth in SEQ ID NOS: 10-43), or an IGHV2 (e.g. any set forth in SEQ ID NOS:44-67); a D_H germline segment that is an IGHD6 (e.g. any set forth in SEQ ID NOS: 268-271); an IGHD1 (e.g. any set forth in any of SEQ ID NOS: 239-243), or an IGHD7 (e.g. set forth in SEQ ID NO:272); and a J_H germline segment that is an IGHJ1 (e.g., set forth in SEQ ID NO:273), an IGHJ2 (e.g. set forth in SEQ ID NO:274), an IGHJ4 (e.g. set forth in any of SEQ ID NOS: 277-279), or an IGHJ6 (e.g. set forth in any of SEQ ID NOS:282-285). Such antibodies also include any that contain a VL chain encoded by a sequence of nucleotides containing germline components compiled from a Vκ germline segment that is a IGKV3 (e.g. any set forth in any of SEQ ID NOS:332-350), a IGKV4 (e.g. set forth in SEQ ID NO:351), or an IGKV2 (e.g. any set forth in SEQ ID NOS:317-331); and a Jκ germline segment that is an IGKJ1 (e.g. set forth in SEQ ID NO: 356). Such antibodies also include any that are encoded by a sequence of nucleotides containing germline segments that are variants of any of the above germline segments, for example due to conservative

mutations or other mutations, so long as the resulting antibody is a functional and productive antibody and binds to ErbB-2 and/or modulates a functional activity.

Exemplary of antibodies against ErbB-2 include an antibody where the VH chain is encoded by a sequence of nucleotides compiled from a V_H germline segment that is a IGHV4-31 (e.g. an IGHV4-31*01, IGHV4-31*02, IGHV4-31*03, IGHV4-31*04, IGHV4-31*05, IGHV4-31*06, IGHV4-31*07, IGHV4-31*08, IGHV4-31*09, IGHV4-31*10), an IGHV1-46 (e.g.,IGHV1-46*01, IGHV1-46*02, IGHV1-46*03), an IGHV2-5 (e.g. IGHV2-5*01, IGHV2-5*02; IGHV2-5*03, IGHV2-5*04, IGHV2-5*05, IGHV2-5*06, IGHV2-5*07, IGHV2-5*08, IGHV2-5*09, IGHV2-5*10) IGHV1-69 (e.g. IGHV1-69*01, IGHV1-69*02, IGHV1-69*03, IGHV1-69*04, IGHV1-69*05, IGHV1-69*06, IGHV1-69*07, IGHV1-69*08, IGHV1-69*09, IGHV1-69*10, IGHV1-69*11, IGHV1-69*12, IGHV1-69*13); a D_H germline segment that is a IGHD6-6 (e.g. IGHD6-6*01), an IGHD6-13 (e.g. IGHD6-13*01), an IGHD1-26 (e.g.IGHD1-26*01), an IGHD7-27*01, or an IGHD1-1*01; and a JH germline segment that is an IGHJ1*01, an IGHJ2*01, an IGHJ4 (e.g. IGHJ4*01, IGHJ4*02, IGHJ4*03) or an IGHJ6 (e.g. IGHJ6*01, IGHJ6*02, IGHJ6*03, IGHJ6*04). The VL chain is encoded by a sequence of nucleotides compiled from a Vκ germline segment that is a IGKV3-20 (e.g. IGHV3-20*01 or IGHV3-20*02), a IGKV4-1 (e.g. IGKV4-1*01), an IGKV3-15*01, or an IGKV2-30*01; and a Jκ germline segment that is a IGKJ1*01. Exemplary antibodies provided herein that modulate an activity of ErbB-2 are set forth in Table 18G.

TABLE 18G: Anti-ErbB2 Antibodies

Heavy Chain Germline Segments	SEQ ID NO		Light Chain Germline Segments	SEQ ID NO	
	nucleotide	Amino acid		nucleotide	Amino acid
IGHV4-31*02; IGHD1-26*01; IGHJ2*01	1344	1760	IGKV3-20*01; IGKJ1*01	1417	1833
IGHV1-46*01, IGHD6-6*01 and IGHJ1*01	1097	1513	IGKV4-1*01; IGKJ1*01	1422	1838
IGHV1-46*01; IGHD6-13*01; IGHJ4*01	1096	1512	IGKV4-1*01; IGKJ1*01	1422	1838
IGHV2-5*01; IGHD7-27*01; IGHJ2*01	1143	1559	IGKV3-15*01; IGKJ1*01	1427	1843
IGHV1-69*06; IGHD1-1*01; IGHJ6*01	1106	1522	IGKV2-30*01; IGKJ1*01	1412	1828

iii. IGF-R1 (Insulin-like Growth Factor 1 Receptor)

Insulin-like Growth Factor 1 Receptor (IGF-R1; set forth in SEQ ID NO:2007) is a transmembrane receptor activated by Insulin-like Growth Factor 1 (IGF-1) and Insulin-like Growth Factor 2 (IFG-2). Overexpression of Insulin-like Growth Factor Receptor-I has been demonstrated in several cancer cell lines and tumor tissues. IGFR1 is overexpressed in 40% of all breast cancer cell lines (Pandini, *et al.*, (1999) Cancer Res. 5: 1935) and in 15% of lung cancer cell lines. In breast cancer tumor tissue, IGFR1 is overexpressed 6-14 fold and IGFR1 exhibits 2-4 fold higher kinase activity as compared to normal tissue (Webster, *et al.*, (1996) Cancer Res. 56: 2781 and Pekonen, *et al.*, (1998) Cancer Res. 48: 1343). Moreover, colorectal cancer tissue has been reported to exhibit strongly elevated IGFR1 levels (Weber *et al.*, Cancer 95 (10): 2086-95 (2002)). Analysis of primary cervical cancer cell cultures and cervical cancer cell lines revealed 3-and 5-fold overexpression of IGFR1, respectively, as compared to normal ectocervical cells (Steller, et a/., (1996) Cancer Res. 56: 1762). Expression of IGFR1 in synovial sarcoma cells also correlated with an aggressive phenotype (i. e. , metastasis and high rate of proliferation; Xie, *et al.*, (1999) Cancer Res. 59: 3588).

Activation of IGF-R1 causes survival and proliferation of mitosis-competent cells and growth in tissues such as skeletal muscle and cardiac muscle. The IGF-1 receptor is implicated in several cancers, most notably breast cancer. IGF-R1 can serve to increase the metastatic potential of the tumor by inferring the ability of the tumor to promote vascularization. In addition, IGF-R1's anti-apoptotic properties allow cancer cells to evade the cytotoxic properties of chemotherapeutic drugs or radiation. Crosstalk can occur between IGF-R1 and EGFR allowing EGFR signaling to resume, even in the presence of EGFR inhibitors. Inhibition of IGF-1R mediated signaling has been shown to reduce tumor growth rate, increase apoptosis, and increase killing of tumors by chemotherapy and other molecular target therapies.

Experimental approaches undertaken to inhibit IGF-1R function in tumors have provided encouraging but limited success, and their effectiveness in treating cancer is yet to be determined in the clinic. The ability of an antibody to inhibit IGF-R1 function was first demonstrated with a mouse monoclonal antibody (α-IR3) targeting an unknown epitope in the α subunit of IGF-1R (Kull *et al.*, (1983) *J. Biol. Chem.* 258:6561-66). Subsequently other antibodies developed to the α subunit of IGF-1R have been shown to inhibit IGF-R1 function to varying degrees in different experimental cancer models. There remains a need for IGF-1R antibodies with different or improved binding, efficacy, and safety characteristics for the treatment of various neoplastic diseases including cancer and metastases thereof.

Antibody libraries provided herein can be screened for modulation of an acitivity by assaying for binding to IGF-R1 and/or assaying for a functional activity, for example, cell proliferation. Assays can be peformed in the presence of IGF-1 or IGF-2. Example 13 exemplifies a binding assay to screen antibody libraries provided herein to select or identify antibodies that bind to IGF-R1.

The antibodies or portions thereof identified from the libraries provided herein that modulate an activity of IGF-R1 can be used for the treatment or prevention of disease states associated with expression and/or activity of IGF-R1. For example, the antibodies or portions thereof can be used in the treatment of rheumatoid arthritis, Grave's disease, multiple sclerosis, systemic lupus erythematosus, Hashimoto's Thyroiditis, Myasthenia Gravis, auto-immune thyroiditis, Bechet's disease, acromegaly, bladder cancer, Wilm's cancer, ovarian cancer, pancreatic cancer, benign prostatic hyperplasia, breast cancer, prostate cancer, bone cancer, lung cancer, colorectal cancer, cervical cancer, synovial sarcoma, diarrhea associated with metastatic carcinoid, vasoactive intestinal peptide secreting tumors, gigantism, psoriasis, atherosclerosis, smooth muscle restenosis of blood vessels or inappropriate microvascular proliferation.

iv. C-Met

C-Met (or hepatocyte growth factor receptor, HGFR; set forth in SEQ ID NO: 2001) is a membrane receptor found in cells of epithelial origin, including stem cells and progenitor cells. Upon stimulation of c-Met by its ligand, hepatocyte growth factor (HGF), c-Met induces several biological responses that trigger invasive growth, including mitogenesis, motogenesis and morphogenesis. C-Met also is expressed in tumor cell lines and in various human solid tumors. Abnormal c-Met activation in cancer cells correlates with poor prognosis and triggers tumor growth, angiogenesis and metastasis. C-Met engages multiple oncogenic signal transduction pathways, including RAS, which leads to morphogenesis; PI3K, which is associated with cell motility; STAT, which induces branching morphogenesis; and beta catenin, which participates in transcriptional regulation of numerous genes. HGF, through c-Met, has also been shown to be a mitogen for certain cell types, including melanocytes, renal tubular cells, keratinocytes, certain endothelial cells and cells of epithelial origin [Matsumoto *et al.*, *Biochem. Biophys. Res. Commun.* 176: 45-51 (1991); Igawa *et al.*, *Biochem. Biophys. Res. Commun.* 174: 831-838 (1991); Han *et al.*, *Biochem.*, 30: 9768-9780 (1991); Rubin *et al.* , *Proc. Natl. Acad. Sci. USA*, 88: 415-419 (1991)].

Several cancer therapies involve interference of c-Met signaling. These therapies include kinase inhibitors, that prevent ATP from binding to c-Met preventing

transphosphorylation; HGF inhibitors, that prevent HGF activation of c-Met; decoy MET inhibitors, that prevent ligand binding and homodimerization; and immunotherapy, including passive immunotherapy which activates CDC or ADCC and active immunotherapy with cytokines triggering non-specific stiulation of immune cells. In view of the important role that this pathway plays in the etiology of various pathological conditions, however, it is clear that there continues to be a need for agents that have clinical attributes that are optimal for development as therapeutic agents.

Antibody libraries provided herein can be screened for modulation of an acitivity by assaying for binding to c-Met and/or assaying for a functional activity, for example, cell proliferation or cell signaling. Assays can be performed in the presence of HGF. Example 13 exemplifies a binding assay to screen antibody libraries provided herein to select or identify antibodies that bind to c-Met.

The antibodies or portions thereof identified from the libraries provided herein that modulate an activity of c-Met can be used for the treatment or prevention of disease states associated with expression and/or activity of c-Met. For example, the antibodies or portions thereof can be used in the treatment of lung cancer, bone cancer, pancreatic cancer, skin cancer, cancer of the head and neck, cutaneous or intraocular melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, colon cancer, breast cancer, gynecologic tumors (e. g. , uterine sarcomas, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina or carcinoma of the vulva), Hodgkin's disease, cancer of the esophagus, cancer of the small intestine, cancer of the endocrine system (e.g., cancer of the thyroid, parathyroid or adrenal glands), sarcomas of soft tissues, cancer of the urethra, cancer of the penis, prostate cancer, chronic or acute leukemia, solid tumors of childhood, lymphocytic lymphomas, cancer of the bladder, cancer of the kidney or ureter (e. g., renal cell carcinoma, carcinoma of the renal pelvis), or neoplasms of the central nervous system (e. g. , primary CNS lymphoma, spinal axis tumors, brain stem gliomas or pituitary adenomas).

Anti-c-Met antibodies provided herein include antibodies having at least one CDR that is a CDRH1, CDRH2, CDRH3, CDRL1, CDRL2 and/or CDRL3. For example, a CDRH1 is GFTFSSYAMS (amino acids 26-35 of SEQ ID NO:3353); a CDRH2 is SISGSGGSTYYADSVKG (amino acids 50-66 of SEQ ID NO:3353); a CDRH3 is EHIVVVIAISYYYYYYGMDV (amino acids 99-118 of SEQ ID NO:3353); a CDRH3 is EDIVVVPAAMSYYYYYYGMDV (amino acids 99-119 of SEQ ID NO:3347); a CDRH3 is EDIVLMVYAISYYYYYYGMDV (amino acids 99-119 of SEQ ID NO:3349); a CDRH3 is

EDIVVVVAATSYYYYYYGMDV (amino acids 99-119 of SEQ ID NO:3351); a CDRL1 is QGDSLRSYYAS (amino acids 22-33 of SEQ ID NO:1870); a CDRL2 is GKNNRPS (amino acids 49-55 of SEQ ID NO:1870); and a CDRL3 is NSRDSSGNHLVV (amino acids 88-99 of SEQ ID NO:1870). Also provided herein is a CDR that exhibits 60 %, 65 %, 70 %, 80 %, 90 %, 91 %, 92 %, 93 %, 94 %, 95 %, 96 %, 97 %, 98 %, 99 % or more sequence identity to any of the above CDRs.

For example, antibodies that modulate an activity of c-Met include any that contain a VH chain encoded by a sequence of nucleotides containing germline components compiled from a V_H germline segment that is an IGHV3 (e.g. any set forth in SEQ ID NOS: 68-152); a D_H germline segment that is an IGHD2 (e.g., any set forth in any of SEQ ID NOS:244-251); and a J_H germline segment that is an IGHJ6 (e.g. any set forth in SEQ ID NOS: 282-285), or is a modified form of a J_H germline segment, for example, set forth in SEQ ID NO: 3455. Such antibodies also include any that contain a VL chain encoded by a sequence of nucleotides containing germline components compiled from a Vλ germline segment that is an IGLV3 (e.g. set forth in SEQ ID NO: 400-417); and a Jλ germline segment that is an IGLJ2 (e.g. set forth in SEQ ID NO: 443). Such antibodies also include any that are encoded by a sequence of nucleotides containing germline segments that are variants of any of the above germline segments, for example due to conservative mutations or other nucleotide mutations, so long as the resulting antibody is a functional and productive antibody and binds to c-Met and/or modulates a functional activity.

Exemplary of antibodies against c-Met include an antibody where the VH chain is encoded by a sequence of nucleotides compiled from a V_H germline segment that is an IGHV3-23 (e.g. IGHV3-23*01, IGHV3-23*02, IGHV3-23*03, IGHV3-23*04 or IGHV3-23*05); a D_H germline segment that is an IGHD2-15*01, an IGHD2-2 (e.g. IGHD2-2*01, IGHD2-2*02, or IGHD2-2*03), an IGHD2-8 (e.g. IGHD2-8*01 or IGHD2-8*02), or an IGHD2-21 (e.g. IGHD2-21*01 or IGHD2-21*02); and a JH germline segment that is an IGHJ6 (e.g. IGHJ6*01, IGHJ6*02, IGHJ6*03, IGHJ6*04), or any modified form thereof, for example, set forth in SEQ ID NOS: 3455. The VL chain is encoded by a sequence of nucleotides compiled from a a Vλ germline segment that is an IGLV3-19*01; and a Jλ germline segment that is an ILGJ2*01. Exemplary antibodies provided herein that modulate an activity of EpoR are set forth in Table 18H.

TABLE 18H: Anti-HGFR Antibodies

Heavy Chain Germline Segments	SEQ ID NO		Light Chain Germline Segments	SEQ ID NO	
	nucleotide	Amino acid		nucleotide	Amino acid

IGHV3-23*01; IGHD2-21*01>3; IGHJ6*01	2663	3353	IGLV3-19*01; IGLJ2*01	1454	1870
IGHV3-23*01; IGHD2-2*01>3; IGHJ6*01	2657	3347	IGLV3-19*01; IGLJ2*01	1454	1870
IGHV3-23*01; IGHD2-8*01>3; IGHJ6*01	2659	3349	IGLV3-19*01; IGLJ2*01	1454	1870
IGHV3-23*01; IGHD2-15*01>3; IGHJ6*01	2661	3351	IGLV3-19*01; IGLJ2*01	1454	1870

v. CD20 – B-lymphocyte antigen

CD20 (human B-lymphocyte-restricted differentiation antigen, Bp35; set forth in SEQ ID NO: 2011), is a hydrophobic transmembrane protein located on pre-B and mature B lymphocytes. CD20 is found on the surface of greater than 90% of B cells from peripheral blood or lymphoid organs and is expressed during early pre-B cell development and remains until plasma cell differentiation. CD20 is present on both normal B cells as well as malignant B cells. In particular, CD20 is expressed on greater than 90% of B cell non-Hodgkin's lymphomas (NHL) (Anderson *et al.* (1984) *Blood* 63(6):1424-1433), but is not found on hematopoietic stem cells, pro-B cells, normal plasma cells, or other normal tissue (Tedder *et al.* (1985) *J. Immunol.* 135(2):973-979). CD20 also is expressed on tumor cells, e.g. NHL.

CD20 regulates an early step in the activation process for cell cycle initiation and differentiation. CD20 functions as an ion channel and operates as a store of calcium facilitating entry of extracellular calcium following BCR-induced emptying of intracellular stores (see e.g., Teeling *et al.* (2006) J Immunol., 177:362-371). Due to the expression of CD20 on almost all B-cells, but not stem cells, it is a target for antigenic modulation via mAb induced antibody-dependent cellular cytotoxicity and complement-dependent cytotoxicity. In addition, when engaged by antibody, CD20 initiates signaling that can control growth and triggering cell death in tumors (Teeling *et al.* (2006) J Immunol., 177:362-371).

CD20 has been validated as a cancer cell target by RITUXAN® (Rituximab), a genetically engineered chimeric murine/human monoclonal antibody directed against the CD20 antigen found on the surface of normal and malignant B lymphocytes (see e.g. United States Patent No. 5,736,137). RITUXAN® has been shown to induce B-cell lysis through apoptosis, complement-dependent cytotoxicity (CDC) and ADCC.

Antibody libraries provided herein can be screened for modulation of an acitivity by assaying for binding to CD20 and/or assaying for a functional activity, for example,

complement-dependent cell-mediate cytotoxicity and killing of cells and apoptosis assays of cells expressing CD20. Example 13 exemplifies a binding assay to screen antibody libraries provided herein to select or identify antibodies that bind to CD20. Example 11 exemplifies a lymphoma apoptosis assay for assessing the function of cross-linked Fab antibodies.

The antibodies or portions thereof identified from the libraries provided herein that modulate an activity of CD20 can be used for the treatment or prevention of disease states associated with expression and/or activity of CD20. For example, the antibodies or portions thereof can be used in the treatment of lymphomas, autoimmune diseases and transplant rejections (e.g, to prevent rejection of organ and tissue grafts by suppressing autoimmune responses.) Lymphomas include, but are not limited to, non-Hodgkin's lymphomas (high-grade lymphomas, intermediate grade lymphomas, and low grade lymphomas), Hodgkin's disease, acute lymphoblastic leukemias, myelomas, chronic lymphocytic leukemias, and myeloblastic leukemias. Autoimmune diseases include, but are not limited to, systemic lupus erythematosus (SLE), rheumatoid arthritis, Crohn's disease, psoriasis, autoimmune thrombocytopenic purpura, multiple sclerosis, ankylosing spondylitis, myasthenia gravis, and pemphigus vulgaris.

vii. Erythropoietin Receptor (Epo-R)

Erythropoietin (Epo; set forth in SEQ ID NO: 2009) is a glycoprotein hormone that induces proliferation and differentiation of erythroid progenitor cells. Epo is responsible for promoting the growth, differentiation and survival of erythroid progenitors, which give rise to mature red blood cells. In response to changes in the level of oxygen in the blood and tissues, erythropoietin appears to stimulate both proliferation and differentiation of immature erythroblasts. It also functions as a growth factor, stimulating the mitotic activity of erythroid progenitor cells, such as erythrocyte burst forming and colony-forming units. It also acts as a differentiation factor, triggering transformation of an erythrocyte colony-forming-unit into a proerythroblast (See Erslev, A., *New Eng. J. Med.*, 316:101-103 (1987)).

The activity of Epo is mediated through the binding and activation of a cell surface receptor referred to as the erythropoietin receptor (EpoR). In the absence of ligands the Epo receptor exists in a preformed dimer. The binding of Epo to its receptor causes a conformational change such that the cytoplasmic domains are placed in close proximity. While not completely understood, it is believed that this "dimerization" plays a role in the activation of the receptor. The activation of the Epo receptor results in a number of biological effects. Some of these activities include stimulation of proliferation, stimulation of differentiation and inhibition of apoptosis (See U.S. Pat. No. 6,319,499, Liboi *et al.*, *PNAS*

USA, 90:11351 (1993), Koury, Science, 248:378 (1990)).Defects in the erythropoietin receptor can produce erythroleukemia and familial erythrocytosis.

Erythropoietin is an important pharmaceutical for use in a variety of therapies where stimulation of red blood cell proliferation (RBC) is desired. Epogen® (epoetin alfa) is a recombinant erythropoietin used to stimulate red blood cell proliferation and thereby treat anemia (see e.g. U.S. Patent Nos. 4,703,008 and 5,955,422).

Antibody libraries provided herein can be screened for modulation of an acitivity by assaying for binding to EpoR and/or assaying for a functional activity, for example, proliferation, apoptosis or cell signaling. Example 13 exemplifies a binding assay to screen antibody libraries provided herein to select or identify antibodies that bind to EpoR. Example 12 and 18 exemplify assays to assess modulation of proliferation or apoptosis induced by EpoR. Hence, such assays can be used to identify agonist antibodies.

The antibodies or portions thereof identified from the libraries provided herein that modulate an activity of EpoR can be used for the treatment or prevention of disease states associated with expression and/or activity of EpoR. For example, the antibodies or portions thereof can be used in the treatment of disorders characterized by low red blood cell levels and/or decreased hemoglobin levels (e.g. anemia). In addition, such antibodies or portions thereof can be used for treating disorders characterized by decreased or subnormal levels of oxygen in the blood or tissue, such as, for example, hypoxemia or chronic tissue hypoxia and/or diseases characterized by inadequate blood circulation or reduced blood flow. Antibodies or antigen-binding portions thereof also can be useful in promoting wound healing or for protecting against neural cell and/or tissue damage, resulting from brain/spinal cord injury, stroke and the like. Non-limiting examples of conditions that can be treatable by the antibodies include anemia, such as chemotherapy-induced anemia, cancer associated anemia, anemia of chronic disease, HIV-associated anemia, bone marrow transplant-associated anemia and the like, heart failure, ischemic heart disease and renal failure.

Provided herein are antibodies that modulate the activity of EpoR and therefore can be used in the treatment of diseases or conditions associated with expression or activity of EpoR. Such antibodies include those that have a VH chain and a VL chain encoded by a sequence of nucleotides compiled from germline segments, or any antibodies optimized therefrom. Exemplary of such antibodies are Fab antibodies. The antibodies further can contain a constant region. The antibodies include those that have a binding affinity for EpoR that is or is about 10^{-6} M, 10^{-7} M, 10^{-8} M, 10^{-9} M, 10^{-10} M, 10^{-11} M, 10^{-12} M or lower, in particular any that have a nanomolar or sub-nanomolar binding affinity.

Anti-EpoR antibodies provided herein include antibodies having at least one CDR that is a CDRH1, CDRH2, CDRH3, CDRL1, CDRL2 and/or CDRL3. For example, a CDRH1 is GYTFTSYYMH (amino acids 26-35 of SEQ ID NO:1509); a CDRH1 is SGYSISSSNWWG (amino acids $26-37 of SEQ ID NO:1759); a CDRH1 is GGSISSGGYYWS (amino acids 26-37 of SEQ ID NO:1769); a CDRH1 is GFTFSSYAMS (amino acids 26-35 of SEQ ID NO:3359); a CDRH2 is IINPSGGSTSYAQKFQG (amino acids 50-66 of SEQ ID NO:1509); a CDRH2 is YIYYSGSTYYNPSLKS (amino acids 51-66 of SEQ ID NO:1759); a CDRH2 is YIYYSGSTYYNPSLKS (amino acids 52-67 of SEQ ID NO:1769); a CDRH2 is SISGSGGSTYYADSVKG (amino acids 50-66 of SEQ ID NO:3359); a CDRH3 is EYYYGSGSYYNDYFDY (amino acids 99-114 of SEQ ID NO:1509); a CDRH3 is EGYSSSWYDYFDY (amino acids 99-111 of SEQ ID NO:1512); a CDRH3 is TNWGAEYFQH (amino acids 99-108 of SEQ ID NO:1759); a CDRH3 is ANWGDNWFDS (amino acids 100-109 of SEQ ID NO:1769); a CDRH3 is ANWGYWYFDL (amino acids 99-108 of SEQ ID NO:1514); a CDRH3 is EGYCSGGSCYSYWYFDL (amino acids 99-115 of SEQ ID NO:1508); a CDRH3 is GITMVRGVIISYYYYYYGMDV (amino acids 99-119 of SEQ ID NO:3359); a CDRL1 is RASQSVSSSYLA (amino acids 24-35 of SEQ ID NO:1833); a CDRL1 is KSSQSVLYSSNNKNYLA (amino acids 24-40 of SEQ ID NO:1838); a CDRL1 is RASQSVSSNLA (amino acids 24-34 of SEQ ID NO:1843); a CDRL1 is RASQSISSWLA (amino acids 24-34 of SEQ ID NO:1841); a CDRL1 is RSSQSLLDSDDGNTYLD (amino acids 24-40 of SEQ ID NO:1853); a CDRL1 is RASQSISSYLN (amino acids 24-34 of SEQ ID NO:1854); a CDRL1 is QGDSLRSYYAS (amino acids 23-33 of SEQ ID NO:1870); a CDRL2 is GASSRAT (amino acids 51-57 of SEQ ID NO:1833); a CDRL2 is WASTRES (amino acids 56-62 of SEQ ID NO:1838); a CDRL2 is GASTRAT (amino acids 50-56 of SEQ ID NO:1843); a CDRL2 is DASSLES (amino acids 50-56 of SEQ ID NO:1841); a CDRL2 is TLSYRAS (amino acids 56-62 of SEQ ID NO:1853); a CDRL2 is AASSLQS (amino acids 50-56 of SEQ ID NO:1854); a CDRL2 is GKNNRPS (amino acids 49-55 of SEQ ID NO:1870); a CDRL3 is QQYGSSPPWT (amino acids 90-99 of SEQ ID NO:1833); a CDRL3 is QQYYSTPPWT (amino acids 95-104 of SEQ ID NO:1838); a CDRL3 is QQYNNWPPWT (amino acids 89-98 of SEQ ID NO:1843); a CDRL3 is QQYNSYSPWT (amino acids 89-98 of SEQ ID NO:1841); a CDRL3 is MQRIEFPSWT (amino acids 95-104 of SEQ ID NO:1853); a CDRL3 is QQSYSTPPWT (amino acids 89-98 of SEQ ID NO:1854); and a CDRL3 is NSRDSSGNHLVV(amino acids 88-99 of SEQ ID NO:1870). Also provided herein is a CDR that exhibits 60 %, 65 %, 70 %,

80 %, 90 %, 91 %, 92 %, 93 %, 94 %, 95 %, 96 %, 97 %, 98 %, 99 % or more sequence identity to any of the above CDRs.

For example, antibodies that modulate an activity of EpoR include any that contain a VH chain encoded by a sequence of nucleotides containing germline components compiled from a V_H germline segment that is an IGHV1 (e.g. any set forth in SEQ ID NOS: 10-43), IGHV3 (e.g. any set forth in SEQ ID NOS: 68-152), or an IGHV4 (e.g. any set forth in SEQ ID NOS: 153-224); a D_H germline segment that is an IGHD6 (e.g. any set forth in SEQ ID NOS: 268-271), an IGHD3 (e.g. any set forth in any of SEQ ID NOS: 252-259), an IGHD7 (e.g. any set forth in SEQ ID NO: 272); an IGHD2 (e.g., any set forth in any of SEQ ID NOS:244-251); and a J_H germline segment that is an IGHJ1 (e.g., set forth in SEQ ID NO:273), IGHJ4 (e.g. set forth in SEQ ID NO:277-279), an IGHJ5 (e.g. set forth in SEQ ID NOS: 280 or 281), an IGHJ2 (e.g. set forth in SEQ ID NOS: 274), or an IGHJ6 (e.g. any set forth in SEQ ID NOS: 282-285), or is a modified form of a JH germline segment, for example, set forth in any of SEQ ID NOS: 3450-3455. Such antibodies also include any that contain a VL chain encoded by a sequence of nucleotides containing germline components compiled from a Vκ germline segment that is an IGKV4 (e.g. set forth in SEQ ID NO:351), an IGKV3 (e.g. set forth in SEQ ID NOS:332-350); an IGKV1 (e.g. set forth in SEQ ID NOS:286-316 and 868); an IGKV2 (e.g. set forth in SEQ ID NOS:317-331); a Jκ germline segment that is an IGKJ1 (e.g. set forth in SEQ ID NO: 356); a Vλ germline segment that is an IGLV3 (e.g. set forth in SEQ ID NO: 400-417); and a Jλ germline segment that is an IGLJ2 (e.g. set forth in SEQ ID NO: 443). Such antibodies also include any that are encoded by a sequence of nucleotides containing germline segments that are variants of any of the above germline segments, for example due to conservative mutations or other nucleotide mutations, so long as the resulting antibody is a functional and productive antibody and binds to EpoR and/or modulates a functional activity.

Exemplary of antibodies against EpoR include an antibody where the VH chain is encoded by a sequence of nucleotides compiled from a V_H germline segment that is a IGHV1-46 (e.g.,IGHV1-46*01, IGHV1-46*02, IGHV1-46*03), an IGHV3-23 (e.g. IGHV3-23*01, IGHV3-23*02, IGHV3-23*03, IGHV3-23*04, IGHV3-23*05), an IGHV4-28 (e.g. IGHV4-28*01, IGHV4-28*02, IGHV4-28*03, IGHV4-28*04, IGHV4-28*05), or an IGHV4-31 (e.g. IGHV4-31*01, IGHV4-31*02, IGHV4-31*03; IGHV4-31*04, IGHV4-31*05, IGHV4-31*06, IGHV4-31*07, IGHV4-31*08, IGHV4-31*09, IGHV4-31*10); a D_H germline segment that is a IGHD6-6 (e.g. IGHD6-6*01), an IGHD6-13 (e.g. IGHD6-13*01), an IGHD3-10 (e.g.IGHD3-10*01 or IGHD3-10*02), an IGHD7-27*01, an IGHD2-15*01, or an

IGHD6-13*01; and a JH germline segment that is an IGHJ1*01, an IGHJ4 (e.g. IGHJ4*01, IGHJ4*02 or IGHJ4*03), an IGHJ5 (e.g. IGHJ5*01, IGHJ5*02), an IGHJ6 (e.g. IGHJ6*01, IGHJ6*02, IGHJ6*03, IGHJ6*04), or an IGHJ2*01, or any modified form thereof, for example, set forth in SEQ ID NOS: 3455. The VL chain is encoded by a sequence of nucleotides compiled from a Vκ germline segment that is an IGKV4-1 (e.g. IGKV4-1*01), an IGKV3-15*01, an IGKV3-20 (e.g. IGKV3*01, IGKV3*02), an IGKV1-5 (e.g. IGKV1-5*01, IGKV1-5*02, IGKV1-5*03), an IGKV1-39*01, or an IGKV2D-40*01; a Jκ germline segment that is a IGKJ1*01; a Vλ germline segment that is an IGLV3-19*01; and a Jλ germline segment that is an ILGJ2*01. Exemplary antibodies provided herein that modulate an activity of EpoR are set forth in Table 18I.

TABLE 18I: Anti-EpoR Antibodies

Heavy Chain Germline Segments	SEQ ID NO		Light Chain Germline Segments	SEQ ID NO	
	nucleotide	Amino acid		nucleotide	Amino acid
IGHV1-46*01; IGHD3-10*01; IGHJ4*01	1093	1509	IGKV4-1*01; IGKJ1*01	1422	1838
IGHV1-46*01; IGHD6-6*01; IGHJ1*01	1097	1513	IGKV4-1*01; IGKJ1*01	1422	1838
IGHV1-46*01; IGHD6-13*01; IGHJ4*01	1096	1512	IGKV4-1*01; IGKJ1*01	1422	1838
IGHV4-28*01; IGHD7-27*01; IGHJ1*01	1343	1759	IGKV3-15*01; IGKJ1*01	1427	1843
IGHV4-31*02; IGHD7-27*01; IGHJ5*01	1353	1769	IGKV3-15*01; IGKJ1*01	1427	1843
IGHV1-46*01; IGHD7-27*01; IGHJ2*01	1098	1514	IGKV3-20*01; IGKJ1*01	1417	1833
IGHV1-46*01; IGHD2-15*01; IGHJ2*01	1092	1508	IGKV3-15*01; IGKJ1*01	1427	1843
IGHV1-46*01; IGHD6-13*01; IGHJ4*01	1096	1512	IGKV3-15*01; IGKJ1*01	1427	1843
IGHV1-46*01; IGHD6-13*01; IGHJ4*01	1096	1512	IGKV3-20*01; IGKJ1*01	1417	1833
IGHV1-46*01; IGHD2-15*01; IGHJ2*01	1092	1508	IGKV1-5*01; IGKJ1*01	1425	1841
IGHV1-46*01;	1093	1509	IGKV2D-40*01;	1437	1853

IGHD3-10*01; IGHJ4*01			IGKJ1*01		
IGHV1-46*01; IGHD6-13*01; IGHJ4*01	1096	1512	IGKV2D-40*01; IGKJ1*01	1437	1853
IGHV3-23*01; IGHD3-10*01>3; IGHJ6*01	2669	3359	IGKV1-39*01; IGKJ1*01	1438	1854
IGHV3-23*01; IGHD3-10*01>3; IGHJ6*01	2669	3359	IGLV3-19*01; IGLJ2*01	1454	1870

viii. Cadherins

Cadherins are a class of calcium dependent, type-1 transmembrane glycoproteins that are involved in cell adhesion, helping to ensure that cells within tissues are bound together. There are multiple classes of cadherin molecules, including but not limited to N-cadherin, E-cadherin and P-cadherin. Members of this family exhibit calcium-dependent homophilic interactions and are responsible for the selective cell-cell recognition and adhesion, which is necessary for allocating different cell types to their proper places during organ development. Cadherins also play an important role in maintaining the integrity of multicellular structures. During embryonic morphogenesis the expression of diverse members of the cadherin family is spatially and temporally regulated facilitating the orderly assembly of various cell types into functional structures. Cadherins are considered to play a significant role in the cellular connections of cancer and metastatic cells.

a) P-Cadherin (P-cad/CDH3)

P-cadherin (P-cad; set forth in SEQ ID NO: 2008) is a single-span type-1 transmembrane glycoprotein found in the placenta that is homologous to E-cadherin (epithelial cadherin, E-cad). Both P-cad and E-cad interact with the cytoskeleton by alpha-catenin. Like other cadherins, p-cadherin plays a role in epithelial cell-cell adhesion. Other major roles include the determination of cell phenotypes and involvement in cell dynamics, including migration and the dissemination of tumor cells. The expression of P-cad in epithelial tissues appears to identify cell populations with proliferative activity, and its expression decreases as cells differentiate.

Expression of P-cadherin, a calcium-dependent cellular adhesion protein, has been reported in poorly differentiated and invasive bladder carcinoma cells. Such bladder carcinoma cells exhibit reduced E-cadherin expression. (Mialhe, A. *et al.*, J. Urol. 164:826 (2000)). Down-regulation of E-cadherin and P-cadherin has also been associated with cultured neoplastic prostate cells. (Wang, J. *et al.*, Urol. Res. 5:308 (2000)). The development

of human colorectal cancer has been attributed, at least in part, to a decrease in cellular levels of the E-cadherin/catenin complex. (Debruyne, P. *et al.*, *Acta Gastroenterol. Belg.* 62(4):393 (1999)) . Aberrant up-regulation of P-cadherin was recently reported to be associated with proliferative cell phenotypes that can be related to neoplastic transformation of tissues of the gastrointestinal tract, particularly metaplastic and adenomatous polyps. (Sanders, D.S., et a/., J. Pathol. 190(5):526 (2000)). Hence, certain cancer types, particularly some digestive cancer types, e.g., colon cancer, are characterized by the upregulation and the overexpression of P-cadherin relative to normal cells. P-cadherin is a valid target for cancer diagnosis, prophylaxis or therapy (see e.g. United States Published Patent Application No. 2003/0194406 and International Published Patent Application No. WO 02/097395).

Antibody libraries provided herein can be screened for modulation of an acitivity by assaying for binding to pCad and/or assaying for a functional activity. Assays for functional activity, include but are not limited to, assays that assess proliferation and/or adhesion of tumor cells, ADCC or CDC activity, anti-apoptotic assays, or cell cycle checkpoint assays. Example 13 exemplifies a binding assay to screen antibody libraries provided herein to select or identify antibodies that bind to pCad. Example 20 exemplifies an assay to assess effects of antibodies on cell to cell adhesion induced by p-cadherin. For example, an antibody that inhibits p-cadherin function can be identified based on the failure of cells to clump in the presence of the antibody.

The antibodies or portions thereof identified from the libraries provided herein that modulate an activity of pCad can be used for the treatment or prevention of disease states associated with expression and/or activity of pCad. For example, the antibodies or portions thereof can be used in the treatment of digestive cancers such as colon cancer, stomach cancer and liver cancer, and other cancers, such as lung cancer and breast cancer.

Provided herein are antibodies that modulate the activity of p-cadherin and therefore can be used in the treatment of diseases or conditions associated with expression or activity of p-cadherin. Such antibodies include those that have a VH chain and a VL chain encoded by a sequence of nucleotides compiled from germline segments, or any antibodies optimized therefrom. Exemplary of such antibodies are Fab antibodies. The antibodies further can contain a constant region. The antibodies include those that have a binding affinity for p-cadherin that is or is about 10^{-6} M, 10^{-7} M, 10^{-8} M, 10^{-9} M, 10^{-10} M, 10^{-11} M, 10^{-12} M or lower, in particular any that have a nanomolar or sub-nanomolar binding affinity.

Anti-p-cadherin antibodies provided herein include antibodies having at least one CDR that is a CDRH1, CDRH2, CDRH3, CDRL1, CDRL2 and/or CDRL3. For example, a

CDRH1 is GYTFTSYYMH (amino acids 26-35 of SEQ ID NO:1512); a CDRH1 is GFTFSSYAMS (amino acids 26-35 of SEQ ID NO:3559); a CDRH2 is IINPSGGSTSYAQKFQG (amino acids 50-66 of SEQ ID NO:1512); a CDRH2 is SISGSGGSTYYADSVKG (amino acids 50-66 of SEQ ID NO:3359); a CDRH3 is EGYSSSWYDYFDY (amino acids 99-111 of SEQ ID NO:1512); a CDRH3 is ANWGYWYFDL (amino acids 99-108 of SEQ ID NO:1514); a CDRH3 is EYYYGSGSYYNDYFDY (amino acids 99-114 of 1509); a CDRH3 is GITMVRGVIISYYYYYYGMDV (amino acids 99-119 of SEQ ID NO:3359); a CDRH3 is VIITPRTIVISYAFDV (amino acids 99-114 of SEQ ID NO:3071; a CDRL1 is RASQSVSSNLA (amino acids 24-35 of SEQ ID NO:1843); a CDRL1 is RASQSVSSSYLA (amino acids 24-35 of SEQ ID NO:1833); a CDRL1 is RASQSISSWLA (amino acids 24-34 of SEQ ID NO:1841); a CDRL1 is RASQSISSYLN (amino acids 24-34 of SEQ ID NO:1854); a CDRL1 is QGDSLRSYYAS (amino acids 23-33 of SEQ ID NO:1870; a CDRL2 is GASTRAT (amino acids 50-56 of SEQ ID NO:1843); a CDRL2 is GASSRAT (amino acids 51-57 of SEQ ID NO:1833); a CDRL2 is DASSLES (amino acids 50-56 of SEQ ID NO:1841); a CDRL2 is AASSLQS (amino acids 50-56 of SEQ ID NO:1854); a CDRL2 is GKNNRPS (amino acids 49-55 of SEQ ID NO:1870); a CDRL3 is QQYNNWPPWT (amino acids 89-98 of SEQ ID NO:1843); a CDRL3 is QQYGSSPPWT (amino acids 90-99 of SEQ ID NO:1833); a CDRL3 is QQYNSYSPWT (amino acids 89-98 of SEQ ID NO:1841); a CDRL3 is QQSYSTPPWT (amino acids 89-98 of SEQ ID NO:1854); and a CDRL3 is NSRDSSGNHLVV (amino acids 88-99 of SEQ ID NO:1870). Also provided herein is a CDR that exhibits 60 %, 65 %, 70 %, 80 %, 90 %, 91 %, 92 %, 93 %, 94 %, 95 %, 96 %, 97 %, 98 %, 99 % or more sequence identity to any of the above CDRs.

For example, antibodies that modulate an activity of p-cadherin include any that contain a VH chain encoded by a sequence of nucleotides containing germline components compiled from a V_H germline segment that is an IGHV1 (e.g. any set forth in any of SEQ ID NOS:1-43) or an IGHV3 (e.g. any set forth in any of SEQ ID NOS:68-152); a D_H germline segment that is an IGHD3 (e.g. any set forth in SEQ ID NOS:252-259), an IGHD6 (e.g. any set forth in SEQ ID NOS: 268-271) or an IGHD7 (e.g. set forth in SEQ ID NO: 272); and a J_H germline segment that is an IGHJ2 (e.g. set forth in SEQ ID NO:274), IGHJ3 (e.g. set forth in SEQ ID NO:275 or 276), is an IGHJ4 (e.g. set forth in SEQ ID NO: 278 or 279), an IGHJ6 (e.g. set forth in any of SEQ ID NOS: 282-285), or is a modified form of a JH germline segment, for example, set forth in any of SEQ ID NOS: 3450-3455. Such antibodies also include any that contain a VL chain encoded by a sequence of nucleotides containing

germline components compiled from a Vκ germline segment that is an IGKV1 (e.g. any set forth in SEQ ID NOS: 286-316), or an IGKV3 (e.g. any set forth in any of SEQ ID NOS:332-350); a Jκ germline segment that is an IGKJ1 (e.g. set forth in SEQ ID NO: 356); a Vλ germline segment that is an IGLV3 (e.g. set forth in SEQ ID NO: 400-417); and a Jλ germline segment that is an IGLJ2 (e.g. set forth in SEQ ID NO: 443). Such antibodies also include any that are encoded by a sequence of nucleotides containing germline segments that are variants of any of the above germline segments, for example due to conservative mutations or other mutations, so long as the resulting antibody is a functional and productive antibody and binds to p-cadherin and/or modulates a functional activity.

Exemplary of antibodies against p-cadherin include an antibody where the VH chain is encoded by a sequence of nucleotides compiled from a V_H germline segment that is a IGHV1-46 (e.g. an IGHV1-46*01, IGHV1-46*01, or an IGHV1-46*03) or an IGHV3-23 (e.g. IGHV3-23*01, IGHV3-23*02, IGHV3-3*03, IGHV3-23*04, IGHV3-23*05); a D_H germline segment that is an IGHD3-10 (e.g. IGHD3-10*01, IGHD3-10*02) or an IGHD6-13 (e.g. IGHD6-13*01) or an IGHD7-27*01; and a JH germline segment that is an IGHJ3 (e.g. IGHJ3*01, IGHJ3*02), IGHJ4 (e.g. IGHJ4*01, IGHJ4*02, IGHJ4*03), an IGHJ6 (e.g. IGHJ6*01, IGHJ6*02, IGHJ6*03, IGHJ6*04), or an IGHJ2*01, or any modified form thereof, for example, set forth in SEQ ID NO: 3452 and 3455 and encoding a J_H region set forth in SEQ ID NO:3458 and 3461, respectively. The VL chain is encoded by a sequence of nucleotides compiled from a Vκ germline segment that is an IGKV1-5 (e.g. IGKV1-5*01, IGKV1-5*02, IGKV1-5*03), IGKV1-39*01, an IGKV3-15 (e.g. IGKV3-15*01), IGKV3-20 (e.g. IGKV3-20*01, IGKV3-20*02) or an IGKV3-11 (e.g. IGKV3-11*01, IGKV3-11*02); a Jκ germline segment that is a IGKJ1*01; a Vλ germline segment that is an IGLV3-19*01; and a Jλ germline segment that is an ILGJ2*01. Exemplary antibodies provided herein that modulate an activity of p-cadherin are set forth in Table 18J.

TABLE 18J: Anti-p-cadherin Antibodies

Heavy Chain Germline Segments or Modified forms thereof	SEQ ID NO		Light Chain Germline Segments	SEQ ID NO	
	nucleotide	Amino acid		nucleotide	Amino acid
IGHV1-46*01; IGHD6-13*01; IGHJ4*01	1096	1512	IGKV3-15*01; IGKJ1*01	1427	1843
IGHV1-46*01; IGHD6-13*01; IGHJ4*01	1096	1512	IGKV3-20*01; IGKJ1*01	1417	1833

IGHV1-46*01; IGHD7-27*01; IGHJ2*01	1098	1514	IGKV3-11*01; IGKJ1*01	1434	1850
IGHV1-46*01; IGHD3-10*01; IGHJ4*01	1093	1509	IGKV1-5*01; IGKJ1*01	1425	1841
IGHV3-23*01; IGHD3-10*01>3; IGHJ6*01	2669	3359	IGKV1-39*01; IGKJ1*01	1438	1854
IGHV3-23*01; IGHD3-10*01>1'; IGHJ3*01	2381	3071	IGKV1-39*01; IGKJ1*01	1438	1854
IGHV3-23*01; IGHD3-10*01>3; IGHJ6*01	2669	3359	IGLV3-19*01; IGLJ2*01	1454	1870

ix. CD44

CD44 (set forth in SEQ ID NO: 2006) is a cell-surface integral membrane glycoprotein involved in cell-to-cell interactions, cell adhesion and migration. Transcripts of the CD44 gene undergo complex alternative splicing resulting in many distinct functional isoform variants. CD44 is a protein which is expressed in several different isoforms on the surface of a wide variety of cell types. The smallest isoform, standard CD44 (CD44s), which is expressed by a variety of different cells, is thought to mediate cell attachment to extracellular matrix components and can transmit a co-stimulus in lymphocyte and monocyte activation. In contrast, expression of splice variants of CD44 which contain the domain v6 (CD44v6) in the extracellular region, is restricted to a subset of epithelia.

CD44 participates in a wide variety of cellular functions, including lymphocyte activation, recirculation and homing, hematopoiesis and tumor metastasis. CD44 is a receptor for hyaluronic acid and can also interact with other ligands such as E-selectin and L-selectin and other ligands such as osteopontin, collagens and matrix metalloproteinases (MMPs). MMPs degrade proteins that keep vessel walls solid allowing endothelial cells to escape into the interstitial matrix causing sprouting angiogenesis. Inhibition of MMPs prevents formation of new capillaries. Interactions of CD44 with hyaluronan mediates cell adhesion interactions. Treatments that disrupt such interactions can be used in the treatment of a number of pathologies.

Some CD44 variations are cell surface markers for breast and prostate cancer cells. Overexpression of CD44 has been linked to the growth and spread of a range of different types of malignancies, particularly lymphomas. CD44v6, as well as other variant exons (CD44v3, CD44v5, CD44v7/v8, CD44v10) has been shown to be a tumor-associated antigen

with a favorable expression pattern in human tumors and normal tissues (Heider K H *et al.* Eur. J. Cancer 31A:2385-2391, 1995; Heider K H *et al.* Cancer Immunology Immunotherapy 43:245-253, 1996; Dall *et al.*, 1996; Beham-Schmid *et al.*, 1998; Tempfer *et al.*, 1998; Wagner *et al.*, 1998) and has been subject to antibody-based diagnostic and therapeutic approaches, in particular radioimmunotherapy (RIT) of tumors (Stroomer J W *et al.* Clin Cancer Res 6(8):3046-55, 2000, WO 95/33771, WO 97/21104). CD44 has been the target of the development of anti-cancer therapeutics (see e.g. United States Patent No. 5,990,299).

Antibody libraries provided herein can be screened for modulation of an acitivity by assaying for binding to CD44 and/or assaying for a functional activity. Example 13 exemplifies a binding assay to screen antibody libraries provided herein to select or identify antibodies that bind to pCad.

The antibodies or portions thereof identified from the libraries provided herein that modulate an activity of CD44 can be used for the treatment or prevention of disease states associated with expression and/or activity of CD44 or a variant thereof. For example, the antibodies or portions thereof can be used in the treatment of a cancer that is a head and neck squamous cell carcinoma (SCC), esophagus SCC, lung SCC, skin SCC, breast adenocarcinoma (AC), lung AC, cervix SCC, pancreas AC, colon AC, or stomach AC. The antibodies or portions thereof also can be used in the treatement of rheumatoid arthritis.

4. Iterative Screening

Upon identification of a "Hit" the methods described in Section C can be repeated to generate a further library for use in the screening methods herein. By virtue of the fact that antibodies are provided in an addressable format, identification of a "Hit" permits instant identification and assessment of the "structure/activity" relationship. For example, upon identification of a "Hit" the component germline segments of the encoded antibody can be immediately envisaged. A subsequent library can be generated that includes antibodies encoded by nucleic acid molecules derived from germline segments "related" to the identified "Hit". Typically, the germline segments are related by sequence similarity, but can also be related by some other shared characteristic such as a CDR, directed peptide, or other biochemical attribute.

Generally, for the generation of a further antibody library in the iterative screening method, all gene families of the germline segments contained in a "Hit" are identified. All V_H, D_H and J_H gene family segments thereof are combined in all possible permutations, or a subset thereof as desired, to generate a recombined nucleic acid molecule encoding a VH chain. All V_κ and J_κ,or V_λ and J_λ gene family segments thereof are combined in all possible

permutation, or a subset thereof as desired, to generate a recombined nucleic acid molecule encoding a VL chain. Vectors and cells expressing the various paired VH and VL members, in all permutations, are generated, proteins expressed, and antibody members purified to generate a further antibody library. The further antibody library can be provided in an addressed format. The further library can be used in screening assays as described herein above to optimize the "Hit".

In addition, it is contemplated herein that because libraries can be created whereby the identify of each member is known, a library might exist already containing the exact desired "related" library members. Thus, those members can be collected to create a sub-library of related "Hits" for screening without having to reperform the method herein.

It also is contemplated that the "Hits" or any subsequent members of a further library can be mutagenized, such as by directed evolution, to further optimize the "Hit".

5. Directed Evolution

Antibody "Hits" identified by the screening methods herein can be further modified, e.g., by mutagenesis, to provide a library of modified antibodies. The modified antibodies are then evaluated to identify one or more antibodies which have altered functional properties (e.g., improved binding, improved stability, lengthened stability in vivo, and/or improved modulation of a functional activity). A further library of modified "Hits" can be generated to select or screen for an improved activity against a target protein. The library can be screened in an addressable format or other display format as described herein above. For example, higher affinity binding proteins can be identified from the second library, e.g., by using higher stringency or more competitive binding and washing conditions. Other screening techniques can also be used.

Various approaches have been used to create mutated antibody repertoires, including chain shuffling (Marks *et al.* (1992) *Bio/Technology* 10:779 and Clackson *et al.* (1991) *Nature* 352:624), error prone PCR (Hawkins *et al.* (1992) *J. Mol. Biol.* 226:889; and Leung *et al.* (1989) *Technique* 1:11-15), use of E. coli mutator strains (Low *et al.* (1996) *J. Mol. Biol.* 260,359), recombination (see, e.g., United States Publication No. 2004-0005709), DNA shuffling using random cleavage (Stemmer (1994) *Nature* 389-391; termed "nucleic acid shuffling"), RACHITT® (Coco *et al.* (2001) *Nature Biotech.* 19:354), or approaches more specifically directed to the complementarity determining regions (CDRs) of the antibody molecule, like CDR walking (Barbas *et al.* (1994) *Proc. Natl. Acad. Sci. USA* 91:3809 and Yang *et al.* (1995) *J. Mol. Biol.* 254:392), site-directed mutagenesis (Zoller *et al.* (1987) *Nucl Acids Res* 10:6487-6504), cassette mutagenesis (Reidhaar-Olson (1991) *Methods Enzymol.*

208:564-586) and incorporation of degenerate oligonucleotides (Griffiths *et al.* (1994) *EMBO J* 13:3245).

In some implementations, the mutagenesis is targeted to regions known or likely to be at the binding interface. For example, mutagenesis can be directed to the CDR regions of the heavy or light chains as described herein. Further, mutagenesis can be directed to framework regions near or adjacent to the CDRs, e.g., framework regions, particular within ten, five, or three amino acids of a CDR junction. Additionally, mutagenesis can also be limited to one or a few of the CDRs, e.g., to make step-wise improvements.

a. Random Mutagenesis

Antibodies bind to antigens via residues in their CDRs. Consequently, mutagenesis of CDRs is widely used to improve the affinity of Fab and Fv fragments of antibodies. Random mutagenesis methods include, for example, use of *E. coli* XL1red, UV irradiation, chemical modification such as by deamination, alkylation, or base analog mutagens, or PCR methods such as DNA shuffling, cassette mutagenesis, site-directed random mutagenesis, error prone PCR (see e.g. U.S. Application No.: 2006-0115874) or the use of commercially available random mutagenesis kits such as, for example, GeneMorph PCR-based random mutagenesis kits (Stratagene) or Diversify random mutagenesis kits (Clontech). The Diversify random mutagenesis kit allows the selection of a desired mutation rate for a given DNA sequence (from 2 to 8 mutations/1000 base pairs) by varying the amounts of manganese (Mn^{2+}) and dGTP in the reaction mixture. Raising manganese levels initially increases the mutation rate, with a further mutation rate increase provided by increased concentration of dGTP. Even higher rates of mutation can be achieved by performing additional rounds of PCR. All of these approaches involve the construction of expression libraries of antibodies with mutations in the CDRs and selection for better binders. Any of a variety of general approaches for directed protein evolution based on mutagenesis can be employed. Any of these, alone or in combination can be used to modify a lead antibody to achieve a desired property. Any method known in the art can be used to modify or alter a lead antibody.

i. Saturation Mutagenesis

In one exemplary embodiment, a saturation mutagenesis technique is used in which the CDR residue(s) are mutated to each of the 20 possible amino acids (see e.g., the Kunkle method, Current Protocols in Molecular Biology, John Wiley and Sons, Inc., Media Pa. and United States Patent No. 6,562,594). In such a technique, a degenerate mutagenic oligonucleotide primer can be synthesized which contains randomization of nucleotides at the desired codon(s) encoding the selected amino acid(s). Exemplary randomization schemes

include NNS- or NNK-randomization, where N represents any nucleotide, S represents guanine or cytosine and K represents guanine or thymine. The degenerate mutagenic primer is annealed to the single stranded DNA template and DNA polymerase is added to synthesize the complementary strand of the template. After ligation, the double stranded DNA template is transformed into *E. coli* for amplification. Alternatively, single amino acid changes are made using standard, commercially available site-directed mutagenesis kits such as QuikChange (Stratagene). In another embodiment, any method commonly known in the art for site specific amino acid mutation can be used.

ii. Error Prone PCR

Error prone PCR can introduce random mutations into nucleic acid sequences (See, e.g., Hawkins *et al.*, (1992) *J. Mol. Biol.* 226(3):889-96). Briefly, PCR is run under conditions which compromise the fidelity of replication, thus introducing random mutations in sequences as those skilled in the art can accomplish. After generation of such random mutants, they can be placed into genetic display formats, panned and thus evaluated for activity.

iii. Cell lines

A mutator strain of bacteria, such as *E. coli* mutD5 or Epicurian Coli® XL1-Red Competent cells (Stratagene, La Jolla, Calif.), can be used during plasmid replication to generate a repertoire of antibodies that include single nucleotide point mutations. The libraries of random mutants are then screened for biological activity using a genetic display format.

iv. DNA shuffling/ antibody chain shuffling

DNA shuffling can be employed to modulate the activities of lead antibodies. In DNA shuffling, variant DNA molecules are generated by *in vitro* homologous recombination by random fragmentation of a parent DNA followed by reassembly using PCR, resulting in randomly introduced point mutations (see e.g. Stemmer, (1994) *Nature* 370:389-391; Stemmer (1994) *Proc. Natl Acad. Sci. USA* 91:10747-10751; United States Patent Nos. 5,605,793, 5,811,238, and 5,830,721; and International Publication Nos. WO 95/022625 and WO 97/20078). This technique can be modified by using a family of parent DNA molecules, such as allelic variants or DNA molecules from different species, to introduce additional variability into the process. Selection or screening for the desired activity, followed by additional iterations of mutagenesis and assay provides for rapid "evolution" of sequences by selecting for desirable mutations while simultaneously selecting against detrimental changes.

In antibody chain shuffling, one selected VH sequence is paired with variety of VL sequences to create new VH/VL partners (see e.g. Kang *et al.* (1991) *Proc. Natl. Acad. Sci.*

USA 88:11120–11123; Collet *et al.* (1992) *Proc. Natl. Acad. Sci. USA* 89:10026-10030; and Marks *et al.* (1992) *Bio/Technology* 10:779)

v. CDR walking

In another example, the generation or selection of higher affinity antibodies can be carried out by CDR walking mutagenesis, which mimics the tertiary immune selection process. For example, saturation mutagenesis of the CDR's of an antibody can be used to generate one or more libraries of antibody fragments which are displayed on the surface of filamentous bacteriophage followed by the subsequent selection of the relevant antibody using immobilized antigen. Sequential and parallel optimization strategies can be used to then select the higher affinity antibody (see e.g. Barbas *et al.* (1994) *Proc. Natl. Acad. Sci. USA* 91:3809-3813; and Yang *et al.* (1995) *J. Mol. Biol* 254(3):392-403).

vi. Framework Stabilization

A mutation can be made in a framework region or constant domain to increase the half-life of the antibody. A mutation in a framework region or constant domain also can be made to alter the immunogenicity of the antibody, to provide a site for covalent or non-covalent binding to another molecule, or to alter such properties as complement fixation, FcR binding and antibody-dependent cell-mediated cytotoxicity (ADCC). A single antibody can have mutations in any one or more of the CDRs or framework regions of the variable domain or in the constant domain. See, e.g., PCT Publication No. WO 00/09560; Ewert *et al.* (2003) *Biochemistry* 42(6):1517-1528; Ewert *et al.* (2004) *Methods* 23(2):184-99; and Knappik *et al.* (1995) *Protein Engineering* 8:81-89.

6. Epitope Mapping

Once a "Hit" is identified its binding epitope can be determined. Hence, antibody libraries provided herein can be used to identify novel epitopes, including but not limited to, previously unidentified epitopes on known antigens or novel epitopes of unknown antigens, for example, those presented by a carcinoma cell line. Methods of epitope mapping are known to one skill in the art (see e.g., Olwyn M.R. Westwood and Frank C. Hay. Epitope Mapping. Oxford University Press, 2001; Sigma Catalog # Z373990 Epitope Mapping Protocols: Methods in Molecular Biology, Vol. 66). Methods for mapping of epitopes recognized by an antibody include, but are not limited to, binding assays such as by using BIAcore or ELISA (Reineke *et al.* 1999), ELISPOT, prediction software, combinatorial synthesis of peptide libraries onto a planar support (i.e. protein chip) followed by exposure of the surface to the antibody, phage display of a library of peptides derived from the sequence of the protein antigen, methods using mass spectrometry methods such as methods using

MALDI or amide H/D exchange (see e.g. Baerga-Ortiz *et al.* (2002) Protein Science, 11:1300-1308) and surface plasma resonance.

7. In Vivo Assays of Identified Hits

Once a "Hit" is identified against a target of interest, it can be assessed in vivo assays associated with aberrant activity of the target. In general, the method involves administering an antibody to a subject, generally a non-human animal model for a disease or condition and determining the effect of the antibody on the on the disease or condition of the model animal. *In vivo* assays include controls, where suitable controls include a sample in the absence of the antibody. Generally a plurality of assay mixtures is run in parallel with different antibody concentrations to obtain a differential response to the various concentrations. Typically, one of these concentrations serves as a negative control, i.e. at zero concentration or below the level of detection. An antibody of interest is one that modulates, i.e., reduces or increases a symptom of the animal model disease or condition by at least about 10%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 80%, at least about 90%, or more, when compared to a control in the absence of the antibody. In general, an antibody of interest will cause a subject animal to be more similar to an equivalent animal that is not suffering from the disease or condition.

Non-human animals models include those induced to have a disease such as by injection with disease and/or phenotype-inducing substances prior to administration of the antibodies to monitor the effects on disease progression. Genetic models also are useful. Animals, such as mice, can be generated which mimic a disease or condition by the overexpression, underexpression or knock-out of one or more genes. Such animals can be generated by transgenic animal production techniques well-known in the art or using naturally-occurring or induced mutant strains. One of skill in the art is familiar with various animal models associated with particular targets.

Such animal model systems include, but are not limited to, mice, rats, rabbits, guinea pigs, sheep, goats, pigs, and non-human primates, e.g. baboons, chimpanzees and monkey. Any animal system well-known in the art can be used. Several aspects of the procedure can vary; said aspects include, but are not limited to, the temporal regime of administering the antibodies (e.g., prophylactic and/or therapeutic agents), whether such antibodies are administered separately or as an admixture, and the frequency of administration of the antibodies.

Recombinant (transgenic) animal models can be engineered by introducing the coding portion of the genes identified herein into the genome of animals of interest, using standard techniques for producing transgenic animals. Animals that can serve as a target for transgenic manipulation include, without limitation, mice, rats, rabbits, guinea pigs, sheep, goats, pigs, and non-human primates, e.g. baboons, chimpanzees and monkeys. Techniques known in the art to introduce a transgene into such animals include pronucleic microinjection (United States Patent No. 4,873,191); retrovirus-mediated gene transfer into germ lines (e.g., Van der Putten *et al.*, (1985) *Proc. Natl. Acad. Sci. USA* 82:6148-615); gene targeting in embryonic stem cells (Thompson *et al.*, (1989) *Cell* 56:313-321); electroporation of embryos (Lo, (1983) *Mol. Cel. Biol.* 3:1803-1814); sperm-mediated gene transfer (Lavitrano *et al.*, (1989) *Cell* 57:717-73). For review, see, for example, U.S. Pat. No. 4,736,866.

Animal models can be used to assess the efficacy of an antibody, a composition, or a combination therapy provided herein. Examples of animal models for lung cancer include, but are not limited to, lung cancer animal models (see e.g. Zhang *et al.*, (1994) *In Vivo* 8(5):755-69) and a transgenic mouse model with disrupted p53 function (see, e.g., Morris *et al.*, (1998) *J La State Med Soc* 150(4):179-85). An example of an animal model for breast cancer includes, but is not limited to, a transgenic mouse that overexpresses cyclin D1 (see, e.g., Hosokawa *et al.*, (2001) *Transgenic Res* 10(5):471-8). An example of an animal model for colon cancer includes, but is not limited to, a TCR b and p53 double knockout mouse (see, e.g., Kado *et al.*, (2001), *Cancer Res* 61(6):2395-8). Examples of animal models for pancreatic cancer include, but are not limited to, a metastatic model of Panc02 murine pancreatic adenocarcinoma (see, e.g., Wang *et al.*, (2001) *Int J Pancreatol* 29(1):37-46) and nu-nu mice generated in subcutaneous pancreatic tumors (see, e.g., Ghaneh *et al.*, (2001) *Gene Ther* 8(3):199-208). Examples of animal models for non-Hodgkin's lymphoma include, but are not limited to, a severe combined immunodeficiency ("SCID") mouse (see, e.g., Bryant *et al.*, (2000) *Lab Invest* 80(4):553-73) and an IgHmu-HOX11 transgenic mouse (see, e.g., Hough *et al.*, (1998) *Proc Natl Acad Sci USA* 95(23):13853-8). An example of an animal model for esophageal cancer includes, but is not limited to, a mouse transgenic for the human papillomavirus type 16 E7 oncogene (see, e.g., Herber *et al.*, (1996) *J Virol* 70(3):1873-81). Examples of animal models for colorectal carcinomas include, but are not limited to, Apc mouse models (see, e.g., Fodde & Smits, (2001) *Trends Mol Med* 7(8):369-73 and Kuraguchi *et al.*, (2000) *Oncogene* 19(50):5755-63).

Animal models for arthritis include, but are not limited to, rheumatoid arthritis rats (see e.g. Pearson, (1956) *Proc. Soc. Exp. Biol. Med.*, 91:95-101) and collagen induced

arthritis in mice and rats (see e.g. Current Protocols in Immunology, Eds. J. E. Cologan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach and W. Strober, John Wiley & Sons, Inc., 1994). An example of an animal model for asthma, includes but is not limited to, a mouse model of pulmonary hypersensitivity (see e.g. Riese *et al.* (1998) *J. Clin. Invest.* 101:2351-2363 and Shi, *et al.* (1999) *Immunity* 10:197-206). Animal models for allogenic rejection include, but are not limited to, rat allogeneic heart transplant models (see e.g. Tanabe *et al.* (1994) *Transplantation* 58:23-27 and Tinubu *et al.* (1994) *J. Immunol.* 153:4330-4338) and rat heterocardiac allograft rejection (Jae-Hyuck Sim *et al.* (2002) *Proc Natl Acad Sci U.S.A.* 99(16):10617-10622). Steel mice are used as a model of human aplastic anemia (see e.g. Jones, (1983) *Exp. Hematol.*, 11:571-580). An example of an animal model for anemia, includes but is not limited to, hemolytic anemia guinea pigs (see e.g. Schreiber, *et al.* (1972) *J. Clin. Invest.* 51:575). An example of an animal model for neutropenia, includes but is not limited to, neutropenia neutropenic CD rats (see, e.g. Nohynek *et al.* (1997) Cancer Chemother. Pharmacol. 39:259-266).

8. Articles of Manufacture/Kits

Pharmaceutical compounds of selected antibodies or nucleic acids encoding selected antibodies, or a derivative or a biologically active portion thereof can be packaged as articles of manufacture containing packaging material, a pharmaceutical composition which is effective for treating the disease or disorder, and a label that indicates that selected antibody or nucleic acid molecule is to be used for treating the disease or disorder.

The articles of manufacture provided herein contain packaging materials. Packaging materials for use in packaging pharmaceutical products are well known to those of skill in the art. See, for example, U.S. Patent Nos. 5,323,907, 5,052,558 and 5,033,252, each of which is incorporated herein in its entirety. Examples of pharmaceutical packaging materials include, but are not limited to, blister packs, bottles, tubes, inhalers, pumps, bags, vials, containers, syringes, bottles, and any packaging material suitable for a selected formulation and intended mode of administration and treatment. A wide array of formulations of the compounds and compositions provided herein are contemplated as are a variety of treatments for any EPO-mediated disease or disorder or therapeutic polypeptide-mediated disease or disorder.

Antibodies and nucleic acid molecules encoding the antibodies thereof also can be provided as kits. Kits can include a pharmaceutical composition described herein and an item for administration. For example, a selected antibody can be supplied with a device for administration, such as a syringe, an inhaler, a dosage cup, a dropper, or an applicator. The kit can, optionally, include instructions for application including dosages, dosing regimens

and instructions for modes of administration. Kits also can include a pharmaceutical composition described herein and an item for diagnosis. For example, such kits can include an item for measuring the concentration, amount or activity of the antibody in a subject.

9. Formulations/Administration and uses of antibodies and polypeptides

The antibodies provided herein can be provided as a formulation for administration. While it is possible for the active ingredient to be administered alone, it is preferable to present it as a pharmaceutical formulation. Formulations contain at least one active ingredient, together with one or more acceptable carriers thereof. Each carrier must be both pharmaceutically and physiologically acceptable in the sense of being compatible with the other ingredients and not injurious to the patient. Formulations include those suitable for oral, rectal, nasal, or parenteral (including subcutaneous, intramuscular, intravenous and intradermal) administration. The formulations can conveniently be presented in unit dosage form and can be prepared by methods well known in the art of pharmacy. See, e.g., Gilman, *et al.* (eds. 1990) Goodman and Gilman's: The Pharmacological Bases of Therapeutics, 8th Ed., Pergamon Press; and Remington's Pharmaceutical Sciences, 17th ed. (1990), Mack Publishing Co., Easton, Pa.; Avis, *et al.* (eds. 1993) Pharmaceutical Dosage Forms: Parenteral Medications Dekker, NY; Lieberman, *et al.* (eds. 1990) Pharmaceutical Dosage Forms: Tablets Dekker, NY; and Lieberman, *et al.* (eds. 1990) Pharmaceutical Dosage Forms: Disperse Systems Dekker, NY.

The route of antibody administration is in accord with known methods, e.g., injection or infusion by intravenous, intraperitoneal, intracerebral, intramuscular, subcutaneous, intraocular, intraarterial, intrathecal, inhalation or intralesional routes, topical or by sustained release systems as noted below. The antibody is preferably administered continuously by infusion or by bolus injection. One can administer the antibodies in a local or systemic manner.

The antibodies provided herein can be prepared in a mixture with a pharmaceutically acceptable carrier. Techniques for formulation and administration of the compounds of the instant application can be found in "Remington's Pharmaceutical Sciences," Mack Publishing Co., Easton, Pa., latest edition. This therapeutic composition can be administered intravenously or through the nose or lung, preferably as a liquid or powder aerosol (lyophilized). The composition also can be administered parenterally or subcutaneously as desired. When administered systematically, the therapeutic composition should be sterile,

pyrogen-free and in a parenterally acceptable solution having due regard for pH, isotonicity, and stability. These conditions are known to those skilled in the art.

Therapeutic formulations can be administered in many conventional dosage formulations. Briefly, dosage formulations of the antibodies provided herein are prepared for storage or administration by mixing the compound having the desired degree of purity with physiologically acceptable carriers, excipients, or stabilizers. Such materials are non-toxic to the recipients at the dosages and concentrations employed, and can include buffers such as TRIS HCl, phosphate, citrate, acetate and other organic acid salts; antioxidants such as ascorbic acid; low molecular weight (less than about ten residues) peptides such as polyarginine, proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidinone; amino acids such as glycine, glutamic acid, aspartic acid, or arginine; monosaccharides, disaccharides, and other carbohydrates including cellulose or its derivatives, glucose, mannose, or dextrins; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; counterions such as sodium and/or nonionic surfactants such as TWEEN, PLURONICS or polyethyleneglycol.

When used for in vivo administration, the antibody formulation must be sterile and can be formulated according to conventional pharmaceutical practice. This is readily accomplished by filtration through sterile filtration membranes, prior to or following lyophilization and reconstitution. The antibody ordinarily will be stored in lyophilized form or in solution. Other vehicles such as naturally occurring vegetable oil like sesame, peanut, or cottonseed oil or a synthetic fatty vehicle like ethyl oleate or the like can be desired. Buffers, preservatives, antioxidants and the like can be incorporated according to accepted pharmaceutical practice.

Pharmaceutical compositions suitable for use include compositions wherein one or more rationally designed antibodies are contained in an amount effective to achieve their intended purpose. Determination of a therapeutically effective amount is well within the capability of those skilled in the art, especially in light of the detailed disclosure provided herein. Therapeutically effective dosages can be determined by using in vitro and in vivo methods.

An effective amount of antibody to be employed therapeutically will depend, for example, upon the therapeutic objectives, the route of administration, and the condition of the patient. In addition, the attending physician takes into consideration various factors known to modify the action of drugs including severity and type of disease, body weight, sex, diet, time and route of administration, other medications and other relevant clinical factors.

Accordingly, it will be necessary for the therapist to titer the dosage and modify the route of administration as required to obtain the optimal therapeutic effect. Typically, the clinician will administer antibody until a dosage is reached that achieves the desired effect. The progress of this therapy is easily monitored by conventional assays.

For any antibody containing a peptide, the therapeutically effective dose can be estimated initially from cell culture assays. For example, a dose can be formulated in animal models to achieve a circulating concentration range that includes the EC50 as determined in cell culture (e.g., the concentration of the test molecule which promotes or inhibits cellular proliferation or differentiation). Such information can be used to more accurately determine useful doses in humans.

Toxicity and therapeutic efficacy of the antibody molecules described herein can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, e.g., for determining the LD50 (the dose lethal to 50% of the population) and the ED50 (the dose therapeutically effective in 50% of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index and it can be expressed as the ratio between LD50 and ED50. Molecules which exhibit high therapeutic indices are preferred. The data obtained from these cell culture assays and animal studies can be used in formulating a range of dosage for use in human. The dosage of such molecules lies within a range of circulating concentrations that include the ED50 with little or no toxicity. The dosage can vary within this range depending upon the dosage form employed and the route of administration utilized. The exact formulation, route of administration and dosage can be chosen by the individual physician in view of the patient's condition. (See e.g., Fingl *et al.*, 1975, in "The Pharmacological Basis of Therapeutics", Ch. 1, p.1).

Dosage amount and interval can be adjusted individually to provide plasma levels of the antibody which are sufficient to promote or inhibit cellular proliferation or differentiation or minimal effective concentration (MEC). The MEC will vary for each antibody, but can be estimated from in vitro data using described assays. Dosages necessary to achieve the MEC will depend on individual characteristics and route of administration. However, HPLC assays or bioassays can be used to determine plasma concentrations.

Dosage intervals can also be determined using MEC value. Antibody molecules should be administered using a regimen which maintains plasma levels above the MEC for 10-90% of the time, typically between 30-90% and most typically between 50-90%.

In cases of local administration or selective uptake, the effective local concentration of the antibody can not be related to plasma concentration.

A typical daily dosage might range from about 1 μ/kg to up to 1000 mg/kg or more, depending on the factors mentioned above. Typically, the clinician will administer the molecule until a dosage is reached that achieves the desired effect. The progress of this therapy is easily monitored by conventional assays.

Depending on the type and severity of the disease, from about 0.001 mg/kg to abut 1000 mg/kg, more typically about 0.01 mg to 100 mg/kg, more typically about 0.010 to 20 mg/kg of the antibody, for example an antagonist or agonist antibody, is an initial candidate dosage for administration to the patient, whether, for example, by one or more separate administrations, or by continuous infusion. For repeated administrations over several days or longer, depending on the condition, the treatment is repeated until a desired suppression of disease symptoms occurs or the desired improvement in the patient's condition is achieved. However, other dosage regimes also are contemplated.

H. EXAMPLES

The following examples are included for illustrative purposes only and are not intended to limit the scope of the invention.

EXAMPLE 1

Materials and Methods

1. Plasmids A and C

Plasmid A (SEQ ID NO:1), Plasmid C (SEQ ID NO:3), Plasmid D (SEQ ID NO:2) and Plasmid E (SEQ ID NO:4), set forth in Figures 3-6, are used to produce recombinant Fab antibodies. They contain high-copy, ColE1 replication origins that are compatible with *E. coli*. In addition, the ColE1 replication origins of plasmids A and D are compatible with the replication origins of plasmids C and E. Moreover, they replicate at similar copy numbers when co-cultured in the same *E. coli* cell. The plasmids contain a STII leader sequence that allows for the Fab to be translocated to the periplasm, to allow for better folding, and an Ara promoter for arabinose inducible gene expression. Plasmid A contains a heavy chain constant region for production of a Fab heavy chain and includes Flag and His tags for protein purification. Plasmid D contains a heavy chain constant region for production of a Fab heavy chain, and includes Flag, LPETG, and His tags for both protein purification and site specific modification using the protein ligase, sortase. Plasmid C contains a kappa light chain constant region for production of a kappa Fab light chain while Plasmid E contains a lambda light chain constant region for production of a lambda Fab light chain . Thus Plasmids A and D encode Fab heavy chain and Plasmids C and E encode Fab light chain. A Fab is produced upon co-transformation of *E. coli* with a plasmid encoding a heavy chain and a plasmid

encoding a light chain, and induction of the promoter to express the heavy or light chain genes.

2. Cell Lines

E. coli strains BL21 (EMD Biosciences) and LMG194 (ATCC) were used for expression of the Fabs. Ramos B-Lymphocyte cells (ATCC) and Jurkat T-Lymphocyte cells (ATCC) were used for the Apo-ONE homogenous Caspase-3/7 Assay. The BaF3 mouse peripheral blood cell line (Harvey Lodish, Massachusetts Institute of Technology) was used for the EPO Fab library cell based assays.

3. DNA Sequence Compilation Software

The DNA Sequence Compilation Software is provided herein. It implements an *in silico* method for recombining heavy chain V, D, and J segment sequences and recombining light chain V and J segments while maintaining functional germline antibody sequences. The software systematically combines DNA encoding the V_H, D_H and J_H and V_L and J_L germline segment sequences, or alternatively a subset of V_H, D_H and J_H and V_L and J_L germline segment sequences, to produce sequences of recombined heavy chain and light chain variable regions from which nucleic acid molecules are produced for production of a Fab library. The germline segment sequences are inputted from a database. Example 2 provides a description of the software. Example 3 describes how to use the software, and Example 4 describes implementation of the software to compile recombined germline sequences and output the sequences for DNA synthesis.

4. Piccolo™ Automated system

Piccolo™ system is a fully automated system for the rapid optimization of recombinant protein production, sold by The Automation Partnership (TAP) (see e.g., Wollerton *et al.* (2006) JALA, 11:291-303, which describes the system). The system combines cell culture with automated harvesting, lysis, and purification units. Example 9 provides details about the specifics of the Piccolo™ system operation.

EXAMPLE 2

DNA Sequence Compilation Software Design

This example describes the DNA Sequence Compilation Software.

A. General Description:

Sequences for V_H, D_H and J_H and V_L and J_L germline segment sequences are inputted from a database file, i.e. SequenceDatabase.txt file described in detail below. The software 1) generates every possible recombination of V_H, D_H and J_H and V_L and J_L germline segments to generate sequences encoding a variable heavy (VH) chain and sequences encoding a variable

light (VL) chain; 2) translates and frame-checks the sequences; 3) stores the sequences in a SequenceHistory.txt file to keep track of sequences in nucleotide format; and 4) outputs sequences as files that represent 96-well plates for ordering for DNA synthesis. Output is generated in the form of a 96-well plate file that lists the distinct heavy chain or light chain sequences as an array designating each locus in the array corresponding to a well in a 96-well plate. DNA molecules can be synthesized in a 96-well plate based on this output. In addition, the software can rank the sequences and generate diversity scores. The software automatically generates all permutions of recombined nucleic acid sequences encoding VH chains and VL chains (kappa and lambda). If desired, the output file can be manually restricted by the user by selecting germline segments to be recombined by the software, or by choosing sequences that are sufficiently diverse from one another using the ranking function.

B. Software Description:

The DNA Sequence Compilation Software was written in the C# programming language using the Visual Studio 2005 Professional Edition development tool. The DNA Sequence compilation Software require the Microsoft .NET framework 2.0 to run under the Windows XP and Vista 32-bit Edition Operating System. The software is composed of ten modules (see Figure 7.) These modules include (a) Blast to Diversity Converter; (b) DNA Sequence Compilation GUI; (c) DNA Sequence Compilation Controls; (d) DNA Sequence Compilation Rules; and (e) DNA Sequence Compilation Rules Test, which are provided herein. The remaining five modules are available from public domain software. They include (f) NUnit; (g) formatdb; (h) BLAST; (i) BLASTClust; and (j) XP Explorer Bar.

The modules contain classes. A class is the formal definition of an object. The class acts as the template from which an instance of an object is created at run time. The class defines the properties of the object and the methods used to control the object's behavior. A singleton class is a class that is globally available to be accessed by all other classes. In this case the singleton class is the sequence compiler module, which has every rule for sequence compilation. A static class contains data and functions that can be accessed without creating an instance of the class. Static class members can be used to separate data and behavior that is independent of any object identity; the data and functions do not change regardless of what happens to the object.

Additionally, the software is grouped into 4 layers: 1) the graphical user interface (GUI); 2) GUI controls; 3) Compilation rules; and 4) NCBI tools. The 4 layers are:

GUI – The GUI is the presentation of information to and interaction with the computer operator. The GUI is made up of the Blast to Diversity Converter, the DNA Sequence Compilation GUI and NUnit.

GUI controls – Custom visible Windows controls that are re-used by the GUI. GUI controls is made up of the XP Explorer Bar and the DNA Sequence Compilation Controls.

Compilation Rules – Implementation of the rules for DNA sequence compilation. The compilation rules are made up of DNA Sequence Compilation Rules and DNA Sequence Compilation Rules Test.

NCBI tools – A set of tools available from NCBI that allows the user to run searches on a local computer.

1. Modules

a. DNA Sequence Compilation GUI

DNA Sequence Compilation GUI is the main application. It interacts with the user and enables all the functionality to be available to the user. As a whole, the DNA Sequence Compilation GUI permits the user to selectively restrict germline segments to compile a sequence; automatically compile all sequences; automatically rank all the sequences in terms of sequence diversity, clusters or similarity; and select compiled DNA sequences to be placed in a 96-well plate.

The DNA Sequence Compilation GUI contains the following classes:

Program – a static class automatically generated that contains the execution entry point to the application;

SplashScreen – a user control that displays a splash screen when the application starts and exits;

MainForm – a form that encapsulates all the functionality that is available to the user. The MainForm also displays the user controls that are implemented in the DNA Sequence Compilation Controls module and initializes the SequenceCompiler singleton defined in the DNA Sequence Compilation Rules module;

Resources – a resource file containing the image for the splash screen;

Settings – an automatically generated class that contains the user settings for the 5' restriction site and 3' restriction site to be placed with the sequence for the IDT order; and

AboutBox – a form that displays the application information to the user. It interacts with the user and enables all the functionality to be available to the user.

b. DNA Sequence Compilation Controls

The DNA Sequence Compilation Controls module contains custom window controls to be used by the DNA Sequence Compilation GUI. It contains the following classes:

FabrusDataGridView – a derived class of .NET framework DataGridView that displays the row number in the row header. A .NET framework is part of windows operating systems that contains a large library of pre-coded solutions to common programming problems and manages the execution of programs written specifically for the framework. The DataGridView control provides a customizable table for displaying data.

WellPlateControl – a custom control that displays 96-well plate information;

AutoHeavySequenceControl – a custom control that displays all of the automatically compiled DNA sequences in a data grid view for user selection into the 96-well plate, while also displaying rank, diversity score, cluster, V(D)J sequence identifier and DNA sequence protein sequence;

AutoLightSequenceControl – a custom control that displays all the automatically compiled DNA sequences in a data grid view for user selection into the 96-well plate, while also displaying rank, diversity score, cluster, V(D)J sequence identifier and DNA sequence protein sequence;

ManualHeavySequenceControl – a custom control that allows the user to manually select a V_H, D_H and J_H sequence with which to compile into a DNA heavy chain sequence;

ManualLightSequenceControl – a custom control that allows the user to manually select a V_L and J_L sequence with which to compile into a DNA light chain sequence;

LightSequenceBlastForm – a custom control that displays in grid format the BLAST results of a light sequence against all other light chains; and

HeavySequenceBlastForm – a custom control that displays in grid format the BLAST results of a heavy chain sequence against all the other heavy chains.

c. DNA Sequence Compilation Rules Module

The DNA Sequence Compilation Rules module contains all of the business logic for the compilation of the DNA sequences. This module includes all the rules for compiling functional recombined VDJ and VJ antibody sequences, including compilation, joint generation, stop codon removal, and sequence ranking.

There are six main classes within the DNA Sequence Compilation Module:

SequenceCompiler is a singleton class that provides all the DNA sequence compilation functionality. This class provides the ability to automatically or manually generate combined DNA sequences from the V(D)J sequences and all its associated information;

BlastTable provides all the information regarding diversity scores, cluster number and performs the BLAST search for a specified sequence;

SequenceHistorian is a class that keeps track of the DNA sequences in nucleotide format that have been ordered from the DNA synthesis company (e.g., IDT, Genscript, Invitrogen, and the like). Persistence is achieved by using a text file named SequenceHistory.txt, which keeps track of all of the sequences in nucleotide format ordered from the DNA Synthesis Company and

SequenceContainer is a class that holds all the V(D)J sequence information and restriction sites as specified in the text file SequencesDatabase.txt.

DnaSequence is the parent class that models the heavy and light chain sequences through the use of HeavyChainDnaSequence and LightChainDnaSequence classes, respectively.

WellPlate_8x12 is a class that models a 96-well plate. It holds references to the DNA sequence instances and allows them to be saved into an order file.

Additionally, there are three helper classes within the DNA Sequence Compilation Rules:

CodonUsageTable is a class that encapsulates the codon usage table for *E. coli* K12;

Translator is a static class that performs the translation of the sixty four codons to their respective amino acid equivalents based on the genetic code; and

ProtoParam is a static class that computes the GRAVY value.

The following is a discussion of each of the six main classes (i-vi) and the three helper classes (vii-ix) of the DNA Sequence Compilation Rules Module.

i. SequenceCompiler

SequenceCompiler is a singleton class that provides all the DNA sequence compilation functionality. This class provides the ability to automatically or manually generate combined DNA sequences from the V(D)J sequences and all its associated information. Sequence Compiler includes the following functionalities:

1) Algorithm for Automatic DNA Sequence Compilation

SequenceCompiler uses the algorithm shown in Figure 8 to generate compiled sequences by computing all the possible combinations of the available V(D)J sequences for the heavy and light chains. The algorithm equates to simply computing all the possible combinations of the available V(D)J sequences for the heavy and light sequences, respectively.

For example, if there are three V_H sequences, three D_H sequences and three J_H sequences, the algorithm computes 3*3*3 combinations, thereby producing all 27 possible combined sequences. Similarly, if there are four V_K sequences and four J_K sequences, the algorithm computes 4*4 combinations, thereby producing 16 possible combined sequences. In addition, the algorithm computes lambda light chains and kappa light chains separately.

2) Sequence Compilation

Actual sequence compilation starts with the identification of a V_H, D_H, and J_H sequence and a V_L and J_L sequence for a heavy and light chain respectively from the SequenceDatabase.txt file. Individual segments are identified as described in Example 4. Once the individual segments are identified, V(D)J joints are created, and finally all nucleotide pieces (the segments and the joints) are joined together thus compiling the sequence (see Figure 9). The rules for joint generation, removal of STOP codons and restriction sites are set forth below under Section Headings "V(D)J Joint Generation," "Stop Codon Removal," and "Codon Usage Table," respectively.

3) V(D)J Joint Generation

The joints in the compiled sequences between the different V(D)J sequences are selected so that the resulting sequences are in frame. SequenceCompiler uses the following three rules for determining reading frames.

1. The V Sequence is always reading frame 1.
2. The D Sequence has a frame that yields the most negative GRAVY (Grand Average of Hydropathy) value.
3. The J Sequence has a reading frame as specified in the SequenceDatabase.txt file (see Example 4.1 entitled "Creating the V(D)J Sequence Database File," which describes that the J sequences are set forth in three letter codonsto designate the reading frame; also see Table 13).

Based on the rules listed above, in the joints between sequences, a codon will not automatically be generated by simply recombining the bases from either of the sequences. SequenceCompiler uses the rules listed in Table 19 to generate a new codon. For example,

when creating a light chain V-J joint where the V sequence is in reading frame 1 and the J sequence is in reading frame 1, a "G" nucleotide will be inserted between the V-J joint, thereby maintaining the reading frame of the entire segment.

Table 19. V(D)J joint generation.

V-D Joints (Heavy Chains)			
V	D	Frame	Rule
0	0	0	NO MANIPULATION
0	1	1	Delete 1 nucleotide from 5' end of D
0	2	2	Add a "G" between V-D
1	0	1	Delete 1 nucleotide from 3' end of V
1	1	2	Add a "G" between V-D
1	2	3	NO MANIPULATION
2	0	2	Add a "G" between V-D
2	1	3	NO MANIPULATION
2	2	4	Delete 1 nucleotide from 3' end of V

D-J Joints (Heavy Chains)			
D	J	Frame	Rule
0	0	0	NO MANIPULATION
0	1	1	Delete 1 nucleotide from 5' end of J
0	2	2	Add a "G" between D-J
1	0	1	Delete 1 nucleotide from 3' end of D
1	1	2	Add a "G" between D-J
1	2	3	NO MANIPULATION
2	0	2	Add a "G" between D-J
2	1	3	NO MANIPULATION
2	2	4	Delete 1 nucleotide from 3' end of D

V-J Joints (Light Chains)			
V	J	Frame	Rule
0	0	0	NO MANIPULATION
0	1	1	Delete 1 nucleotide from 5' end of J
0	2	2	Add a "G" between V-J
1	0	1	Delete 1 nucleotide from 3' end of V
1	1	2	Add a "G" between V-J
1	2	3	NO MANIPULATION
2	0	2	Add a "G" between V-J
2	1	3	NO MANIPULATION
2	2	4	Delete 1 nucleotide from 3' end of V

4) Stop Codon Removal

There are situations where V(D)J joint generation will generate a STOP codon (TAA, TAG or TGA). SequenceCompiler removes detrimental STOP codons according to the following rules, whereby nucleotides encoding a Stop Codon are replaced with the designated new codon:

STOP Codon	New Codon
TAA	TAT
TAG	TAT
TGA	TCA

Once SequenceCompiler has completed the successive steps of V(D)J joint generation and STOP codon removal, the protein sequence is complete and functional.

5) Algorithm for Ranking Sequences

Once sequences are compiled, each sequence is ranked and presented to the user in order of highest diversity to lowest diversity (See Table 20 and Figures 17 and 19). This presentation of ranked sequences allows the user several options when selecting sequences to be placed in the 96-well plate order file. The user can select the most diverse sequences, or sequences that are most similar to each other.

Compiled sequences are ranked by the software by using a combination of the diversity score and cluster number information for the sequences. Diversity scores are generated by the blast to diversity converter module, as described in Section B.1.e, and cluster information is generated by BLASTClust, as described in Section B.1.i. The sequence ranking algorithm flowchart is shown in Figure 10. The algorithm picks from each cluster the sequence with the lowest diversity score, orders those sequences in terms of diversity from the lowest diversity number to the highest diversity number (a low diversity score indicates lack of similarity, and therefore highest diversity), ranks the sequences in that order, eliminates those sequences from the respective clusters, and then iteratively applies the previous procedure until all the sequences are ranked.

An example of the ranking of Sequences using this algorithm is set forth in Table 20 . The sequences in the table are ordered from highest diversity to lowest diversity. The sequence with the lowest diversity score indicates the highest diversity and receives the rank of 1. The second sequence belongs to the same cluster as the first sequences, and receives the rank of 64. This data also indicates to the user that there are a total of 63 clusters defined, since sequence 001 and sequence 002 are both in cluster 39 and they have consecutive diversity scores.

Table 20. Ranking of Sequences

	Selected	Rank	Cluster	Diversity Score	V Sequence	J Sequence	Amino Acid Sequence	SEQ ID NO
001		1	39	73.202	V3-4	IGLJ6*01	QTWTQEPSFSVSP...	1905
002		64	39	73.305	V3-4	IGLJ7*01	QTWTQEPSFSVSP...	1906
003		2	21	73.560	V4-2	IGLJ6*01	QAVLTQPSSLSASP...	1907
004		65	32	73.603	V4-2	IGLJ7*01	QAVLTQPSSLSASP...	1908
005		3	32	73.876	V1-22	IGLJ6*01	NFMLTQPHSVSES...	1909
006		66	24	74.017	V1-22	IGLJ7*01	NFMLTQPHSVSES...	1910
007		4	24	74.040	V5-1	IGLJ7*01	LPVLTQPPSASALL...	1911
008		67	39	74.056	V5-1	IGLJ6*01	LPVLTQPPSASALL...	1912
009		127	39	74.081	V3-4	IGLJ1*01	QTWTQEPSFSVSP...	1881
010		190	21	74.399	V3-4	IGLJ4*01	QTWTQEPSFSVSP...	1913
011		128	39	74.458	V4-2	IGLJ1*01	QAVLTQPSSLSASP...	1914

012		253	21	74.571	V3-4	IGLJ5*01	QTWTQEPSFSVSP...	1915
013		191	21	74.577	V4-2	IGLJ4*01	QAVLTQPSSLSASP...	1883

ii. BlastTable

BlastTable provides all the information regarding diversity scores, cluster number and performs the BLAST search for a specified sequence;

iii. SequenceHistorian

SequenceHistorian is a class that keeps track of the DNA sequences in nucleotide format that have been ordered for DNA synthesis. The persistence is achieved by using a text file named SequenceHistory.txt.

iv. SequenceContainer

SequenceContainer is a class that reads V(D)J sequences and restriction sites from a text file and stores them in memory for later retrieval for either manual (i.e. restricted selection) or automatic compilation.

v. DnaSequence

DnaSequence is the parent class that models the heavy and light chain sequences through the use of HeavyChainDnaSequence and LightChainDnaSequence classes, respectively. The only difference between the HeavyChainDnaSequence and LightChainDnaSequence classes is in the way the sequence is compiled which is implemented in the constructor of each class.

Each class contains Fields, Properties and Methods. In addition, the parent DnaSequence class contains events and Nested Types. Thus, DnaSequence implements all the functionality that is common to heavy chain and light chain sequences. This includes the fields such as AminoAcids, Cluster, DiversityScore, _SEQ_ID, Name, Notes, Nucleotides, Rank, and RestrictionSites and methods such as removing restriction sites, removing stop codons and silencing restriction sites. HeavyChainDnaSequence class contains fields for the V_H, J_H and D_H sequences, the V_H-J_H and J_H-D_H joints and methods to generate the V_H-J_H and J_H-D_H joints. LightChainDnaSequence class contains fields for the V_L and J_L sequences, the V_L-J_L joint and methods to generate the V_L-J_L joint.

vi. WellPlate_8x12

WellPlate_8x12 is a class that models a 96-well plate. It holds references to the DNA sequence instances and allows them to be saved into an order file.

vii CodonUsageTable

CodonUsageTable is a class that encapsulates the codon usage table for *E. coli* K12 (see, Table 14). The CodonUsageTable is used by the software to modify reading frame

problems as well as restriction site silencing. The software is programmed to recognize restriction sites that will be used to insert the DNA into the desired plasmid. When these restriction sites are observed in the compiled DNA sequence, the software modifies the nucleotide sequence to modify the undesired restriction site while maintaining the appropriate amino acid sequence. The above mentioned codon redundancy is used to modify codons. A codon change is used to provide a beneficial increase in the frequency of usage of the possible newly used codon. In addition, modifying the last base of a codon (the degenerate position) is preferred over modifying the first or second base of the codon.

viii. Translator

Translator is a static class that performs the translation of the sixty four codons to their respective amino acid equivalents based on the genetic code.

Table 20. DNA Codon table.

Amino Acid	SLC	DNA codons
Isoleucine	I	ATT, ATC, ATA
Leucine	L	CTT, CTC, CTA, CTG, TTA, TTG
Valine	V	GTT, GTC, GTA, GTG
Phenylalanine	F	TTT, TTC
Methionine	M	ATG
Cysteine	C	TGT, TGC
Alanine	A	GCT, GCC, GCA, GCG
Glycine	G	GGT, GGC, GGA, GGG
Proline	P	CCT, CCC, CCA, CCG
Threonine	T	ACT, ACC, ACA, ACG
Serine	S	TCT, TCC, TCA, TCG, AGT, AGC
Tyrosine	Y	TAT, TAC
Tryptophan	W	TGG
Glutamine	Q	CAA, CAG
Asparagine	N	AAT, AAC
Histidine	H	CAT, CAC
Glutamic acid	E	GAA, GAG
Aspartic acid	D	GAT, GAC
Lysine	K	AAA, AAG
Arginine	R	CGT, CGC, CGA, CGG, AGA, AGG
Stop codons	Stop	TAA, TAG, TGA

In this table, the twenty amino acids found in proteins are listed, along with the single-letter code used to represent these amino acids in protein data bases. The DNA codons representing each amino acid are also listed. All 64 possible 3-letter combinations of the DNA coding units T, C, A and G are used either to encode one of these amino acids or as one of the three stop codons that signals the end of a sequence. While DNA can be decoded unambiguously, it is not possible to predict a DNA sequence from its protein sequence. Because most amino acids have multiple codons, a number of possible DNA sequences might represent the same protein sequence.

ix. ProtoParam

ProtoParam is a static class that computes the GRAVY value. The GRAVY (Grand Average of Hydropathy) value for a peptide or protein is calculated as the sum of hydropathy values of all the amino acids divided by the number of residues in the sequence (Table 21). In essence, the GRAVY score is the relative value for the hydrophobic residues of the protein. This information is used by the V(D)J joint generation software when computing the D sequence reading frame. This reading frame is determined by the most negative GRAVY value.

Table 21. Hydropathy Values

Amino Acid	Hydropathy Value
Ala	1.800
Arg	-4.500
Asn	-3.500
Asp	-3.500
Cys	2.500
Gln	-3.500
Glu	-3.500
Gly	-0.400
His	-3.200
Ile	4.500
Leu	3.800
Lys	-3.900
Met	1.900
Phe	2.800
Pro	-1.600
Ser	-0.800
Thr	-0.700
Trp	-0.900
Tyr	-1.300
Val	4.200

d. DNA Sequence Compilation Rules Test Module

The DNA Sequence Compilation Rules Test module is a collection of NUnit automated tests that perform unit tests for each class. These tests help to ensure the individual modules and classes listed are running properly. These nine classes include:

BlastTableTest;

CodonUsageTableTest;

HeavyChainDnaSequenceTester;

LightChainDnaSequenceTester;

ProtoParamTest;

SequenceCompilerTest,

SequenceContainerTest;

TranslatorTest; and

TranslatorWrapper.

e. Blast to Diversity Converter Module

The Blast to Diversity Converter is an executable that takes a BLAST output file and outputs a diversity score. It contains five classes:

Program – a static class that is automatically generated and contains the execution entry point to the application;

Main Form – a button for the operator to click on to select a file to be converted;

Resources – an empty resource file that is created by default;

Settings – an automatically generated class that contains the user settings; and

BlastConverter – a class that contains the implementation of the conversion of the BLAST output file to a diversity score file.

i. BLAST Converter Algorithm

The BLAST converter algorithm takes a BLAST output file and applies the following equation to compute a sequence's diversity score.

$$DiversityScore(seq_i) = \sqrt{\frac{1}{N}\sum_{k=1,k\neq i}^{N} BLAST(i,k)^2}$$

The algorithm computes a standard deviation for the BLAST scores by taking all the individual BLAST numbers, squaring them, adding up all the squares, normalizing by the number of samples (N), and then taking the square root.

For example, a sequence's diversity score was computed by applying the algorithm to the following BLAST output file (-m 9 BLAST switch, i.e.Alignment view options, tablular with comment lines; see Section B.1.h.):

```
# BLASTP 2.2.17
# Query: gnl|Fabrus|V4-2_IGLJ2*01
# Database: AllLightChainSequences.txt
# Fields: Query id, Subject id, % identity, alignment length, mismatches, gap openings, q.
start, q. end, s. start, s. end, e-value, bit score
gnl|Fabrus|V4-2_IGLJ2*01      gnl|Fabrus|V4-2_IGLJ2*01      100.00  116     0       0       1
       116     1       116     1e-050  186
gnl|Fabrus|V4-2_IGLJ2*01      gnl|Fabrus|V4-2_IGLJ7*01      98.28   116     2       0       1
       116     1       116     2e-049  182
...
gnl|Fabrus|V4-2_IGLJ2*01      gnl|Fabrus|A5_IGKJ1*01 38.82   85      46      3       31      115
       34      112     2e-007  43.1
# BLASTP 2.2.17
# Query: gnl|Fabrus|V4-2_IGLJ1*01
# Database: AllLightChainSequences.txt
# Fields: Query id, Subject id, % identity, alignment length, mismatches, gap openings, q.
start, q. end, s. start, s. end, e-value, bit score
gnl|Fabrus|V4-2_IGLJ1*01      gnl|Fabrus|V4-2_IGLJ1*01      100.00  116     0       0       1
       116     1       116     3e-050  185
gnl|Fabrus|V4-2_IGLJ1*01      gnl|Fabrus|V4-2_IGLJ6*01      98.28   116     2       0       1
       116     1       116     4e-049  181
...
```

The following output file is generated, which provide diversity scores for the respective variable heavy chain sequences. The lowest diversity score indicates the least similarity between the sequence and the next most related sequence, and therefore has the highest diversity.

```
gnl|Fabrus|VH1-69_IGHD7-27*01_IGHJ2*01        119.675348536301
gnl|Fabrus|VH3-15_IGHD5-24*01_IGHJ2*01        136.102291820977
gnl|Fabrus|VH2-26_IGHD1-7*01_IGHJ4*01         111.073223319952
gnl|Fabrus|VH3-13_IGHD1-14*01_IGHJ1*01        136.760646289454
gnl|Fabrus|VH3-30_IGHD6-13*01_IGHJ6*01        139.423052600581
```

f. NUnit

NUnit is a unit-testing framework for all .Net languages. NUnit testing tools provide a means to test an object model, and is useful in ensuring that the application and its logic work correctly. Initially ported from JUnit, the current production release, version 2.4.2, is the fifth major release of this xUnit based unit testing tool for Microsoft .NET. It is written entirely in C# and has been completely redesigned to take advantage of many .NET language features, for example custom attributes and other reflection related capabilities. NUnit brings xUnit to all .NET languages. NUnit is available free to the public from the organization NUnit.

g. Formatdb

Formatdb must be used in order to format protein or nucleotide source databases before these databases can be searched by blastall, blastpgp or MegaBLAST. The source database can be in either FASTA or ASN.1 format. Once a source database has been formatted by formatdb it is not needed by BLAST.

The following Command Line Options are used when generating output files with formatdb:

-i Input File for formatting

-p Type of File (T – protein; F – nucleotide; Default = T)

-o Parse options

T – True: Parse SeqID and create indexes

F – False: Do not parse SeqID. Do not create indexes.

The version win32-ia32 (2.2.17) is currently used. Formatdb can be downloaded from the National Center for Biotechnology Information.

h. The Basic Local Alignment Search Tool (BLAST)

The Basic Local Alignment Search Tool (BLAST) finds regions of local similarity between sequences. The program compares nucleotide or protein sequences to sequence databases and calculates the statistical significance of matches. BLAST can be used to infer functional and evolutionary relationships between sequences as well as help identify members of gene families.

The following Command Line Options are used when generating output files with blastall:

-p Program Name ("blastp", "blastn", "blastx", "tblastn", or "tblastx")

-d Database

-I Query File

-o BLAST report Output File

-m Alignment View Options (0=default; 9=tabular with comment lines)

-b Number of Database Sequence to show alignments for (B) [Integer]

The version win32-ia32 (2.2.17) is currently used. BLAST can be downloaded from the National Center for Biotechnology Information.

i. BLASTClust

BLASTClust is a program within the stand alone BLAST package used to cluster either protein or nucleotide sequences. The program begins with pairwise matches and places a sequence in a cluster if the sequence matches at least one sequence already in the cluster. In

the case of proteins, the blastp algorithm is used to compute the pairwise matches; in the case of nucleotide sequences, the Megablast algorithm is used.

In the simplest case, BLASTClust takes as input a file containing concatenated FASTA format sequences, each with a unique identifier at the start of the definition line. BLASTClust formats the input sequence to produce a temporary BLAST database, performs the clustering, and removes the database at completion. Hence, there is no need to run formatdb in advance to use BLASTClust. The output of BLASTClust is a file, with one cluster to a line, of sequence identifiers separated by spaces. The clusters are sorted from the largest cluster to the smallest.

The following Command Line Options are used when generating output files with blastclust:

-d Sequence Database Name

-o Output File to save cluster list

-S Similarity Threshold

if <3 then the threshold is set as a BLAST score density (0.0 to 0.3; default = 1.75)

if >3 then the threshold is set as a percent of identical residues (3 to 100)

The version win32-ia32 (2.2.17) is currently used. BLASTClust can be downloaded from the National Center for Biotechnology Information

j. XPExplorerBar

The **XPExplorerBar** is a fully customizable Windows XP style Explorer Bar that supports Windows XP themes and animated expand/collapse with transparency. The XP Explorer Bar is available as free public domain software.

EXAMPLE 3

Sequence Database

The DNA Sequence compilation software requires a file containing sequence information used by the program to perform sequence compilation in accordance with sequence compilation rules. This is called the SequenceDatabase.txt file. All recombined sequences are generated from the sequence data in the file. Hence, the file contains all sequences that are used in performing the sequence compilation by the software. For example, the file contains nucleotide sequences for all desired germline segments and also contains nucleotide recognition sequences for restriction enzyme. The sequences in the database include any known sequence, and can be updated manually at any time. V, D, and J antibody germline sequences of human origin were obtained from the NCBI IgBLAST

database (available from the National Center for Biotechnology Information) and the International ImMunoGeneTics Information system (IMGT) and were entered into a sequence database file. The database file served as an input file for the Sequence Compilation Software.

The format of the SequenceDatabast.txt file is illustrated in Figure 11. The SequencesDatabase.txt file is updated by simply manually adding new sequences according to the following rules:

- All sequences must be specified using the FASTA format.
- Three letter codons are specified for J sequences.
- All sequences must have a "blank line" between them.
- // is used a the beginning of any line containing extraneous comments.
- Section titles are indicated by the following designations:
  - [VH] – List of V_H sequence to follow.
  - [DH] – List of D_H sequence to follow.
  - [JH] – List of J_H sequence to follow.
  - [VK] – List of V_K sequence to follow.
  - [JK] – List of J_K sequence to follow.
  - [VL] – List of V_L sequence to follow.
  - [JL] – List of J_L sequence to follow.
  - [Restriction Sites] – List of restriction sites to follow.

EXAMPLE 4

Generation of Heavy and Light Chain DNA Files and Ranking Analysis

This example describes methods for generating recombined heavy and light chain sequence files that will be used by the DNA Sequence Compilation Software. The files were created immediately upon initiating the software. The files are created from the SequenceDatabase.txt file and are analyzed using public domain software, such as NCBI's formatdb, BLAST and BLASTclust, to compute diversity and clustering information for the sequences included in the database file. The ranking function of the software is performed automatically, but can optionally be used by the user to rank the sequences for selction and ordering for DNA synthesis.

To generate sequence files, a database file that contains DNA sequences for all desired V, (D), and J variable regions sequences was generated as described in Example 3. The DNA Sequence Compilation Software mechanically recombined all heavy chain variable germline segments and light chain variable germline segment sequences in the database into

nucleic acid molecules encoding functional amino acid sequences. The software translated the nucleic acid sequence into an amino acid sequence to create sequence files. The recombined amino acid sequences were compared to determine the similarity of each compiled sequence to every other compiled sequence, which was subsequently used to generate a diversity score. Finally, the compiled sequences were clustered by sequence similarity. These various steps of the software were performed immediately upon initiating the software and are described below.

1. Compiling Heavy Chains and Light Chains

Once the database file was updated and contains all the desired V(D)J sequences, the database file was used as an input file by DNA Sequence Compilation software to mechanically compile full length heavy chain or light chain sequences in accordance with the DNA sequence compilation rules as described in Example 2, Section B.1.c. The software created files containing the full-length amino acid sequences encoded by compiled variable heavy and light chain germline segments. These are contained in the following two files:

- TempLightChainSequences.txt – This file contains all the lambda and kappa light chain sequence combinations in the amino-acid format.
- TempHeavyChainSequences.txt – This file contains all the heavy chain sequence combinations in the amino-acid format.

The compiled light and heavy chain amino acid sequences are each identified with a unique sequence ID (gnl|Fabrus|V_(D)_J), examples of which are illustrated below.

>gnl|Fabrus|V4-2_IGLJ2*01 (SEQ ID NO:2027)
QAVLTQPSSLSASPGASASLTCTLRSGINVGTYRIYWYQQKPGSPPQYLLRYKSDSDKQQGSGVPSRFSGSKDASA
NAGILLISGLQSEDEADYYCMIWHSSASVVFGGGTKLTVL

>gnl|Fabrus|VH1-2_IGHD2-21*01_IGHJ1*01 (SEQ ID NO:2028)
QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPGQGLEWMGWINPNSGGTNYAQKFQGRVTMTRDTSI
STAYMELSRLRSDDTAVYYCAREAYCGGDCYSAEYFQHWGQGTLVTVSS

2. Ranking Recombined Variable Heavy and Light Chains

Recombined variable heavy and light chain sequences were compared by the software for sequence similarity between and among all recombined sequences. This is performed using the NCBI utility BLAST. The Blast bit score is used to generate a diversity score. Recombined variable heavy and light chain sequences also were analyzed for sequence similarity using cluster analysis (*e.g.* BLASTclust).

As described in Example 2, under the heading "Alogrithm for ranking Sequences," compiled sequences were ranked by the software by using a combination of the diversity

score and cluster number information for the sequences. The ranking occurs automatically upon intiation of the program, and can be viewed by the user using the auto compilation function as described in Example 5 below. For example, Figures 17 and 19 exemplify screen shots following auto compilation, and depict columns indiating the cluster, diversity score and rank for exemplary heavy and light chain sequences.

The following sections describe the various steps for determining the diversity score and the cluster in order to rank the sequences using the Alogrithm described in Example 2.

a. Calculating Compiled Sequence Similarity and Diversity Scores

The compiled sequences were compared in order to determine the similarity of each compiled sequence to every other compiled sequence. This information was used to generate a diversity score. To start, the TempLightChainSequences.txt and TempHeavyChainSequences.txt files were copied to a folder (as created by the user) and a DOS command prompt window was opened. The NCBI DNA utility formatdb was used to prepare the files for use by BLAST by first using the following command prompts for the respective light chain and heavy chain files:

Run `formatdb -i TempLightChainSequences.txt -p T -o F`

Run `formatdb -i TempHeavyChainSequences.txt -p T -o F`

Formatdb must be installed in the folder for which the DOS command prompt window is opened or the utility will not be found. Alternatively, a path can be added to direct the DOS command to utilize formatdb from the folder it was previously installed in. For example, if all the NCBI utilities are downloaded into a folder entitled "NCBIUtilities" then the command prompts are be as follows:

Run `NCBIUtilities\bin\formatdb -i TempLightChainSequences.txt -p T -o F`

Run `NCBIUtilities\bin\formatdb -i TempHeavyChainSequences.txt -p T -o F`

BLAST command prompts were then used to generate output files LightChainBlastResults.txt and HeavyChainBlastResults.txt. The command prompts are as follows:

- Run `blastall -p blastp -d TempLightChainSequences.txt -I TempLightChainSequences.txt -o LightChainBlastResults.txt -m 9 -b 500`

(The -b value must be equal to or greater than the number of sequences to BLAST.)

- Run `blastall -p blastp -d TempHeavyChainSequences.txt -I TempHeavyChainSequences.txt -o HeavyChainBlastResults.txt -m 9 -b 8000`

(The –b value must be equal to or greater than the number of sequences to BLAST.)

Once the BLAST output files were generated, the BLAST bit score is used to calculate a diversity score for each sequence using the algorithm shown in Example 2, under the sub-section heading "Blast Converter Algorithm" using the following commands:

(a) Run `BlastToDiversityConverter.exe` (This file runs automatically each time the software is started.)

(b) Open the file LightChainBlastResults.txt

(c) Save this file as AllLightChainSequencesDiversityScores.txt

(d) Open the file HeavyChainBlastResults.txt

(e) Save this file as AllHeavyChainSequencesDiversityScores.txt

b. Clustering Compiled Sequences by Sequence Similarity

Finally, the sequences are clustered based on sequence similarity by generating pairwise matches using the NCBI utility BLASTClust. BLASTClust is used to generate two output files, AllLightChainsBLastClust.txt and AllHeavyChainsBlastClust.txt. The current example dictates that two sequences must be either 95 % or 96 % identical to register a pairwise match. The command prompts are as follows:

- Run `blastclust -d TempLightChainSequences.txt -o AllLightChainsBlastClust.txt -S 95`
- Run `blastclust -d TempHeavyChainSequences.txt -o AllHeavyChainsBlastClust.txt -S 96`

The BlastClust setting (-S) can be modified to in order to better suit any individual requirements that are necessary.

Once all the files are generated (as indicated above), the following files are manually copied into the installation folder of the DNA Sequence Compilation Tool.

(a) AllHeavyChainsBlastClust.txt

(b) AllLightChainsBlastClust.txt

(c) AllLightChainSequencesDiversityScores.txt

(d) AllHeavyChainSequencesDiversityScores.txt

EXAMPLE 5

Installation and Graphical User Interface of the DNA Sequence Compilation Tool Software

The DNA Sequence Compilation Software is used to recombine heavy and light chain antibody sequences and subsequently select desired sequences to populate a 96-well plate output file, which serves as an order file for purchasing DNA sequences in nucleotide format from a DNA Synthesis Company. This example illustrates the software requirements as well as the controls the user encounters when using the DNA Sequence Compilation Software, including Main Menu Options and Explorer Bar Options.

A. Software Overview

The software is designed to run on a computer that uses Windows XP or Windows Vista as the operating system. The software is installed by running the executable file setup.exe and installing the program in a folder of the users choice. Once installed, the user encounters Main Menu Options as well as Explorer Bar Options. The details are described below.

1. System Requirements

The DNA Sequence Compilation Software has been designed to run on a local machine as a stand alone application.

Operating System:	Windows XP / Vista 32-bit Edition
Internet Connection:	Not Required
Database Server:	None

2. Installation of the DNA Sequence Compilation Tool Program

To install the program, run the executable file setup.exe and install the program in a folder of your choice.

3. Main Menu Options (see Figure 12)

There are three main menu options.

File – The file menu is used to close the application.

Well-Plate – The well-plate menu is used to generate an order, clear the entire plate or a selected well, or configure the restriction sites for the well-plate order generation.

Help – The help menu is used to find out what version of the software you are running.

4. Explorer Bar Options

There are three explorer bar options (see Figure 12; left column):

Manual Compilation – Manual compilation contains items used to display the light chain or heavy chain manual compilation form, which allows users selection of germline segments.

Auto Compilation –Auto compilation contains items used to display the light chain or heavy chain automatic compilation form.

Well Plate – Well plate contains items used to display the well plate form.

C. Starting the Application

The software is launched either by clicking on the Fabrus DNA Compilation Tool on the All Programs Windows menu or by double-clicking the Fabrus DNA Compilation Tool shortcut on the desktop. A Splash Screen (Figure 13) appears upon application startup and then fades into the background.

D. Generating an output plate using the DNA Sequence Compilation Software

The DNA Sequence Compilation Software is used to recombine heavy and light chain antibody sequences and subsequently select desired sequences to populate a 96-well plate output file which serves as an order file for purchasing DNA sequences in nucleotide format from a DNA Synthesis Company. In addition to the plate file, a SequenceHistory.txt file is generated to keep track of all sequences ordered. Users can select either manual compilation or auto compilation in order to generate sequences and subsequently select individual sequences for inclusion into the 96-well plate grid, as described below in sections C.2-4. The software program also computes a diversity score for all sequences. The following sections describe user options for selecting and compiling germline sequences encoding variable heavy and light chains for DNA synthesis ordering.

1. The 96-well plate screen

When the application launches, the 96 Well-Plate screen is displayed. As is shown in Figure 12, the 96-well plate is empty at application startup. The Main Menu is observed horizontally along the top of the screen, underneath the title DNA Sequence Compilation. The Explorer Bar is observed vertically along the left side of the screen. The user must populate the empty 96-well plate with DNA sequences that will be selected for manufacture as described herein below using either the manual compilation function or the automatic compilation function. The operating functions within the 96-well plate screen that permit population of the screen include the following:

a. Selecting Well Plate Restriction Sites

Restriction enzyme sequences are selected by the user from the Sequencedatabase.txt file to add to the compiled DNA sequence at the 5' and 3' ends for cloning purposes. The

following commands are used to specify the 5' and 3' restriction sites that are added to the plate order according to antibody chain type:

Heavy Chains:

- **Well Plate > Configuration > Heavy Chains > 5' End → choose;** and **Well Plate >Configuration > Heavy Chains > 3' End → choose.**

Kappa Light Chains:

- **Well Plate > Configuration > Kappa Light Chains > 5' End → choose;** and **Well Plate> Configuration > Kappa Light Chains > 3' End → choose.**

Lambda Light Chains:

- **Well Plate > Configuration > Lambda Light Chains > 5' End → choose;** and **WellPlate > Configuration > Lambda Light Chains > 3' End → choose.**

This defines the restriction site that is prefixed and suffixed to each sequence chain type in the order file and can be viewed in the IDT Order Well Plate Start/Stop Restriction Sites box (See Figure 12 and Figure 14). The compilation software includes a function to internally search compiled sequences for the chosen restriction site and modify the nucleotide sequence in accord with codon usage to remove any internal restriction sites that can be incompatible for cloning purposes. This is completed prior to placing the sequences in the well plate for ordering such that only those sequences "with restriction sites silenced" are ordered. This is described in Example 2 in the section entitled "Codon usage Tables," and in Section 2 below.

b. Placing Sequences in the well plate

The selection of sequences is performed from either manual compilation or auto compilation screens as described below in Sections C.2 and C.3. As described below, in the manual compilation or auto compilation screens, following compilation, sequences are selected by checking the "Selected" column (for auto compilation) or clicking the "Add to Well Plate" button (for manual compilation).

c. Displaying Well Sequence Information

The sequence of a compiled sequence placed in a well is displayed by clicking on the well. The well for the selected sequence is highlighted. For example, Figure 14 shows a model screen for a single 96-well plate containing compiled sequences which the user has selected for ordering. In row A of the Figure, columns 1-3 (shaded in medium gray) indicate a cell with a compiled heavy chain sequence; columns 3-6 (shaded in light gray) indicate a

cell with a compiled light chain sequence. The highlighted cell (row A, column 5, indicated in dark shading) indicates the cell for which the individual data is observed in the Sequence Information box at the bottom of the display.

The Sequence Information text box is then updated with the sequence information for that well. The Sequence Information box lists all the pertinent information for a particular sequence, including the name, the nucleotide sequence, the amino acid sequence, the diversity score and individual component titles for the V(D)J recombination. For example, in Figure 14, the highlighted sequence is a variable light chain compiled from the V_L germline segment V3-4 and the J_L germline segment IGLJ7*01.

d. Generating an order

An order is generated for the 96-well plate regardless of how many samples are placed in the plate, i.e. from one (1) to 96 sequences can be ordered from a 96-well plate. To generate an order, the option **Well Plate > Generate Order** is chosen and a filename is inputed when requested. The order file is saved in a comma separated variable (.csv) format. Example 4 describes compilation, output and ordering of exemplary sequences compiled using the Software compilation software.

e. Clearing a Selected Well of a Well Plate

In order to clear a specific well in the plate, click on the selected well, then choose **WellPlate > Clear > Selected Well** or, alternatively, right click on the desired well and select "Clear Selected Well".

f. Clearing all sequences from an entire Well Plate

The Well Plate is not automatically cleared when an order is generated. In order to clear the entire Well-Plate, choose **Well Plate > Clear > Entire Plate**.

2. Manual Compilation of Sequences

Compiled sequences can be generated manually by user selection using the Manual Compilation option.

a. Manual Compilation of Light Chains

To manually compile a light chain, choose the option **Manual Compilation > Light Chain** from the explorer bar. The manual compilation screen is displayed in Figure 15. The manual compilation light chain screen allows the user to compile either a Lambda or Kappa sequence. This option is available under the heading Type and is chosen by selecting the circle in front of either Lambda or Kappa at the top of the screen. The software does not allow the combination of a V_λ and a J_κ sequence or vice-versa.

i. Compiling Lambda Light Chains

The following steps show how to compile a Lambda Light Chain.

- Select **Type > Lambda**.
- Select the desired V_λ Sequence from the **VL Sequence Combo box**. All of the available V_λ nucleotide sequences that are entered in the SequenceDatabase.txt file appear in the drop down menu box underneath.
- Select the desired J_λ Sequence from the **JL Sequence Combo Box**. All of the available J_λ nucleotide sequences that are entered in the SequenceDatabase.txt file appear in the drop down menu box underneath.
- Click "**Add to Well Plate**" button to add the compiled sequence to the well plate.

Two boxes are observed under the Dna Sequence heading. The "**No Silencing of restricted Sites**" box displays the individual V_λ and J_λ nucleotide sequences plus any V-J joints generated in accord with the sequence compilation rules. The corresponding encoded amino acid sequence also is displayed. For example, in Figure 15, the first sequence displayed in the "no silencing of restricted sites" box corresponds to the selected V_λ sequence (in this case V1-11). Following this is a depiction of three nucleotides "cct" encoding proline (P), which correspond to the joint region created by performance of the compilation method in order to generate a functional nucleic acid molecule. The last sequence displayed corresponds to the selected J_λ sequence (in this case IGLJ1*01). The "**With Restriction Sites Silenced**" box displays the compiled sequence containing any necessary nucleotide modifications to the sequence to silence restriction sites, while maintaining codon usage. Any restriction sites silenced by the software are displayed in the "**Notes**" box. The sequence with the restriction sites silenced is the sequence that is placed in the order file.

(ii) Compiling Kappa Light Chains

The following steps show how to compile a Kappa Light Chain.

- Select **Type > Kappa**.
- Select the desired V_K Sequence from the **VK Sequence Combo box**. All of the available V_K nucleotide sequences that are entered in the SequenceDatabase.txt file appear in the box underneath.
- Select the desired J_K Sequence from the **JK Sequence Combo Box**. All of the available J_K nucleotide sequences that are entered in the SequenceDatabase.txt file appear in the box underneath.

- Click "**Add to Well Plate**" button to add the compiled sequence to the well plate. All compiled sequences are added to the well plate for ordering for DNA synthesis.

As above for compiling lambda light chain sequences, two boxes are observed under the Dna Sequence heading. The "**No Silencing of restricted Sites**" box displays the individual Vκ and Jκ sequences plus any V-J joints generated. The "**With Restriction Sites Silenced**" box displays the compiled sequence with any sequence modifications to silence selected restriction sites. Any restriction sites silenced by the software are displayed in the "**Notes**" box. The sequence with the restriction sites silenced is the sequence that is placed in the order file.

b. Manual Compilation of Heavy Chains

To manually compile a heavy chain, choose the option **Manual Compilation > Heavy Chain** on the explorer bar. The manual compilation screen is displayed in Figure 16. The manual compilation heavy chain screen allows the user to concatenate V_H, D_H and J_H sequences. The following steps show how to compile a heavy chain.

- Select the desired V_H Sequence from the **VH Sequence Combo box**. All of the available V_H nucleotide sequences that are entered in the SequenceDatabase.txt file appear in the drop down menu box underneath.
- Select the desired D_H Sequence from the **DH Sequence Combo Box**. All of the available D_H nucleotide sequences that are entered in the SequencDatabase.txt file appear in the drop down menu box underneath.
- Select the desired D_H reading frame from the DH Reading Frame Box. The GRAVY value is updated according to the reading frame selection. The user should select the reading frame that corresponds to the lowest GRAVY value.
- Select the desired J_H Sequence from the **JH Sequence Combo Box**. All of the available J_H nucleotide sequences that are entered in the SequenceDatabase.txt file appear in the box underneath.
- Click "**Add to Well Plate**" button to add the compiled sequence to the well plate. All compiled sequences are added to the well plate for ordering for DNA synthesis.

Two boxes are observed in under the Dna Sequence heading. The "**No Silencing of restricted Sites**" box displays the individual V_H, D_H and J_H sequences plus any V-D-J joints generated in accord with the sequence compilation rules. The corresponding encoded amino acid sequence also is displayed. For example, in Figure 16, the first sequence displayed in the

"no silencing of restricted sites" box corresponds to the selected V_H sequence (in this case VH1-18). Following this is a depiction of three nucleotides "gag" encoding glutamic acid (E), which correspond to the V-D joint region created by performance of the compilation method in order to generate a functional nucleic acid molecule. The next sequence displayed corresponds to the selected D_H sequence (in this case IGHD1-1*01). That sequence is followed by depiction of three nucleotides "acg" encoding threonine (T), which correspond to the D-J joint region created by performance of the compilation method in order to generate a functional nucleic acid molecule. The last sequence displayed corresponds to the J_H selected sequence (in this case IGHJ1*01). The "**With Restriction Sites Silenced**" box displays the compiled sequence with any restriction sites that are present silenced. Any restriction sites silenced are displayed in the "**Notes**" box. **The sequence with the restriction sites silenced is the sequence that is placed in the order file**.

3. Auto Compilation of Sequences

Compiled chains are generated automatically by using the Auto Compilation option. As discussed in Example 4, compilation of all sequences is performed mechanically by the computer upon initiation and stored in files. The auto compilation function permits the user to view these sequences.

a. Auto Compilation of Light Chains

To automatically compile a light chain, choose the option **Auto Compilation > Light Chain** on the explorer bar. The auto compilation screen is displayed in Figure 17. The auto compilation light chain screen displays all the possible combinations of V_K and J_K, and V_λ and J_λ sequences.

The auto compilation screen shows a grid with the following columns:

- **Selected** – This column contains a box that is either checked or unchecked to add or remove a sequence to or from the well plate.
- **Rank** – This column indicates the rank order in terms of diversity. A value of 1 indicates the most diverse sequence.
- **Cluster** – This column lists the cluster that the sequence is grouped into. The cluster number is simply an identifier and its value is not associated to any sort of ranking.
- **Diversity Score** – This column lists a score based on the root mean square of the BLAST Bit score results of this sequence against all other sequences in this list. A low value indicates a more diverse sequence.

- **V Sequence** – This column lists the V sequence identifier that is used for this sequence.
- **J Sequence** – This column lists the J sequence identifier that is used for this sequence.
- **Amino Acid Sequence** – This column lists the compiled sequence in protein format.

b. Auto Compilation of Heavy Chains

To automatically compile heavy chains, choose the option **Auto Compilation > Heavy Chain** on the explorer bar. The auto compilation screen is displayed in Figure 19. The auto compilation heavy chain screen displays all the possible combinations of V_H, D_H and J_H sequences.

The auto compilation screen shows a grid with the following columns:

- **Selected** – This column contains a box that is either checked or unchecked to add or remove a sequence to or from the well plate.
- **Rank** – This column indicates the rank order in terms of diversity. A value of 1 indicates the most diverse sequence.
- **Cluster** – This column lists the cluster that the sequence is grouped into. The cluster number is simply an identifier and its value is not associated to any sort of ranking.
- **Diversity Score** – This column lists a score based on the root mean square of the BLAST Bit score results of this sequence against all other sequences in this list. A low value indicates a more diverse sequence.
- **V Sequence** – This column lists the V sequence identifier that is used for this sequence.
- **D Sequence** – This column lists the D sequence identifier that is used for this sequence.
- **J Sequence** – This column lists the J sequence identifier that is used for this sequence.
- **Amino Acid Sequence** – This column lists the compiled sequence in protein format.

4. Other functionalities associated with compilation of light chain and heavy chain sequences

a. Changing the sorting option of the Auto Compilation Screen

The view of the sequences listed in the auto compilation screen can be reorganized by clicking on the desired column header. For example, to view sequences based on diversity score, the column header "Diversity Score" is clicked and the sequences are reordered in terms of lowest to highest diversity score.

b. Status Indicators

The auto compilation screen uses color conventions to identify the status of compiled sequences. For example, grey indicates the sequence has already been ordered, blue indicates the sequence has neither been ordered nor placed in the 96-Well Plate, and bold blue indicates the sequence has been placed in the 96-Well Plate. For example, the bolded items in rows 022, 023 and 024 in Figure 17 indicate that the compiled sequences have been placed in the 96-well plate for ordering, which also is indicated by the check mark in the "selected" column. For example, the bolded items in rows 0103-0107 in Figure 19 indicate that the compiled sequences have been placed in the 96-well plate for ordering, which also is indicated by the check mark in the "selected" column.

c. Placing Multiple Sequences in the 96-well plate

Multiple sequences can be placed into the 96-well plate by clicking on the box for multiple selected sequences. This can be down by selecting a first sequence with the mouse, and then, holding down the **Shift** key and clicking on the box for the last selected sequence. Alternatively, the **Ctrl** key can be used to select individual sequences by holding down the **Ctrl** key and clicking on the individual boxes for all selected sequences. Once VL sequences are selected to add to the 96-well plate, right Click on the row header and select "**Copy to Well Plate**". All selected sequences are added to the well plate for ordering for DNA synthesis.

d. Placing a Single Sequence in the 96-well plate

To place a single sequences into the 96-well plate, click the box in the "**Selected**" Column; or alternatively, right Click on the Row Header for the sequence and click "**Copy to Well Plate**". Only the selected sequence is added to the well place for ordering for DNA synthesis.

e. BLAST of a selected sequence against all the other sequences in the compilation.

Once the sequences are compiled by auto compilation, the software allows the user the option of performing a BLAST search of a single sequence against all the other sequences in the list. This function provides an output indicator, the BLAST bit score, which is a value calculated from the number of gaps and substitutions associated with each aligned sequence.

The higher the score, the more significant the alignment. This data is useful if the user is trying to select sequences that have either the most diversity or alternatively, the least diversity to every other selected sequence. An example of generated data for selected VL sequences is illustrated in Figure 18 and an example of generated data for selected VH sequences is illustrated in Figure 20.

The compiled sequences are then compared in order to determine the similarity of each compiled sequence to every other compiled sequence and this information is used to generate a diversity score. For example, the NCBI utility BLAST can be used to find regions of local similarity between sequences, by comparing nucleotide or protein sequences and calculating the statistical significance of matches.

To perform BLAST, the sequence to be compared is selected by clicking on the sequence. The user can select the BLAST option by right clicking the sequence. For example, for VL sequences, Figure 18 illustrates a BLAST grid form generated by selecting on the V4-2_IGLJ2*01 sequence on a manual compilation or auto compilation screen, followed by right clicking the sequence and selecting Blast. A new grid form was generated, illustrated in Figure 18, which provides the Blast bit score of other compiled sequences aligned with the selected sequence. For example, for VH sequences, Figure 20 illustrates a BLAST grid form generated by selecting on the VH4-39_IGHD5-24*01_IGHJ6*01 sequence on a manual compilation or auto compilation screen, followed by right clicking the sequence and selecting Blast. A new grid was generated, illustrated in Figure 20, which provides the Blast bit score of other compiled sequences aligned with the selected sequence. Sequences can be selected from this new grid form for insertion into the 96-well plate file for ordering for DNA synthesis as indicated by checking the box in the "selected" column.

The BLAST form is a grid with the columns:

- **Selected** – This column contains a box that is either checked or unchecked to add or remove a sequence to or from the well plate.
- **Rank** – This column indicates the rank order in terms of diversity. A value of 1 indicates the most diverse sequence.
- **BLAST Bit Score** – This column indicates the BLAST Bit score for this particular sequence against the selected sequence.
- **V Sequence** – This column lists the V sequence identifier that is used for this sequence.
- **J Sequence** – This column lists the J sequence identifier that is used for this sequence.

- **Amino Acid Sequence** – This column lists the compiled sequence in protein format.

EXAMPLE 6

Generation of Heavy and Light Chain Germline Recombined DNA Sequences

This example describes methods for generating heavy and light chain DNA sequences by the DNA Sequence Compilation Software. The first step in compilation is to select either manual compilation or automatic compilation of sequences as discussed in Example 5 above. Manual compilation is useful as it gives the user complete control over the selected sequences. This allows the user to cater a library to any desired circumstance, such as creating a library where every sequence contains a particular segment that is the same, or by controlling the diversity by selecting sequences that are different (*e.g.* from different gene families).

Using manual compilation germline segments were selected by selecting a germline segment from each gene family of a V_H, D_H, J_H, Vκ, Jκ , V_λ or J_λ germline segment. Compilation of the variable heavy chain was performed separate from the light chain. Also compilation of the variable kappa light chain was performed separate from the variable lambda chain. Hence, separate 96-well plate files were created for the variable heavy chain, variable kappa light chain and variable lambda light chain.

For example, for a variable heavy chain, one V_H germline segment from the IGHV1-18 gene family was selected, i.e. IGHV1-18*01; one V_H germline segment from the IGHV1-2 gene family was selected, i.e. IGHV1-2*01; and so on. Similar selections were made for D_H germline segments and J_H germline segments. The D_H germline segments were selected in a reading frame to give the lowest gravy score where possible. A combination of $V_HD_HJ_H$ germline segments were made one at at time in the Manual compilation screen. In addition, the restriction enzyme sites NcoI and Nhe I were selected from the "well plate" menu for each $V_HD_HJ_H$ combination for inclusion at the 5' and 3' ends of the recombined segments to allow for subcloning into appropriate vectors (see Example 8). This resulted in the software automatically viewing in the DNA Sequence Window the sequence of the selected sequence with "no silencing of restricted sites" and "with restriction sites silenced," (i.e. in this case any NcoI or NheI restriction sites present internally in the sequence were silenced by modification using the codon usage table). Generated V-D and D-J joints also were created by the software in accordance with the sequence compilation rules and indicated in the DNA sequence window (an exemplary selection is set forth in Figure 16). Once germline segment

components for a rearranged sequence were selected, it was "added to the well plate." This was repeated for all variable heavy chain germline segment combinations.

Similar selections also were made for the Vκ and Jκ light chain germline by selecting a combination of Vκ and Jκ germline segments (only one gene family member from each germline segment was ever selected) one at a time in the manual compilation screen. In addition, the restriction enzyme sites Nco I and BsiW I were selected from the "well plate" menu for each Vκ and Jκ combination for inclusion at the 5' and 3' ends of the recombined segments to allow for subcloning into appropriate vectors (see Example 8). This resulted in the software automatically displaying in the DNA Sequence Window the sequence of the selected sequence with "no silencing of restricted sites" and "with restriction sites silenced," (i.e. in this case any Nco I or BsiW I restriction sites present internally in the sequence were silenced by nucleotide modification using the codon usage table.) Generated V-J joints also were created by the software in accordance with the sequence compilation rules and indicated in the DNA sequence window. Once germline segment components for a rearranged sequence were selected, it was "added to the well plate." This was repeated for all variable kappa light chain germline segment combinations.

Similar selections also were made for the V_λ or J_λ light chain germline segments by selecting a combination of V_λ or J_λ germline segments (only one gene family member from each germline segment was ever selected) one at at time in the manual compilation screen. In addition, the restriction enzyme sites Nco I and Avr II were selected from the "well plate" menu for each V_λ and J_λ combination for inclusion at the 5' and 3' ends of the recombined segments to allow for subcloning into appropriate vectors (see Example 8) This resulted in the software automatically displaying in the DNA Sequence Window the sequence of the selected sequence with "no silencing of restricted sites" and "with restriction sites silenced," (i.e: in this case any Nco I or Avr II restriction sites present internally in the sequence were silenced by nucleotide modification using the codon usage table.) Generated V-J joints also were created by the software in accordance with the sequence compilation rules and indicated in the DNA sequence window (an exemplary selection is set forth in Figure 15). Once germline segment components for a rearranged sequence were selected, it was "added to the well plate." This was repeated for all variable lambda light chain germline segment combinations.

The choice of Nhe I, Bsi WI and Avr II sites allow for complete amino acid conservation for their respective heavy and light chains thereby maintaining the natural human V and C regions.

Once all sequences were selected, the selected sequences were viewed under the 96-well plate view (see e.g., Figure 12 and Figure 14). A DNA synthesis order was generated using the Generate Order function. The DNA Compilation Software outputted the selected sequences in arrays that mapped to the 96-well format. The sequences in this format were sent to a DNA synthesis vendor (Genscript Corp.) to generate synthetic antibody variable heavy and light chain sequences. The synthesized nucleic acid molecules were returned and identified by the 96-well format. Table 22 lists sequences generated by the Sequence Compilation Software, ordered and synthesized.

Table 22: Exemplary Sequences Generated by DNA Compilation Software

Heavy Chain		
Number	Name	SEQ ID NO.
3	gnl|Fabrus|VH1-18_IGHD1-26*01_IGHJ2*01	454
4	gnl|Fabrus|VH1-18_IGHD2-21*01_IGHJ2*01	455
5	gnl|Fabrus|VH1-18_IGHD3-16*01_IGHJ6*01	456
6	gnl|Fabrus|VH1-18_IGHD3-22*01_IGHJ4*01	457
7	gnl|Fabrus|VH1-18_IGHD4-23*01_IGHJ1*01	458
8	gnl|Fabrus|VH1-18_IGHD5-12*01_IGHJ4*01	459
9	gnl|Fabrus|VH1-18_IGHD6-6*01_IGHJ1*01	460
10	gnl|Fabrus|VH1-2_IGHD1-1*01_IGHJ3*01	461
11	gnl|Fabrus|VH1-24_IGHD1-7*01_IGHJ4*01	462
12	gnl|Fabrus|VH1-24_IGHD2-15*01_IGHJ2*01	463
13	gnl|Fabrus|VH1-24_IGHD3-10*01_IGHJ4*01	464
14	gnl|Fabrus|VH1-24_IGHD3-16*01_IGHJ4*01	465
15	gnl|Fabrus|VH1-24_IGHD4-23*01_IGHJ2*01	466
16	gnl|Fabrus|VH1-24_IGHD5-12*01_IGHJ4*01	467
17	gnl|Fabrus|VH1-24_IGHD5-18*01_IGHJ6*01	468
18	gnl|Fabrus|VH1-24_IGHD6-19*01_IGHJ4*01	469
19	gnl|Fabrus|VH1-3_IGHD2-15*01_IGHJ2*01	470
20	gnl|Fabrus|VH1-3_IGHD2-2*01_IGHJ5*01	471
21	gnl|Fabrus|VH1-3_IGHD3-9*01_IGHJ6*01	472
22	gnl|Fabrus|VH1-3_IGHD4-23*01_IGHJ4*01	473
23	gnl|Fabrus|VH1-3_IGHD5-18*01_IGHJ4*01	474
24	gnl|Fabrus|VH1-3_IGHD6-6*01_IGHJ1*01	475
25	gnl|Fabrus|VH1-3_IGHD7-27*01_IGHJ4*01	476
26	gnl|Fabrus|VH1-45_IGHD1-26*01_IGHJ4*01	477
27	gnl|Fabrus|VH1-45_IGHD2-15*01_IGHJ6*01	478
28	gnl|Fabrus|VH1-45_IGHD2-8*01_IGHJ3*01	479
29	gnl|Fabrus|VH1-45_IGHD3-10*01_IGHJ4*01	480
30	gnl|Fabrus|VH1-45_IGHD3-16*01_IGHJ2*01	481
31	gnl|Fabrus|VH1-45_IGHD4-23*01_IGHJ4*01	482
32	gnl|Fabrus|VH1-45_IGHD5-24*01_IGHJ4*01	483
33	gnl|Fabrus|VH1-45_IGHD6-19*01_IGHJ4*01	484
34	gnl|Fabrus|VH1-45_IGHD7-27*01_IGHJ6*01	485
35	gnl|Fabrus|VH1-46_IGHD1-26*01_IGHJ4*01	486
36	gnl|Fabrus|VH1-46_IGHD2-15*01_IGHJ2*01	487
37	gnl|Fabrus|VH1-46_IGHD3-10*01_IGHJ4*01	488
38	gnl|Fabrus|VH1-46_IGHD4-17*01_IGHJ4*01	489
39	gnl|Fabrus|VH1-46_IGHD5-18*01_IGHJ4*01	490

40	gnl|Fabrus|VH1-46_IGHD6-13*01_IGHJ4*01	491
41	gnl|Fabrus|VH1-46_IGHD6-6*01_IGHJ1*01	492
42	gnl|Fabrus|VH1-46_IGHD7-27*01_IGHJ2*01	493
43	gnl|Fabrus|VH1-58_IGHD1-26*01_IGHJ4*01	494
44	gnl|Fabrus|VH1-58_IGHD2-15*01_IGHJ2*01	495
45	gnl|Fabrus|VH1-58_IGHD3-10*01_IGHJ6*01	496
46	gnl|Fabrus|VH1-58_IGHD4-17*01_IGHJ4*01	497
47	gnl|Fabrus|VH1-58_IGHD5-18*01_IGHJ4*01	498
48	gnl|Fabrus|VH1-58_IGHD6-6*01_IGHJ1*01	499
49	gnl|Fabrus|VH1-58_IGHD7-27*01_IGHJ5*01	500
50	gnl|Fabrus|VH1-69_IGHD1-1*01_IGHJ6*01	501
51	gnl|Fabrus|VH1-69_IGHD1-14*01_IGHJ4*01	502
52	gnl|Fabrus|VH1-69_IGHD2-2*01_IGHJ4*01	503
53	gnl|Fabrus|VH1-69_IGHD2-8*01_IGHJ6*01	504
54	gnl|Fabrus|VH1-69_IGHD3-16*01_IGHJ4*01	505
55	gnl|Fabrus|VH1-69_IGHD3-3*01_IGHJ4*01	506
56	gnl|Fabrus|VH1-69_IGHD3-9*01_IGHJ6*01	507
57	gnl|Fabrus|VH1-69_IGHD4-17*01_IGHJ4*01	508
58	gnl|Fabrus|VH1-69_IGHD5-12*01_IGHJ4*01	509
59	gnl|Fabrus|VH1-69_IGHD5-24*01_IGHJ6*01	510
60	gnl|Fabrus|VH1-69_IGHD6-19*01_IGHJ4*01	511
61	gnl|Fabrus|VH1-69_IGHD6-6*01_IGHJ1*01	512
62	gnl|Fabrus|VH1-69_IGHD7-27*01_IGHJ4*01	513
63	gnl|Fabrus|VH1-8_IGHD1-26*01_IGHJ4*01	514
64	gnl|Fabrus|VH1-8_IGHD2-15*01_IGHJ6*01	515
65	gnl|Fabrus|VH1-8_IGHD2-2*01_IGHJ6*01	516
66	gnl|Fabrus|VH1-8_IGHD3-10*01_IGHJ4*01	517
67	gnl|Fabrus|VH1-8_IGHD4-17*01_IGHJ4*01	518
68	gnl|Fabrus|VH1-8_IGHD5-5*01_IGHJ4*01	519
69	gnl|Fabrus|VH1-8_IGHD7-27*01_IGHJ4*01	520
70	gnl|Fabrus|VH2-26_IGHD1-20*01_IGHJ4*01	521
71	gnl|Fabrus|VH2-26_IGHD2-15*01_IGHJ2*01	522
72	gnl|Fabrus|VH2-26_IGHD2-2*01_IGHJ4*01	523
73	gnl|Fabrus|VH2-26_IGHD3-10*01_IGHJ4*01	524
74	gnl|Fabrus|VH2-26_IGHD3-9*01_IGHJ6*01	525
75	gnl|Fabrus|VH2-26_IGHD4-11*01_IGHJ4*01	526
76	gnl|Fabrus|VH2-26_IGHD5-12*01_IGHJ4*01	527
77	gnl|Fabrus|VH2-26_IGHD5-18*01_IGHJ4*01	528
78	gnl|Fabrus|VH2-26_IGHD6-13*01_IGHJ4*01	529
79	gnl|Fabrus|VH2-26_IGHD7-27*01_IGHJ4*01	530
80	gnl|Fabrus|VH2-26_IGHD7-27*01_IGHJ4*01	531
81	gnl|Fabrus|VH2-5_IGHD1-1*01_IGHJ5*01	532
82	gnl|Fabrus|VH2-5_IGHD2-15*01_IGHJ6*01	533
83	gnl|Fabrus|VH2-5_IGHD3-16*01_IGHJ4*01	534
84	gnl|Fabrus|VH2-5_IGHD3-9*01_IGHJ6*01	535
85	gnl|Fabrus|VH2-5_IGHD5-12*01_IGHJ4*01	536
86	gnl|Fabrus|VH2-5_IGHD6-13*01_IGHJ4*01	537
87	gnl|Fabrus|VH2-5_IGHD7-27*01_IGHJ2*01	538
88	gnl|Fabrus|VH2-70_IGHD1-1*01_IGHJ2*01	539
89	gnl|Fabrus|VH2-70_IGHD2-15*01_IGHJ2*01	540
90	gnl|Fabrus|VH2-70_IGHD3-22*01_IGHJ4*01	541
91	gnl|Fabrus|VH2-70_IGHD3-9*01_IGHJ6*01	542
92	gnl|Fabrus|VH2-70_IGHD5-12*01_IGHJ4*01	543
93	gnl|Fabrus|VH2-70_IGHD7-27*01_IGHJ2*01	544

94	gnl|Fabrus|VH3-11_IGHD1-26*01_IGHJ4*01	545
95	gnl|Fabrus|VH3-11_IGHD2-2*01_IGHJ6*01	546
96	gnl|Fabrus|VH3-11_IGHD3-16*01_IGHJ4*01	547
97	gnl|Fabrus|VH3-11_IGHD3-9*01_IGHJ6*01	548
98	gnl|Fabrus|VH3-11_IGHD4-23*01_IGHJ5*01	549
99	gnl|Fabrus|VH3-11_IGHD5-18*01_IGHJ4*01	550
100	gnl|Fabrus|VH3-11_IGHD6-19*01_IGHJ6*01	551
101	gnl|Fabrus|VH3-11_IGHD6-6*01_IGHJ1*01	552
102	gnl|Fabrus|VH3-11_IGHD7-27*01_IGHJ4*01	553
103	gnl|Fabrus|VH3-13_IGHD1-26*01_IGHJ4*01	554
104	gnl|Fabrus|VH3-13_IGHD2-8*01_IGHJ5*01	555
105	gnl|Fabrus|VH3-13_IGHD3-3*01_IGHJ1*01	556
106	gnl|Fabrus|VH3-13_IGHD3-9*01_IGHJ6*01	557
107	gnl|Fabrus|VH3-13_IGHD4-23*01_IGHJ5*01	558
108	gnl|Fabrus|VH3-13_IGHD5-5*01_IGHJ4*01	559
109	gnl|Fabrus|VH3-13_IGHD6-6*01_IGHJ1*01	560
110	gnl|Fabrus|VH3-13_IGHD7-27*01_IGHJ5*01	561
111	gnl|Fabrus|VH3-15_IGHD1-26*01_IGHJ4*01	562
112	gnl|Fabrus|VH3-15_IGHD2-15*01_IGHJ2*01	563
113	gnl|Fabrus|VH3-15_IGHD2-15*01_IGHJ6*01	564
114	gnl|Fabrus|VH3-15_IGHD3-10*01_IGHJ4*01	565
115	gnl|Fabrus|VH3-15_IGHD3-9*01_IGHJ2*01	566
116	gnl|Fabrus|VH3-15_IGHD5-12*01_IGHJ4*01	567
117	gnl|Fabrus|VH3-15_IGHD6-6*01_IGHJ1*01	568
118	gnl|Fabrus|VH3-16_IGHD1-1*01_IGHJ1*01	569
119	gnl|Fabrus|VH3-16_IGHD1-7*01_IGHJ6*01	570
120	gnl|Fabrus|VH3-16_IGHD2-15*01_IGHJ2*01	571
121	gnl|Fabrus|VH3-16_IGHD2-2*01_IGHJ2*01	572
122	gnl|Fabrus|VH3-16_IGHD3-10*01_IGHJ4*01	573
123	gnl|Fabrus|VH3-16_IGHD4-4*01_IGHJ2*01	574
124	gnl|Fabrus|VH3-16_IGHD5-24*01_IGHJ4*01	575
125	gnl|Fabrus|VH3-16_IGHD6-13*01_IGHJ4*01	576
126	gnl|Fabrus|VH3-16_IGHD7-27*01_IGHJ2*01	577
127	gnl|Fabrus|VH3-20_IGHD1-14*01_IGHJ4*01	578
128	gnl|Fabrus|VH3-20_IGHD2-15*01_IGHJ2*01	579
129	gnl|Fabrus|VH3-20_IGHD2-8*01_IGHJ4*01	580
130	gnl|Fabrus|VH3-20_IGHD3-10*01_IGHJ4*01	581
131	gnl|Fabrus|VH3-20_IGHD3-9*01_IGHJ6*01	582
132	gnl|Fabrus|VH3-20_IGHD4-23*01_IGHJ4*01	583
133	gnl|Fabrus|VH3-20_IGHD5-12*01_IGHJ4*01	584
134	gnl|Fabrus|VH3-20_IGHD6-13*01_IGHJ4*01	585
135	gnl|Fabrus|VH3-20_IGHD7-27*01_IGHJ2*01	586
136	gnl|Fabrus|VH3-21_IGHD1-26*01_IGHJ4*01	587
137	gnl|Fabrus|VH3-21_IGHD2-2*01_IGHJ5*01	588
138	gnl|Fabrus|VH3-21_IGHD3-22*01_IGHJ4*01	589
139	gnl|Fabrus|VH3-21_IGHD4-23*01_IGHJ5*01	590
140	gnl|Fabrus|VH3-21_IGHD5-24*01_IGHJ5*01	591
141	gnl|Fabrus|VH3-21_IGHD6-19*01_IGHJ1*01	592
142	gnl|Fabrus|VH3-21_IGHD7-27*01_IGHJ4*01	593
143	gnl|Fabrus|VH3-23_IGHD1-1*01_IGHJ1*01	594
144	gnl|Fabrus|VH3-23_IGHD1-1*01_IGHJ4*01	595
145	gnl|Fabrus|VH3-23_IGHD1-20*01_IGHJ3*01	596
146	gnl|Fabrus|VH3-23_IGHD1-26*01_IGHJ4*01	597
147	gnl|Fabrus|VH3-23_IGHD2-15*01_IGHJ4*01	598

148	gnl|Fabrus|VH3-23_IGHD2-21*01_IGHJ1*01	599
149	gnl|Fabrus|VH3-23_IGHD3-10*01_IGHJ4*01	600
150	gnl|Fabrus|VH3-23_IGHD3-16*01_IGHJ4*01	601
151	gnl|Fabrus|VH3-23_IGHD3-22*01_IGHJ4*01	602
152	gnl|Fabrus|VH3-23_IGHD3-3*01_IGHJ5*01	603
153	gnl|Fabrus|VH3-23_IGHD4-11*01_IGHJ4*01	604
154	gnl|Fabrus|VH3-23_IGHD4-23*01_IGHJ2*01	605
155	gnl|Fabrus|VH3-23_IGHD5-12*01_IGHJ4*01	606
156	gnl|Fabrus|VH3-23_IGHD5-24*01_IGHJ1*01	607
157	gnl|Fabrus|VH3-23_IGHD5-5*01_IGHJ4*01	608
158	gnl|Fabrus|VH3-23_IGHD6-13*01_IGHJ4*01	609
159	gnl|Fabrus|VH3-23_IGHD6-25*01_IGHJ2*01	610
160	gnl|Fabrus|VH3-23_IGHD6-6*01_IGHJ1*01	611
161	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ4*01	612
162	gnl|Fabrus|VH3-23_IGHD7-27*01_IGHJ6*01	613
163	gnl|Fabrus|VH3-30_IGHD1-1*01_IGHJ6*01	614
164	gnl|Fabrus|VH3-30_IGHD1-26*01_IGHJ1*01	615
165	gnl|Fabrus|VH3-30_IGHD1-26*01_IGHJ4*01	616
166	gnl|Fabrus|VH3-30_IGHD2-15*01_IGHJ2*01	617
167	gnl|Fabrus|VH3-30_IGHD2-2*01_IGHJ6*01	618
168	gnl|Fabrus|VH3-30_IGHD3-10*01_IGHJ1*01	619
169	gnl|Fabrus|VH3-30_IGHD3-16*01_IGHJ6*01	620
170	gnl|Fabrus|VH3-30_IGHD4-17*01_IGHJ4*01	621
171	gnl|Fabrus|VH3-30_IGHD5-12*01_IGHJ4*01	622
172	gnl|Fabrus|VH3-30_IGHD5-18*01_IGHJ1*01	623
173	gnl|Fabrus|VH3-30_IGHD6-13*01_IGHJ4*01	624
174	gnl|Fabrus|VH3-30_IGHD6-6*01_IGHJ1*01	625
175	gnl|Fabrus|VH3-35_IGHD1-1*01_IGHJ2*01	626
176	gnl|Fabrus|VH3-35_IGHD1-20*01_IGHJ6*01	627
177	gnl|Fabrus|VH3-35_IGHD2-15*01_IGHJ2*01	628
178	gnl|Fabrus|VH3-35_IGHD2-21*01_IGHJ6*01	629
179	gnl|Fabrus|VH3-35_IGHD3-10*01_IGHJ4*01	630
180	gnl|Fabrus|VH3-35_IGHD3-9*01_IGHJ6*01	631
181	gnl|Fabrus|VH3-35_IGHD5-12*01_IGHJ4*01	632
182	gnl|Fabrus|VH3-35_IGHD6-13*01_IGHJ4*01	633
183	gnl|Fabrus|VH3-35_IGHD7-27*01_IGHJ1*01	634
184	gnl|Fabrus|VH3-38_IGHD1-14*01_IGHJ5*01	635
185	gnl|Fabrus|VH3-38_IGHD1-20*01_IGHJ6*01	636
186	gnl|Fabrus|VH3-38_IGHD2-15*01_IGHJ6*01	637
187	gnl|Fabrus|VH3-38_IGHD2-2*01_IGHJ1*01	638
188	gnl|Fabrus|VH3-38_IGHD3-10*01_IGHJ4*01	639
189	gnl|Fabrus|VH3-38_IGHD3-16*01_IGHJ1*01	640
190	gnl|Fabrus|VH3-38_IGHD4-17*01_IGHJ2*01	641
191	gnl|Fabrus|VH3-38_IGHD5-24*01_IGHJ3*01	642
192	gnl|Fabrus|VH3-38_IGHD6-6*01_IGHJ1*01	643
193	gnl|Fabrus|VH3-38_IGHD7-27*01_IGHJ6*01	644
194	gnl|Fabrus|VH3-43_IGHD1-26*01_IGHJ5*01	645
195	gnl|Fabrus|VH3-43_IGHD1-7*01_IGHJ6*01	646
196	gnl|Fabrus|VH3-43_IGHD2-2*01_IGHJ3*01	647
197	gnl|Fabrus|VH3-43_IGHD2-21*01_IGHJ6*01	648
198	gnl|Fabrus|VH3-43_IGHD3-16*01_IGHJ6*01	649
199	gnl|Fabrus|VH3-43_IGHD3-22*01_IGHJ4*01	650
200	gnl|Fabrus|VH3-43_IGHD4-23*01_IGHJ3*01	651
201	gnl|Fabrus|VH3-43_IGHD5-18*01_IGHJ5*01	652

202	gnl|Fabrus|VH3-43_IGHD6-13*01_IGHJ4*01	653
203	gnl|Fabrus|VH3-43_IGHD7-27*01_IGHJ1*01	654
204	gnl|Fabrus|VH3-48_IGHD6-6*01_IGHJ1*01	655
205	gnl|Fabrus|VH3-49_IGHD1-26*01_IGHJ4*01	656
206	gnl|Fabrus|VH3-49_IGHD1-7*01_IGHJ6*01	657
207	gnl|Fabrus|VH3-49_IGHD2-2*01_IGHJ6*01	658
208	gnl|Fabrus|VH3-49_IGHD2-8*01_IGHJ4*01	659
209	gnl|Fabrus|VH3-49_IGHD3-22*01_IGHJ4*01	660
210	gnl|Fabrus|VH3-49_IGHD3-9*01_IGHJ6*01	661
211	gnl|Fabrus|VH3-49_IGHD5-18*01_IGHJ4*01	662
212	gnl|Fabrus|VH3-49_IGHD6-13*01_IGHJ4*01	663
213	gnl|Fabrus|VH3-49_IGHD7-27*01_IGHJ1*01	664
214	gnl|Fabrus|VH3-53_IGHD1-14*01_IGHJ6*01	665
215	gnl|Fabrus|VH3-53_IGHD1-7*01_IGHJ1*01	666
216	gnl|Fabrus|VH3-53_IGHD2-2*01_IGHJ2*01	667
217	gnl|Fabrus|VH3-53_IGHD3-22*01_IGHJ3*01	668
218	gnl|Fabrus|VH3-53_IGHD4-23*01_IGHJ1*01	669
219	gnl|Fabrus|VH3-53_IGHD5-5*01_IGHJ4*01	670
220	gnl|Fabrus|VH3-53_IGHD6-13*01_IGHJ3*01	671
221	gnl|Fabrus|VH3-53_IGHD7-27*01_IGHJ4*01	672
222	gnl|Fabrus|VH3-64_IGHD1-26*01_IGHJ4*01	673
223	gnl|Fabrus|VH3-64_IGHD1-7*01_IGHJ6*01	674
224	gnl|Fabrus|VH3-64_IGHD2-2*01_IGHJ5*01	675
225	gnl|Fabrus|VH3-64_IGHD3-3*01_IGHJ4*01	676
226	gnl|Fabrus|VH3-64_IGHD4-17*01_IGHJ4*01	677
227	gnl|Fabrus|VH3-64_IGHD5-12*01_IGHJ4*01	678
228	gnl|Fabrus|VH3-64_IGHD6-19*01_IGHJ1*01	679
229	gnl|Fabrus|VH3-64_IGHD7-27*01_IGHJ4*01	680
230	gnl|Fabrus|VH3-66_IGHD6-6*01_IGHJ1*01	681
231	gnl|Fabrus|VH3-7_IGHD1-20*01_IGHJ3*01	682
232	gnl|Fabrus|VH3-7_IGHD1-7*01_IGHJ6*01	683
233	gnl|Fabrus|VH3-7_IGHD2-21*01_IGHJ5*01	684
234	gnl|Fabrus|VH3-7_IGHD2-8*01_IGHJ6*01	685
235	gnl|Fabrus|VH3-7_IGHD3-22*01_IGHJ3*01	686
236	gnl|Fabrus|VH3-7_IGHD3-9*01_IGHJ6*01	687
237	gnl|Fabrus|VH3-7_IGHD4-17*01_IGHJ4*01	688
238	gnl|Fabrus|VH3-7_IGHD5-12*01_IGHJ4*01	689
239	gnl|Fabrus|VH3-7_IGHD5-24*01_IGHJ4*01	690
240	gnl|Fabrus|VH3-7_IGHD6-19*01_IGHJ6*01	691
241	gnl|Fabrus|VH3-7_IGHD6-6*01_IGHJ1*01	692
242	gnl|Fabrus|VH3-7_IGHD7-27*01_IGHJ2*01	693
243	gnl|Fabrus|VH3-72_IGHD1-1*01_IGHJ4*01	694
244	gnl|Fabrus|VH3-72_IGHD2-15*01_IGHJ1*01	695
245	gnl|Fabrus|VH3-72_IGHD3-22*01_IGHJ4*01	696
246	gnl|Fabrus|VH3-72_IGHD3-9*01_IGHJ6*01	697
247	gnl|Fabrus|VH3-72_IGHD4-23*01_IGHJ2*01	698
248	gnl|Fabrus|VH3-72_IGHD5-18*01_IGHJ4*01	699
249	gnl|Fabrus|VH3-72_IGHD5-24*01_IGHJ6*01	700
250	gnl|Fabrus|VH3-72_IGHD6-6*01_IGHJ1*01	701
251	gnl|Fabrus|VH3-72_IGHD7-27*01_IGHJ2*01	702
252	gnl|Fabrus|VH3-73_IGHD1-1*01_IGHJ5*01	703
253	gnl|Fabrus|VH3-73_IGHD2-8*01_IGHJ2*01	704
254	gnl|Fabrus|VH3-73_IGHD3-22*01_IGHJ4*01	705
255	gnl|Fabrus|VH3-73_IGHD3-9*01_IGHJ6*01	706

256	gnl|Fabrus|VH3-73_IGHD4-11*01_IGHJ6*01	707
257	gnl|Fabrus|VH3-73_IGHD4-23*01_IGHJ5*01	708
258	gnl|Fabrus|VH3-73_IGHD5-12*01_IGHJ4*01	709
259	gnl|Fabrus|VH3-73_IGHD6-19*01_IGHJ1*01	710
260	gnl|Fabrus|VH3-73_IGHD7-27*01_IGHJ5*01	711
261	gnl|Fabrus|VH3-74_IGHD1-1*01_IGHJ6*01	712
262	gnl|Fabrus|VH3-74_IGHD1-26*01_IGHJ4*01	713
263	gnl|Fabrus|VH3-74_IGHD2-2*01_IGHJ5*01	714
264	gnl|Fabrus|VH3-74_IGHD3-22*01_IGHJ5*01	715
265	gnl|Fabrus|VH3-74_IGHD4-17*01_IGHJ1*01	716
266	gnl|Fabrus|VH3-74_IGHD5-12*01_IGHJ4*01	717
267	gnl|Fabrus|VH3-74_IGHD6-6*01_IGHJ1*01	718
268	gnl|Fabrus|VH3-74_IGHD7-27*01_IGHJ4*01	719
269	gnl|Fabrus|VH3-9_IGHD1-1*01_IGHJ6*01	720
270	gnl|Fabrus|VH3-9_IGHD1-7*01_IGHJ5*01	721
271	gnl|Fabrus|VH3-9_IGHD2-2*01_IGHJ4*01	722
272	gnl|Fabrus|VH3-9_IGHD3-16*01_IGHJ6*01	723
273	gnl|Fabrus|VH3-9_IGHD3-22*01_IGHJ4*01	724
274	gnl|Fabrus|VH3-9_IGHD4-11*01_IGHJ4*01	725
275	gnl|Fabrus|VH3-9_IGHD5-24*01_IGHJ1*01	726
276	gnl|Fabrus|VH3-9_IGHD6-13*01_IGHJ4*01	727
277	gnl|Fabrus|VH3-9_IGHD6-25*01_IGHJ6*01	728
278	gnl|Fabrus|VH3-9_IGHD7-27*01_IGHJ2*01	729
279	gnl|Fabrus|VH4-28_IGHD1-20*01_IGHJ1*01	730
280	gnl|Fabrus|VH4-28_IGHD1-7*01_IGHJ6*01	731
281	gnl|Fabrus|VH4-28_IGHD2-15*01_IGHJ6*01	732
282	gnl|Fabrus|VH4-28_IGHD3-16*01_IGHJ2*01	733
283	gnl|Fabrus|VH4-28_IGHD3-9*01_IGHJ6*01	734
284	gnl|Fabrus|VH4-28_IGHD4-4*01_IGHJ4*01	735
285	gnl|Fabrus|VH4-28_IGHD5-5*01_IGHJ1*01	736
286	gnl|Fabrus|VH4-28_IGHD6-13*01_IGHJ4*01	737
287	gnl|Fabrus|VH4-28_IGHD7-27*01_IGHJ1*01	738
288	gnl|Fabrus|VH4-31_IGHD1-26*01_IGHJ2*01	739
289	gnl|Fabrus|VH4-31_IGHD2-15*01_IGHJ2*01	740
290	gnl|Fabrus|VH4-31_IGHD2-2*01_IGHJ6*01	741
291	gnl|Fabrus|VH4-31_IGHD3-10*01_IGHJ4*01	742
292	gnl|Fabrus|VH4-31_IGHD3-9*01_IGHJ6*01	743
293	gnl|Fabrus|VH4-31_IGHD4-17*01_IGHJ5*01	744
294	gnl|Fabrus|VH4-31_IGHD5-12*01_IGHJ4*01	745
295	gnl|Fabrus|VH4-31_IGHD6-13*01_IGHJ4*01	746
296	gnl|Fabrus|VH4-31_IGHD6-6*01_IGHJ1*01	747
297	gnl|Fabrus|VH4-31_IGHD7-27*01_IGHJ5*01	748
298	gnl|Fabrus|VH4-34_IGHD1-7*01_IGHJ4*01	749
299	gnl|Fabrus|VH4-34_IGHD2-2*01_IGHJ4*01	750
300	gnl|Fabrus|VH4-34_IGHD3-16*01_IGHJ4*01	751
301	gnl|Fabrus|VH4-34_IGHD3-22*01_IGHJ6*01	752
302	gnl|Fabrus|VH4-34_IGHD4-17*01_IGHJ4*01	753
303	gnl|Fabrus|VH4-34_IGHD5-12*01_IGHJ4*01	754
304	gnl|Fabrus|VH4-34_IGHD6-13*01_IGHJ4*01	755
305	gnl|Fabrus|VH4-34_IGHD6-25*01_IGHJ6*01	756
306	gnl|Fabrus|VH4-34_IGHD6-6*01_IGHJ6*01	757
307	gnl|Fabrus|VH4-34_IGHD7-27*01_IGHJ4*01	758
308	gnl|Fabrus|VH4-39_IGHD1-14*01_IGHJ1*01	759
309	gnl|Fabrus|VH4-39_IGHD1-20*01_IGHJ6*01	760

310	gnl|Fabrus|VH4-39_IGHD2-21*01_IGHJ3*01	761
311	gnl|Fabrus|VH4-39_IGHD3-10*01_IGHJ4*01	762
312	gnl|Fabrus|VH4-39_IGHD3-16*01_IGHJ2*01	763
313	gnl|Fabrus|VH4-39_IGHD3-9*01_IGHJ6*01	764
314	gnl|Fabrus|VH4-39_IGHD4-23*01_IGHJ2*01	765
315	gnl|Fabrus|VH4-39_IGHD5-12*01_IGHJ4*01	766
316	gnl|Fabrus|VH4-39_IGHD6-6*01_IGHJ1*01	767
317	gnl|Fabrus|VH4-4_IGHD1-20*01_IGHJ3*01	768
318	gnl|Fabrus|VH4-4_IGHD2-8*01_IGHJ4*01	769
319	gnl|Fabrus|VH4-4_IGHD3-22*01_IGHJ2*01	770
320	gnl|Fabrus|VH4-4_IGHD4-23*01_IGHJ4*01	771
321	gnl|Fabrus|VH4-4_IGHD5-12*01_IGHJ5*01	772
322	gnl|Fabrus|VH4-4_IGHD6-6*01_IGHJ4*01	773
323	gnl|Fabrus|VH4-4_IGHD7-27*01_IGHJ6*01	774
324	gnl|Fabrus|VH4-59_IGHD6-25*01_IGHJ3*01	775
325	gnl|Fabrus|VH5-51_IGHD1-14*01_IGHJ4*01	776
326	gnl|Fabrus|VH5-51_IGHD1-26*01_IGHJ6*01	777
327	gnl|Fabrus|VH5-51_IGHD2-8*01_IGHJ4*01	778
328	gnl|Fabrus|VH5-51_IGHD3-10*01_IGHJ6*01	779
329	gnl|Fabrus|VH5-51_IGHD3-3*01_IGHJ4*01	780
330	gnl|Fabrus|VH5-51_IGHD4-17*01_IGHJ4*01	781
331	gnl|Fabrus|VH5-51_IGHD5-18*01>3_IGHJ4*01	782
332	gnl|Fabrus|VH5-51_IGHD5-18*01>1_IGHJ4*01	783
333	gnl|Fabrus|VH5-51_IGHD6-25*01_IGHJ4*01	784
334	gnl|Fabrus|VH5-51_IGHD7-27*01_IGHJ4*01	785
335	gnl|Fabrus|VH6-1_IGHD1-1*01_IGHJ4*01	786
336	gnl|Fabrus|VH6-1_IGHD1-20*01_IGHJ6*01	787
337	gnl|Fabrus|VH6-1_IGHD2-15*01_IGHJ4*01	788
338	gnl|Fabrus|VH6-1_IGHD2-21*01_IGHJ6*01	789
339	gnl|Fabrus|VH6-1_IGHD3-16*01_IGHJ5*01	790
340	gnl|Fabrus|VH6-1_IGHD3-3*01_IGHJ4*01	791
341	gnl|Fabrus|VH6-1_IGHD4-11*01_IGHJ6*01	792
342	gnl|Fabrus|VH6-1_IGHD4-23*01_IGHJ4*01	793
343	gnl|Fabrus|VH6-1_IGHD5-5*01_IGHJ4*01	794
344	gnl|Fabrus|VH6-1_IGHD6-13*01_IGHJ4*01	795
345	gnl|Fabrus|VH6-1_IGHD6-25*01_IGHJ6*01	796
346	gnl|Fabrus|VH6-1_IGHD7-27*01_IGHJ4*01	797
347	gnl|Fabrus|VH7-81_IGHD1-14*01_IGHJ4*01	798
348	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ2*01	799
349	gnl|Fabrus|VH7-81_IGHD2-21*01_IGHJ6*01	800
350	gnl|Fabrus|VH7-81_IGHD3-16*01_IGHJ6*01	801
351	gnl|Fabrus|VH7-81_IGHD4-23*01_IGHJ1*01	802
352	gnl|Fabrus|VH7-81_IGHD5-12*01_IGHJ6*01	803
353	gnl|Fabrus|VH7-81_IGHD6-25*01_IGHJ4*01	804
354	gnl|Fabrus|VH7-81_IGHD7-27*01_IGHJ4*01	805
Light Chain		
Number	Name	SEQ ID NO.
1	gnl|Fabrus|A14_IGKJ1*01	806
2	gnl|Fabrus|A17_IGKJ1*01	807
3	gnl|Fabrus|A2_IGKJ1*01	808
4	gnl|Fabrus|A20_IGKJ1*01	809
5	gnl|Fabrus|A23_IGKJ1*01	810
6	gnl|Fabrus|A26_IGKJ1*01	811

7	gnl|Fabrus|A27_IGKJ1*01	812
8	gnl|Fabrus|A27_IGKJ3*01	813
9	gnl|Fabrus|A30_IGKJ1*01	814
10	gnl|Fabrus|B2_IGKJ1*01	815
11	gnl|Fabrus|B2_IGKJ3*01	816
12	gnl|Fabrus|B3_IGKJ1*01	817
14	gnl|Fabrus|L11_IGKJ1*01	819
15	gnl|Fabrus|L12_IGKJ1*01	820
16	gnl|Fabrus|L14_IGKJ1*01	821
17	gnl|Fabrus|L2_IGKJ1*01	822
18	gnl|Fabrus|L22_IGKJ3*01	823
19	gnl|Fabrus|L23_IGKJ1*01	824
20	gnl|Fabrus|L25_IGKJ1*01	825
21	gnl|Fabrus|L25_IGKJ3*01	826
22	gnl|Fabrus|L4/18a_IGKJ1*01	827
23	gnl|Fabrus|L5_IGKJ1*01	828
24	gnl|Fabrus|L6_IGKJ1*01	829
25	gnl|Fabrus|L8_IGKJ1*01	830
26	gnl|Fabrus|L9_IGKJ2*01	831
27	gnl|Fabrus|O1_IGKJ1*01	832
28	gnl|Fabrus|O12_IGKJ1*01	833
29	gnl|Fabrus|O18_IGKJ1*01	834
31	gnl|Fabrus|V1-11_IGLJ2*01	836
32	gnl|Fabrus|V1-13_IGLJ5*01	837
33	gnl|Fabrus|V1-16_IGLJ6*01	838
34	gnl|Fabrus|V1-18_IGLJ2*01	839
35	gnl|Fabrus|V1-2_IGLJ7*01	840
36	gnl|Fabrus|V1-20_IGLJ6*01	841
37	gnl|Fabrus|V1-3_IGLJ1*01	842
38	gnl|Fabrus|V1-4_IGLJ4*01	843
39	gnl|Fabrus|V1-5_IGLJ2*01	844
40	gnl|Fabrus|V1-7_IGLJ1*01	845
41	gnl|Fabrus|V1-9_IGLJ6*01	846
42	gnl|Fabrus|V2-1_IGLJ6*01	847
43	gnl|Fabrus|V2-11_IGLJ7*01	848
44	gnl|Fabrus|V2-13_IGLJ2*01	849
45	gnl|Fabrus|V2-14_IGLJ4*01	850
46	gnl|Fabrus|V2-15_IGLJ7*01	851
47	gnl|Fabrus|V2-17_IGLJ2*01	852
48	gnl|Fabrus|V2-19_IGLJ4*01	853
49	gnl|Fabrus|V2-6_IGLJ4*01	854
50	gnl|Fabrus|V2-7_IGLJ2*01	855
51	gnl|Fabrus|V2-7_IGLJ7*01	856
52	gnl|Fabrus|V2-8_IGLJ6*01	857
53	gnl|Fabrus|V3-2_IGLJ4*01	858
54	gnl|Fabrus|V3-3_IGLJ7*01	859
55	gnl|Fabrus|V3-4_IGLJ1*01	860
56	gnl|Fabrus|V4-1_IGLJ4*01	861
57	gnl|Fabrus|V4-2_IGLJ4*01	862
58	gnl|Fabrus|V4-3_IGLJ4*01	863
59	gnl|Fabrus|V4-4_IGLJ5*01	864
60	gnl|Fabrus|V4-6_IGLJ4*01	865
61	gnl|Fabrus|V5-4_IGLJ2*01	866
62	gnl|Fabrus|V5-6_IGLJ1*01	867

EXAMPLE 7

Comparison of Fab Secretion By Different Leader Sequences

In this Example, the effect of different leader sequences on expression of encoded Fabs was assessed. In order to assure properly folded Fab proteins, disulfide bonds must form in an oxidizing environment and therefore it is necessary to translocate the Fab proteins into the periplasm by using a pathway such as Sec, SRP and TAT. The SRP pathway does not require unfolding of any proteins. SRP leader sequences are shown in Table 23.

Table 23. SRP Leader Sequences

Name	SEQ ID NO.	Sequence
DsbA	5	MKKIWLALAGLVLAFSASA
SfmC	6	MMTKIKLLMLIIFYLIISASAHA
TolB	7	MKQALRVAFGFLILWASVLHA
TorT	8	MRVLLFLLLSLRMLPAFS

Plasmid A (SEQ ID NO:1) and plasmid C (SEQ ID NO:3) were modified to contain either a DsbA leader sequence (SEQ ID NO:5) or a mutant DsbA leader sequence (SEQ ID NO:965) and a ribosomal binding site (RBS) variation. Overlap PCR was performed using three forward primers containing RBS variations and the sequence corresponding to the N-terminus of DsbA (set forth in SEQ ID NOS:966-968) and two reverse primers corresponding to the C-terminus of either DsbA or mutant DsbA (set forth in SEQ ID NOS:969-970). The PCR resulted in six different leader sequences (Table 24). These leader sequences were then inserted into Plasmid A and Plasmid C between EcoRI and NcoI sites upstream of the start codon, ATG. Plasmids A and C containing the DsbA leader sequence with the RBS variations are set forth in SEQ ID NO:1015-1017 and 1021-1023, respectively. Plasmids A and C containing the mutant DsbA leader sequence with the RBS variations are set forth in SEQ ID NO:1018-1020 and 1024-1026, respectively.

Table 24. DsbA and mutant DsbA leader sequences with RBS variations

Name	Leader Sequence	SEQ ID NO.
DS1	GAATTCTAAGGAG**GT**TTCACCATGAAAAAGATTTGGCTGGCGC TGGCTGGTTTAGTTTTAGCGTTTAGC GCC ATG G	971
DS2	GAATTCTAAGGAG**TA**TTCACCATGAAAAAGATTTGGCTGGCGCT GGCTGGTTTAGTTTTAGCGTTTAGC GCC ATG G	972
DS3	GAATTCT**TA**GGA**TTA**TTCACCATGAAAAAGATTTGGCTGGCGCT GGCTGGTTTAGTTTTAGCGTTTAGC GCC ATG G	973
DM1	GAATTCTAAGGAG**GT**TTCACCATGAAAAAGATTTGGCTGGCGC TGGCTGGTTTAGTTTTAGCGTTTAGCGCATCG GCG GCC ATG GCA	974
DM2	GAATTCTAAGGAG**TA**TTCACCATGAAAAAGATTTGGCTGGCGCT GGCTGGTTTAGTTTTAGCGTTTAGCGCATCG GCG GCC ATG GCA	975
DM3	GAATTCT**TA**GGA**TTA**TTCACCATGAAAAAGATTTGGCTGGCGCT GGCTGGTTTAGTTTTAGCGTTTAGCGCATCG GCG GCC ATG GCA	976

To assess the effect of the different leader sequences on the expression of a Fab antibody, expression of Rituxan was assessed. Rituxan heavy chain (SEQ ID NO:453) was cloned in-frame to the C_H sequence present on the respective Plasmid A vector and Rituxan light chain (SEQ ID NO:835) was cloned in-frame to the Cκ sequence present in the respective Plasmid C vector. Briefly, the V_H and Vκ chains were cloned into the Plasmid A or C vectors (containing an STII leader sequence, a DsbA leader sequence or a mutant DsbA leader sequence) by digestion of the plasmids with NheI and NcoI (for the heavy chain DNA) or with NcoI and BsiWI (for the light chain DNA) followed by ligation. Plasmids encoding a heavy and light chain were co-transformed into LMG194 cells as described in Example 8 below and grown for 36 hours at 20 °C in terrific broth (TB) medium in the presence of 0.4% glucose and 0.008% arabinose. Expressed Fabs were extracted from the whole cells using Bugbuster® (Novagen), and purified using a Ni^{2+} affinity column (EMD), and analyzed by SDS-PAGE followed by Western Blot. The results show that in the absence of an inducer little to no protein was expressed. Upon induction, expression of the Fabs under the control of the DsbA leader sequence (for each of the three RBS variations) was equal to expression under the control of the STII leader sequence. Mutated DsbA resulted in lower expression. There was no significant difference in expression among the various RBS variations of the DsbA leader sequence.

EXAMPLE 8

Cloning and Co-transformation of Synthesized Variable Heavy and Light Chains

In this Example, a Fab library was created by cloning heavy or light chain DNA into their respective Plasmids followed by co-transformation and protein growth/purification. Following synthesis of the DNA molecules generated from the Sequence Compilation Software as described in Example 6, the DNA molecules were cloned into plasmids containing constant heavy or light chains as appropriate for co-transformation and expression of combinatorial Fabs. Plasmid A (SEQ ID NO:1) and plasmid D (SEQ ID NO:2) contain heavy chain constant regions sequences. Plasmid C (SEQ ID NO:3) contains a kappa light chain constant region sequence and Plasmid E (SEQ ID NO:4) contains a lambda light chain constant region sequence.

Synthetic recombined nucleic acid encoding a variable heavy chain were digested with Nhe I and Nco I and ligated into Plasmid A with a StII leader sequence using standard molecular techniques. Synthetic recombined nucleic acid encoding a variable kappa light chain were digested with NcoI and BsiWI and synthetic recombined nucleic acid encoding a variable lambda chain were digested with NcoI and AvrII, and were ligated into Plasmid C or

Plasmid E, respectively, with a StII leader sequence, using standard molecular biology techniques.

Plasmid A and one of either Plasmid C or Plasmid E, each containing various combinations of variable heavy and light chains, were co-transformed into *E. coli*. The process was repeated for all combinations of heavy and light chains. Briefly, plasmid A (encoding a Fab heavy chain) and plasmid C or Plasmid E (encoding a Fab light chain) were resuspended separately in TE buffer to a final concentration of 1 ng/μl. One (1) μL of heavy chain plasmid and 1 μL of light chain plasmid were combined in a PCR tube or a PCR plate and were mixed with 20 μL ice cold LMG194 competent cells. The transformation reaction was incubated on ice for 10 minutes followed by heat shock in a preheated PCR block at 42 °C for 45 seconds. The tube was then placed on ice for an additional 2 minutes followed by addition of 200 μL SOC medium. The cells were allowed to recover for 1.5 hours at 37 °C. A 100 μL aliquot of the transformation culture was used to inoculate 0.9 mL LB (Luria-Bertani Broth) containing 0.4% (w/v) glucose, 17 μg/mL kanamycin (Sigma Aldrich) and 34 μg/mL chloramphenicol (Sigma Aldrich). The culture was grown at 30 °C with vigorous shaking for 20 hours. The transformation culture was grown and purified using the Piccolo™ system as described in Example 9.

EXAMPLE 9

High throughput Growth and Purification of Fab libraries

In this Example, Fab libraries are generated and purified using high throughput techniques. High throughput transformation of pairs of heavy chains (plasmid A) and light chains (plasmid C or E) was performed as described in Example 8, except that a 96-well PCR plate was used instead of individual PCR tubes. After transformation, the cells were grown overnight in 2 ml deep well 96-well plates (VWR) block covered with breathable tape. The overnight culture was used directly for inoculation in Piccolo™ (Wollerton *et al.* (2006) JALA, 11:291-303.)

High throughput, parallel expression and purification of antibody Fab fragments was performed using Piccolo™ (The Automation Partnership (TAP)), which automates protein expression and purification. The expression and purification parameters for Piccolo™ were prepared using Run Composer software (TAP). A 'Strain File' was generated mapping the location of each clone in the seed culture plate. This was submitted to the Run Composer software and the basic machine settings were set as follows: Pre-induction Incubator set at 30° C; Expression Incubator 1 set at 16 °C; Centrifuge set at 6 °C and 5000 x g; Media Pump 1 primed with TB (Terrific Broth; per liter contains 12 g tryptone, 24 g yeast extract, 9.4 g

potassium phosphate, dibasic, and 2.2 g potassium phosphate, monobasic) (EMD Biosciences; catalog No. 71754), 50 μg/mL kanamycin (Sigma Aldrich), 35 μg/mL chloramphenicol (Sigma Aldrich), 0.4% (w/v) glucose (Sigma Aldrich) and 0.015% (v/v) Antifoam 204 (Sigma Aldrich); Inducer Pump 1 primed with 0.2% (w/v) arabinose (EMD Biosciences); Incubator Gassing Rate set at 2 sec with 51% oxygen, 0.1 mL inoculation volume; Induction Statistic Mean set w/o Outliers (i.e. block mean OD_{600} determined after excluding the 3 highest and 3 lowest values); culture vessel blocks (CVB) pre-induction delay set at 1 hr 20 min and Expression Incubator Acclimatization set at 30 min.

The seed cultures were prepared and loaded into Piccolo™ along with the necessary labware: 24-well culture vessel blocks (CVBs; The Automation Partnership), 24-well Filter Plates (The Automation Partnership), 24-well Output Plates (Seahorse Bioscience) and Pipette Tip Boxes (MBP) as specified by the manufacturer. The TB media supplemented as described above, arabinose inducer and associated pumps were prepared under sterile conditions and attached to the machine. The centrifuge counterbalance weight was set and placed inside the centrifuge. Lastly, purification reagents were prepared and attached to the system pumps (lysis buffer, resin, wash buffer and elution buffer as described below). Once this was complete, the machine was started and processing began.

Before inoculation, the inocula were mapped to specific wells of 24-well CVB, and expression and induction conditions were set as described in Table 25 below. Each well of the CVBs were filled with 10 mL of TB media supplemented as described above prior to inoculation from the seed plate. Each well of each CVB was inoculated with 0.1 mL seed culture and then returned to the storage carousel to await scheduled admission to pre-induction incubation. Once a CVB was queued to begin pre-induction incubation it was removed from the storage carousel and coupled to an aeration assembly (which provides agitation, well sealing and a means for controlled administration of oxygen/air) and then placed in the pre-induction incubator. OD_{600} readings were taken upon commencement of incubation and approximately every 30 minutes thereafter. Piccolo operation control software monitors the OD_{600} measurements to predict when each CVB will reach the 1.0 OD_{600} set point. Approximately 30 minutes prior to the CVB reaching the OD_{600} set point the assembly was moved to the expression incubator to equilibrate to the desired expression temperature, and then the cultures in the CVB were induced by addition of the predetermined volume of arabinose as set forth in Table 25. Cell growth was monitored by measuring the OD_{600} every 30 minutes after induction and plotting the data showing total incubation time versus optical density reading. The 6 CVB expressions/purifications schemes from Table 25 were analyzed.

CVB01 through CVB04 exhibited the same growth patterns with the OD_{600} maxing out around 20 after approximately 1700 minutes. In these plates, growth of the Fab cultures in each of the individual wells of the plates were similar, with a somewhat greater variability in growth rates per well observed in the CVB03 and CVB04 conditions. CVB05 and CVB06 showed slower growth, with the OD_{600} still increasing at the last time point tested, i.e. total incubation time of 2300 minutes after induction. The growth of the Fab cultures varied between wells of each plate; the maximum OD_{600} between wells varied between OD_{600} =10 to OD_{600}=16-18.

TABLE 25: Growth Curves of CVB plates Under Various Conditions

Culture Vessel Block	Inocula Wells of 96-well plate	Post-establishment chill Incubation	Pre-Induction Incubation	Induction Time	Expression Conditions	Induction Conditions
CVB01	A1,3,5,7,9,11 B1,3,5,7,9,11 C1,3,5,7,9,11 D1,3,5,7,9,11	41 min 47 s	7 hr 56 min @ 30° C	509 min	30 hours @ 16° C	0.008%(w/v) arabinose at OD=2
CVB02	A1,3,5,7,9,11 B1,3,5,7,9,11 C1,3,5,7,9,11 D1,3,5,7,9,11	4 hr 26 min 25 s	7 hr 40 min @ 30° C	492 min	36 hours @ 16° C	0.008%(w/v) arabinose at OD=2
CVB03	E1,3,5,7,9,11 F1,3,5,7,9,11 G1,3,5,7,9,11 H1,3,5,7,9,11	1 hr 45 min 40 s	8 hr 11 min @ 30° C	525 min	30 hours @ 16° C	0.008%(w/v) arabinose at OD=2
CVB04	E1,3,5,7,9,11 F1,3,5,7,9,11 G1,3,5,7,9,11 H1,3,5,7,9,11	5 hr 31 min 34 s	8 hr 12 min @ 30° C	525 min	36 hours @ 16° C	0.008%(w/v) arabinose at OD=2
CVB05	E2,4,6,8,10,12 F2,4,6,8,10,12 G2,4,6,8,10,12 H2,4,6,8,10,12	3 hr 11 min 23 s	8 hr 18 min @ 30° C	532 min	30 hours @ 16° C	0.008%(w/v) arabinose at OD=2
CVB06	E2,4,6,8,10,12 F2,4,6,8,10,12 G2,4,6,8,10,12 H2,4,6,8,10,12	6 hr 46 min 46 s	8 hr 35 min @ 30° C	549 min	36 hours @ 16° C	0.008%(w/v) arabinose at OD=2

Following culture inoculation and growth induction of cultures, the cells were harvested and lysed for purification of Fabs. Piccolo™ was used for purification of the expressed Fab proteins using an automated expression and purification 'Lifecycle' of a whole culture purification. After controlled expression, CVBs were chilled for 30 minutes at 6 °C in the storage carousel prior to lysis. The CVB was moved to the liquid handling bed and lysis

buffer (2.5 mL of Popculture with 1:1000 Lysonase (EMD Biosciences)) was added to each well with thorough mixing. The lysis proceeded for 10 minutes and then the CVB was centrifuged for 10 minutes at 5000 x *g* to pellet cell debris. During centrifugation, a Filter Plate was placed in the filter bed and resin (2 mL of a 50% slurry of Ni-charged His-Bind resin (EMD Biosciences)) was added to each well. Soluble lysate was added to the corresponding wells of the filter plate containing resin and allowed to bind for 10 minutes prior to draining to waste. Wash buffer (12 mL of wash buffer (50 mM Sodium Phosphate, 300 mM NaCl, 30 mM Imidazole, pH 8.0)) was added in two steps to each well and allowed to drain to waste. Finally, an Output Plate was placed under the Filter Plate in the filter bed and IMAC elution buffer ((50 mM Sodium Phosphate, 300 mM NaCl, 500 mM Imidazole)) was added in two steps draining into the output plate. The output plate was returned to the storage carousel as was all other labware. Once this process was complete for each CVB in the designed run, the machine was unloaded.

Using similar Piccolo™ runs with the same clones allowed for the optimization of incubation temperatures for expression, concentration of arabinose inducer and time of expression. Global optimal results were obtained by use of a two-step temperature incubation where the pre-induction samples are incubated at 30 °C. Following induction, protein expression was carried out at 20 °C. Optimal expression yields were obtained using 0.032% arabinose inducer followed by 45 hours of expression.

EXAMPLE 10

Orthogonal Secondary Purification of Fab antibodies

To rapidly further purify partially pure Fabs generated after the Piccolo™ process, an orthogonal method of purification was developed. Fabs were expressed and purified as described above in Example 9 using the Piccolo™ machine. Approximately 1.8 mL of the IMAC elution per Fab sample obtained from Piccolo™ purification was further purified on a 1 mL Hi-Trap Protein G column (GE Healthcare) at 4 °C using the Akta purifier (GE Healthcare) and A-905 autosampler (GE Healthcare) according to the manufacturer's protocol. The protein samples were transferred to a deep well 96-well block (VWR), which was covered by aluminum foil tape to prevent evaporation. The autosampler was set for multiple injections (typically four injections of 450 µL per sample) onto the Hi-Trap Protein G column. The column was then washed with 2 column volumes of 50 mM sodium phosphate pH7.2, 150 mM NaCl. The Fab was eluted with six column volumes of 100 mM glycine pH2.8. The elution peak fractions (appoximately 0.8 mL) were collected in a deep well 96-well plate block. The eluted protein was immediately neutralized with 100 µL

saturated dibasic sodium phosphate pH9.0. Protein concentration was determined by measuring absorbance at A280 on a Molecular Dynamic plate reader and calculated from the exctinction coefficient of the corresponding Fab. Extinction coefficients are calculated based on the total numbers of Tyrosine + Tryptophane + Phenylalanine in the Fab heavy and light chains. Following purification using the Piccolo™ system, expressed protein was generally less than 20% pure. After orthogonal purifiation with protein G, Fab purity was greater than 95% pure as indicated by SDS-PAGE.

Table 17 sets forth Fab antibodies generated by Piccolo and further purified in a secondary purification. The amino acid sequences of the Fab antibodies correspond to sequences containing variable heavy chain sequences set forth in any of SEQ ID NOS: 1475-1826 and variable light chain sequences set forth in SEQ ID NO: 1827-1838, 1840-1855 and 1857-188. The sequences of the heavy and light chain Fab library members also further contains a sequence for a constant region included in Plasmid A, C or E.

EXAMPLE 11

Lymphoma Apoptosis Assay

To identify unique Fabs from an antibody library, assays can be performed to assess any desired function, property or activity. As an example of an assay for protein function, cross-linked anti-CD20 Fab (heavy chain set forth in SEQ ID NO:453 and light chain set forth in SEQ ID NO:835) was tested in a cell based assay for the ability to induce apoptosis in lymphoma cells. Anti-CD20 Fabs were cross-linked by adding equal molar concentration of polyclonal anti human kappa light chain antibodies that recognize different parts of the anti-CD20 kappa light chain.

Apoptosis was determined using the Apo-ONE homogenous Caspase-3/7 Assay (Promega). Ramos B-Lymphocyte cells were grown in RPMI1640 media containing 10% FBS (fetal bovine serum), P-S (penicillin-streptomycin) and arrayed into a clear 96-well plate (Costar 3595, Corning, $2.5x10^4$ cells per well). Jurkat T-Lymphocyte cells were grown in RPMI1640 with 10% FBS and P-S, and arrayed into a clear 96-well plate (Costar 3595, Corning, $2.5x10^4$ cells per well). Crosslinked anti-CD20 Fab was added to each well at concentrations of 0, 25, 50, 100 and 200 nM together with equal molar concentrations of polyclonal antibody against human kappa light chain (Sigma). Anti-Fas monoclonal antibody (20-100 ng/ml) or staurosporine (1.0 μM) were added for postive controls and trastuzumab Fab was used as a negative control. An equal volume of Apo-ONE Caspase-3/7 Reagent (rhodamine 110, bis-(N-CBZ-L-aspartyl-L-glutamyl-L-valyl-L-aspartic acid amide, Z-DEVD-R110) was added and the plate was incubated for one hour at room temperature. The

presence of rhodamine 110 was detected by measuring fluorescence in a fluorescent plate reader at 485 nm exitation/521 nm emission. The increase in the percentage of apoptosis was calculated according to the equation: 100 x [(Fluorescence for Fab)-(Fluorescence for background)]/(Fluorescence for background).

EXAMPLE 12

Erythropoietin binding Fab library

As an alternative to "naïve" libraries, directed Fab libraries are constructed to a known target. In this example, a directed library was constructed in which a 16 amino acid erythropoietin peptide (EPO) was inserted into various CDRs of an antibody to identify Fabs that induce activation of recombinant EPO (EpoR). Because there are variations in the number of amino acid residues that occur in a CDR (see, e.g., Table 26), CDRs with larger inserts were selected for insertion of the EPO peptide. These CDRs include CDR-H2, CDR-H3, CDR-L1, and CDR-L3.

Table 26: Amino Acid Length of CDR

	Heavy Chain	Light Chain
CDR1	10-12	10-17
CDR2	16-19	7
CDR3	3-25	7-11

To randomize the orientation of the peptide insert to expose the active surface of the peptide, two extra amino acid residues, either proline or glycine, were added to the N-terminus and C-terminus of the EPO peptide, yielding sixteen different peptides (SEQ ID NO:874-889). A Fab, containing heavy chain VH3-23 (SEQ ID NO:869) and light chain A17 (SEQ ID NO:871), served as a parent antibody for the EPO peptide library. BsaI restriction sites were introduced into the nucleic acid sequences of the EPO peptides and the nucleic acid sequences of the heavy and light chain variable regions in order to allow the cloning of the DNA encoding the EPO peptides into the respective CDRs. Heavy chain VH3-23 DNA was modified to create VH3-23B (SEQ ID NO:896) containing BsaI sites at CDR2 and VH3-23R (SEQ ID NO:913) containing BsaI sites at CDR3. Light chain A17 DNA was modified to create A17P (SEQ ID NO:872) containing BsaI sites at CDR1 and A17Q (SEQ ID NO:873) containing BsaI sites at CDR3. Sixteen different genes encoding the EPO peptides were cloned into the respective heavy (CDR2 and CDR3) or light (CDR1 and CDR3) chain sequences and the resulting Fabs were expressed and purified as described in Example 9. Table 27 lists the resulting 64 EPO containing Fabs.

Table 27. EPO Peptide containing Fab Library

HEAVY CHAIN	LIGHT CHAIN

NAME	SEQ ID NO	NAME	SEQ ID NO
H2-EP14 (VH3-23B)	897	A17	871
H2-EP18 (VH3-23B)	898	A17	871
H2-EP19 (VH3-23B)	899	A17	871
H2-EP20 (VH3-23B)	900	A17	871
H2-EP21 (VH3-23B)	901	A17	871
H2-EP22 (VH3-23B)	902	A17	871
H2-EP23 (VH3-23B)	903	A17	871
H2-EP24 (VH3-23B)	904	A17	871
H2-EP25 (VH3-23B)	905	A17	871
H2-EP26 (VH3-23B)	906	A17	871
H2-EP27 (VH3-23B)	907	A17	871
H2-EP28 (VH3-23B)	908	A17	871
H2-EP29 (VH3-23B)	909	A17	871
H2-EP30 (VH3-23B)	910	A17	871
H2-EP31 (VH3-23B)	911	A17	871
H2-EP32 (VH3-23B)	912	A17	871
H3-EP14 (VH3-23R)	914	A17	871
H3-EP18 (VH3-23R)	915	A17	871
H3-EP19 (VH3-23R)	916	A17	871
H3-EP20 (VH3-23R)	917	A17	871
H3-EP21 (VH3-23R)	918	A17	871
H3-EP22 (VH3-23R)	919	A17	871
H3-EP23 (VH3-23R)	920	A17	871
H3-EP24 (VH3-23R)	921	A17	871
H3-EP25 (VH3-23R)	922	A17	871
H3-EP26 (VH3-23R)	923	A17	871
H3-EP27 (VH3-23R)	924	A17	871
H3-EP28 (VH3-23R)	925	A17	871
H3-EP29 (VH3-23R)	926	A17	871
H3-EP30 (VH3-23R)	927	A17	871
H3-EP31 (VH3-23R)	928	A17	871
H3-EP32 (VH3-23R)	929	A17	871
VH3-23	869	L1-EP14 (A17P)	930
VH3-23	869	L1-EP18 (A17P)	931
VH3-23	869	L1-EP19 (A17P)	932
VH3-23	869	L1-EP20 (A17P)	933
VH3-23	869	L1-EP21 (A17P)	934
VH3-23	869	L1-EP22 (A17P)	935
VH3-23	869	L1-EP23 (A17P)	936
VH3-23	869	L1-EP24 (A17P)	937
VH3-23	869	L1-EP25 (A17P)	938
VH3-23	869	L1-EP26 (A17P)	939
VH3-23	869	L1-EP27 (A17P)	940
VH3-23	869	L1-EP28 (A17P)	941
VH3-23	869	L1-EP29 (A17P)	942
VH3-23	869	L1-EP30 (A17P)	943
VH3-23	869	L1-EP31 (A17P)	944
VH3-23	869	L1-EP32 (A17P)	945
VH3-23	869	L3-EP14 (A17Q)	946
VH3-23	869	L3-EP18 (A17Q)	947
VH3-23	869	L3-EP19 (A17Q)	948
VH3-23	869	L3-EP20 (A17Q)	949

VH3-23	869	L3-EP21 (A17Q)	950
VH3-23	869	L3-EP22 (A17Q)	951
VH3-23	869	L3-EP23 (A17Q)	952
VH3-23	869	L3-EP24 (A17Q)	953
VH3-23	869	L3-EP25 (A17Q)	954
VH3-23	869	L3-EP26 (A17Q)	955
VH3-23	869	L3-EP27 (A17Q)	956
VH3-23	869	L3-EP28 (A17Q)	957
VH3-23	869	L3-EP29 (A17Q)	958
VH3-23	869	L3-EP30 (A17Q)	959
VH3-23	869	L3-EP31 (A17Q)	960
VH3-23	869	L3-EP32 (A17Q)	961

Screening to identify Fabs that modulated activation of the Epo Receptor (EpoR, SEQ ID NO:962) was performed in BaF3 cells stably transfected with EpoR-encoding cDNA.

a. MTT Cell Proliferation Assay

The tetrazolium ring of MTT (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyl tetrazolium bromide) is cleaved by mitochondrial dehydrogenase of viable cells to produce purple MTT formazan crystals that are insoluble in aqueous solution but can be solubilized in acidified isopropanol. BaF3/EpoR cells ($5x10^3$-$5x10^5$) were incubated for one or two days in the presence and in the absence of the Epo Fabs. MTT solution (10% of the culture volume) was added to cells and incubated 3-4 hrs at 37 °C in a CO_2 incubator. An equal volume of 0.1 N HCl in isopropanol was added. Absorbance was measured at 570 nm and the number of cells was calculated based on the standard curve.

b. Luciferase Reporter Assay

Activation of EpoR leads to activation of STAT5 transcription factor, which in turn induces transcription of genes including c-myc, bcl-2, pim-1 and cyclin-D. Transcription can be detected by linking the promotor of any one of the above genes to a reporter gene, thus creating a reporter plasmid. Two reporter plasmids were created to assess activation of the EpoR. The first reporter plasmid was constructed by placing the mouse cyclin-D promoter (SEQ ID NO:963) at the 5' end of the luciferase gene in the pGL4.70 vector (Promega; SEQ ID NO:1997). Briefly, pGL4.70 was digested with restriction enzymes NheI and HindIII and the cyclin D promoter was inserted between nucleotides 28-66 of the plasmid using standard molecular biology protocols.

An EPO Fab that is capable of activating EpoR will cause activation of STAT5, thereby activating the cyclin-D promoter causing induction and expression of the luciferase gene. Hence, a second reporter plasmid was created for STAT5 by using the pGL4.23 vector (Promega; SEQ ID NO: 1998), a vector that contains a minimal promoter at the 5' end of the translation start site for luciferase that allows for activation of a promoterless-response

element to drive expression. Six repeats of a DNA element for STAT5 binding (SEQ ID NO:964) were cloned directly upstream of the minimal promoter. Briefly, pGL4.23 was digested with restriction enzymes NheI and HindIII and the DNA element repeats of STAT5 was inserted between nucleotides 28-66 of the plasmid using standard molecular biology protocols.

An EPO Fab capable of activating EpoR will cause the activation of STAT5 and the direct expression of the luciferase gene. BaF3 cells, previously transfected with EpoR-encoding cDNA, were transiently transfected with one of the reporter plasmids above. The resulting cells are incubated in the presence and absence of EPO Fabs. An equal volume of lysis buffer containing luciferase substrate is added to the cell culture. Relative luminescence was measured for 10 seconds using a luminometer after 5 min incubation with the substrate.

EXAMPLE 13

Electrochemiluminescence Binding Assay

In this example, an electrochemiluminescence (ECL) binding assay was used to screen a 960 member Fab library for antibodies capable of binding to one of nine different antigens, including the human epidermal growth factor 2 receptor (ErbB2), epidermal growth factor receptor (EGF R), hepatocyte growth factor receptor (HGF R/c-Met), Notch-1, CD44, insulin-like growth factor-1 soluble receptor (IGF-1 sR), P-cadherin, erythropoietin receptor (Epo R) and delta-like protein 4 (DLL4). In an ECL assay, an antigen-antibody interaction is detected by addition of a detection antibody labeled with ruthenium tri-bispyridine-(4-methysulfone) ($Ru(bpy)_2^{2+}$). Upon application of an electric current, the $Ru(bpy)_2^{2+}$-label undergoes an oxidation-reduction cycle in the presence of a co-reactant and light is emitted. A signal is only generated when the $Ru(bpy)_2^{2+}$-label is in close proximity to the electrode, eliminating the need for washing. Detected light intensity is proportional to the amount of captured protein.

Recombinant human proteins were obtained from R&D Systems and included: rHuman ErbB2/Fc Chimera, CF (Cat# 1129-ER); rHuman EGF R/Fc Chimera, CF (Cat# 344-ER); rHuman HGF R/c-MET/Fc Chimera, CF (Cat# 358-MT/CF); rHuman Notch-1/Fc Chimera, CF (Cat# 3647-TK); rHuman CD44/Fc Chimera, CF (Cat# 3660-CD); rHuman IGF-1 sR,(IGF-1 sR), CF (Cat# 391-GR); rHuman P-Cadherin/Fc Chimera, CF (Cat# 861-PC); rHuman Erythropoietin R/Fc Chimera, CF (Cat# 963-ER); and Recombinant Human DLL4 (Cat# 1506-D4/CF). The proteins were immobilized onto each well of 10 plates by spotting 50 nanoliters (nl) of each protein (of a 60 μg/mL antigen) on the surface of a 96-well

Multi-Spot 10 Highbind plate (Meso Scale Discovery; Gaithersburg MD). Spot 10 was left blank as a control.

An 150 µl aliquot of 1% Bovine Serum Albumin (BSA) in Tris-buffered Saline Tween (TBST) was added to each well and allowed to incubate for 30 min at 20 °C followed by washing and tap drying to completely remove any residual solution. Subsequently, a 12.5 µl aliquot of 1% BSA TBST was added to each well followed by the addition of a 12.5 µl aliquot of a purified Fab. The plate was sealed and incubated for 1 hour at 20 °C with shaking.

Detection antibodies were prepared by individually conjugating both goat anti-human Kappa light chain polyclonal antibody (K3502-1MG, Sigma-Aldrich) and goat anti-human Lambda light chain polyclonal antibody (L1645-1ML, Sigma-Aldrich) with Ruthenium (II) tris-bipyridine-(4-methylsulfone)-N-hydroxysuccinimide (SULFO-TAG NHS-ester, Meso Scale Discovery) according to the manufacturer's instructions. TAG-detection antibody at 25 µl was added to each well and allowed to incubate for 1 hour at 20 °C with shaking. Finally, 15 µl of Read Buffer P with Surfactant (Cat # R92PC-1, Meso Scale Discovery) was added to each well. The electrochemiluminescence was measured using a Sector Imager 2400 (Meso Scale Discovery). Data was analyzed by comparing the ECL signals for an antigen to the blank of each well. A signal to blank ratio of 4 or more was considered a "Hit" Fab.

Ten plates, each containing 96 different Fabs, were screened using the ECL assay. The results of the initial screen are shown in Tables 28-28B, below. Table 28, below, lists the 6 Fabs (including the heavy chain and light chain) that were identified as "hits" in the initial ECL screen. A "hit" was a Fab antibody with signal to blank ratio of greater than 4. Three Fabs were identified that bind to recombinant human delta-like protein 4 (DLL4). One Fab was identified that binds to recombinant human epidermal growth factor 2 (ErbB2) and one Fab was identified that binds to recombinant human erythropoietin receptor (Epo R). An additional Fab was identified that binds to both ErbB2 and EpoR. The results of the initial MSD assay screen at a single Fab concentration are listed in Table 28B below. Table 28B lists the 6 Fabs (the Fab No. corresponds each of the Fabs identified in Table 28), the Fab concentration, the 9 recombinant human target/protein antigens, and the ECL signals from the initial MSD assay screen at the given Fab concentration.

To confirm a "Hit" from the intial ECL screening, a Fab concentration dependent titration was carried out to determine the Fab-antigen binding affinity. The assay procedure was the same as described above, except that the concentration of Fab antibody was varied

between wells from 0.1 nM to 2.4 μM. The data are set forth in Tables 29-34 below. The data were graphed using Microsoft Excel and the binding affinity was estimated from the 50% binding signal. As noted, binding affinity can be assay dependent (see Example 16).

The results show that Fab VH1-46_IGHD6-6*01_IGHJ1*01 & L6_IGKJ1*01 specifically binds Human DLL4 with high affinity in the lower nanomolar range at or about 10 nM or lower, whereas Fabs VH5-51_IGHD5-18*01>3_IGHJ4*01 & V3-4_IGLJ1*01, and VH6-1_IGHD3-3*01_IGHJ4*01 & V4-3_IGLJ4*01 bind Human DLL4 in the micromolar range. Since the three Fabs contain different heavy and light chains, the results suggest that the binding epiotopes on DL44 recognized by the antibodies can be different.

The results further show that Fab VH4-31_IGHD1-26*01_IGHJ2*01 & A27_IGKJ1*01 binds Human ErbB2/Fc chimera at a concentration of approximately 100 nM and Fab VH1-46_IGHD3-10*01_IGHJ4*01 & B3_IGKJ1*01 binds Human Erythropoietin R/Fc chimera at a concentration of approximately 100 nM. One Fab, VH1-46_IGHD6-13*01_IGH41*01 & B3_IGKJ1*01, shows affinity for both Human ErbB2/Fc and Human Erythropoietin R/Fc chimeras. It is unlikely that this Fab is binding to the Fc region of the chimera proteins, since no binding was observed to five other antigens that were Fc fusion proteins.

TABLE 28 – Identified Fab "Hits"

Fab No.	Target	Heavy Chain	SEQ ID NO	Light Chain	SEQ ID NO
1	rHuman DLL4	VH1-46_IGHD6-6*01_IGHJ1*01	1513	L6_IGKJ1*01	1850
2	rHuman DLL4	VH5-51_IGHD5-18*01>3_IGHJ4*01	1803	V3-4_IGLJ1*01	1881
3	rHuman DLL4	VH6-1_IGHD3-3*01_IGHJ4*01	1812	V4-3_IGLJ4*01	1884
4	rHuman ErbB2/Fc chimera	VH4-31_IGHD1-26*01_IGHJ2*01	1760	A27_IGKJ1*01	1833
5	rHuman Epo R/Fc chimera	VH1-46_IGHD3-10*01_IGHJ4*01	1509	B3_IGKJ1*01	1838
6	rHuman ErbB2/Fc chimera and rHuman Epo R/Fc chimera	VH1-46_IGHD6-13*01_IGHJ4*01	1512	B3_IGKJ1*01	1838

Table 28B. ECL Signals for Identified Fab "Hits" from 960 Fab Library Screen

Fab No.	[Fab] uM	rHuman Target									
		ErbB2	EGFR	HGFR	Notch-1	CD44	IGF-1	P-cad	EPOR	DLL4	Blank
1	0.14	870	823	848	614	515	663	423	693	19293	237
2	2.38	594	681	931	636	666	691	1224	834	12172	526
3	0.21	9229	815	744	949	837	763	890	1115	1069	529

4	0.23	1251	942	954	722	675	982	508	777	2808	363
5	0.74	562	652	633	980	682	593	1155	4108	1000	692
6	0.43	16499	1233	1138	1793	1497	1139	5245	12985	2538	879

Table 29. Binding affinity of Fab VH1-46_IGHD6-6*01_IGHJ1*01 & L6_IGKJ1*01								
Fab[nM]	**2383**	**595.8**	**148.9**	**37.2**	**9.3**	**2.3**	**0.6**	**0.1**
ErbB2/Fc	454	321	247	384	354	291	215	306
EGF R/Fc	621	403	290	228	424	289	309	311
HGF R/Fc	762	353	205	207	324	253	256	286
Notch-1/Fc	690	306	375	402	492	333	337	378
CD44/Fc	559	372	348	356	396	317	238	323
IGF-1 sR	527	335	322	295	315	231	313	241
P-Cadherin/Fc	728	617	687	649	452	401	321	235
EPO R/Fc	658	378	373	315	306	429	337	373
DLL4	11794	17203	16253	16717	13210	3055	508	317
Blank	344	285	218	199	287	234	226	201

Table 30. Binding affinity of Fab VH5-51_IGHD5-18*01>3_IGHJ4*01 & V3-4_IGLJ1*01				
Fab[nM]	**154**	**51**	**17**	**6**
ErbB2/Fc	1593	1248	1033	873
EGF R/Fc	1398	816	805	742
HGF R/Fc	1520	1044	914	831
Notch-1/Fc	929	685	558	464
CD44/Fc	960	651	518	547
IGF-1 sR	1396	1051	872	854
P-Cadherin/Fc	1733	854	542	358
EPO R/Fc	1195	750	620	548
DLL4	40392	17025	7158	1946
Blank	447	335	143	191

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Table 31. Binding affinity of Fab VH6-1_IGHD3-3*01_IGHJ4*01 & V4-3_IGLJ4*01								
Fab[nM]	**480**	**240**	**120**	**60**	**30**	**15**	**7.5**	**3.8**
ErbB2/Fc	965	833	822	777	726	713	695	714
EGF R/Fc	877	690	658	679	585	584	582	511
HGF R/Fc	951	834	785	623	640	694	558	519
Notch-1/Fc	545	368	472	415	425	508	392	383
CD44/Fc	541	470	442	434	484	454	444	419
IGF-1 sR	741	625	813	654	697	705	642	463
P-Cadherin/Fc	596	383	450	372	440	351	352	281
EPO R/Fc	621	478	431	423	325	397	443	407
DLL4	1532	1273	938	875	736	690	598	462
Blank	362	316	363	237	213	261	217	198

Table 32. Binding affinity of Fab VH4-31_IGHD1-26*01_IGHJ2*01 & A27_IGKJ1*01

Fab[nM]	410	205	102.5	51.3	25.6	12.8	6.4	3.2
ErbB2/Fc	5422	5260	4355	3588	2992	2255	1796	868
EGF R/Fc	734	595	455	379	373	320	249	254
HGF R/Fc	753	735	425	456	382	258	234	294
Notch-1/Fc	804	722	607	408	270	249	279	275
CD44/Fc	767	613	461	409	332	273	240	295
IGF-1 sR	600	565	443	316	311	323	209	313
P-Cadherin/Fc	814	769	714	424	323	245	197	206
EPO R/Fc	797	595	587	498	409	338	264	233
DLL4	859	599	550	474	384	268	256	242
Blank	637	430	437	337	345	227	133	172

Table 33. Binding affinity of Fab VH1-46_IGHD3-10*01_IGHJ4*01 & B3_IGKJ1*01

Fab[nM]	1410	705	352.5	176.3	88.1	44.1	22	11
ErbB2/Fc	932	671	514	448	200	347	363	216
EGF R/Fc	1071	692	769	428	376	428	312	201
HGF R/Fc	903	839	606	418	392	336	203	268
Notch-1/Fc	1034	958	715	664	440	331	389	404
CD44/Fc	885	693	556	376	340	302	317	296
IGF-1 sR	426	630	528	393	273	309	347	289
P-Cadherin/Fc	1059	827	649	532	278	343	215	270
EPO R/Fc	4314	4894	4105	3519	3368	2387	2241	1824
DLL4	1265	981	660	460	434	388	342	254
Blank	709	483	494	346	301	200	289	212

Table 34. Binding affinity of Fab VH1-46_IGHD6-13*01_IGHJ4*01 & B3_IGKJ1*01

Fab[nM]	1000	500	250	125	62.5	31.3	15.6	7.8
ErbB2/Fc	8731	10241	11026	12956	13124	13911	14791	13220
EGF R/Fc	2236	1468	1138	860	602	447	346	379
HGF R/Fc	2109	1371	1221	778	578	299	293	282
Notch-1/Fc	2267	1975	1241	802	536	563	418	486
CD44/Fc	1966	1685	1175	764	591	439	473	409
IGF-1 sR	1667	1334	993	654	491	385	349	353
P-Cadherin/Fc	4495	3447	2784	1481	1173	1105	971	695
EPO R/Fc	8594	10305	8535	9237	7749	7878	8357	6765
DLL4	2785	2319	1560	912	715	528	525	407
Blank	1133	680	590	403	268	250	294	316

Example 14

VH3-23 Heavy Chain Library

In this example, a library of 690 different VH3-23 containing heavy chains was generated using standard molecular biology protocols. Library diversity was generated by 1) use of 6 different J_H segments; 2) including the DIRECT sequence and INVERTED sequence (or reverse complement) of each D_H segment; and 3) translating each DIRECT and

INVERTED D_H segment in all 3 reading frames. This resulted in the initial generation of six pF-VH3-23-IGHJ plasmids and115 different D_H segments. Simultaneous cloning of each individual D_H segment into each pF-VH3-23-IGHJ plasmid resulted in the 690 member heavy chain library. The library was then transformed with various previously generated light chains (see Example 8) to generate a 3012 member Fab library.

A. Generation of pF-VH3-23-IGHJ1 to pF-VH3-23-IGHJ6 Plasmids

In this example, 6 plasmids, each encoding the VH3-23 V_H segment and one of six J_H segments, were generated. The plasmids were modified such that BsaI sites were incorporated to 1) allow the cloning of individual J_H segments (see Table 35); and 2) subsequently allow the cloning of any individual D_H segment (see Table 37). To this end, Plasmid A (SEQ ID NO:1) and V_H segment VH3-23R (SEQ ID NO:2050) were first modified to remove internal BsaI sites (SEQ ID NO:3719). Subsequently, VH3-23R was further modified to add two BsaI sites, including 1) at the 3' end of the VH3-23 V_H segment; and 2) at the 5' end of the nucleotides encoding framework region 4 (amino acids WGQGTLVTVSSAS of SEQ ID NOS:3456-3461, see Table 35 below) of the J_H segment. VH3-23R (SEQ ID NO:2050) was then synthesized using standard DNA synthesis protocols. VH3-23R was digested with NcoI (SEQ ID NO:977) and NheI (SEQ ID NO:978) and ligated into the modified Plasmid A creating plasmid pF-VH3-23R (SEQ ID NO:2051).

A series of forward and reverse oligos (see Table 36, below) encoding segments IGHJ1-IGHJ6 (see Table 35, and SEQ ID NOS:3450-3455 and SEQ ID NOS:3456-3461) were generated by standard DNA synthesis protocols. Pairs of oligos (encoding a particular IGHJ segment) were digested with BsaI and ligated into similarly digested plasmid pF-VH3-23R (SEQ ID NO:2051), thereby generating 6 new plasmids: pF-VH3-23-IGHJ1 (SEQ ID NO:2064), pF-VH3-23-IGHJ2 (SEQ ID NO:2065), pF-VH3-23-IGHJ3 (SEQ ID NO:2066), pF-VH3-23-IGHJ4 (SEQ ID NO:2067), pF-VH3-23-IGHJ5 (SEQ ID NO:2068), and pF-VH3-23-IGHJ6 (SEQ ID NO:2069). For each of the new plasmids, this resulted in the removal of the BsaI site at the 5' end of the nucleotides encoding framework region 4 and the generation of a new BsaI site at the 5' end of the J_H segment to allow subsequent cloning of a single D_H segment into all six vectors simultaneously thereby creating six different genes per each D_H segment.

Table 35. IGHJ1 to IGHJ6 Segments

Segment	Nucleotide Sequence
IGHJ1 (SEQ ID NO:3450)	GCT GAA TAC TTC CAG CAC TGG GGC CAA GGA ACC CTG GTC ACC GTC TCC TCA G
IGHJ2 (SEQ ID NO:3451)	C TAC TGG TAC TTC GAT TCC TGG GGC CAA GGA ACC CTG GTC ACC GTC TCC TCA G

IGHJ3 (SEQ ID NO:3452)	T GCT TTT GAT GTC TGG GGC CAA GGA ACC CTG GTC ACC GTC TCC TCA G
IGHJ4 (SEQ ID NO:3453)	AC TAC TTT GAC TAC TGG GGC CAA GGA ACC CTG GTC ACC GTC TCC TCA G
IGHJ5 (SEQ ID NO:3454)	AC AAC TGG TTC GAC TAC TGG GGC CAA GGA ACC CTG GTC ACC GTC TCC TCA G
IGHJ6 (SEQ ID NO:3455)	AT TAC TAC TAC TAC TAC GGT ATG GAC GTC TGG GGC CAA GGA ACC CTG GTC ACC GTC TCC TCA G
Segment	**Protein Sequence**
IGHJ1 (SEQ ID NO:3456)	AEYFQHWGQGTLVTVSSAS
IGHJ2 (SEQ ID NO:3457)	YWYFDSWGQGTLVTVSSAS
IGHJ3 (SEQ ID NO:3458)	AFDVWGQGTLVTVSSAS
IGHJ4 (SEQ ID NO:3459)	YFDYWGQGTLVTVSSAS
IGHJ5 (SEQ ID NO:3460)	NWFDYWGQGTLVTVSSAS
IGHJ6 (SEQ ID NO:3461)	YYYYYGMDVWGQGTLVTVSSAS

Table 36. Oligos used to generate J1 to J6 plasmids

Oligo	Nucleotide Sequence
J1_F (SEQ ID NO:2052)	CGAAAGAGACCTACTATGGTTCGGGTCTCTCCTACGCTGAATACTTCCAG CACT
J1_R (SEQ ID NO:2053)	CCCCAGTGCTGGAAGTATTCAGCGTAGGAGAGACCCGAACCATAGTAGGT CTCT
J2_F (SEQ ID NO:2054)	CGAAAGAGACCTACTATGGTTCGGGTCTCTCCTACTACTGGTACTTCGAT TCCT
J2_R (SEQ ID NO:2055)	CCCCAGGAATCGAAGTACCAGTAGTAGGAGAGACCCGAACCATAGTAGGT CTCT
J3_F (SEQ ID NO:2056)	CGAAAGAGACCTACTATGGTTCGGGTCTCTCCTATGCTTTTGATGTCT
J3_R (SEQ ID NO:2057)	CCCCAGACATCAAAAGCATAGGAGAGACCCGAACCATAGTAGGTCTCT
J4_F (SEQ ID NO:2058)	CGAAAGAGACCTACTATGGTTCGGGTCTCTCCTACTACTTTGACTACT
J4_R (SEQ ID NO:2059)	CCCCAGTAGTCAAAGTAGTAGGAGAGACCCGAACCATAGTAGGTCTCT
J5_F (SEQ ID NO:2060)	CGAAAGAGACCTACTATGGTTCGGGTCTCTCCTACAACTGGTTCGACTAC T
J5_R (SEQ ID NO:2061)	CCCCAGGAGTCGAACCAGTTGTAGGAGAGACCCGAACCATAGTAGGTCTC T
J6_F (SEQ ID NO:2062)	CGAAAGAGACCTACTATGGTTCGGGTCTCTCCTATTACTACTACTACTAC GGTATGGACGTCT
J6_R (SEQ ID NO:2063)	CCCCAGACGTCCATACCGTAGTAGTAGTAGTAATAGGAGAGACCCGAACC ATAGTAGGTCTCT

B. Generation and cloning of modified D_H oligos into pF-VH3-23-IGHJ plasmids

In this example, pairs of D_H oligos were generated and cloned into the pF-VH3-23-IGHJ plasmids thereby generating 690 new VH3-23 heavy chains as follows. Twenty seven (27) D_H segments (see Table 37 below) were selected for cloning into each

modified pF-VH3-23-IGHJ plasmid. Library diversity in the CDR3 region was generated by 1) including the DIRECT sequence and INVERTED sequence (or reverse complement) of each D_H segment; and 2) translating each DIRECT and INVERTED D_H segment in all 3 reading frames. If the translation of a reading frame for any given D_H segment resulted in a stop codon, that particular sequence and reading frame were excluded from the library. Table 37 below indicates the open reading frames for each particular D_H segment that were included in the library, thereby resulting in 115 different D_H segments.

Table 37. D_H segments included in heavy chain library

Number	D segment	DIRECT (SEQ ID NO)	Reading Frames	INVERTED (SEQ ID NO)	Reading Frames
1	IGHD1-1*01	239	1, 2, 3	3462	1, 2, 3
2	IGHD1-7*01	243	1, 3	3463	1, 3
3	IGHD1-14*01	240	1, 3	3464	1, 2, 3
4	IGHD1-20*01	241	1, 3	3465	1, 2, 3
5	IGHD1-26*01	242	1, 3	3466	1, 3
6	IGHD2-2*01	245	2, 3	3467	1, 3
7	IGHD2-8*01	250	2, 3	3468	1
8	IGHD2-15*01	244	2, 3	3469	1, 3
9	IGHD2-21*01	248	2, 3	3470	1, 3
10	IGHD3-3*01	258	1, 2, 3	3471	1, 3
11	IGHD3-9*01	259	2	3472	1, 3
12	IGHD3-10*01	252	2, 3	3473	1, 3
13	IGHD3-16*01	254	2, 3	3474	1, 3
14	IGHD3-22*01	256	2, 3	3475	1, 3
15	IGHD4-4*01	263	2, 3	3476	1, 3
16	IGHD4-11*01	260	2, 3	3477	1, 3
17	IGHD4-17*01	261	2, 3	3478	1, 3
18	IGHD4-23*01	262	2, 3	3479	1, 3
19	IGHD5-5*01	267	1, 2, 3	3480	1, 3
20	IGHD5-12*01	264	1, 3	3481	1, 3
21	IGHD5-18*01	265	1, 2, 3	3482	1, 3
22	IGHD5-24*01	266	1, 3	3483	1, 3
23	IGHD6-6*01	271	1, 2	3484	1, 2, 3
24	IGHD6-13*01	268	1, 2	3485	1, 2, 3
25	IGHD6-19*01	269	1, 2	3486	1, 2, 3
26	IGHD6-25*01	270	1, 2	3487	1, 3
27	IGHD7-27*01	272	1, 3	3488	1, 2

The following rules (see Table 38) were used to design pairs of D oligos for cloning into the six different vectors to ensure that the resulting heavy chain sequences are in frame. The rules were applied to both the direct and inverted D_H segments. In order to facilite cloning into the BsaI sites of the pF-VH3-23-IGHJ plasmids, the following nucleotides were added to the D_H segment oligonucleotides:

DIRECT 5' End: CGAAA;

DIRECT 3' End: T;

INDIRECT 5' End: CGAAA;

INDIRECT 3' End: T.

The resulting oligos for each particular D_H segment are listed in Tables 39-40 below. The nucleotides added to facilite cloning are in lower case letters. The nucleotides encoding the D_H segment are in upper case letters. The oligos were synthesized by standard DNA synthesis technology. Pairs of oligos (encoding a particular D_H segment) were digested with BsaI and ligated into similarly digested plasmids pF-VH3-23-IGHJ1 to pF-VH3-23-IGHJ6 thereby generating a VH3-23 library of 690 members, listed in Table 41 below. The VH3-23 heavy chain library was co-transformed with various light chains (as described in Example 8) creating a Fab library of 3012 members.

Table 38. Rules for generation of D_H segment oligos

Frame	No. of nucleotides	Manipulation
1	3N	NONE
1	3N+1	Remove nucleotide at 3' end
1	3N+2	Add G to 3' end
2	3N	Remove nucleotide at 5' end, add G to 3' end
2	3N+1	Remove nucleotide at 5' end
2	3N+2	Remove nucleotide at 5' end, add GG to 3' end
3	3N	Add G to 5' end, remove nucleotide at 3' end
3	3N+1	Add G to 5' end, remove 2 nucleotides at 3' end
3	3N+2	Add G to 5' end

Table 39. Direct D_H segment oligos

D segment	Forward	SEQ ID NO	Reverse	SEQ ID NO
1_IGHD1-1*01	cgaaaGGTACAACTGGAACGACGt	3489	taggaCGTCGTTCCAGTTGTACCt	3490
2_IGHD1-1*01	cgaaaGTACAACTGGAACGACGGt	3491	taggaCCGTCGTTCCAGTTGTACt	3492
3_IGHD1-1*01	cgaaaGGGTACAACTGGAACGACt	3493	taggaGTCGTTCCAGTTGTACCCt	3494
1_IGHD1-7*01	cgaaaGGTATAACTGGAACTACGt	3495	taggaCGTAGTTCCAGTTATACCt	3496
3_IGHD1-7*01	cgaaaGGGTATAACTGGAACTACt	3497	taggaGTAGTTCCAGTTATACCCt	3498
1_IGHD1-14*01	cgaaaGGTATAACCGGAACCACGt	3499	taggaCGTGGTTCCGGTTATACCt	3500
3_IGHD1-14*01	cgaaaGGGTATAACCGGAACCACt	3501	taggaGTGGTTCCGGTTATACCCt	3502
1_IGHD1-20*01	cgaaaGGTATAACTGGAACGACGt	3503	taggaCGTCGTTCCAGTTATACCt	3504
3_IGHD1-20*01	cgaaaGGGTATAACTGGAACGACt	3505	taggaGTCGTTCCAGTTATACCCt	3506
1_IGHD1-26*01	cgaaaGGTATAGTGGGAGCTACTACGt	3507	taggaCGTAGTAGCTCCCACTATACCt	3508

3_IGHD1-26*01	cgaaaGGGTATAGTGGGAGCTACTACt	3509	taggaGTAGTAGCTCCCACTATACCCt	3510
2_IGHD2-2*01	cgaaaGGATATTGTAGTAGTACCAGCTGCTATGCCt	3511	taggaGGCATAGCAGCTGGTACTACTACAATATCCt	3512
3_IGHD2-2*01	cgaaaGAGGATATTGTAGTAGTACCAGCTGCTATGt	3513	taggaCATAGCAGCTGGTACTACTACAATATCCTCt	3514
2_IGHD2-8*01	cgaaaGGATATTGTACTAATGGTGTATGCTATACCt	3515	taggaGGTATAGCATACACCATTAGTACAATATCCt	3516
3_IGHD2-8*01	cgaaaGAGGATATTGTACTAATGGTGTATGCTATAt	3517	taggaTATAGCATACACCATTAGTACAATATCCTCt	3518
2_IGHD2-15*01	cgaaaGGATATTGTAGTGGTGGTAGCTGCTACTCCt	3519	taggaGGAGTAGCAGCTACCACCACTACAATATCCt	3520
3_IGHD2-15*01	cgaaaGAGGATATTGTAGTGGTGGTAGCTGCTACTt	3521	taggaAGTAGCAGCTACCACCACTACAATATCCTCt	3522
2_IGHD2-21*01	cgaaaGCATATTGTGGTGGTGATTGCTATTCCt	3523	taggaGGAATAGCAATCACCACCACAATATGCt	3524
3_IGHD2-21*01	cgaaaGAGCATATTGTGGTGGTGATTGCTATTt	3525	taggaAATAGCAATCACCACCACAATATGCTCt	3526
1_IGHD3-3*01	cgaaaGTATTACGATTTTTGGAGTGGTTATTATACt	3527	taggaGTATAATAACCACTCCAAAAATCGTAATACt	3528
2_IGHD3-3*01	cgaaaTATTACGATTTTTGGAGTGGTTATTATACCt	3529	taggaGGTATAATAACCACTCCAAAAATCGTAATAt	3530
3_IGHD3-3*01	cgaaaGGTATTACGATTTTTGGAGTGGTTATTATAt	3531	taggaTATAATAACCACTCCAAAAATCGTAATACCt	3532
2_IGHD3-9*01	cgaaaTATTACGATATTTTGACTGGTTATTATAACt	3533	taggaGTTATAATAACCAGTCAAAATATCGTAATAt	3534
2_IGHD3-10*01	cgaaaTATTACTATGGTTCGGGGAGTTATTATAACt	3535	taggaGTTATAATAACTCCCCGAACCATAGTAATAt	3536
3_IGHD3-10*01	cgaaaGGTATTACTATGGTTCGGGGAGTTATTATAt	3537	taggaTATAATAACTCCCCGAACCATAGTAATACCt	3538
2_IGHD3-16*01	cgaaaTATTATGATTACGTTTGGGGGAGTTATGCTTATACCt	3539	taggaGGTATAAGCATAACTCCCCCAAACGTAATCATAATAt	3540
3_IGHD3-16*01	cgaaaGGTATTATGATTACGTTTGGGGGAGTTATGCTTATAt	3541	taggaTATAAGCATAACTCCCCCAAACGTAATCATAATACCt	3542
2_IGHD3-22*01	cgaaaTATTACTATGATAGTAGTGGTTATTACTACt	3543	taggaGTAGTAATAACCACTACTATCATAGTAATAt	3544
3_IGHD3-22*01	cgaaaGGTATTACTATGATAGTAGTGGTTATTACTt	3545	taggaAGTAATAACCACTACTATCATAGTAATACCt	3546
2_IGHD4-4*01 (1)	cgaaaGACTACAGTAACTACt	3547	taggaGTAGTTACTGTAGTCt	3548
3_IGHD4-4*01 (1)	cgaaaGTGACTACAGTAACTt	3549	taggaAGTTACTGTAGTCAC t	3550
2_IGHD4-11*01 (1)	cgaaaGACTACAGTAACTACt	3551	taggaGTAGTTACTGTAGTCt	3552
3_IGHD4-11*01 (1)	cgaaaGTGACTACAGTAACTt	3553	taggaAGTTACTGTAGTCAC t	3554
2_IGHD4-17*01	cgaaaGACTACGGTGACTACt	3555	taggaGTAGTCACCGTAGTCt	3556
3_IGHD4-17*01	cgaaaGTGACTACGGTGACTt	3557	taggaAGTCACCGTAGTCAC t	3558
2_IGHD4-23*01	cgaaaGACTACGGTGGTAACTCCt	3559	taggaGGAGTTACCACCGTAGTCt	3560
3_IGHD4-23*01	cgaaaGTGACTACGGTGGTAACTt	3561	taggaAGTTACCACCGTAGTCACt	3562

1_IGHD5-5*01 (2)	cgaaaGTGGATACAGCTATGGTTACGt	3563	taggaCGTAACCATAGCTGTATCCACt	3564
2_IGHD5-5*01 (2)	cgaaaTGGATACAGCTATGGTTACGGt	3565	taggaCCGTAACCATAGCTGTATCCAt	3566
3_IGHD5-5*01 (2)	cgaaaGGTGGATACAGCTATGGTTACt	3567	taggaGTAACCATAGCTGTATCCACCt	3568
1_IGHD5-12*01	cgaaaGTGGATATAGTGGCTACGATTACGt	3569	taggaCGTAATCGTAGCCACTATATCCACt	3570
3_IGHD5-12*01	cgaaaGGTGGATATAGTGGCTACGATTACt	3571	taggaGTAATCGTAGCCACTATATCCACCt	3572
1_IGHD5-18*01 (2)	cgaaaGTGGATACAGCTATGGTTACGt	3573	taggaCGTAACCATAGCTGTATCCACt	3574
2_IGHD5-18*01 (2)	cgaaaTGGATACAGCTATGGTTACGGt	3575	taggaCCGTAACCATAGCTGTATCCAt	3576
3_IGHD5-18*01 (2)	cgaaaGGTGGATACAGCTATGGTTACt	3577	taggaGTAACCATAGCTGTATCCACCt	3578
1_IGHD5-24*01	cgaaaGTAGAGATGGCTACAATTACGt	3579	taggaCGTAATTGTAGCCATCTCTACt	3580
3_IGHD5-24*01	cgaaaGGTAGAGATGGCTACAATTACt	3581	taggaGTAATTGTAGCCATCTCTACCt	3582
1_IGHD6-6*01	cgaaaGAGTATAGCAGCTCGTCCt	3583	taggaGGACGAGCTGCTATACTCt	3584
2_IGHD6-6*01	cgaaaAGTATAGCAGCTCGTCCGt	3585	taggaCGGACGAGCTGCTATACTt	3586
1_IGHD6-13*01	cgaaaGGGTATAGCAGCAGCTGGTACt	3587	taggaGTACCAGCTGCTGCTATACCCt	3588
2_IGHD6-13*01	cgaaaGGTATAGCAGCAGCTGGTACGt	3589	taggaCGTACCAGCTGCTGCTATACCt	3590
1_IGHD6-19*01	cgaaaGGGTATAGCAGTGGCTGGTACt	3591	taggaGTACCAGCCACTGCTATACCCt	3592
2_IGHD6-19*01	cgaaaGGTATAGCAGTGGCTGGTACGt	3593	taggaCGTACCAGCCACTGCTATACCt	3594
1_IGHD6-25*01	cgaaaGGGTATAGCAGCGGCTACt	3595	taggaGTAGCCGCTGCTATACCCt	3596
2_IGHD6-25*01	cgaaaGGTATAGCAGCGGCTACGt	3597	taggaCGTAGCCGCTGCTATACCt	3598
1_IGHD7-27*01	cgaaaCTAACTGGGGAGt	3599	taggaCTCCCCAGTTAGt	3600
3_IGHD7-27*01	cgaaaGCTAACTGGGGAt	3601	taggaTCCCCAGTTAGCt	3602

Table 40. Inverted D_H segment oligos

D segment	Forward	SEQ ID NO	Reverse	SEQ ID NO
1'_IGHD1-1*01	cgaaaGTCGTTCCAGTTGTACCGt	3603	taggaCGGTACAACTGGAACGACt	3604
2'_IGHD1-1*01	cgaaaTCGTTCCAGTTGTACCGGt	3605	taggaCCGGTACAACTGGAACGAt	3606
3'_IGHD1-1*01	cgaaaGGTCGTTCCAGTTGTACCt	3607	taggaGGTACAACTGGAACGACCt	3608
1'_IGHD1-7*01	cgaaaGTAGTTCCAGTTATACCGt	3609	taggaCGGTATAACTGGAACTACt	3610
3'_IGHD1-7*01	cgaaaGGTAGTTCCAGTTATACCt	3611	taggaGGTATAACTGGAACTACCt	3612
1'_IGHD1-14*01	cgaaaGTGGTTCCGGTTATACCGt	3613	taggaCGGTATAACCGGAACCACt	3614

2' IGHD1-14*01	cgaaaTGGTTCCGGTTATACCGGt	3615	taggaCCGGTATAACCGGAACCAt	3616
3' IGHD1-14*01	cgaaaGGTGGTTCCGGTTATACCt	3617	taggaGGTATAACCGGAACCACCt	3618
1' IGHD1-20*01	cgaaaGTCGTTCCAGTTATACCGt	3619	taggaCGGTATAACTGGAACGACt	3620
2' IGHD1-20*01	cgaaaTCGTTCCAGTTATACCGGt	3621	taggaCCGGTATAACTGGAACGAt	3622
3' IGHD1-20*01	cgaaaGGTCGTTCCAGTTATACCt	3623	taggaGGTATAACTGGAACGACCt	3624
1' IGHD1-26*01	cgaaaGTAGTAGCTCCCACTATACCGt	3625	taggaCGGTATAGTGGGAGCTACTACt	3626
3' IGHD1-26*01	cgaaaGGTAGTAGCTCCCACTATACCt	3627	taggaGGTATAGTGGGAGCTACTACCt	3628
1' IGHD2-2*01	cgaaaGGCATAGCAGCTGGTACTACTACAATATCCt	3629	taggaGGATATTGTAGTAGTACCAGCTGCTATGCCt	3630
3' IGHD2-2*01	cgaaaGGGCATAGCAGCTGGTACTACTACAATATCt	3631	taggaGATATTGTAGTAGTACCAGCTGCTATGCCCt	3632
1' IGHD2-8*01	cgaaaGGTATAGCATACACCATTAGTACAATATCCt	3633	taggaGGATATTGTACTAATGGTGTATGCTATACCt	3634
1' IGHD2-15*01	cgaaaGGAGTAGCAGCTACCACCACTACAATATCCt	3635	taggaGGATATTGTAGTGGTGGTAGCTGCTACTCCt	3636
3' IGHD2-15*01	cgaaaGGGAGTAGCAGCTACCACCACTACAATATCt	3637	taggaGATATTGTAGTGGTGGTAGCTGCTACTCCCt	3638
1' IGHD2-21*01	cgaaaGGAATAGCAATCACCACCACAATATGCt	3639	taggaGCATATTGTGGTGGTGATTGCTATTCCt	3640
3' IGHD2-21*01	cgaaaGGGAATAGCAATCACCACCACAATATGt	3641	taggaCATATTGTGGTGGTGATTGCTATTCCCt	3642
1' IGHD3-3*01	cgaaaGGTATAATAACCACTCCAAAAATCGTAATAt	3643	taggaTATTACGATTTTTGGAGTGGTTATTATACCt	3644
3' IGHD3-3*01	cgaaaGGGTATAATAACCACTCCAAAAATCGTAATt	3645	taggaATTACGATTTTTGGAGTGGTTATTATACCCt	3646
1' IGHD3-9*01	cgaaaGTTATAATAACCAGTCAAAATATCGTAATAt	3647	taggaTATTACGATATTTTGACTGGTTATTATAACt	3648
3' IGHD3-9*01	cgaaaGGTTATAATAACCAGTCAAAATATCGTAATt	3649	taggaATTACGATATTTTGACTGGTTATTATAACCt	3650
1' IGHD3-10*01	cgaaaGTTATAATAACTCCCCGAACCATAGTAATAt	3651	taggaTATTACTATGGTTCGGGGAGTTATTATAACt	3652
3' IGHD3-10*01	cgaaaGGTTATAATAACTCCCCGAACCATAGTAATt	3653	taggaATTACTATGGTTCGGGGAGTTATTATAACCt	3654
1' IGHD3-16*01	cgaaaGGTATAAGCATACTCCCCCAAACGTAATCATAATAt	3655	taggaTATTATGATTACGTTTGGGGGAGTTATGCTTATACCt	3656
3' IGHD3-16*01	cgaaaGGGTATAAGCATAACTCCCCCAAACGTAATCATAATt	3657	taggaATTATGATTACGTTTGGGGGAGTTATGCTTATACCCt	3658
1' IGHD3-22*01	cgaaaGTAGTAATAACCACTACTATCATAGTAATAt	3659	taggaTATTACTATGATAGTAGTGGTTATTACTACt	3660
1' IGHD4-4*01 (1)	cgaaaGTAGTTACTGTAGTCt	3661	taggaGACTACAGTAACTACt	3662
3' IGHD4-4*01 (1)	cgaaaGGTAGTTACTGTAGTt	3663	taggaACTACAGTAACTACCt	3664
1' IGHD4-11*01 (1)	cgaaaGTAGTTACTGTAGTCt	3665	taggaGACTACAGTAACTACt	3666
3' IGHD4-11*01 (1)	cgaaaGGTAGTTACTGTAGTt	3667	taggaACTACAGTAACTACCt	3668

1'_IGHD4-17*01	cgaaaGTAGTCACCGTAGTCt	3669	taggaGACTACGGTGACTACt	3670
3'_IGHD4-17*01	cgaaaGGTAGTCACCGTAGTt	3671	taggaACTACGGTGACTACCt	3672
1'_IGHD4-23*01	cgaaaGGAGTTACCACCGTAGTCt	3673	taggaGACTACGGTGGTAACTCCt	3674
3'_IGHD4-23*01	cgaaaGGGAGTTACCACCGTAGTt	3675	taggaACTACGGTGGTAACTCCCt	3676
1'_IGHD5-5*01 (2)	cgaaaGTAACCATAGCTGTATCCACGt	3677	taggaCGTGGATACAGCTATGGTTACt	3678
3'_IGHD5-5*01 (2)	cgaaaGGTAACCATAGCTGTATCCACt	3679	taggaGTGGATACAGCTATGGTTACCt	3680
1'_IGHD5-12*01	cgaaaGTAATCGTAGCCACTATATCCACGt	3681	taggaCGTGGATATAGTGGCTACGATTACt	3682
3'_IGHD5-12*01	cgaaaGGTAATCGTAGCCACTATATCCACt	3683	taggaGTGGATATAGTGGCTACGATTACCt	3684
1'_IGHD5-18*01 (2)	cgaaaGTAACCATAGCTGTATCCACGt	3685	taggaCGTGGATACAGCTATGGTTACt	3686
3'_IGHD5-18*01 (2)	cgaaaGGTAACCATAGCTGTATCCACt	3687	taggaGTGGATACAGCTATGGTTACCt	3688
1'_IGHD5-24*01	cgaaaGTAATTGTAGCCATCTCTACGt	3689	taggaCGTAGAGATGGCTACAATTACt	3690
3'_IGHD5-24*01	cgaaaGGTAATTGTAGCCATCTCTACt	3691	taggaGTAGAGATGGCTACAATTACCt	3692
1'_IGHD6-6*01	cgaaaGGACGAGCTGCTATACTCt	3693	taggaGAGTATAGCAGCTCGTCCt	3694
2'_IGHD6-6*01	cgaaaGACGAGCTGCTATACTCGt	3695	taggaCGAGTATAGCAGCTCGTCt	3696
3'_IGHD6-6*01	cgaaaGGGACGAGCTGCTATACTt	3697	taggaAGTATAGCAGCTCGTCCCt	3698
1'_IGHD6-13*01	cgaaaGTACCAGCTGCTGCTATACCCt	3699	taggaGGGTATAGCAGCAGCTGGTACt	3700
2'_IGHD6-13*01	cgaaaTACCAGCTGCTGCTATACCCGt	3701	taggaCGGGTATAGCAGCAGCTGGTAt	3702
3'_IGHD6-13*01	cgaaaGGTACCAGCTGCTGCTATACCt	3703	taggaGGTATAGCAGCAGCTGGTACCt	3704
1'_IGHD6-19*01	cgaaaGTACCAGCCACTGCTATACCCt	3705	taggaGGGTATAGCAGTGGCTGGTACt	3706
2'_IGHD6-19*01	cgaaaTACCAGCCACTGCTATACCCGt	3707	taggaCGGGTATAGCAGTGGCTGGTAt	3708
3'_IGHD6-19*01	cgaaaGGTACCAGCCACTGCTATACCt	3709	taggaGGTATAGCAGTGGCTGGTACCt	3710
1'_IGHD6-25*01	cgaaaGTAGCCGCTGCTATACCCt	3711	taggaGGGTATAGCAGCGGCTACt	3712
3'_IGHD6-25*01	cgaaaGGTAGCCGCTGCTATACCt	3713	taggaGGTATAGCAGCGGCTACCt	3714
1'_IGHD7-27*01	cgaaaTCCCCAGTTAGGt	3715	taggaCCTAACTGGGGAt	3716
2'_IGHD7-27*01	cgaaaCCCCAGTTAGGGt	3717	taggaCCCTAACTGGGGt	3718

Table 41. VH3-23 Library

No.	Heavy Chain	Nuc. SEQ ID NO	Prot. SEQ ID NO
1	>gi|Fabrus|VH3-23_IGHD1-1*01>1_IGHJ1*01	2070	2760

2	>gi|Fabrus|VH3-23_IGHD1-1*01>2_IGHJ1*01	2071	2761
3	>gi|Fabrus|VH3-23_IGHD1-1*01>3_IGHJ1*01	2072	2762
4	>gi|Fabrus|VH3-23_IGHD1-7*01>1_IGHJ1*01	2073	2763
5	>gi|Fabrus|VH3-23_IGHD1-7*01>3_IGHJ1*01	2074	2764
6	>gi|Fabrus|VH3-23_IGHD1-14*01>1_IGHJ1*01	2075	2765
7	>gi|Fabrus|VH3-23_IGHD1-14*01>3_IGHJ1*01	2076	2766
8	>gi|Fabrus|VH3-23_IGHD1-20*01>1_IGHJ1*01	2077	2767
9	>gi|Fabrus|VH3-23_IGHD1-20*01>3_IGHJ1*01	2078	2768
10	>gi|Fabrus|VH3-23_IGHD1-26*01>1_IGHJ1*01	2079	2769
11	>gi|Fabrus|VH3-23_IGHD1-26*01>3_IGHJ1*01	2080	2770
12	>gi|Fabrus|VH3-23_IGHD2-2*01>2_IGHJ1*01	2081	2771
13	>gi|Fabrus|VH3-23_IGHD2-2*01>3_IGHJ1*01	2082	2772
14	>gi|Fabrus|VH3-23_IGHD2-8*01>2_IGHJ1*01	2083	2773
15	>gi|Fabrus|VH3-23_IGHD2-8*01>3_IGHJ1*01	2084	2774
16	>gi|Fabrus|VH3-23_IGHD2-15*01>2_IGHJ1*01	2085	2775
17	>gi|Fabrus|VH3-23_IGHD2-15*01>3_IGHJ1*01	2086	2776
18	>gi|Fabrus|VH3-23_IGHD2-21*01>2_IGHJ1*01	2087	2777
19	>gi|Fabrus|VH3-23_IGHD2-21*01>3_IGHJ1*01	2088	2778
20	>gi|Fabrus|VH3-23_IGHD3-3*01>1_IGHJ1*01	2089	2779
21	>gi|Fabrus|VH3-23_IGHD3-3*01>2_IGHJ1*01	2090	2780
22	>gi|Fabrus|VH3-23_IGHD3-3*01>3_IGHJ1*01	2091	2781
23	>gi|Fabrus|VH3-23_IGHD3-9*01>2_IGHJ1*01	2092	2782
24	>gi|Fabrus|VH3-23_IGHD3-10*01>2_IGHJ1*01	2093	2783
25	>gi|Fabrus|VH3-23_IGHD3-10*01>3_IGHJ1*01	2094	2784
26	>gi|Fabrus|VH3-23_IGHD3-16*01>2_IGHJ1*01	2095	2785
27	>gi|Fabrus|VH3-23_IGHD3-16*01>3_IGHJ1*01	2096	2786
28	>gi|Fabrus|VH3-23_IGHD3-22*01>2_IGHJ1*01	2097	2787
29	>gi|Fabrus|VH3-23_IGHD3-22*01>3_IGHJ1*01	2098	2788
30	>gi|Fabrus|VH3-23_IGHD4-4*01(1)>2_IGHJ1*01	2099	2789
31	>gi|Fabrus|VH3-23_IGHD4-4*01(1)>3_IGHJ1*01	2100	2790
32	>gi|Fabrus|VH3-23_IGHD4-11*01(1)>2_IGHJ1*01	2101	2791
33	>gi|Fabrus|VH3-23_IGHD4-11*01(1)>3_IGHJ1*01	2102	2792
34	>gi|Fabrus|VH3-23_IGHD4-17*01>2_IGHJ1*01	2103	2793
35	>gi|Fabrus|VH3-23_IGHD4-17*01>3_IGHJ1*01	2104	2794
36	>gi|Fabrus|VH3-23_IGHD4-23*01>2_IGHJ1*01	2105	2795
37	>gi|Fabrus|VH3-23_IGHD4-23*01>3_IGHJ1*01	2106	2796
38	>gi|Fabrus|VH3-23_IGHD5-5*01(2)>1_IGHJ1*01	2107	2797
39	>gi|Fabrus|VH3-23_IGHD5-5*01(2)>2_IGHJ1*01	2108	2798
40	>gi|Fabrus|VH3-23_IGHD5-5*01(2)>3_IGHJ1*01	2109	2799
41	>gi|Fabrus|VH3-23_IGHD5-12*01>1_IGHJ1*01	2110	2800
42	>gi|Fabrus|VH3-23_IGHD5-12*01>3_IGHJ1*01	2111	2801
43	>gi|Fabrus|VH3-23_IGHD5-18*01(2)>1_IGHJ1*01	2112	2802
44	>gi|Fabrus|VH3-23_IGHD5-18*01(2)>2_IGHJ1*01	2113	2803
45	>gi|Fabrus|VH3-23_IGHD5-18*01(2)>3_IGHJ1*01	2114	2804
46	>gi|Fabrus|VH3-23_IGHD5-24*01>1_IGHJ1*01	2115	2805
47	>gi|Fabrus|VH3-23_IGHD5-24*01>3_IGHJ1*01	2116	2806
48	>gi|Fabrus|VH3-23_IGHD6-6*01>1_IGHJ1*01	2117	2807
49	>gi|Fabrus|VH3-23_IGHD6-6*01>2_IGHJ1*01	2118	2808
50	>gi|Fabrus|VH3-23_IGHD6-13*01>1_IGHJ1*01	2119	2809
51	>gi|Fabrus|VH3-23_IGHD6-13*01>2_IGHJ1*01	2120	2810
52	>gi|Fabrus|VH3-23_IGHD6-19*01>1_IGHJ1*01	2121	2811
53	>gi|Fabrus|VH3-23_IGHD6-19*01>2_IGHJ1*01	2122	2812
54	>gi|Fabrus|VH3-23_IGHD6-25*01>1_IGHJ1*01	2123	2813
55	>gi|Fabrus|VH3-23_IGHD6-25*01>2_IGHJ1*01	2124	2814

56	>gi|Fabrus|VH3-23_IGHD7-27*01>1_IGHJ1*01	2125	2815
57	>gi|Fabrus|VH3-23_IGHD7-27*01>3_IGHJ1*01	2126	2816
58	>gi|Fabrus|VH3-23_IGHD1-1*01>1'_IGHJ1*01	2127	2817
59	>gi|Fabrus|VH3-23_IGHD1-1*01>2'_IGHJ1*01	2128	2818
60	>gi|Fabrus|VH3-23_IGHD1-1*01>3'_IGHJ1*01	2129	2819
61	>gi|Fabrus|VH3-23_IGHD1-7*01>1'_IGHJ1*01	2130	2820
62	>gi|Fabrus|VH3-23_IGHD1-7*01>3'_IGHJ1*01	2131	2821
63	>gi|Fabrus|VH3-23_IGHD1-14*01>1'_IGHJ1*01	2132	2822
64	>gi|Fabrus|VH3-23_IGHD1-14*01>2'_IGHJ1*01	2133	2823
65	>gi|Fabrus|VH3-23_IGHD1-14*01>3'_IGHJ1*01	2134	2824
66	>gi|Fabrus|VH3-23_IGHD1-20*01>1'_IGHJ1*01	2135	2825
67	>gi|Fabrus|VH3-23_IGHD1-20*01>2'_IGHJ1*01	2136	2826
68	>gi|Fabrus|VH3-23_IGHD1-20*01>3'_IGHJ1*01	2137	2827
69	>gi|Fabrus|VH3-23_IGHD1-26*01>1'_IGHJ1*01	2138	2828
70	>gi|Fabrus|VH3-23_IGHD1-26*01>3'_IGHJ1*01	2139	2829
71	>gi|Fabrus|VH3-23_IGHD2-2*01>1'_IGHJ1*01	2140	2830
72	>gi|Fabrus|VH3-23_IGHD2-2*01>3'_IGHJ1*01	2141	2831
73	>gi|Fabrus|VH3-23_IGHD2-8*01>1'_IGHJ1*01	2142	2832
74	>gi|Fabrus|VH3-23_IGHD2-15*01>1'_IGHJ1*01	2143	2833
75	>gi|Fabrus|VH3-23_IGHD2-15*01>3'_IGHJ1*01	2144	2834
76	>gi|Fabrus|VH3-23_IGHD2-21*01>1'_IGHJ1*01	2145	2835
77	>gi|Fabrus|VH3-23_IGHD2-21*01>3'_IGHJ1*01	2146	2836
78	>gi|Fabrus|VH3-23_IGHD3-3*01>1'_IGHJ1*01	2147	2837
79	>gi|Fabrus|VH3-23_IGHD3-3*01>3'_IGHJ1*01	2148	2838
80	>gi|Fabrus|VH3-23_IGHD3-9*01>1'_IGHJ1*01	2149	2839
81	>gi|Fabrus|VH3-23_IGHD3-9*01>3'_IGHJ1*01	2150	2840
82	>gi|Fabrus|VH3-23_IGHD3-10*01>1'_IGHJ1*01	2151	2841
83	>gi|Fabrus|VH3-23_IGHD3-10*01>3'_IGHJ1*01	2152	2842
84	>gi|Fabrus|VH3-23_IGHD3-16*01>1'_IGHJ1*01	2153	2843
85	>gi|Fabrus|VH3-23_IGHD3-16*01>3'_IGHJ1*01	2154	2844
86	>gi|Fabrus|VH3-23_IGHD3-22*01>1'_IGHJ1*01	2155	2845
87	>gi|Fabrus|VH3-23_IGHD4-4*01(1)>1'_IGHJ1*01	2156	2846
88	>gi|Fabrus|VH3-23_IGHD4-4*01(1)>3'_IGHJ1*01	2157	2847
89	>gi|Fabrus|VH3-23_IGHD4-11*01(1)>1'_IGHJ1*01	2158	2848
90	>gi|Fabrus|VH3-23_IGHD4-11*01(1)>3'_IGHJ1*01	2159	2849
91	>gi|Fabrus|VH3-23_IGHD4-17*01>1'_IGHJ1*01	2160	2850
92	>gi|Fabrus|VH3-23_IGHD4-17*01>3'_IGHJ1*01	2161	2851
93	>gi|Fabrus|VH3-23_IGHD4-23*01>1'_IGHJ1*01	2162	2852
94	>gi|Fabrus|VH3-23_IGHD4-23*01>3'_IGHJ1*01	2163	2853
95	>gi|Fabrus|VH3-23_IGHD5-5*01(2)>1'_IGHJ1*01	2164	2854
96	>gi|Fabrus|VH3-23_IGHD5-5*01(2)>3'_IGHJ1*01	2165	2855
97	>gi|Fabrus|VH3-23_IGHD5-12*01>1'_IGHJ1*01	2166	2856
98	>gi|Fabrus|VH3-23_IGHD5-12*01>3'_IGHJ1*01	2167	2857
99	>gi|Fabrus|VH3-23_IGHD5-18*01(2)>1'_IGHJ1*01	2168	2858
100	>gi|Fabrus|VH3-23_IGHD5-18*01(2)>3'_IGHJ1*01	2169	2859
101	>gi|Fabrus|VH3-23_IGHD5-24*01>1'_IGHJ1*01	2170	2860
102	>gi|Fabrus|VH3-23_IGHD5-24*01>3'_IGHJ1*01	2171	2861
103	>gi|Fabrus|VH3-23_IGHD6-6*01>1'_IGHJ1*01	2172	2862
104	>gi|Fabrus|VH3-23_IGHD6-6*01>2'_IGHJ1*01	2173	2863
105	>gi|Fabrus|VH3-23_IGHD6-6*01>3'_IGHJ1*01	2174	2864
106	>gi|Fabrus|VH3-23_IGHD6-13*01>1'_IGHJ1*01	2175	2865
107	>gi|Fabrus|VH3-23_IGHD6-13*01>2'_IGHJ1*01	2176	2866
108	>gi|Fabrus|VH3-23_IGHD6-13*01>3'_IGHJ1*01	2177	2867
109	>gi|Fabrus|VH3-23_IGHD6-19*01>1'_IGHJ1*01	2178	2868

110	>gi|Fabrus|VH3-23_IGHD6-19*01>2'_IGHJ1*01	2179	2869
111	>gi|Fabrus|VH3-23_IGHD6-19*01>3'_IGHJ1*01	2180	2870
112	>gi|Fabrus|VH3-23_IGHD6-25*01>1'_IGHJ1*01	2181	2871
113	>gi|Fabrus|VH3-23_IGHD6-25*01>3'_IGHJ1*01	2182	2872
114	>gi|Fabrus|VH3-23_IGHD7-27*01>1'_IGHJ1*01	2183	2873
115	>gi|Fabrus|VH3-23_IGHD7-27*01>2'_IGHJ1*01	2184	2874
116	>gi|Fabrus|VH3-23_IGHD1-1*01>1_IGHJ2*01	2185	2875
117	>gi|Fabrus|VH3-23_IGHD1-1*01>2_IGHJ2*01	2186	2876
118	>gi|Fabrus|VH3-23_IGHD1-1*01>3_IGHJ2*01	2187	2877
119	>gi|Fabrus|VH3-23_IGHD1-7*01>1_IGHJ2*01	2188	2878
120	>gi|Fabrus|VH3-23_IGHD1-7*01>3_IGHJ2*01	2189	2879
121	>gi|Fabrus|VH3-23_IGHD1-14*01>1_IGHJ2*01	2190	2880
122	>gi|Fabrus|VH3-23_IGHD1-14*01>3_IGHJ2*01	2191	2881
123	>gi|Fabrus|VH3-23_IGHD1-20*01>1_IGHJ2*01	2192	2882
124	>gi|Fabrus|VH3-23_IGHD1-20*01>3_IGHJ2*01	2193	2883
125	>gi|Fabrus|VH3-23_IGHD1-26*01>1_IGHJ2*01	2194	2884
126	>gi|Fabrus|VH3-23_IGHD1-26*01>3_IGHJ2*01	2195	2885
127	>gi|Fabrus|VH3-23_IGHD2-2*01>2_IGHJ2*01	2196	2886
128	>gi|Fabrus|VH3-23_IGHD2-2*01>3_IGHJ2*01	2197	2887
129	>gi|Fabrus|VH3-23_IGHD2-8*01>2_IGHJ2*01	2198	2888
130	>gi|Fabrus|VH3-23_IGHD2-8*01>3_IGHJ2*01	2199	2889
131	>gi|Fabrus|VH3-23_IGHD2-15*01>2_IGHJ2*01	2200	2890
132	>gi|Fabrus|VH3-23_IGHD2-15*01>3_IGHJ2*01	2201	2891
133	>gi|Fabrus|VH3-23_IGHD2-21*01>2_IGHJ2*01	2202	2892
134	>gi|Fabrus|VH3-23_IGHD2-21*01>3_IGHJ2*01	2203	2893
135	>gi|Fabrus|VH3-23_IGHD3-3*01>1_IGHJ2*01	2204	2894
136	>gi|Fabrus|VH3-23_IGHD3-3*01>2_IGHJ2*01	2205	2895
137	>gi|Fabrus|VH3-23_IGHD3-3*01>3_IGHJ2*01	2206	2896
138	>gi|Fabrus|VH3-23_IGHD3-9*01>2_IGHJ2*01	2207	2897
139	>gi|Fabrus|VH3-23_IGHD3-10*01>2_IGHJ2*01	2208	2898
140	>gi|Fabrus|VH3-23_IGHD3-10*01>3_IGHJ2*01	2209	2899
141	>gi|Fabrus|VH3-23_IGHD3-16*01>2_IGHJ2*01	2210	2900
142	>gi|Fabrus|VH3-23_IGHD3-16*01>3_IGHJ2*01	2211	2901
143	>gi|Fabrus|VH3-23_IGHD3-22*01>2_IGHJ2*01	2212	2902
144	>gi|Fabrus|VH3-23_IGHD3-22*01>3_IGHJ2*01	2213	2903
145	>gi|Fabrus|VH3-23_IGHD4-4*01(1)>2_IGHJ2*01	2214	2904
146	>gi|Fabrus|VH3-23_IGHD4-4*01(1)>3_IGHJ2*01	2215	2905
147	>gi|Fabrus|VH3-23_IGHD4-11*01(1)>2_IGHJ2*01	2216	2906
148	>gi|Fabrus|VH3-23_IGHD4-11*01(1)>3_IGHJ2*01	2217	2907
149	>gi|Fabrus|VH3-23_IGHD4-17*01>2_IGHJ2*01	2218	2908
150	>gi|Fabrus|VH3-23_IGHD4-17*01>3_IGHJ2*01	2219	2909
151	>gi|Fabrus|VH3-23_IGHD4-23*01>2_IGHJ2*01	2220	2910
152	>gi|Fabrus|VH3-23_IGHD4-23*01>3_IGHJ2*01	2221	2911
153	>gi|Fabrus|VH3-23_IGHD5-5*01(2)>1_IGHJ2*01	2222	2912
154	>gi|Fabrus|VH3-23_IGHD5-5*01(2)>2_IGHJ2*01	2223	2913
155	>gi|Fabrus|VH3-23_IGHD5-5*01(2)>3_IGHJ2*01	2224	2914
156	>gi|Fabrus|VH3-23_IGHD5-12*01>1_IGHJ2*01	2225	2915
157	>gi|Fabrus|VH3-23_IGHD5-12*01>3_IGHJ2*01	2226	2916
158	>gi|Fabrus|VH3-23_IGHD5-18*01(2)>1_IGHJ2*01	2227	2917
159	>gi|Fabrus|VH3-23_IGHD5-18*01(2)>2_IGHJ2*01	2228	2918
160	>gi|Fabrus|VH3-23_IGHD5-18*01(2)>3_IGHJ2*01	2229	2919
161	>gi|Fabrus|VH3-23_IGHD5-24*01>1_IGHJ2*01	2230	2920
162	>gi|Fabrus|VH3-23_IGHD5-24*01>3_IGHJ2*01	2231	2921
163	>gi|Fabrus|VH3-23_IGHD6-6*01>1_IGHJ2*01	2232	2922

164	>gi|Fabrus|VH3-23_IGHD6-6*01>2_IGHJ2*01	2233	2923
165	>gi|Fabrus|VH3-23_IGHD6-13*01>1_IGHJ2*01	2234	2924
166	>gi|Fabrus|VH3-23_IGHD6-13*01>2_IGHJ2*01	2235	2925
167	>gi|Fabrus|VH3-23_IGHD6-19*01>1_IGHJ2*01	2236	2926
168	>gi|Fabrus|VH3-23_IGHD6-19*01>2_IGHJ2*01	2237	2927
169	>gi|Fabrus|E06_VH3-23_IGHD6-25*01>1_IGHJ2*01	2238	2928
170	>gi|Fabrus|E07_VH3-23_IGHD6-25*01>2_IGHJ2*01	2239	2929
171	>gi|Fabrus|E08_VH3-23_IGHD7-27*01>1_IGHJ2*01	2240	2930
172	>gi|Fabrus|E09_VH3-23_IGHD7-27*01>3_IGHJ2*01	2241	2931
173	>gi|Fabrus|A01_VH3-23_IGHD1-1*01>1'_IGHJ2*01	2242	2932
174	>gi|Fabrus|A02_VH3-23_IGHD1-1*01>2'_IGHJ2*01	2243	2933
175	>gi|Fabrus|A03_VH3-23_IGHD1-1*01>3'_IGHJ2*01	2244	2934
176	>gi|Fabrus|A04_VH3-23_IGHD1-7*01>1'_IGHJ2*01	2245	2935
177	>gi|Fabrus|A05_VH3-23_IGHD1-7*01>3'_IGHJ2*01	2246	2936
178	>gi|Fabrus|A06_VH3-23_IGHD1-14*01>1'_IGHJ2*01	2247	2937
179	>gi|Fabrus|A07_VH3-23_IGHD1-14*01>2'_IGHJ2*01	2248	2938
180	>gi|Fabrus|A08_VH3-23_IGHD1-14*01>3'_IGHJ2*01	2249	2939
181	>gi|Fabrus|A09_VH3-23_IGHD1-20*01>1'_IGHJ2*01	2250	2940
182	>gi|Fabrus|A10_VH3-23_IGHD1-20*01>2'_IGHJ2*01	2251	2941
183	>gi|Fabrus|A11_VH3-23_IGHD1-20*01>3'_IGHJ2*01	2252	2942
184	>gi|Fabrus|A12_VH3-23_IGHD1-26*01>1'_IGHJ2*01	2253	2943
185	>gi|Fabrus|B01_VH3-23_IGHD1-26*01>3'_IGHJ2*01	2254	2944
186	>gi|Fabrus|B02_VH3-23_IGHD2-2*01>1'_IGHJ2*01	2255	2945
187	>gi|Fabrus|B03_VH3-23_IGHD2-2*01>3'_IGHJ2*01	2256	2946
188	>gi|Fabrus|B04_VH3-23_IGHD2-8*01>1'_IGHJ2*01	2257	2947
189	>gi|Fabrus|B05_VH3-23_IGHD2-15*01>1'_IGHJ2*01	2258	2948
190	>gi|Fabrus|B06_VH3-23_IGHD2-15*01>3'_IGHJ2*01	2259	2949
191	>gi|Fabrus|B07_VH3-23_IGHD2-21*01>1'_IGHJ2*01	2260	2950
192	>gi|Fabrus|B08_VH3-23_IGHD2-21*01>3'_IGHJ2*01	2261	2951
193	>gi|Fabrus|B09_VH3-23_IGHD3-3*01>1'_IGHJ2*01	2262	2952
194	>gi|Fabrus|B10_VH3-23_IGHD3-3*01>3'_IGHJ2*01	2263	2953
195	>gi|Fabrus|B11_VH3-23_IGHD3-9*01>1'_IGHJ2*01	2264	2954
196	>gi|Fabrus|B12_VH3-23_IGHD3-9*01>3'_IGHJ2*01	2265	2955
197	>gi|Fabrus|C01_VH3-23_IGHD3-10*01>1'_IGHJ2*01	2266	2956
198	>gi|Fabrus|C02_VH3-23_IGHD3-10*01>3'_IGHJ2*01	2267	2957
199	>gi|Fabrus|C03_VH3-23_IGHD3-16*01>1'_IGHJ2*01	2268	2958
200	>gi|Fabrus|C04_VH3-23_IGHD3-16*01>3'_IGHJ2*01	2269	2959
201	>gi|Fabrus|C05_VH3-23_IGHD3-22*01>1'_IGHJ2*01	2270	2960
202	>gi|Fabrus|C06_VH3-23_IGHD4-4*01(1)>1'_IGHJ2*01	2271	2961
203	>gi|Fabrus|C07_VH3-23_IGHD4-4*01(1)>3'_IGHJ2*01	2272	2962
204	>gi|Fabrus|C08_VH3-23_IGHD4-11*01(1)>1'_IGHJ2*01	2273	2963
205	>gi|Fabrus|C09_VH3-23_IGHD4-11*01(1)>3'_IGHJ2*01	2274	2964
206	>gi|Fabrus|C10_VH3-23_IGHD4-17*01>1'_IGHJ2*01	2275	2965
207	>gi|Fabrus|C11_VH3-23_IGHD4-17*01>3'_IGHJ2*01	2276	2966
208	>gi|Fabrus|C12_VH3-23_IGHD4-23*01>1'_IGHJ2*01	2277	2967
209	>gi|Fabrus|D01_VH3-23_IGHD4-23*01>3'_IGHJ2*01	2278	2968
210	>gi|Fabrus|D02_VH3-23_IGHD5-5*01(2)>1'_IGHJ2*01	2279	2969
211	>gi|Fabrus|D03_VH3-23_IGHD5-5*01(2)>3'_IGHJ2*01	2280	2970
212	>gi|Fabrus|D04_VH3-23_IGHD5-12*01>1'_IGHJ2*01	2281	2971
213	>gi|Fabrus|D05_VH3-23_IGHD5-12*01>3'_IGHJ2*01	2282	2972
214	>gi|Fabrus|D06_VH3-23_IGHD5-18*01(2)>1'_IGHJ2*01	2283	2973
215	>gi|Fabrus|D07_VH3-23_IGHD5-18*01(2)>3'_IGHJ2*01	2284	2974
216	>gi|Fabrus|D08_VH3-23_IGHD5-24*01>1'_IGHJ2*01	2285	2975
217	>gi|Fabrus|D09_VH3-23_IGHD5-24*01>3'_IGHJ2*01	2286	2976

218	>gi|Fabrus|D10_VH3-23_IGHD6-6*01>1'_IGHJ2*01	2287	2977
219	>gi|Fabrus|D11_VH3-23_IGHD6-6*01>2'_IGHJ2*01	2288	2978
220	>gi|Fabrus|D12_VH3-23_IGHD6-6*01>3'_IGHJ2*01	2289	2979
221	>gi|Fabrus|E01_VH3-23_IGHD6-13*01>1'_IGHJ2*01	2290	2980
222	>gi|Fabrus|E02_VH3-23_IGHD6-13*01>2'_IGHJ2*01	2291	2981
223	>gi|Fabrus|E03_VH3-23_IGHD6-13*01>3'_IGHJ2*01	2292	2982
224	>gi|Fabrus|E04_VH3-23_IGHD6-19*01>1'_IGHJ2*01	2293	2983
225	>gi|Fabrus|E05_VH3-23_IGHD6-19*01>2'_IGHJ2*01	2294	2984
226	>gi|Fabrus|E06_VH3-23_IGHD6-19*01>3'_IGHJ2*01	2295	2985
227	>gi|Fabrus|E07_VH3-23_IGHD6-25*01>1'_IGHJ2*01	2296	2986
228	>gi|Fabrus|E08_VH3-23_IGHD6-25*01>3'_IGHJ2*01	2297	2987
229	>gi|Fabrus|E09_VH3-23_IGHD7-27*01>1'_IGHJ2*01	2298	2988
230	>gi|Fabrus|E10_VH3-23_IGHD7-27*01>2'_IGHJ2*01	2299	2989
231	>gi|Fabrus|A01_VH3-23_IGHD1-1*01>1_IGHJ3*01	2300	2990
232	>gi|Fabrus|A02_VH3-23_IGHD1-1*01>2_IGHJ3*01	2301	2991
233	>gi|Fabrus|A03_VH3-23_IGHD1-1*01>3_IGHJ3*01	2302	2992
234	>gi|Fabrus|A04_VH3-23_IGHD1-7*01>1_IGHJ3*01	2303	2993
235	>gi|Fabrus|A05_VH3-23_IGHD1-7*01>3_IGHJ3*01	2304	2994
236	>gi|Fabrus|A06_VH3-23_IGHD1-14*01>1_IGHJ3*01	2305	2995
237	>gi|Fabrus|A07_VH3-23_IGHD1-14*01>3_IGHJ3*01	2306	2996
238	>gi|Fabrus|A08_VH3-23_IGHD1-20*01>1_IGHJ3*01	2307	2997
239	>gi|Fabrus|A09_VH3-23_IGHD1-20*01>3_IGHJ3*01	2308	2998
240	>gi|Fabrus|A10_VH3-23_IGHD1-26*01>1_IGHJ3*01	2309	2999
241	>gi|Fabrus|A11_VH3-23_IGHD1-26*01>3_IGHJ3*01	2310	3000
242	>gi|Fabrus|A12_VH3-23_IGHD2-2*01>2_IGHJ3*01	2311	3001
243	>gi|Fabrus|B01_VH3-23_IGHD2-2*01>3_IGHJ3*01	2312	3002
244	>gi|Fabrus|B02_VH3-23_IGHD2-8*01>2_IGHJ3*01	2313	3003
245	>gi|Fabrus|B03_VH3-23_IGHD2-8*01>3_IGHJ3*01	2314	3004
246	>gi|Fabrus|B04_VH3-23_IGHD2-15*01>2_IGHJ3*01	2315	3005
247	>gi|Fabrus|B05_VH3-23_IGHD2-15*01>3_IGHJ3*01	2316	3006
248	>gi|Fabrus|B06_VH3-23_IGHD2-21*01>2_IGHJ3*01	2317	3007
249	>gi|Fabrus|B07_VH3-23_IGHD2-21*01>3_IGHJ3*01	2318	3008
250	>gi|Fabrus|B08_VH3-23_IGHD3-3*01>1_IGHJ3*01	2319	3009
251	>gi|Fabrus|B09_VH3-23_IGHD3-3*01>2_IGHJ3*01	2320	3010
252	>gi|Fabrus|B10_VH3-23_IGHD3-3*01>3_IGHJ3*01	2321	3011
253	>gi|Fabrus|B11_VH3-23_IGHD3-9*01>2_IGHJ3*01	2322	3012
254	>gi|Fabrus|B12_VH3-23_IGHD3-10*01>2_IGHJ3*01	2323	3013
255	>gi|Fabrus|C01_VH3-23_IGHD3-10*01>3_IGHJ3*01	2324	3014
256	>gi|Fabrus|C02_VH3-23_IGHD3-16*01>2_IGHJ3*01	2325	3015
257	>gi|Fabrus|C03_VH3-23_IGHD3-16*01>3_IGHJ3*01	2326	3016
258	>gi|Fabrus|C04_VH3-23_IGHD3-22*01>2_IGHJ3*01	2327	3017
259	>gi|Fabrus|C05_VH3-23_IGHD3-22*01>3_IGHJ3*01	2328	3018
260	>gi|Fabrus|C06_VH3-23_IGHD4-4*01(1)>2_IGHJ3*01	2329	3019
261	>gi|Fabrus|C07_VH3-23_IGHD4-4*01(1)>3_IGHJ3*01	2330	3020
262	>gi|Fabrus|C08_VH3-23_IGHD4-11*01(1)>2_IGHJ3*01	2331	3021
263	>gi|Fabrus|C09_VH3-23_IGHD4-11*01(1)>3_IGHJ3*01	2332	3022
264	>gi|Fabrus|C10_VH3-23_IGHD4-17*01>2_IGHJ3*01	2333	3023
265	>gi|Fabrus|C11_VH3-23_IGHD4-17*01>3_IGHJ3*01	2334	3024
266	>gi|Fabrus|C12_VH3-23_IGHD4-23*01>2_IGHJ3*01	2335	3025
267	>gi|Fabrus|D01_VH3-23_IGHD4-23*01>3_IGHJ3*01	2336	3026
268	>gi|Fabrus|D02_VH3-23_IGHD5-5*01(2)>1_IGHJ3*01	2337	3027
269	>gi|Fabrus|D03_VH3-23_IGHD5-5*01(2)>2_IGHJ3*01	2338	3028
270	>gi|Fabrus|D04_VH3-23_IGHD5-5*01(2)>3_IGHJ3*01	2339	3029
271	>gi|Fabrus|D05_VH3-23_IGHD5-12*01>1_IGHJ3*01	2340	3030

272	>gi|Fabrus|D06_VH3-23_IGHD5-12*01>3_IGHJ3*01	2341	3031
273	>gi|Fabrus|D07_VH3-23_IGHD5-18*01(2)>1_IGHJ3*01	2342	3032
274	>gi|Fabrus|D08_VH3-23_IGHD5-18*01(2)>2_IGHJ3*01	2343	3033
275	>gi|Fabrus|D09_VH3-23_IGHD5-18*01(2)>3_IGHJ3*01	2344	3034
276	>gi|Fabrus|D10_VH3-23_IGHD5-24*01>1_IGHJ3*01	2345	3035
277	>gi|Fabrus|D11_VH3-23_IGHD5-24*01>3_IGHJ3*01	2346	3036
278	>gi|Fabrus|D12_VH3-23_IGHD6-6*01>1_IGHJ3*01	2347	3037
279	>gi|Fabrus|E01_VH3-23_IGHD6-6*01>2_IGHJ3*01	2348	3038
280	>gi|Fabrus|E02_VH3-23_IGHD6-13*01>1_IGHJ3*01	2349	3039
281	>gi|Fabrus|E03_VH3-23_IGHD6-13*01>2_IGHJ3*01	2350	3040
282	>gi|Fabrus|E04_VH3-23_IGHD6-19*01>1_IGHJ3*01	2351	3041
283	>gi|Fabrus|E05_VH3-23_IGHD6-19*01>2_IGHJ3*01	2352	3042
284	>gi|Fabrus|E06_VH3-23_IGHD6-25*01>1_IGHJ3*01	2353	3043
285	>gi|Fabrus|E07_VH3-23_IGHD6-25*01>2_IGHJ3*01	2354	3044
286	>gi|Fabrus|E08_VH3-23_IGHD7-27*01>1_IGHJ3*01	2355	3045
287	>gi|Fabrus|E09_VH3-23_IGHD7-27*01>3_IGHJ3*01	2356	3046
288	>gi|Fabrus|A01_VH3-23_IGHD1-1*01>1'_IGHJ3*01	2357	3047
289	>gi|Fabrus|A02_VH3-23_IGHD1-1*01>2'_IGHJ3*01	2358	3048
290	>gi|Fabrus|A03_VH3-23_IGHD1-1*01>3'_IGHJ3*01	2359	3049
291	>gi|Fabrus|A04_VH3-23_IGHD1-7*01>1'_IGHJ3*01	2360	3050
292	>gi|Fabrus|A05_VH3-23_IGHD1-7*01>3'_IGHJ3*01	2361	3051
293	>gi|Fabrus|A06_VH3-23_IGHD1-14*01>1'_IGHJ3*01	2362	3052
294	>gi|Fabrus|A07_VH3-23_IGHD1-14*01>2'_IGHJ3*01	2363	3053
295	>gi|Fabrus|A08_VH3-23_IGHD1-14*01>3'_IGHJ3*01	2364	3054
296	>gi|Fabrus|A09_VH3-23_IGHD1-20*01>1'_IGHJ3*01	2365	3055
297	>gi|Fabrus|A10_VH3-23_IGHD1-20*01>2'_IGHJ3*01	2366	3056
298	>gi|Fabrus|A11_VH3-23_IGHD1-20*01>3'_IGHJ3*01	2367	3057
299	>gi|Fabrus|A12_VH3-23_IGHD1-26*01>1'_IGHJ3*01	2368	3058
300	>gi|Fabrus|B01_VH3-23_IGHD1-26*01>3'_IGHJ3*01	2369	3059
301	>gi|Fabrus|B02_VH3-23_IGHD2-2*01>1'_IGHJ3*01	2370	3060
302	>gi|Fabrus|B03_VH3-23_IGHD2-2*01>3'_IGHJ3*01	2371	3061
303	>gi|Fabrus|B04_VH3-23_IGHD2-8*01>1'_IGHJ3*01	2372	3062
304	>gi|Fabrus|B05_VH3-23_IGHD2-15*01>1'_IGHJ3*01	2373	3063
305	>gi|Fabrus|B06_VH3-23_IGHD2-15*01>3'_IGHJ3*01	2374	3064
306	>gi|Fabrus|B07_VH3-23_IGHD2-21*01>1'_IGHJ3*01	2375	3065
307	>gi|Fabrus|B08_VH3-23_IGHD2-21*01>3'_IGHJ3*01	2376	3066
308	>gi|Fabrus|B09_VH3-23_IGHD3-3*01>1'_IGHJ3*01	2377	3067
309	>gi|Fabrus|B10_VH3-23_IGHD3-3*01>3'_IGHJ3*01	2378	3068
310	>gi|Fabrus|B11_VH3-23_IGHD3-9*01>1'_IGHJ3*01	2379	3069
311	>gi|Fabrus|B12_VH3-23_IGHD3-9*01>3'_IGHJ3*01	2380	3070
312	>gi|Fabrus|C01_VH3-23_IGHD3-10*01>1'_IGHJ3*01	2381	3071
313	>gi|Fabrus|C02_VH3-23_IGHD3-10*01>3'_IGHJ3*01	2382	3072
314	>gi|Fabrus|C03_VH3-23_IGHD3-16*01>1'_IGHJ3*01	2383	3073
315	>gi|Fabrus|C04_VH3-23_IGHD3-16*01>3'_IGHJ3*01	2384	3074
316	>gi|Fabrus|C05_VH3-23_IGHD3-22*01>1'_IGHJ3*01	2385	3075
317	>gi|Fabrus|C06_VH3-23_IGHD4-4*01(1)>1'_IGHJ3*01	2386	3076
318	>gi|Fabrus|C07_VH3-23_IGHD4-4*01(1)>3'_IGHJ3*01	2387	3077
319	>gi|Fabrus|C08_VH3-23_IGHD4-11*01(1)>1'_IGHJ3*01	2388	3078
320	>gi|Fabrus|C09_VH3-23_IGHD4-11*01(1)>3'_IGHJ3*01	2389	3079
321	>gi|Fabrus|C10_VH3-23_IGHD4-17*01>1'_IGHJ3*01	2390	3080
322	>gi|Fabrus|C11_VH3-23_IGHD4-17*01>3'_IGHJ3*01	2391	3081
323	>gi|Fabrus|C12_VH3-23_IGHD4-23*01>1'_IGHJ3*01	2392	3082
324	>gi|Fabrus|D01_VH3-23_IGHD4-23*01>3'_IGHJ3*01	2393	3083
325	>gi|Fabrus|D02_VH3-23_IGHD5-5*01(2)>1'_IGHJ3*01	2394	3084

326	>gi|Fabrus|D03_VH3-23_IGHD5-5*01(2)>3'_IGHJ3*01	2395	3085
327	>gi|Fabrus|D04_VH3-23_IGHD5-12*01>1'_IGHJ3*01	2396	3086
328	>gi|Fabrus|D05_VH3-23_IGHD5-12*01>3'_IGHJ3*01	2397	3087
329	>gi|Fabrus|D06_VH3-23_IGHD5-18*01(2)>1'_IGHJ3*01	2398	3088
330	>gi|Fabrus|D07_VH3-23_IGHD5-18*01(2)>3'_IGHJ3*01	2399	3089
331	>gi|Fabrus|D08_VH3-23_IGHD5-24*01>1'_IGHJ3*01	2400	3090
332	>gi|Fabrus|D09_VH3-23_IGHD5-24*01>3'_IGHJ3*01	2401	3091
333	>gi|Fabrus|D10_VH3-23_IGHD6-6*01>1'_IGHJ3*01	2402	3092
334	>gi|Fabrus|D11_VH3-23_IGHD6-6*01>2'_IGHJ3*01	2403	3093
335	>gi|Fabrus|D12_VH3-23_IGHD6-6*01>3'_IGHJ3*01	2404	3094
336	>gi|Fabrus|E01_VH3-23_IGHD6-13*01>1'_IGHJ3*01	2405	3095
337	>gi|Fabrus|E02_VH3-23_IGHD6-13*01>2'_IGHJ3*01	2406	3096
338	>gi|Fabrus|E03_VH3-23_IGHD6-13*01>3'_IGHJ3*01	2407	3097
339	>gi|Fabrus|E04_VH3-23_IGHD6-19*01>1'_IGHJ3*01	2408	3098
340	>gi|Fabrus|E05_VH3-23_IGHD6-19*01>2'_IGHJ3*01	2409	3099
341	>gi|Fabrus|E06_VH3-23_IGHD6-19*01>3'_IGHJ3*01	2410	3100
342	>gi|Fabrus|E07_VH3-23_IGHD6-25*01>1'_IGHJ3*01	2411	3101
343	>gi|Fabrus|E08_VH3-23_IGHD6-25*01>3'_IGHJ3*01	2412	3102
344	>gi|Fabrus|E09_VH3-23_IGHD7-27*01>1'_IGHJ3*01	2413	3103
345	>gi|Fabrus|E10_VH3-23_IGHD7-27*01>2'_IGHJ3*01	2414	3104
346	>gi|Fabrus|A01_VH3-23_IGHD1-1*01>1_IGHJ4*01	2415	3105
347	>gi|Fabrus|A02_VH3-23_IGHD1-1*01>2_IGHJ4*01	2416	3106
348	>gi|Fabrus|A03_VH3-23_IGHD1-1*01>3_IGHJ4*01	2417	3107
349	>gi|Fabrus|A04_VH3-23_IGHD1-7*01>1_IGHJ4*01	2418	3108
350	>gi|Fabrus|A05_VH3-23_IGHD1-7*01>3_IGHJ4*01	2419	3109
351	>gi|Fabrus|A06_VH3-23_IGHD1-14*01>1_IGHJ4*01	2420	3110
352	>gi|Fabrus|A07_VH3-23_IGHD1-14*01>3_IGHJ4*01	2421	3111
353	>gi|Fabrus|A08_VH3-23_IGHD1-20*01>1_IGHJ4*01	2422	3112
354	>gi|Fabrus|A09_VH3-23_IGHD1-20*01>3_IGHJ4*01	2423	3113
355	>gi|Fabrus|A10_VH3-23_IGHD1-26*01>1_IGHJ4*01	2424	3114
356	>gi|Fabrus|A11_VH3-23_IGHD1-26*01>3_IGHJ4*01	2425	3115
357	>gi|Fabrus|A12_VH3-23_IGHD2-2*01>2_IGHJ4*01	2426	3116
358	>gi|Fabrus|B01_VH3-23_IGHD2-2*01>3_IGHJ4*01	2427	3117
359	>gi|Fabrus|B02_VH3-23_IGHD2-8*01>2_IGHJ4*01	2428	3118
360	>gi|Fabrus|B03_VH3-23_IGHD2-8*01>3_IGHJ4*01	2429	3119
361	>gi|Fabrus|B04_VH3-23_IGHD2-15*01>2_IGHJ4*01	2430	3120
362	>gi|Fabrus|B05_VH3-23_IGHD2-15*01>3_IGHJ4*01	2431	3121
363	>gi|Fabrus|B06_VH3-23_IGHD2-21*01>2_IGHJ4*01	2432	3122
364	>gi|Fabrus|B07_VH3-23_IGHD2-21*01>3_IGHJ4*01	2433	3123
365	>gi|Fabrus|B08_VH3-23_IGHD3-3*01>1_IGHJ4*01	2434	3124
366	>gi|Fabrus|B09_VH3-23_IGHD3-3*01>2_IGHJ4*01	2435	3125
367	>gi|Fabrus|B10_VH3-23_IGHD3-3*01>3_IGHJ4*01	2436	3126
368	>gi|Fabrus|B11_VH3-23_IGHD3-9*01>2_IGHJ4*01	2437	3127
369	>gi|Fabrus|B12_VH3-23_IGHD3-10*01>2_IGHJ4*01	2438	3128
370	>gi|Fabrus|C01_VH3-23_IGHD3-10*01>3_IGHJ4*01	2439	3129
371	>gi|Fabrus|C02_VH3-23_IGHD3-16*01>2_IGHJ4*01	2440	3130
372	>gi|Fabrus|C03_VH3-23_IGHD3-16*01>3_IGHJ4*01	2441	3131
373	>gi|Fabrus|C04_VH3-23_IGHD3-22*01>2_IGHJ4*01	2442	3132
374	>gi|Fabrus|C05_VH3-23_IGHD3-22*01>3_IGHJ4*01	2443	3133
375	>gi|Fabrus|C06_VH3-23_IGHD4-4*01(1)>2_IGHJ4*01	2444	3134
376	>gi|Fabrus|C07_VH3-23_IGHD4-4*01(1)>3_IGHJ4*01	2445	3135
377	>gi|Fabrus|C08_VH3-23_IGHD4-11*01(1)>2_IGHJ4*01	2446	3136
378	>gi|Fabrus|C09_VH3-23_IGHD4-11*01(1)>3_IGHJ4*01	2447	3137
379	>gi|Fabrus|C10_VH3-23_IGHD4-17*01>2_IGHJ4*01	2448	3138

380	>gi|Fabrus|C11_VH3-23_IGHD4-17*01>3_IGHJ4*01	2449	3139
381	>gi|Fabrus|C12_VH3-23_IGHD4-23*01>2_IGHJ4*01	2450	3140
382	>gi|Fabrus|D01_VH3-23_IGHD4-23*01>3_IGHJ4*01	2451	3141
383	>gi|Fabrus|D02_VH3-23_IGHD5-5*01(2)>1_IGHJ4*01	2452	3142
384	>gi|Fabrus|D03_VH3-23_IGHD5-5*01(2)>2_IGHJ4*01	2453	3143
385	>gi|Fabrus|D04_VH3-23_IGHD5-5*01(2)>3_IGHJ4*01	2454	3144
386	>gi|Fabrus|D05_VH3-23_IGHD5-12*01>1_IGHJ4*01	2455	3145
387	>gi|Fabrus|D06_VH3-23_IGHD5-12*01>3_IGHJ4*01	2456	3146
388	>gi|Fabrus|D07_VH3-23_IGHD5-18*01(2)>1_IGHJ4*01	2457	3147
389	>gi|Fabrus|D08_VH3-23_IGHD5-18*01(2)>2_IGHJ4*01	2458	3148
390	>gi|Fabrus|D09_VH3-23_IGHD5-18*01(2)>3_IGHJ4*01	2459	3149
391	>gi|Fabrus|D10_VH3-23_IGHD5-24*01>1_IGHJ4*01	2460	3150
392	>gi|Fabrus|D11_VH3-23_IGHD5-24*01>3_IGHJ4*01	2461	3151
393	>gi|Fabrus|D12_VH3-23_IGHD6-6*01>1_IGHJ4*01	2462	3152
394	>gi|Fabrus|E01_VH3-23_IGHD6-6*01>2_IGHJ4*01	2463	3153
395	>gi|Fabrus|E02_VH3-23_IGHD6-13*01>1_IGHJ4*01	2464	3154
396	>gi|Fabrus|E03_VH3-23_IGHD6-13*01>2_IGHJ4*01	2465	3155
397	>gi|Fabrus|E04_VH3-23_IGHD6-19*01>1_IGHJ4*01	2466	3156
398	>gi|Fabrus|E05_VH3-23_IGHD6-19*01>2_IGHJ4*01	2467	3157
399	>gi|Fabrus|E06_VH3-23_IGHD6-25*01>1_IGHJ4*01	2468	3158
400	>gi|Fabrus|E07_VH3-23_IGHD6-25*01>2_IGHJ4*01	2469	3159
401	>gi|Fabrus|E08_VH3-23_IGHD7-27*01>1_IGHJ4*01	2470	3160
402	>gi|Fabrus|E09_VH3-23_IGHD7-27*01>3_IGHJ4*01	2471	3161
403	>gi|Fabrus|A01_VH3-23_IGHD1-1*01>1'_IGHJ4*01	2472	3162
404	>gi|Fabrus|A02_VH3-23_IGHD1-1*01>2'_IGHJ4*01	2473	3163
405	>gi|Fabrus|A03_VH3-23_IGHD1-1*01>3'_IGHJ4*01	2474	3164
406	>gi|Fabrus|A04_VH3-23_IGHD1-7*01>1'_IGHJ4*01	2475	3165
407	>gi|Fabrus|A05_VH3-23_IGHD1-7*01>3'_IGHJ4*01	2476	3166
408	>gi|Fabrus|A06_VH3-23_IGHD1-14*01>1'_IGHJ4*01	2477	3167
409	>gi|Fabrus|A07_VH3-23_IGHD1-14*01>2'_IGHJ4*01	2478	3168
410	>gi|Fabrus|A08_VH3-23_IGHD1-14*01>3'_IGHJ4*01	2479	3169
411	>gi|Fabrus|A09_VH3-23_IGHD1-20*01>1'_IGHJ4*01	2480	3170
412	>gi|Fabrus|A10_VH3-23_IGHD1-20*01>2'_IGHJ4*01	2481	3171
413	>gi|Fabrus|A11_VH3-23_IGHD1-20*01>3'_IGHJ4*01	2482	3172
414	>gi|Fabrus|A12_VH3-23_IGHD1-26*01>1'_IGHJ4*01	2483	3173
415	>gi|Fabrus|B01_VH3-23_IGHD1-26*01>3'_IGHJ4*01	2484	3174
416	>gi|Fabrus|B02_VH3-23_IGHD2-2*01>1'_IGHJ4*01	2485	3175
417	>gi|Fabrus|B03_VH3-23_IGHD2-2*01>3'_IGHJ4*01	2486	3176
418	>gi|Fabrus|B04_VH3-23_IGHD2-8*01>1'_IGHJ4*01	2487	3177
419	>gi|Fabrus|B05_VH3-23_IGHD2-15*01>1'_IGHJ4*01	2488	3178
420	>gi|Fabrus|B06_VH3-23_IGHD2-15*01>3'_IGHJ4*01	2489	3179
421	>gi|Fabrus|B07_VH3-23_IGHD2-21*01>1'_IGHJ4*01	2490	3180
422	>gi|Fabrus|B08_VH3-23_IGHD2-21*01>3'_IGHJ4*01	2491	3181
423	>gi|Fabrus|B09_VH3-23_IGHD3-3*01>1'_IGHJ4*01	2492	3182
424	>gi|Fabrus|B10_VH3-23_IGHD3-3*01>3'_IGHJ4*01	2493	3183
425	>gi|Fabrus|B11_VH3-23_IGHD3-9*01>1'_IGHJ4*01	2494	3184
426	>gi|Fabrus|B12_VH3-23_IGHD3-9*01>3'_IGHJ4*01	2495	3185
427	>gi|Fabrus|C01_VH3-23_IGHD3-10*01>1'_IGHJ4*01	2496	3186
428	>gi|Fabrus|C02_VH3-23_IGHD3-10*01>3'_IGHJ4*01	2497	3187
429	>gi|Fabrus|C03_VH3-23_IGHD3-16*01>1'_IGHJ4*01	2498	3188
430	>gi|Fabrus|C04_VH3-23_IGHD3-16*01>3'_IGHJ4*01	2499	3189
431	>gi|Fabrus|C05_VH3-23_IGHD3-22*01>1'_IGHJ4*01	2500	3190
432	>gi|Fabrus|C06_VH3-23_IGHD4-4*01(1)>1'_IGHJ4*01	2501	3191
433	>gi|Fabrus|C07_VH3-23_IGHD4-4*01(1)>3'_IGHJ4*01	2502	3192

434	>gi|Fabrus|C08_VH3-23_IGHD4-11*01(1)>1'_IGHJ4*01	2503	3193
435	>gi|Fabrus|C09_VH3-23_IGHD4-11*01(1)>3'_IGHJ4*01	2504	3194
436	>gi|Fabrus|C10_VH3-23_IGHD4-17*01>1'_IGHJ4*01	2505	3195
437	>gi|Fabrus|C11_VH3-23_IGHD4-17*01>3'_IGHJ4*01	2506	3196
438	>gi|Fabrus|C12_VH3-23_IGHD4-23*01>1'_IGHJ4*01	2507	3197
439	>gi|Fabrus|D01_VH3-23_IGHD4-23*01>3'_IGHJ4*01	2508	3198
440	>gi|Fabrus|D02_VH3-23_IGHD5-5*01(2)>1'_IGHJ4*01	2509	3199
441	>gi|Fabrus|D03_VH3-23_IGHD5-5*01(2)>3'_IGHJ4*01	2510	3200
442	>gi|Fabrus|D04_VH3-23_IGHD5-12*01>1'_IGHJ4*01	2511	3201
443	>gi|Fabrus|D05_VH3-23_IGHD5-12*01>3'_IGHJ4*01	2512	3202
444	>gi|Fabrus|D06_VH3-23_IGHD5-18*01(2)>1'_IGHJ4*01	2513	3203
445	>gi|Fabrus|D07_VH3-23_IGHD5-18*01(2)>3'_IGHJ4*01	2514	3204
446	>gi|Fabrus|D08_VH3-23_IGHD5-24*01>1'_IGHJ4*01	2515	3205
447	>gi|Fabrus|D09_VH3-23_IGHD5-24*01>3'_IGHJ4*01	2516	3206
448	>gi|Fabrus|D10_VH3-23_IGHD6-6*01>1'_IGHJ4*01	2517	3207
449	>gi|Fabrus|D11_VH3-23_IGHD6-6*01>2'_IGHJ4*01	2518	3208
450	>gi|Fabrus|D12_VH3-23_IGHD6-6*01>3'_IGHJ4*01	2519	3209
451	>gi|Fabrus|E01_VH3-23_IGHD6-13*01>1'_IGHJ4*01	2520	3210
452	>gi|Fabrus|E02_VH3-23_IGHD6-13*01>2'_IGHJ4*01	2521	3211
453	>gi|Fabrus|E03_VH3-23_IGHD6-13*01>3'_IGHJ4*01	2522	3212
454	>gi|Fabrus|E04_VH3-23_IGHD6-19*01>1'_IGHJ4*01	2523	3213
455	>gi|Fabrus|E05_VH3-23_IGHD6-19*01>2'_IGHJ4*01	2524	3214
456	>gi|Fabrus|E06_VH3-23_IGHD6-19*01>3'_IGHJ4*01	2525	3215
457	>gi|Fabrus|E07_VH3-23_IGHD6-25*01>1'_IGHJ4*01	2526	3216
458	>gi|Fabrus|E08_VH3-23_IGHD6-25*01>3'_IGHJ4*01	2527	3217
459	>gi|Fabrus|E09_VH3-23_IGHD7-27*01>1'_IGHJ4*01	2528	3218
460	>gi|Fabrus|E10_VH3-23_IGHD7-27*01>2'_IGHJ4*01	2529	3219
461	>gi|Fabrus|A01_VH3-23_IGHD1-1*01>1_IGHJ5*01	2530	3220
462	>gi|Fabrus|A02_VH3-23_IGHD1-1*01>2_IGHJ5*01	2531	3221
463	>gi|Fabrus|A03_VH3-23_IGHD1-1*01>3_IGHJ5*01	2532	3222
464	>gi|Fabrus|A04_VH3-23_IGHD1-7*01>1_IGHJ5*01	2533	3223
465	>gi|Fabrus|A05_VH3-23_IGHD1-7*01>3_IGHJ5*01	2534	3224
466	>gi|Fabrus|A06_VH3-23_IGHD1-14*01>1_IGHJ5*01	2535	3225
467	>gi|Fabrus|A07_VH3-23_IGHD1-14*01>3_IGHJ5*01	2536	3226
468	>gi|Fabrus|A08_VH3-23_IGHD1-20*01>1_IGHJ5*01	2537	3227
469	>gi|Fabrus|A09_VH3-23_IGHD1-20*01>3_IGHJ5*01	2538	3228
470	>gi|Fabrus|A10_VH3-23_IGHD1-26*01>1_IGHJ5*01	2539	3229
471	>gi|Fabrus|A11_VH3-23_IGHD1-26*01>3_IGHJ5*01	2540	3230
472	>gi|Fabrus|A12_VH3-23_IGHD2-2*01>2_IGHJ5*01	2541	3231
473	>gi|Fabrus|B01_VH3-23_IGHD2-2*01>3_IGHJ5*01	2542	3232
474	>gi|Fabrus|B02_VH3-23_IGHD2-8*01>2_IGHJ5*01	2543	3233
475	>gi|Fabrus|B03_VH3-23_IGHD2-8*01>3_IGHJ5*01	2544	3234
476	>gi|Fabrus|B04_VH3-23_IGHD2-15*01>2_IGHJ5*01	2545	3235
477	>gi|Fabrus|B05_VH3-23_IGHD2-15*01>3_IGHJ5*01	2546	3236
478	>gi|Fabrus|B06_VH3-23_IGHD2-21*01>2_IGHJ5*01	2547	3237
479	>gi|Fabrus|B07_VH3-23_IGHD2-21*01>3_IGHJ5*01	2548	3238
480	>gi|Fabrus|B08_VH3-23_IGHD3-3*01>1_IGHJ5*01	2549	3239
481	>gi|Fabrus|B09_VH3-23_IGHD3-3*01>2_IGHJ5*01	2550	3240
482	>gi|Fabrus|B10_VH3-23_IGHD3-3*01>3_IGHJ5*01	2551	3241
483	>gi|Fabrus|B11_VH3-23_IGHD3-9*01>2_IGHJ5*01	2552	3242
484	>gi|Fabrus|B12_VH3-23_IGHD3-10*01>2_IGHJ5*01	2553	3243
485	>gi|Fabrus|C01_VH3-23_IGHD3-10*01>3_IGHJ5*01	2554	3244
486	>gi|Fabrus|C02_VH3-23_IGHD3-16*01>2_IGHJ5*01	2555	3245
487	>gi|Fabrus|C03_VH3-23_IGHD3-16*01>3_IGHJ5*01	2556	3246

488	>gi|Fabrus|C04_VH3-23_IGHD3-22*01>2_IGHJ5*01	2557	3247
489	>gi|Fabrus|C05_VH3-23_IGHD3-22*01>3_IGHJ5*01	2558	3248
490	>gi|Fabrus|C06_VH3-23_IGHD4-4*01(1)>2_IGHJ5*01	2559	3249
491	>gi|Fabrus|C07_VH3-23_IGHD4-4*01(1)>3_IGHJ5*01	2560	3250
492	>gi|Fabrus|C08_VH3-23_IGHD4-11*01(1)>2_IGHJ5*01	2561	3251
493	>gi|Fabrus|C09_VH3-23_IGHD4-11*01(1)>3_IGHJ5*01	2562	3252
494	>gi|Fabrus|C10_VH3-23_IGHD4-17*01>2_IGHJ5*01	2563	3253
495	>gi|Fabrus|C11_VH3-23_IGHD4-17*01>3_IGHJ5*01	2564	3254
496	>gi|Fabrus|C12_VH3-23_IGHD4-23*01>2_IGHJ5*01	2565	3255
497	>gi|Fabrus|D01_VH3-23_IGHD4-23*01>3_IGHJ5*01	2566	3256
498	>gi|Fabrus|D02_VH3-23_IGHD5-5*01(2)>1_IGHJ5*01	2567	3257
499	>gi|Fabrus|D03_VH3-23_IGHD5-5*01(2)>2_IGHJ5*01	2568	3258
500	>gi|Fabrus|D04_VH3-23_IGHD5-5*01(2)>3_IGHJ5*01	2569	3259
501	>gi|Fabrus|D05_VH3-23_IGHD5-12*01>1_IGHJ5*01	2570	3260
502	>gi|Fabrus|D06_VH3-23_IGHD5-12*01>3_IGHJ5*01	2571	3261
503	>gi|Fabrus|D07_VH3-23_IGHD5-18*01(2)>1_IGHJ5*01	2572	3262
504	>gi|Fabrus|D08_VH3-23_IGHD5-18*01(2)>2_IGHJ5*01	2573	3263
505	>gi|Fabrus|D09_VH3-23_IGHD5-18*01(2)>3_IGHJ5*01	2574	3264
506	>gi|Fabrus|D10_VH3-23_IGHD5-24*01>1_IGHJ5*01	2575	3265
507	>gi|Fabrus|D11_VH3-23_IGHD5-24*01>3_IGHJ5*01	2576	3266
508	>gi|Fabrus|D12_VH3-23_IGHD6-6*01>1_IGHJ5*01	2577	3267
509	>gi|Fabrus|E01_VH3-23_IGHD6-6*01>2_IGHJ5*01	2578	3268
510	>gi|Fabrus|E02_VH3-23_IGHD6-13*01>1_IGHJ5*01	2579	3269
511	>gi|Fabrus|E03_VH3-23_IGHD6-13*01>2_IGHJ5*01	2580	3270
512	>gi|Fabrus|E04_VH3-23_IGHD6-19*01>1_IGHJ5*01	2581	3271
513	>gi|Fabrus|E05_VH3-23_IGHD6-19*01>2_IGHJ5*01	2582	3272
514	>gi|Fabrus|E06_VH3-23_IGHD6-25*01>1_IGHJ5*01	2583	3273
515	>gi|Fabrus|E07_VH3-23_IGHD6-25*01>2_IGHJ5*01	2584	3274
516	>gi|Fabrus|E08_VH3-23_IGHD7-27*01>1_IGHJ5*01	2585	3275
517	>gi|Fabrus|E09_VH3-23_IGHD7-27*01>3_IGHJ5*01	2586	3276
518	>gi|Fabrus|A01_VH3-23_IGHD1-1*01>1'_IGHJ5*01	2587	3277
519	>gi|Fabrus|A02_VH3-23_IGHD1-1*01>2'_IGHJ5*01	2588	3278
520	>gi|Fabrus|A03_VH3-23_IGHD1-1*01>3'_IGHJ5*01	2589	3279
521	>gi|Fabrus|A04_VH3-23_IGHD1-7*01>1'_IGHJ5*01	2590	3280
522	>gi|Fabrus|A05_VH3-23_IGHD1-7*01>3'_IGHJ5*01	2591	3281
523	>gi|Fabrus|A06_VH3-23_IGHD1-14*01>1'_IGHJ5*01	2592	3282
524	>gi|Fabrus|A07_VH3-23_IGHD1-14*01>2'_IGHJ5*01	2593	3283
525	>gi|Fabrus|A08_VH3-23_IGHD1-14*01>3'_IGHJ5*01	2594	3284
526	>gi|Fabrus|A09_VH3-23_IGHD1-20*01>1'_IGHJ5*01	2595	3285
527	>gi|Fabrus|A10_VH3-23_IGHD1-20*01>2'_IGHJ5*01	2596	3286
528	>gi|Fabrus|A11_VH3-23_IGHD1-20*01>3'_IGHJ5*01	2597	3287
529	>gi|Fabrus|A12_VH3-23_IGHD1-26*01>1'_IGHJ5*01	2598	3288
530	>gi|Fabrus|B01_VH3-23_IGHD1-26*01>3'_IGHJ5*01	2599	3289
531	>gi|Fabrus|B02_VH3-23_IGHD2-2*01>1'_IGHJ5*01	2600	3290
532	>gi|Fabrus|B03_VH3-23_IGHD2-2*01>3'_IGHJ5*01	2601	3291
533	>gi|Fabrus|B04_VH3-23_IGHD2-8*01>1'_IGHJ5*01	2602	3292
534	>gi|Fabrus|B05_VH3-23_IGHD2-15*01>1'_IGHJ5*01	2603	3293
535	>gi|Fabrus|B06_VH3-23_IGHD2-15*01>3'_IGHJ5*01	2604	3294
536	>gi|Fabrus|B07_VH3-23_IGHD2-21*01>1'_IGHJ5*01	2605	3295
537	>gi|Fabrus|B08_VH3-23_IGHD2-21*01>3'_IGHJ5*01	2606	3296
538	>gi|Fabrus|B09_VH3-23_IGHD3-3*01>1'_IGHJ5*01	2607	3297
539	>gi|Fabrus|B10_VH3-23_IGHD3-3*01>3'_IGHJ5*01	2608	3298
540	>gi|Fabrus|B11_VH3-23_IGHD3-9*01>1'_IGHJ5*01	2609	3299
541	>gi|Fabrus|B12_VH3-23_IGHD3-9*01>3'_IGHJ5*01	2610	3300

542	>gi|Fabrus|C01_VH3-23_IGHD3-10*01>1'_IGHJ5*01	2611	3301
543	>gi|Fabrus|C02_VH3-23_IGHD3-10*01>3'_IGHJ5*01	2612	3302
544	>gi|Fabrus|C03_VH3-23_IGHD3-16*01>1'_IGHJ5*01	2613	3303
545	>gi|Fabrus|C04_VH3-23_IGHD3-16*01>3'_IGHJ5*01	2614	3304
546	>gi|Fabrus|C05_VH3-23_IGHD3-22*01>1'_IGHJ5*01	2615	3305
547	>gi|Fabrus|C06_VH3-23_IGHD4-4*01(1)>1'_IGHJ5*01	2616	3306
548	>gi|Fabrus|C07_VH3-23_IGHD4-4*01(1)>3'_IGHJ5*01	2617	3307
549	>gi|Fabrus|C08_VH3-23_IGHD4-11*01(1)>1'_IGHJ5*01	2618	3308
550	>gi|Fabrus|C09_VH3-23_IGHD4-11*01(1)>3'_IGHJ5*01	2619	3309
551	>gi|Fabrus|C10_VH3-23_IGHD4-17*01>1'_IGHJ5*01	2620	3310
552	>gi|Fabrus|C11_VH3-23_IGHD4-17*01>3'_IGHJ5*01	2621	3311
553	>gi|Fabrus|C12_VH3-23_IGHD4-23*01>1'_IGHJ5*01	2622	3312
554	>gi|Fabrus|D01_VH3-23_IGHD4-23*01>3'_IGHJ5*01	2623	3313
555	>gi|Fabrus|D02_VH3-23_IGHD5-5*01(2)>1'_IGHJ5*01	2624	3314
556	>gi|Fabrus|D03_VH3-23_IGHD5-5*01(2)>3'_IGHJ5*01	2625	3315
557	>gi|Fabrus|D04_VH3-23_IGHD5-12*01>1'_IGHJ5*01	2626	3316
558	>gi|Fabrus|D05_VH3-23_IGHD5-12*01>3'_IGHJ5*01	2627	3317
559	>gi|Fabrus|D06_VH3-23_IGHD5-18*01(2)>1'_IGHJ5*01	2628	3318
560	>gi|Fabrus|D07_VH3-23_IGHD5-18*01(2)>3'_IGHJ5*01	2629	3319
561	>gi|Fabrus|D08_VH3-23_IGHD5-24*01>1'_IGHJ5*01	2630	3320
562	>gi|Fabrus|D09_VH3-23_IGHD5-24*01>3'_IGHJ5*01	2631	3321
563	>gi|Fabrus|D10_VH3-23_IGHD6-6*01>1'_IGHJ5*01	2632	3322
564	>gi|Fabrus|D11_VH3-23_IGHD6-6*01>2'_IGHJ5*01	2633	3323
565	>gi|Fabrus|D12_VH3-23_IGHD6-6*01>3'_IGHJ5*01	2634	3324
566	>gi|Fabrus|E01_VH3-23_IGHD6-13*01>1'_IGHJ5*01	2635	3325
567	>gi|Fabrus|E02_VH3-23_IGHD6-13*01>2'_IGHJ5*01	2636	3326
568	>gi|Fabrus|E03_VH3-23_IGHD6-13*01>3'_IGHJ5*01	2637	3327
569	>gi|Fabrus|E04_VH3-23_IGHD6-19*01>1'_IGHJ5*01	2638	3328
570	>gi|Fabrus|E05_VH3-23_IGHD6-19*01>2'_IGHJ5*01	2639	3329
571	>gi|Fabrus|E06_VH3-23_IGHD6-19*01>3'_IGHJ5*01	2640	3330
572	>gi|Fabrus|E07_VH3-23_IGHD6-25*01>1'_IGHJ5*01	2641	3331
573	>gi|Fabrus|E08_VH3-23_IGHD6-25*01>3'_IGHJ5*01	2642	3332
574	>gi|Fabrus|E09_VH3-23_IGHD7-27*01>1'_IGHJ5*01	2643	3333
575	>gi|Fabrus|E10_VH3-23_IGHD7-27*01>2'_IGHJ5*01	2644	3334
576	>gi|Fabrus|A01_VH3-23_IGHD1-1*01>1_IGHJ6*01	2645	3335
577	>gi|Fabrus|A02_VH3-23_IGHD1-1*01>2_IGHJ6*01	2646	3336
578	>gi|Fabrus|A03_VH3-23_IGHD1-1*01>3_IGHJ6*01	2647	3337
579	>gi|Fabrus|A04_VH3-23_IGHD1-7*01>1_IGHJ6*01	2648	3338
580	>gi|Fabrus|A05_VH3-23_IGHD1-7*01>3_IGHJ6*01	2649	3339
581	>gi|Fabrus|A06_VH3-23_IGHD1-14*01>1_IGHJ6*01	2650	3340
582	>gi|Fabrus|A07_VH3-23_IGHD1-14*01>3_IGHJ6*01	2651	3341
583	>gi|Fabrus|A08_VH3-23_IGHD1-20*01>1_IGHJ6*01	2652	3342
584	>gi|Fabrus|A09_VH3-23_IGHD1-20*01>3_IGHJ6*01	2653	3343
585	>gi|Fabrus|A10_VH3-23_IGHD1-26*01>1_IGHJ6*01	2654	3344
586	>gi|Fabrus|A11_VH3-23_IGHD1-26*01>3_IGHJ6*01	2655	3345
587	>gi|Fabrus|A12_VH3-23_IGHD2-2*01>2_IGHJ6*01	2656	3346
588	>gi|Fabrus|B01_VH3-23_IGHD2-2*01>3_IGHJ6*01	2657	3347
589	>gi|Fabrus|B02_VH3-23_IGHD2-8*01>2_IGHJ6*01	2658	3348
590	>gi|Fabrus|B03_VH3-23_IGHD2-8*01>3_IGHJ6*01	2659	3349
591	>gi|Fabrus|B04_VH3-23_IGHD2-15*01>2_IGHJ6*01	2660	3350
592	>gi|Fabrus|B05_VH3-23_IGHD2-15*01>3_IGHJ6*01	2661	3351
593	>gi|Fabrus|B06_VH3-23_IGHD2-21*01>2_IGHJ6*01	2662	3352
594	>gi|Fabrus|B07_VH3-23_IGHD2-21*01>3_IGHJ6*01	2663	3353
595	>gi|Fabrus|B08_VH3-23_IGHD3-3*01>1_IGHJ6*01	2664	3354

596	>gi|Fabrus|B09_VH3-23_IGHD3-3*01>2_IGHJ6*01	2665	3355
597	>gi|Fabrus|B10_VH3-23_IGHD3-3*01>3_IGHJ6*01	2666	3356
598	>gi|Fabrus|B11_VH3-23_IGHD3-9*01>2_IGHJ6*01	2667	3357
599	>gi|Fabrus|B12_VH3-23_IGHD3-10*01>2_IGHJ6*01	2668	3358
600	>gi|Fabrus|C01_VH3-23_IGHD3-10*01>3_IGHJ6*01	2669	3359
601	>gi|Fabrus|C02_VH3-23_IGHD3-16*01>2_IGHJ6*01	2670	3360
602	>gi|Fabrus|C03_VH3-23_IGHD3-16*01>3_IGHJ6*01	2671	3361
603	>gi|Fabrus|C04_VH3-23_IGHD3-22*01>2_IGHJ6*01	2672	3362
604	>gi|Fabrus|C05_VH3-23_IGHD3-22*01>3_IGHJ6*01	2673	3363
605	>gi|Fabrus|C06_VH3-23_IGHD4-4*01(1)>2_IGHJ6*01	2674	3364
606	>gi|Fabrus|C07_VH3-23_IGHD4-4*01(1)>3_IGHJ6*01	2675	3365
607	>gi|Fabrus|C08_VH3-23_IGHD4-11*01(1)>2_IGHJ6*01	2676	3366
608	>gi|Fabrus|C09_VH3-23_IGHD4-11*01(1)>3_IGHJ6*01	2677	3367
609	>gi|Fabrus|C10_VH3-23_IGHD4-17*01>2_IGHJ6*01	2678	3368
610	>gi|Fabrus|C11_VH3-23_IGHD4-17*01>3_IGHJ6*01	2679	3369
611	>gi|Fabrus|C12_VH3-23_IGHD4-23*01>2_IGHJ6*01	2680	3370
612	>gi|Fabrus|D01_VH3-23_IGHD4-23*01>3_IGHJ6*01	2681	3371
613	>gi|Fabrus|D02_VH3-23_IGHD5-5*01(2)>1_IGHJ6*01	2682	3372
614	>gi|Fabrus|D03_VH3-23_IGHD5-5*01(2)>2_IGHJ6*01	2683	3373
615	>gi|Fabrus|D04_VH3-23_IGHD5-5*01(2)>3_IGHJ6*01	2684	3374
616	>gi|Fabrus|D05_VH3-23_IGHD5-12*01>1_IGHJ6*01	2685	3375
617	>gi|Fabrus|D06_VH3-23_IGHD5-12*01>3_IGHJ6*01	2686	3376
618	>gi|Fabrus|D07_VH3-23_IGHD5-18*01(2)>1_IGHJ6*01	2687	3377
619	>gi|Fabrus|D08_VH3-23_IGHD5-18*01(2)>2_IGHJ6*01	2688	3378
620	>gi|Fabrus|D09_VH3-23_IGHD5-18*01(2)>3_IGHJ6*01	2689	3379
621	>gi|Fabrus|D10_VH3-23_IGHD5-24*01>1_IGHJ6*01	2690	3380
622	>gi|Fabrus|D11_VH3-23_IGHD5-24*01>3_IGHJ6*01	2691	3381
623	>gi|Fabrus|D12_VH3-23_IGHD6-6*01>1_IGHJ6*01	2692	3382
624	>gi|Fabrus|E01_VH3-23_IGHD6-6*01>2_IGHJ6*01	2693	3383
625	>gi|Fabrus|E02_VH3-23_IGHD6-13*01>1_IGHJ6*01	2694	3384
626	>gi|Fabrus|E03_VH3-23_IGHD6-13*01>2_IGHJ6*01	2695	3385
627	>gi|Fabrus|E04_VH3-23_IGHD6-19*01>1_IGHJ6*01	2696	3386
628	>gi|Fabrus|E05_VH3-23_IGHD6-19*01>2_IGHJ6*01	2697	3387
629	>gi|Fabrus|E06_VH3-23_IGHD6-25*01>1_IGHJ6*01	2698	3388
630	>gi|Fabrus|E07_VH3-23_IGHD6-25*01>2_IGHJ6*01	2699	3389
631	>gi|Fabrus|E08_VH3-23_IGHD7-27*01>1_IGHJ6*01	2700	3390
632	>gi|Fabrus|E09_VH3-23_IGHD7-27*01>3_IGHJ6*01	2701	3391
633	>gi|Fabrus|A01_VH3-23_IGHD1-1*01>1'_IGHJ6*01	2702	3392
634	>gi|Fabrus|A02_VH3-23_IGHD1-1*01>2'_IGHJ6*01	2703	3393
635	>gi|Fabrus|A03_VH3-23_IGHD1-1*01>3'_IGHJ6*01	2704	3394
636	>gi|Fabrus|A04_VH3-23_IGHD1-7*01>1'_IGHJ6*01	2705	3395
637	>gi|Fabrus|A05_VH3-23_IGHD1-7*01>3'_IGHJ6*01	2706	3396
638	>gi|Fabrus|A06_VH3-23_IGHD1-14*01>1'_IGHJ6*01	2707	3397
639	>gi|Fabrus|A07_VH3-23_IGHD1-14*01>2'_IGHJ6*01	2708	3398
640	>gi|Fabrus|A08_VH3-23_IGHD1-14*01>3'_IGHJ6*01	2709	3399
641	>gi|Fabrus|A09_VH3-23_IGHD1-20*01>1'_IGHJ6*01	2710	3400
642	>gi|Fabrus|A10_VH3-23_IGHD1-20*01>2'_IGHJ6*01	2711	3401
643	>gi|Fabrus|A11_VH3-23_IGHD1-20*01>3'_IGHJ6*01	2712	3402
644	>gi|Fabrus|A12_VH3-23_IGHD1-26*01>1'_IGHJ6*01	2713	3403
645	>gi|Fabrus|B01_VH3-23_IGHD1-26*01>3'_IGHJ6*01	2714	3404
646	>gi|Fabrus|B02_VH3-23_IGHD2-2*01>1'_IGHJ6*01	2715	3405
647	>gi|Fabrus|B03_VH3-23_IGHD2-2*01>3'_IGHJ6*01	2716	3406
648	>gi|Fabrus|B04_VH3-23_IGHD2-8*01>1'_IGHJ6*01	2717	3407
649	>gi|Fabrus|B05_VH3-23_IGHD2-15*01>1'_IGHJ6*01	2718	3408

650	>gi|Fabrus|B06_VH3-23_IGHD2-15*01>3'_IGHJ6*01	2719	3409
651	>gi|Fabrus|B07_VH3-23_IGHD2-21*01>1'_IGHJ6*01	2720	3410
652	>gi|Fabrus|B08_VH3-23_IGHD2-21*01>3'_IGHJ6*01	2721	3411
653	>gi|Fabrus|B09_VH3-23_IGHD3-3*01>1'_IGHJ6*01	2722	3412
654	>gi|Fabrus|B10_VH3-23_IGHD3-3*01>3'_IGHJ6*01	2723	3413
655	>gi|Fabrus|B11_VH3-23_IGHD3-9*01>1'_IGHJ6*01	2724	3414
656	>gi|Fabrus|B12_VH3-23_IGHD3-9*01>3'_IGHJ6*01	2725	3415
657	>gi|Fabrus|C01_VH3-23_IGHD3-10*01>1'_IGHJ6*01	2726	3416
658	>gi|Fabrus|C02_VH3-23_IGHD3-10*01>3'_IGHJ6*01	2727	3417
659	>gi|Fabrus|C03_VH3-23_IGHD3-16*01>1'_IGHJ6*01	2728	3418
660	>gi|Fabrus|C04_VH3-23_IGHD3-16*01>3'_IGHJ6*01	2729	3419
661	>gi|Fabrus|C05_VH3-23_IGHD3-22*01>1'_IGHJ6*01	2730	3420
662	>gi|Fabrus|C06_VH3-23_IGHD4-4*01(1)>1'_IGHJ6*01	2731	3421
663	>gi|Fabrus|C07_VH3-23_IGHD4-4*01(1)>3'_IGHJ6*01	2732	3422
664	>gi|Fabrus|C08_VH3-23_IGHD4-11*01(1)>1'_IGHJ6*01	2733	3423
665	>gi|Fabrus|C09_VH3-23_IGHD4-11*01(1)>3'_IGHJ6*01	2734	3424
666	>gi|Fabrus|C10_VH3-23_IGHD4-17*01>1'_IGHJ6*01	2735	3425
667	>gi|Fabrus|C11_VH3-23_IGHD4-17*01>3'_IGHJ6*01	2736	3426
668	>gi|Fabrus|C12_VH3-23_IGHD4-23*01>1'_IGHJ6*01	2737	3427
669	>gi|Fabrus|D01_VH3-23_IGHD4-23*01>3'_IGHJ6*01	2738	3428
670	>gi|Fabrus|D02_VH3-23_IGHD5-5*01(2)>1'_IGHJ6*01	2739	3429
671	>gi|Fabrus|D03_VH3-23_IGHD5-5*01(2)>3'_IGHJ6*01	2740	3430
672	>gi|Fabrus|D04_VH3-23_IGHD5-12*01>1'_IGHJ6*01	2741	3431
673	>gi|Fabrus|D05_VH3-23_IGHD5-12*01>3'_IGHJ6*01	2742	3432
674	>gi|Fabrus|D06_VH3-23_IGHD5-18*01(2)>1'_IGHJ6*01	2743	3433
675	>gi|Fabrus|D07_VH3-23_IGHD5-18*01(2)>3'_IGHJ6*01	2744	3434
676	>gi|Fabrus|D08_VH3-23_IGHD5-24*01>1'_IGHJ6*01	2745	3435
677	>gi|Fabrus|D09_VH3-23_IGHD5-24*01>3'_IGHJ6*01	2746	3436
678	>gi|Fabrus|D10_VH3-23_IGHD6-6*01>1'_IGHJ6*01	2747	3437
679	>gi|Fabrus|D11_VH3-23_IGHD6-6*01>2'_IGHJ6*01	2748	3438
680	>gi|Fabrus|D12_VH3-23_IGHD6-6*01>3'_IGHJ6*01	2749	3439
681	>gi|Fabrus|E01_VH3-23_IGHD6-13*01>1'_IGHJ6*01	2750	3440
682	>gi|Fabrus|E02_VH3-23_IGHD6-13*01>2'_IGHJ6*01	2751	3441
683	>gi|Fabrus|E03_VH3-23_IGHD6-13*01>3'_IGHJ6*01	2752	3442
684	>gi|Fabrus|E04_VH3-23_IGHD6-19*01>1'_IGHJ6*01	2753	3443
685	>gi|Fabrus|E05_VH3-23_IGHD6-19*01>2'_IGHJ6*01	2754	3444
686	>gi|Fabrus|E06_VH3-23_IGHD6-19*01>3'_IGHJ6*01	2755	3445
687	>gi|Fabrus|E07_VH3-23_IGHD6-25*01>1'_IGHJ6*01	2756	3446
688	>gi|Fabrus|E08_VH3-23_IGHD6-25*01>3'_IGHJ6*01	2757	3447
689	>gi|Fabrus|E09_VH3-23_IGHD7-27*01>1'_IGHJ6*01	2758	3448
690	>gi|Fabrus|E10_VH3-23_IGHD7-27*01>2'_IGHJ6*01	2759	3449

EXAMPLE 15

Electrochemiluminescence Binding Assay

The electrochemiluminescence (ECL) binding assay described in Example 13 was further used to screen a 5,376 member Fab library and 15 modified Fab antibodies set forth in rows 22-36 in Table 77 below for antibodies capable of binding to one of the nine different antigens. As noted in Example 13 above, data were analyzed by comparing the ECL signals

for an antigen to the blank of each well. A signal to blank ratio of 4 or more was considered a "Hit" Fab.

Fifty-six (56) plates, each containing 96 different Fabs, were screened using the ECL assay. Thirty-six (36) Fabs were identified with specific binding affinity to one or more of the protein antigens, as indicated in Tables 42-44. Table 42, below, summarizes the results of the ECL assay, including the recombinant human target/protein antigen, the number of antibody hits per target and the % of hits per target (number of hits/5376 antibodies screened). Eleven Fabs were identified that bind to recombinant human delta-like protein 4 (DLL4) whereas only 2 hits were identified that bind to to recombinant human epidermal growth factor 2 (ErbB2). Ten Fabs were identified that bind to recombinant human erythropoietin receptor (Epo R) and 6 Fabs were identified that bind to recombinant human P-cadherin. Additionally, 3 Fabs were identified that bind to recombinant human epidermal growth factor 2 (ErbB2) and 3 Fabs were identified that bind to recombinant human Notch-1. Table 43, below, lists the 21 Fabs (including the heavy chain and light chain) that were identified as "hits" in the initial ECL screen. A "hit" was a Fab antibody with signal to blank ratio of greater than 4. The results of the initial MSD assay screen at a single Fab concentration are listed in Table 44 below. Table 44 lists the 21 Fabs (the Fab No. corresponds each of the Fabs identified in Table 43), the Fab concentration, the 9 recombinant human target/protein antigens, and the ECL signals from the initial MSD assay screen at the given Fab concentration.

Table 42. Summary of 5376 Fab Library ECL Screen

rHuman Antigen	Number of Hits	% Per Target
ErbB2/Fc chimera	2	0.037
EGF R/Fc chimera	3	0.056
HGF R/Fc chimera	0	n/a
Notch-1/Fc chimera	3	0.056
CD44/Fc chimera	0	n/a
IGF-1 sR	0	n/a
P-cadherin/Fc chimera	6	0.112
Epo R/Fc chimera	10	0.186
DLL4	11	0.205

Table 43. Fab Antibody "Hits" identified in ECL Screen

Fab No.	Heavy Chain	Light Chain
1	VH4-28_IGHD7-27*01_IGHJ1*01	L2_IGKJ1*01
2	VH4-31_IGHD7-27*01_IGHJ5*01	L2_IGKJ1*01
3	VH2-5_IGHD7-27*01_IGHJ2*01	L2_IGKJ1*01
4	VH1-46_IGHD7-27*01_IGHJ2*01	A27_IGKJ1*01
5	VH1-69_IGHD1-1*01_IGHJ6*01	A17_IGKJ1*01
6	VH1-46_IGHD2-15*01_IGHJ2*01	L2_IGKJ1*01
7	VH1-46_IGHD6-13*01_IGHJ4*01	L2_IGKJ1*01

8	VH4-34_IGHD7-27*01_IGHJ4*01	L5_IGKJ1*01
9	VH1-46_IGHD6-13*01_IGHJ4*01	A27_IGKJ1*01
10	VH1-46_IGHD7-27*01_IGHJ2*01	L6_IGKJ1*01
11	VH1-3_IGHD4-23*01_IGHJ4*01	L12_IGKJ1*01
12	VH1-46_IGHD2-15*01_IGHJ2*01	L12_IGKJ1*01
13	VH1-46_IGHD3-10*01_IGHJ4*01	L12_IGKJ1*01
14	VH1-8_IGHD2-2*01_IGHJ6*01	L12_IGKJ1*01
15	VH1-46_IGHD3-10*01_IGHJ4*01	O1_IGKJ1*01
16	VH1-46_IGHD6-13*01_IGHJ4*01	O1_IGKJ1*01
17	VH4-34_IGHD7-27*01_IGHJ4*01	V1-4_IGLJ4*01
18	VH4-31_IGHD2-15*01_IGHJ2*01	V1-4_IGLJ4*01
19	VH4-34_IGHD7-27*01_IGHJ4*01	V4-6_IGLJ4*01
20	VH3-23_IGHD3-10*01>3_IGHJ6*01	O12_IGKJ1*01
21	VH3-23_IGHD3-10*01>1'_IGHJ3*01	O12_IGKJ1*01

Table 44. ECL Signals for Identified Fab "Hits" from 5376 Fab Library Screen

Fab No.	[Fab] µM	rHuman Target									
		ErbB2	EGFR	HGFR	Notch-1	CD44	IGF-1	P-cad	EPOR	DLL4	Blank
1	0.36	2028	3803	2034	3813	2482	1703	2741	19375	3911	1948
2	0.61	581	1222	539	1195	1048	596	782	3065	1006	570
3	0.03	2556	381	311	563	421	344	352	492	476	373
4	0.36	1474	1405	1225	1921	1542	1081	1795	2434	9082	928
5	0.65	2940	662	437	1336	797	656	695	922	849	441
6	0.25	15169	88015	5912	10346	10436	4929	16145	30118	14728	3693
7	1.19	18514	32030	17322	41739	27596	14089	34551	141492	39645	11543
8	0.51	1705	1807	1738	2876	1879	1742	3176	2563	5648	1393
9	0.48	6940	9043	6313	12759	9979	5468	15301	67194	13726	2877
10	1.56	2452	2497	3116	3953	2281	1919	5418	4129	3770	1129
11	0.06	1569	1755	1910	2232	1683	2325	2432	1973	13614	842
12	0.28	4314	8327	5182	5281	4561	4643	8057	8071	8151	1773
13	0.93	10795	15559	13790	23657	10634	13930	26366	16729	74294	4760
14	0.13	840	859	969	1324	932	1167	1641	1106	9848	786
15	1.57	904	1403	1039	1256	836	985	2029	6393	1496	797
16	0.93	1610	1855	2596	1918	1453	1787	2422	4241	9632	859
17	0.58	1262	1022	1706	739	761	1198	725	768	3128	403
18	0.21	1308	1297	1531	809	868	1557	915	885	3332	489
19	0.34	900	738	914	912	694	871	935	907	2561	356
20	0.12	4578	4060	5472	5501	4213	3137	17528	11210	6646	2225
21	0.42	702	759	935	919	748	844	3178	1504	922	450

To confirm a "Hit" identified in the intial ECL screening (see Tables 42-44 above), a Fab concentration dependent titration was carried out to determine the Fab-antigen binding affinity. The assay procedure was the same as described Example 13 above, except that the concentration of Fab antibody was varied between wells from 0.0628 nM to 1.57 µM. The results of the dose response assays are set forth in Tables 45-61 below. Tables 62-76 below list the results of the dose response assays for 15 modified anti-DLL4 antibodies (set forth in rows 22-36 of Table 77, below). The modified anti-DLL4 antibodies have at least one

mutation in the heavy or light chain as compared to the previously identified germline antibodies.

Table 45. Binding affinity of Fab VH4-28_IGHD7-27*01_IGHJ1*01 & L2_IGKJ1*01		
Fab[nM]	**360**	**36**
ErbB2/Fc	647	600
EGF R/Fc	957	711
HGF R/Fc	581	613
Notch-1/Fc	1026	773
CD44/Fc	740	679
IGF-1 sR	535	486
P-Cadherin/Fc	636	693
EPO R/Fc	4715	2977
DLL4	866	799
Blank	462	413

Table 46. Binding affinity of Fab VH1-46_IGHD2-15*01_IGHJ2*01 & L2_IGKJ1*01				
Fab[μM]	**0.25**	**0.0625**	**0.01563**	**0.00391**
ErbB2/Fc	29608	9033	4495	1667
EGF R/Fc	116674	94778	70836	35936
HGF R/Fc	13427	4108	1998	913
Notch-1/Fc	21447	5848	2800	1282
CD44/Fc	23015	6746	3182	1295
IGF-1 sR	11050	3150	1742	822
P-Cadherin/Fc	25459	7739	4945	1962
EPO R/Fc	49177	21136	11342	5022
DLL4	27691	8051	4015	1551
Blank	6344	1738	906	576

Table 47. Binding affinity of Fab VH1-46_IGHD6-13*01_IGHJ4*01 & L2_IGKJ1*01				
Fab[μM]	**1.19**	**0.2975**	**0.07438**	**0.01859**
ErbB2/Fc	38410	15111	7551	5531
EGF R/Fc	62454	42213	16605	11750
HGF R/Fc	45494	17396	6611	4566
Notch-1/Fc	72018	37503	21990	17565
CD44/Fc	47145	28601	10922	7322
IGF-1 sR	35187	17389	5804	3779
P-Cadherin/Fc	69710	26043	14807	11672
EPO R/Fc	192967	167064	153692	188065
DLL4	74900	34726	20719	18888
Blank	24999	5019	2504	1776

Table 48. Binding affinity of Fab VH4-34_IGHD7-27*01_IGHJ4*01 & L5_IGKJ1*01

Fab[μM]	0.51	0.1275	0.03188	0.00797
ErbB2/Fc	1532	857	584	493
EGF R/Fc	2363	1061	694	530
HGF R/Fc	1989	853	693	419
Notch-1/Fc	2773	1497	849	654
CD44/Fc	2012	926	653	490
IGF-1 sR	2236	1045	765	564
P-Cadherin/Fc	2389	957	775	502
EPO R/Fc	2624	1067	789	566
DLL4	5183	2382	1282	872
Blank	1096	530	536	364

Table 49. Binding affinity of Fab VH1-46_IGHD6-13*01_IGHJ4*01 & A27_IGKJ1*01			
Fab[μM]	0.48	0.096	0.0192
ErbB2/Fc	11287	3365	2313
EGF R/Fc	14638	4509	3115
HGF R/Fc	8002	2328	1582
Notch-1/Fc	15931	4802	3041
CD44/Fc	13445	4320	2915
IGF-1 sR	8927	2449	1826
P-Cadherin/Fc	15595	6654	5040
EPO R/Fc	70938	57356	62037
DLL4	16065	5586	3555
Blank	2945	917	751

Table 50. Binding affinity of Fab VH1-46_IGHD7-27*01_IGHJ2*01 & L6_IGKJ1*01			
Fab[μM]	1.56	0.312	0.0624
ErbB2/Fc	7577	3659	2146
EGF R/Fc	7832	4328	2415
HGF R/Fc	10267	4691	2453
Notch-1/Fc	9447	4462	2352
CD44/Fc	7595	4171	2110
IGF-1 sR	6913	3508	2034
P-Cadherin/Fc	15016	7098	4226
EPO R/Fc	9480	5020	2678
DLL4	10897	5484	2585
Blank	4357	1977	960

Table 51. Binding affinity of Fab VH1-3_IGHD4-23*01_IGHJ4*01 & L12_IGKJ1*01				
Fab[nM]	60	15	3.75	0.9375
ErbB2/Fc	2155	740	291	268
EGF R/Fc	2563	842	371	224
HGF R/Fc	2298	743	394	243

Notch-1/Fc	2886	1058	375	348
CD44/Fc	2355	748	307	251
IGF-1 sR	2666	859	314	204
P-Cadherin/Fc	2662	837	331	191
EPO R/Fc	3214	970	358	238
DLL4	17270	7728	1569	453
Blank	1433	536	191	153

Table 52. Binding affinity of Fab VH1-46_IGHD2-15*01_IGHJ2*01 & L12_IGKJ1*01				
Fab[nM]	**280**	**70**	**17.5**	**4.375**
ErbB2/Fc	3953	1358	541	384
EGF R/Fc	6667	2574	1305	542
HGF R/Fc	3564	1289	565	193
Notch-1/Fc	4382	1492	680	480
CD44/Fc	4069	1370	664	424
IGF-1 sR	3533	1319	626	369
P-Cadherin/Fc	5400	1817	949	469
EPO R/Fc	8496	2485	1262	594
DLL4	8111	2747	1219	558
Blank	1691	635	304	305

Table 53. Binding affinity of Fab VH1-46_IGHD3-10*01_IGHJ4*01 & L12_IGKJ1*01				
Fab[nM]	**920**	**230**	**57.5**	**14.375**
ErbB2/Fc	10924	4078	2447	1594
EGF R/Fc	13406	5723	3858	2672
HGF R/Fc	10708	3934	2297	1600
Notch-1/Fc	20086	9737	5886	4206
CD44/Fc	9698	3817	2313	1488
IGF-1 sR	10246	4764	2833	1746
P-Cadherin/Fc	16666	6484	4110	2318
EPO R/Fc	16429	6949	4038	2718
DLL4	73638	119436	144126	125422
Blank	4082	1656	954	738

Table 54. Binding affinity of Fab VH1-8_IGHD2-2*01_IGHJ6*01 & L12_IGKJ1*01				
Fab[nM]	**130**	**32.5**	**8.1**	**2.0**
ErbB2/Fc	1533	556	557	382
EGF R/Fc	1746	645	560	424
HGF R/Fc	1882	525	551	356
Notch-1/Fc	1759	706	612	539
CD44/Fc	1754	573	528	447
IGF-1 sR	1973	561	518	367
P-Cadherin/Fc	1845	556	573	250

EPO R/Fc	2151	673	660	433
DLL4	7738	2989	1548	605
Blank	1153	473	435	316

Table 55. Binding affinity of Fab FabVH1-46_IGHD3-10*01_IGHJ4*01 & O1_IGKJ1*01				
Fab[nM]	**1570**	**392.5**	**98.1**	**24.5**
ErbB2/Fc	1263	539	247	241
EGF R/Fc	2481	744	4386	317
HGF R/Fc	1638	581	335	211
Notch-1/Fc	1639	749	313	434
CD44/Fc	1381	498	265	267
IGF-1 sR	1428	466	309	239
P-Cadherin/Fc	1793	459	347	257
EPO R/Fc	6121	5863	5628	4531
DLL4	2701	735	402	339
Blank	866	338	210	149

Table 56. Binding affinity of Fab VH1-46_IGHD6-13*01_IGHJ4*01 & O1_IGKJ1*01				
Fab[nM]	**930**	**232.5**	**58.1**	**14.5**
ErbB2/Fc	2225	779	322	274
EGF R/Fc	3110	803	444	357
HGF R/Fc	2344	790	432	373
Notch-1/Fc	2206	778	388	317
CD44/Fc	1917	607	375	212
IGF-1 sR	1915	569	343	234
P-Cadherin/Fc	2438	655	478	277
EPO R/Fc	3009	1472	829	660
DLL4	8162	3586	1876	1149
Blank	1206	460	225	117

Table 57. Binding affinity of Fab VH4-34_IGHD7-27*01_IGHJ4*01 & V1-4_IGLJ4*01				
Fab[nM]	**580**	**145**	**36.3**	**9.1**
ErbB2/Fc	1712	1123	1029	987
EGF R/Fc	1631	856	831	800
HGF R/Fc	2341	1173	1065	894
Notch-1/Fc	1585	860	633	754
CD44/Fc	1228	692	629	607
IGF-1 sR	1364	794	799	788
P-Cadherin/Fc	2240	850	684	589
EPO R/Fc	1579	845	722	697
DLL4	4420	2140	1399	1030
Blank	679	357	314	276

Table 58. Binding affinity of Fab VH4-31_IGHD2-15*01_IGHJ2*01 & V1-4_IGLJ4*01				
Fab[nM]	**210**	**52.5**	**13.1**	**3.3**
ErbB2/Fc	1977	1511	930	1031
EGF R/Fc	1617	1109	824	847
HGF R/Fc	2060	1286	981	849
Notch-1/Fc	1972	1323	669	726
CD44/Fc	1395	897	708	621
IGF-1 sR	1431	911	814	743
P-Cadherin/Fc	4410	2161	1062	678
EPO R/Fc	2123	1319	776	695
DLL4	4108	1951	1107	922
Blank	833	467	376	359

Table 59. Binding affinity of Fab VH4-34_IGHD7-27*01_IGHJ4*01 & V4-6_IGLJ4*01				
Fab[nM]	**340**	**170**	**85.0**	**42.5**
ErbB2/Fc	1226	964	844	866
EGF R/Fc	1208	826	1001	528
HGF R/Fc	1238	757	998	607
Notch-1/Fc	1209	816	780	649
CD44/Fc	959	660	693	522
IGF-1 sR	1042	832	891	646
P-Cadherin/Fc	1160	744	709	421
EPO R/Fc	1255	790	817	494
DLL4	2332	1462	1311	877
Blank	554	262	292	162

Table 60. Binding affinity of Fab VH3-23_IGHD3-10*01>3_IGHJ6*01 & O12_IGKJ1*01				
Fab[nM]	**120**	**12**	**1.2**	**0.12**
ErbB2/Fc	17294	4358	677	287
EGF R/Fc	14925	1984	464	272
HGF R/Fc	15917	2703	412	287
Notch-1/Fc	14382	2582	660	218
CD44/Fc	13519	1321	341	291
IGF-1 sR	13265	1135	181	175
P-Cadherin/Fc	61714	28490	1684	318
EPO R/Fc	33268	10966	1014	260
DLL4	20627	2510	319	210
Blank	6749	573	227	264

Table 61. Binding affinity of Fab VH3-23_IGHD3-10*01>1'_IGHJ3*01 & O12_IGKJ1*01		
Fab[nM]	**421.12**	**42.112**

ErbB2/Fc	868	524
EGF R/Fc	765	422
HGF R/Fc	1202	565
Notch-1/Fc	1061	437
CD44/Fc	903	360
IGF-1 sR	1065	364
P-Cadherin/Fc	2949	1546
EPO R/Fc	1299	759
DLL4	1090	404
Blank	639	323

Table 62. Binding affinity of Fab VH5-51_IGHD5-18*01>3_IGHJ4*01_G100K & V3-4_IGLJ1*01

Fab[nM]	**1000**	**200**	**40**	**8**	**1.6**
ErbB2/Fc	1251	1467	1394	1232	1320
EGF R/Fc	1029	1371	1149	1033	1180
HGF R/Fc	1199	1428	1306	1260	1438
Notch-1/Fc	1176	1247	875	831	816
CD44/Fc	1025	1162	857	853	938
IGF-1 sR	1134	1320	1271	1203	1437
P-Cadherin/Fc	1043	1126	744	788	811
EPO R/Fc	1122	1226	979	881	899
DLL4	29554	45421	35876	11408	2423
Blank	630	588	518	489	565

Table 63. Binding affinity of Fab VH5-51_IGHD5-18*01>3_IGHJ4*01_G100R & V3-4_IGLJ1*01

Fab[nM]	**1000**	**200**	**40**	**8**	**1.6**	**0.32**
ErbB2/Fc	945	1448	1421	1326	1439	1485
EGF R/Fc	721	1017	1113	1078	1204	1221
HGF R/Fc	778	1164	1234	1240	1206	1287
Notch-1/Fc	761	1330	1014	916	1052	983
CD44/Fc	559	895	824	786	997	877
IGF-1 sR	733	1110	1243	1107	1329	1253
P-Cadherin/Fc	762	815	1020	669	666	656
EPO R/Fc	666	1175	994	911	920	851
DLL4	23398	29772	19481	5472	1541	1212
Blank	427	529	502	479	449	513

Table 64. Binding affinity of Fab VH1-46_IGHD6-6*01>1_IGHJ1*01_S104F & L6_IGKJ1*01

Fab[nM]	**1000**	**200**	**40**	**8**	**1.6**	**0.32**
ErbB2/Fc	7472	5434	3428	1775	1008	611
EGF R/Fc	3575	2921	2297	1473	987	709
HGF R/Fc	3314	2836	2110	1619	861	710
Notch-1/Fc	9798	6377	3990	2003	1114	684

CD44/Fc	5105	4071	2711	1523	1016	679
IGF-1 sR	3074	2778	2141	1517	966	630
P-Cadherin/Fc	5955	6263	5103	2634	1369	750
EPO R/Fc	5162	4593	3233	2040	1132	673
DLL4	35253	58743	62035	44781	5920	916
Blank	2186	1787	1442	1117	713	518

Table 65. Binding affinity of Fab VH1-46_IGHD6-6*01_IGHJ1*01_S104A & L6_IGKJ1*01						
Fab[nM]	**1000**	**200**	**40**	**8**	**1.6**	**0.32**
ErbB2/Fc	7419	4038	2231	1902	1168	766
EGF R/Fc	3481	2951	1843	1298	862	660
HGF R/Fc	3531	2443	1545	1305	830	574
Notch-1/Fc	8058	5705	3479	2196	1166	739
CD44/Fc	4734	3189	2677	1487	1017	684
IGF-1 sR	3348	2603	1897	1287	815	611
P-Cadherin/Fc	5632	3993	2602	1916	1139	649
EPO R/Fc	8292	3997	3510	1982	1117	739
DLL4	14331	14838	13637	9329	2130	646
Blank	2142	1659	1229	1188	648	428

Table 66. Binding affinity of Fab VH5-51_IGHD5-18*01>3_IGHJ4*01_G104T & V3-4_IGLJ1*01		
Fab[nM]	**1000**	**10**
ErbB2/Fc	3532	1517
EGF R/Fc	3937	1188
HGF R/Fc	3769	1392
Notch-1/Fc	3342	933
CD44/Fc	3378	841
IGF-1 sR	3992	1118
P-Cadherin/Fc	3426	705
EPO R/Fc	3376	910
DLL4	29776	5229
Blank	1742	427

Table 67. Binding affinity of Fab VH1-46_IGHD6-6*01_IGHJ1*01_S103P & L6_IGKJ1*01		
Fab[nM]	**1000**	**10**
ErbB2/Fc	1276	847
EGF R/Fc	1909	773
HGF R/Fc	1359	859
Notch-1/Fc	1210	792
CD44/Fc	1220	746
IGF-1 sR	1336	814

P-Cadherin/Fc	1376	846
EPO R/Fc	1511	802
DLL4	29752	55127
Blank	760	550

Table 68. Binding affinity of Fab VH1-46_IGHD6-6*01_IGHJ1*01_S102A & L6_IGKJ1*01		
Fab[nM]	**1000**	**10**
ErbB2/Fc	946	670
EGF R/Fc	1601	677
HGF R/Fc	1658	698
Notch-1/Fc	1253	647
CD44/Fc	1087	681
IGF-1 sR	1167	657
P-Cadherin/Fc	1502	691
EPO R/Fc	1320	761
DLL4	22225	38724
Blank	1121	418

Table 69. Binding affinity of Fab VH1-46_IGHD6-6*01_IGHJ1*01_S102A_S103P_S104F & L6_IGKJ1*01		
Fab[nM]	**1000**	**10**
ErbB2/Fc	1292	842
EGF R/Fc	2434	809
HGF R/Fc	1581	691
Notch-1/Fc	1620	1144
CD44/Fc	1314	887
IGF-1 sR	1175	720
P-Cadherin/Fc	2499	894
EPO R/Fc	1656	1109
DLL4	73307	345030
Blank	731	680

Table 70. Binding affinity of Fab VH5-51_IGHD5-18*01>3_IGHJ4*01_G100K_G104T & V3-4_IGLJ1*01				
Fab[nM]	**500**	**25**	**1.25**	**0.0625**
ErbB2/Fc	957	927	695	692
EGF R/Fc	1106	821	729	736
HGF R/Fc	1299	805	774	643
Notch-1/Fc	703	440	312	439
CD44/Fc	923	570	444	394
IGF-1 sR	1114	780	674	537
P-Cadherin/Fc	815	269	374	331

EPO R/Fc	828	597	448	332
DLL4	25941	77931	38837	1014
Blank	480	206	256	239

Table 71. Binding affinity of Fab VH1-46_IGHD6-6*01_IGHJ1*01_S102A_S103P_S104F_H111F & L6_IGKJ1*01			
Fab[nM]	**500**	**50**	**5**
ErbB2/Fc	2621	2114	1377
EGF R/Fc	2514	2042	1158
HGF R/Fc	2043	1282	1016
Notch-1/Fc	4376	2726	1170
CD44/Fc	2912	1610	1132
IGF-1 sR	1872	1226	917
P-Cadherin/Fc	3665	2491	1663
EPO R/Fc	5518	2462	1835
DLL4	29919	94200	149972
Blank	1016	774	626

Table 72. Binding affinity of Fab VH1-46_IGHD6-6*01_IGHJ1*01_S102A_S103P_S104F_H111Y & L6_IGKJ1*01				
Fab[nM]	**500**	**50**	**5**	**0.5**
ErbB2/Fc	713	589	315	331
EGF R/Fc	898	523	311	273
HGF R/Fc	523	325	323	319
Notch-1/Fc	644	475	383	263
CD44/Fc	664	433	413	279
IGF-1 sR	592	460	320	164
P-Cadherin/Fc	939	626	437	215
EPO R/Fc	1212	631	377	359
DLL4	93071	206919	84945	2971
Blank	410	433	367	365

Table 73. Binding affinity of Fab VH1-46_IGHD6-6*01_IGHJ1*01_S102A_S103P_S104Y_H111Y & L6_IGKJ1*01				
Fab[nM]	**500**	**50**	**5**	**0.5**
ErbB2/Fc	596	470	2855	1721
EGF R/Fc	758	489	2980	1751
HGF R/Fc	841	312	3101	1688
Notch-1/Fc	689	389	3232	1756
CD44/Fc	604	345	2756	1563
IGF-1 sR	747	399	3033	1662
P-Cadherin/Fc	1195	470	4162	2628
EPO R/Fc	1273	533	3582	1840
DLL4	105743	201050	73428	5150
Blank	436	329	2104	1309

Table 74. Binding affinity of Fab VH1-46_IGHD6-6*01_IGHJ1*01_S102A_S103P_S104F & L6_IGKJ1*01_S28P				
Fab[nM]	**50**	**10**	**2**	**0.4**
ErbB2/Fc	384	136	176	275
EGF R/Fc	328	207	352	246
HGF R/Fc	183	136	255	199
Notch-1/Fc	477	280	307	248
CD44/Fc	340	212	266	257
IGF-1 sR	355	152	205	172
P-Cadherin/Fc	431	216	223	191
EPO R/Fc	527	392	251	147
DLL4	37653	26851	6103	1140
Blank	274	146	130	138

Table 75. Binding affinity of Fab VH1-46_IGHD6-6*01_IGHJ1*01_S102A_S103P_S104F & L6_IGKJ1*01_S30N				
Fab[nM]	**50**	**10**	**2**	**0.4**
ErbB2/Fc	395	274	138	203
EGF R/Fc	294	245	171	173
HGF R/Fc	135	239	207	120
Notch-1/Fc	279	253	274	197
CD44/Fc	271	286	209	176
IGF-1 sR	240	233	296	141
P-Cadherin/Fc	143	283	395	111
EPO R/Fc	500	420	294	224
DLL4	37208	33374	11375	1039
Blank	299	165	205	179

Table 76. Binding affinity of Fab VH1-46_IGHD6-6*01_IGHJ1*01_S102A_S103P_S104F & L6_IGKJ1*01_S31K				
Fab[nM]	**50**	**10**	**2**	**0.4**
ErbB2/Fc	397	303	337	159
EGF R/Fc	350	297	197	175
HGF R/Fc	257	271	183	119
Notch-1/Fc	355	388	202	197
CD44/Fc	262	352	146	190
IGF-1 sR	257	214	222	65
P-Cadherin/Fc	411	240	351	151
EPO R/Fc	574	392	326	217
DLL4	35274	29781	10534	1259
Blank	183	267	197	255

Summary

Table 77, below, summarizes the results of the MSD assay. Table 77 lists the recombinant human target/protein antigen(s) and the Fabs, as designated by their respective heavy and light chains (including SEQ ID NOS). As is indicated in Table 77, below, several Fabs were identified that bind to multiple targets. For example, Fab VH1-46_IGHD2-15*01_IGHJ2*01 & L12_IGKJ1*01 binds to EGF R, Epo R and DLL4 while Fab VH1-46_IGHD3-10*01_IGHJ4*01 & L12_IGKJ1*01 binds to Notch-1, P-cadherin and DLL4. Table 77 below also lists the 15 additional modified Fabs (set forth in rows 22-36) that bind to DLL4.

Table 77. Selected Fabs and their targets

Fab No.	rHuman Target	Heavy Chain	SEQ ID NO	Light Chain	SEQ ID NO
1	Epo R/Fc chimera	VH4-28_IGHD7-27*01_IGHJ1*01	1759	L2_IGKJ1*01	1843
2	Epo R/Fc chimera	VH4-31_IGHD7-27*01_IGHJ5*01	1769	L2_IGKJ1*01	1843
3	ErbB2/Fc chimera	VH2-5_IGHD7-27*01_IGHJ2*01	1559	L2_IGKJ1*01	1843
4	Epo R/Fc chimera	VH1-46_IGHD7-27*01_IGHJ2*01	1514	A27_IGKJ1*01	1833
5	ErbB2/Fc chimera	VH1-69_IGHD1-1*01_IGHJ6*01	1522	A17_IGKJ1*01	1828
6	Epo R/Fc chimera and EGF R/Fc chimera	VH1-46_IGHD2-15*01_IGHJ2*01	1508	L2_IGKJ1*01	1843
7	EGF R/Fc chimera, Notch-1/Fc chimera, P-cadherin/Fc chimera, Epo R/Fc chimera and DLL4	VH1-46_IGHD6-13*01_IGHJ4*01	1512	L2_IGKJ1*01	1843
8	DLL4	VH4-34_IGHD7-27*01_IGHJ4*01	1779	L5_IGKJ1*01	1849
9	Notch-1/Fc chimera, P-cadherin/Fc chimera, Epo R/Fc chimera and DLL4	VH1-46_IGHD6-13*01_IGHJ4*01	1512	A27_IGKJ1*01	1833
10	P-cadherin/Fc chimera	VH1-46_IGHD7-27*01_IGHJ2*01	1514	L6_IGKJ1*01	1850
11	DLL4	VH1-3_IGHD4-23*01_IGHJ4*01	1494	L12_IGKJ1*01	1841
12	EGF R/Fc chimera, Epo R/Fc chimera and DLL4	VH1-46_IGHD2-15*01_IGHJ2*01	1508	L12_IGKJ1*01	1841
13	Notch-1/Fc chimera, P-	VH1-46_IGHD3-10*01_IGHJ4*01	1509	L12_IGKJ1*01	1841

	cadherin/Fc chimera and DLL4				
14	DLL4	VH1-8_IGHD2-2*01_IGHJ6*01	1537	L12_IGKJ1*01	1841
15	Epo R/Fc chimera	VH1-46_IGHD3-10*01_IGHJ4*01	1509	O1_IGKJ1*01	1853
16	Epo R/Fc chimera and DLL4	VH1-46_IGHD6-13*01_IGHJ4*01	1512	O1_IGKJ1*01	1853
17	DLL4	VH4-34_IGHD7-27*01_IGHJ4*01	1779	V1-4_IGLJ4*01	1864
18	DLL4	VH4-31_IGHD2-15*01_IGHJ2*01	1761	V1-4_IGLJ4*01	1864
19	DLL4	VH4-34_IGHD7-27*01_IGHJ4*01	1779	V4-6_IGLJ4*01	1886
20	P-cadherin/Fc chimera and Epo R/Fc chimera	VH3-23_IGHD3-10*01>3_IGHJ6*01	3359	O12_IGKJ1*01	1854
21	P-cadherin/Fc chimera	VH3-23_IGHD3-10*01>1'_IGHJ3*01	3071	O12_IGKJ1*01	1854
22	DLL4	VH5-51_IGHD5-18*01>3_IGHJ4*01_G100K	3720	V3-4_IGLJ1*01	1881
23	DLL4	VH5-51_IGHD5-18*01>3_IGHJ4*01_G100R	3721	V3-4_IGLJ1*01	1881
24	DLL4	VH1-46_IGHD6-6*01>1_IGHJ1*01_S104F	3722	L6_IGKJ1*01	1850
25	DLL4	VH1-46_IGHD6-6*01_IGHJ1*01_S104A	3723	L6_IGKJ1*01	1850
26	DLL4	VH5-51_IGHD5-18*01>3_IGHJ4*01_G104T	3724	V3-4_IGLJ1*01	1881
27	DLL4	VH1-46_IGHD6-6*01_IGHJ1*01_S103P	3725	L6_IGKJ1*01	1850
28	DLL4	VH1-46_IGHD6-6*01_IGHJ1*01_S102A	3726	L6_IGKJ1*01	1850
29	DLL4	VH1-46_IGHD6-6*01_IGHJ1*01_S102A_S103P_S104F	3727	L6_IGKJ1*01	1850
30	DLL4	VH5-51_IGHD5-18*01>3_IGHJ4*01_G100K_G104T	3728	V3-4_IGLJ1*01	1881
31	DLL4	VH1-46_IGHD6-6*01_IGHJ1*01_S102A_S103P_S104F_H111F	3729	L6_IGKJ1*01	1850
32	DLL4	VH1-46_IGHD6-6*01_IGHJ1*01_S102A_S103P_S104F_H111Y	3730	L6_IGKJ1*01	1850
33	DLL4	VH1-46_IGHD6-6*01_IGHJ1*01_S102A_S103P_S104Y_H111Y	3731	L6_IGKJ1*01	1850
34	DLL4	VH1-46_IGHD6-	3727	L6_IGKJ1*01_	3732

		6*01_IGHJ1*01_S102A_ S103P_S104F		S28P	
35	DLL4	VH1-46_IGHD6-6*01_IGHJ1*01_S102A_ S103P_S104F	3727	L6_IGKJ1*01_ S30N	3733
36	DLL4	VH1-46_IGHD6-6*01_IGHJ1*01_S102A_ S103P_S104F	3727	L6_IGKJ1*01_ S31K	3734

Example 16

Surface Plasmon Resonance

In this example, the binding affinities of selected Fabs (see Tables 78-79) to recombinant human DLL4 (R&D Systems) were analyzed using Surface Plasmon Resonance (SPR) (Biosensor Tools, Salt Lake City, UT). The Fabs (see Table 78) include germline antibodies identified in the initial ECL screen as binding to DLL4 (as shown in Example 13) and modified Fabs that contain one or more mutations in the heavy or light chain as compared to the initially identified anti-DLL4 Fabs.

The results are shown in Table 79 below. Table 79 lists Fab (by Fab No.), the k_a ($M^{-1}s^{-1}$), the k_d (s^{-1}), and the K_D (nM) and the standard deviation (in parentheses). The results indicate that the Fabs have binding affinity for DLL4 ranging from 48.5 nM to 38 uM. Germline Fab VH5-51_IGHD5-18*01>3_IGHJ4*01 & V3-4_IGLJ1*01 has an average K_D of 4.8 uM while variant Fab VH5-51_IGHD5-18*01>3_IGHJ4*01_ G100K_G104T & V3-4_IGLJ1*01 has an improved K_D of 355 nM. Germline Fab VH1-46_IGHD6-6*01_IGHJ1*01 & L6_IGKJ1*01 binds DLL4 with an average K_D of 730 nM while the variant Fabs (rows 5-6 and 8-10 of Tables 78 and 79 below) bind DLL4 with improved K_Ds ranging from 70.6 nM to 388 nM. Germline Fab VH6-1_IGHD3-3*01_IGHJ4*01 & V4-3_IGLJ4*01 has an average binding affinity of 38 uM while germline Fab VH1-46_IGHD3-10*01_IGHJ4*01 & L12_IGKJ1*01 has an average K_D of 500 nM.

Table 78. DLL4 Fabs for Surface Plasmon Resonance

Fab No	Heavy Chain	Light Chain
1	VH5-51_IGHD5-18*01>3_IGHJ4*01	V3-4_IGLJ1*01
2	VH1-46_IGHD6-6*01_IGHJ1*01	L6_IGKJ1*01
3	VH6-1_IGHD3-3*01_IGHJ4*01	V4-3_IGLJ4*01
4	VH1-46_IGHD3-10*01_IGHJ4*01	L12_IGKJ1*01
5	VH1-46_IGHD6-6*01>1_IGHJ1*01_S104F	L6_IGKJ1*01
6	VH1-46_IGHD6-6*01_IGHJ1*01_ S102A_S103P_S104F	L6_IGKJ1*01
7	VH5-51_IGHD5-18*01>3_IGHJ4*01_ G100K_G104T	V3-4_IGLJ1*01
8	VH1-46_IGHD6-6*01_IGHJ1*01_ S102A_S103P_S104F_H111F	L6_IGKJ1*01

9	VH1-46_IGHD6-6*01_IGHJ1*01_ S102A_S103P_S104F_H111Y	L6_IGKJ1*01
10	VH1-46_IGHD6-6*01_IGHJ1*01_ S102A_S103P_S104F	L6_IGKJ1*01_S31K

Table 79. Binding affinity of DLL4 Fabs

Fab No	k_a ($M^{-1}s^{-1}$)	k_d (s^{-1})	K_D (nM)
1	n/a	n/a	4800(200)
2	1.63(3)e5	0.101(2)	730(130)
3	n/a	n/a	38000(4000)
4	5(1)e5	0.29(2)	500(100)
5	5.0(8)e5	0.19(1)	380(60)
6	4.05(5)e5	0.0492(4)	122(1)
7	0.645(0.92)e5	0.023	355(7)
8	4.25(4)e5	0.0300(2)	70.6(7)
9	3.40(3)e5	0.0317(2)	93.1(9)
10	3.50(5)e5	0.0392(4)	112(2)

Example 17

Inhibition of DLL4-Notch interaction

In this example, four Fabs previously identified as binding to DLL4 were functionally screened for their ability to block the binding of Notch-Fc to DLL4.

In this ELISA assay, recombinant human DLL4 bound to the plate followed by the addition of both the Fab and Notch-Fc. An anti-human FC-HRP conjugated antibody was used as a detection molecule therefore if Notch-Fc binds to DLL4, a strong signal will be observed at A_{450}. Alternatively , if the Fab is capable of blocking the bind of Notch-Fc to DLL4, no signal should be observed. The Fabs that were assayed included Fab VH1-46_IGHD6-6*01_IGHJ1*01_S102A_S103P_S104F & L6_IGKJ1*01, Fab VH1-46_IGHD6-6*01_IGHJ1*01_S102A_S103P_S104F_H111F & L6_IGKJ1*01, Fab VH5-51_IGHD5-18*01>3_IGHJ4*01_G100K_G104T & V3-4_IGLJ1*01 and Fab VH1-46_IGHD3-10*01_IGHJ4*01 & L12_IGKJ1*01.

In short, Maxisorp Nunc 96-well plates were coated with 0.5 μg/ml recombinant human DLL4 extracellular domain (R&D Systems) for at least 2 hours. The wells were washed and then blocked with 4% BSA. Following blocking, Fabs VH1-46_IGHD6-6*01_IGHJ1*01_S102A_S103P_S104F & L6_IGKJ1*01, VH1-46_IGHD6-6*01_IGHJ1*01_S102A_S103P_S104F_H111F & L6_IGKJ1*01, VH5-51_IGHD5-18*01>3_IGHJ4*01_G100K_G104T & V3-4_IGLJ1*01 and VH1-46_IGHD3-10*01_IGHJ4*01 & L12_IGKJ1*01 at concentrations from 0.004 and 5 μM were added together with recombinant human Fc-Notch extracellular domain (R&D Systems) at a

concentration of 10 nM. After incubation for one to two hours, the wells were washed and Notch binding was measure using a mouse anti-human FC-HRP conjugated antibody (Southern Biotech) at an 1:1000 dilution. HRP activity was detected using TMB substrate (Pierce) followed by acid neutralization. The A_{450} was measured on a SpectraMax Plus 384.

Results show that the addition of Fabs VH1-46_IGHD6-6*01_IGHJ1*01 _S102A_S103P_S104F & L6_IGKJ1*01, VH1-46_IGHD6-6*01_IGHJ1*01 _S102A_S103P_S104F_H111F & L6_IGKJ1*01 or VH5-51_IGHD5-18*01>3_ IGHJ4*01_G100K_G104T & V3-4_IGLJ1*01 resulted in a decreased signal therefore indicating their ability to block the binding of Notch-Fc to DLL4. The addition of Fab VH1-46_IGHD3-10*01_IGHJ4*01 & L12_IGKJ1*01did not result an any loss of activity, indicating that Fab VH1-46_IGHD3-10*01_IGHJ4*01 & L12_IGKJ1*01does not block the Notch-DLL4 interaction. This result also indicates that Fabs VH1-46_IGHD6-6*01_IGHJ1*01_S102A_S103P_S104F & L6_IGKJ1*01, VH1-46_IGHD6-6*01_IGHJ1*01_S102A_S103P_S104F_H111F & L6_IGKJ1*01 or VH5-51_IGHD5-18*01>3_IGHJ4*01_G100K_G104T & V3-4_IGLJ1*01 bind different epitopes of DLL4 than Fab VH1-46_IGHD3-10*01_IGHJ4*01 & L12_IGKJ1*01.

Example 18

EpoR Cell Based Assay for Receptor Stimulation

In this example, Fabs were analyzed for their ability to stimulate the erythropoietin receptor using a cell based assay. The cell lines used included Ba/F3 cells transfected with the human erythropoietin receptor (EpoR) and parental Ba/F3 cells cells lacking EpoR. The parental Ba/F3 cells do not respond to receptor agonist and both cell lines required IL-3 for growth.

In short, Ba/F3 cells (with and without EpoR) were propagated in RPMI 1640 media with 10% FBS, antibiotics, and 5 ng/L recombinant mouse IL-3, washed into equivalent media lacking IL-3 and plated into 96 well plates at 5000 cells/well in 50 µl. Following plating, cells were treated with 10 µl of Fabs, agonist control EMP16 (TYSCHFGPLTWVCKPQ, SEQ ID NO:3735), or vehicle, and grown for 4 days at 37 °C in humid 5% CO_2 atmosphere. To measure cell viability and proliferation, a resazurin-based viability assay reagent was added to test wells for 24 hours. Reduction of the reagent by metabolically active cells produced the readily-quantifiable fluorescent molecule resorufin. Average fluorescence for each treatment was divided by the average fluorescence of vehicle controls to give fold proliferation.

The results show that 40 nM Fab VH1-46_IGHD2-15*01_IGHJ2*01 & L2_IGKJ1*01 showed receptor dependent proliferation, while 54 nM Fab VH1-46_IGHD6-13*01_IGHJ4*01 & O1_IGKJ1*01 showed little proliferation over vehicle in both receptor-expressing cells and parental cells. The known receptor agonist peptide EMP16 (TYSCHFGPLTWVCKPQ, SEQ ID NO:3735), added at a concentration of 2.5 μM, showed strong cell proliferation.

Example 19

Inhibition of DLL4/Jag1

In this example, a cellular assay is described in which activation of the Notch pathway prevents C2C12 myoblast cell differentiation (see e.g., Jarriault et al., 1998 Molecular and Cellular Biology, 18:7423-7431). In order to activate the Notch pathway, Notch ligands, such as DLL4 or Jag1, must be expressed as full-length proteins on the cell surface. To achieve this Notch activation, non-adherent cells naturally or ectopically expressing Notch ligands DLL4 or Jag1 are co-cultured with C2C12 cells and selected Fabs. Functional inhibition of DLL4 or Jag1 is assessed by the ability of the Fab to promote differentiation, indicating Notch pathway inactivation. The differentiation into tube-like structures is easily discernible morphologically and additionally can be detected with an antibody against troponin t (Sigma-Aldrich).

In short, C2C12 mouse myoblast cells are cultured in the presence and absence of Jag1-expressing IM9 cells (a human lymphoblast cell line) and Fabs. The cells are plated onto glass coverslips in 12 well dishes in DMEM containing 10% FBS (fetal bovine serum). The next day attached C2C12 cells are transferred into DMEM containing 1% FBS to induce differentiation. Following incubation, the cells are visualized to observe whether differentiation into myotubes occurred. Low serum conditions will induce the differentiation of myotubes while Jag1-expressing IM9 cells maintain C2C12 cells in an undifferentiated state in low serum conditions.

Example 20

Inhibition of p-cadherin

In this example, a cellular assay is described in which the ability of an antibody to inhibit P-cadherin is observed by the failure of cells to "clump". P-cadherin is involved in cell-to-cell adhesion and therefore inhibition of P-cadherin leads to cell scattering.

In short, A431 epidermoid carcinoma cells are plated at 10,000 cells/well (96-well in DMEM with 10% FBS into 96-well dishes. The next day, Fab is added to wells at 100 μg/ml. Function blocking p-cadherin antibody (Abcam) is used as a positive control and DMEM with

10% FBS alone is used as a negative control (see e.g. Shimoyama, Y. et al., 1989 Cancer Research, 49:2128-2133). After 3.5 hours cells are examined for "scattering" and photographed. Cells that are incubated with media only exhibit significant "clumping" while cells that are incubated with an anti-P-cadherin Fab or antibody are scattered.

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Since modifications will be apparent to those of skill in this art, it is intended that this invention be limited only by the scope of the appended claims.

CLAIMS:

1. A human combinatorial antibody library, comprising a plurality of antibodies, wherein:

a) each member antibody contains a variable light (VL) chain and a variable heavy (VH) chain or a sufficient portion thereof to form an antigen binding site; wherein:

i) each VL chain is encoded by a nucleic acid molecule that comprises a V_κ and a J_κ human germline segment or degenerate codons thereof, or a V_λ and a J_λ human germline segment or degenerate codons thereof, whereby the segments are linked in-frame;

ii) each VH chain is encoded by a nucleic acid molecule that comprises a human V_H and a human J_H germline segment and any sequence of nucleotides between the V_H and a J_H germline segments, whereby the segments are linked in-frame; and

b) the library comprises at least about or 50 or 100 or more different members.

2. The human combinatorial antibody library of claim 1, wherein:

the V_H germline segment, the sequence of nucleotides between the V_H and J_H and the J_H germline segment of the nucleic acid molecule encoding a VH chain are linked such that the V_H segment is 5' to the sequence of nucleotides between the V_H and J_H which is 5' to the J_H segment; and

the V_κ and J_κ or V_λ and J_λ germline segments of the nucleic acid molecule encoding a VL chain are linked such that the V_κ segment is 5' to the J_κ segment or the V_λ segment is 5' to the J_λ segment.

3. The human combinatorial antibody library of claim 1, wherein the sequence of nucleotides between the V_H and J_H germline segments is at or is about 5, 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 nucleotides in length.

4. The human combinatorial antibody library of any of claims 1-3, wherein the sequence of nucleotides between the V_H and J_H germline segments encodes a peptide mimetic.

5. A human combinatorial antibody library, comprising a plurality of antibodies wherein:

a) each member antibody contains a modified variable light (VL) chain and/or a modified variable heavy chain (VH) chain or a sufficient portion thereof to form an antigen binding site; wherein:

i) each VL chain is encoded by a nucleic acid molecule that comprises a V_κ and a J_κ human germline segment or degenerate codons thereof, or a V_λ and a J_λ human germline segment or degenerate codons thereof, whereby the segments are linked in-frame;

ii) each VH chain is encoded by a nucleic acid molecule that comprises a V_H, D_H and a J_H human germline segment or degenerate codons thereof, whereby the segments are linked in-frame; and

b) the VL chain and/or VH chain is modified by replacement or insertion of amino acids into a CDR.

6. The human combinatorial antibody library of claim 5, wherein the CDR is selected from among a CDRH1, CDRH2, CDRH3, CDRL1, CDRL2 and CDRL3.

7. The human combinatorial antibody library of claim 6, wherein the CDR is CDRH3.

8. The human combinatorial antibody library of any of claims 5-7, wherein the amino acids that are inserted or replaced correspond to a peptide mimetic.

9. The human combinatorial antibody library of claim 4 or claim 8, wherein the peptide mimetic is selected from among selected from among a TPO, EPO, G-CSF, IL-5, human brain natriuretic peptide (hBNP-32), exendin 4, GLP-1, GLP-2, glucagon, PACAP-38, CD209L, TNF, VEGF, MMP inhibitor, or CTLA-4 peptide mimetic.

10. The human combinatorial antibody library of claim 4 or claim 5, wherein the peptide mimetic further contains a flanking sequence at the carboxy and/or N-terminal end.

11. The human combinatorial antibody library of claim 6, wherein the flanking sequence is glycine or proline.

12. The human combinatorial antibody library of any of claims 4-7, wherein the peptide mimetic has a sequence of amino acids selected from among SEQ ID NOS: 891, 987-1014.

13. The human combinatorial antibody library of claim 1, wherein the sequence of nucleotides between the V_H and J_H germline segments is a human germline D_H segment or degenerate codons thereof.

14. A human combinatorial antibody library, comprising a plurality of antibodies wherein:

a) each member antibody contains a variable light (VL) chain and a variable heavy (VH) chain or a sufficient portion thereof to form an antigen binding site; wherein:

i) each VL chain is encoded by a nucleic acid molecule that comprises a V_κ and a J_κ human germline segment or degenerate codons thereof, or a V_λ and a J_λ human germline segment or degenerate codons thereof, whereby the segments are linked in-frame;

ii) each VH chain is encoded by a nucleic acid molecule that comprises a V_H, D_H and a J_H germline segment, whereby the segments are linked in-frame; and

b) the library comprises at least about or 50 or 100 or more different members.

15. The human combinatorial antibody library of claim 1- 14 that is an addressable library.

16. The human combinatorial antibody library of claim 15, wherein the antibody within each address is the same antibody and is different from the antibodies at all other addresses.

17. The human combinatorial antibody library of claim 13 - 16, wherein:

the V_H, D_H and J_H segments of the nucleic acid molecule encoding a VH chain are linked such that the V_H segment is 5' to the D_H segment which is 5' to the J_H segment; and

the V_κ and J_κ or V_λ and J_λ germline segments of the nucleic acid molecule encoding a VL chain are linked such that the V_κ segment is 5' to the J_κ segment or the V_λ segment is 5' to the J_λ segment.

18. The human combinatorial antibody library of any of claims 1 - 17, wherein:

a plurality of nucleic acid molecules encode a VH chain and a plurality of nucleic acid molecules encode a VL chain; and

the plurality of nucleic acid molecules encoding the VH chain and the VL chain are sufficient to generate at least about or 50 or 100 different antibodies.

19. The human combinatorial antibody library of claim 18, wherein:

all or a subset of germline V_H segments are linked with all or a subset of D_H segments which are linked with all or a subset of germline J_H segments to generate the plurality of nucleic acid molecules encoding a VH chain; and

all or a subset of germline V_κ segments are linked with all or a subset of germline J_κ segments, or all or a subset of germline V_λ segments are linked to all or a subset of germline J_λ segments to generate a plurality of nucleic acid molecules encoding a VL chain.

20. The human combinatorial antibody library of any of claims 1-19, wherein the V_H germline segment is selected from among an IGHV1, IGHV2, IGHV3, IGHV4, IGHV5, IGHV6 and IGHV7 and genes and alleles thereof.

21. The human combinatorial antibody library of claim 20, wherein the V_H is selected from among any of SEQ ID NOS: 10-238.

22. The human combinatorial antibody library of any of claims 9-21, wherein the D_H segment is selected from among IGHD1, IGHD2, IGHD3, IGHD4, IGHD5, IGHD6, and IGHD7 and genes and alleles thereof.

23. The human combinatorial antibody library of claim 22, wherein the D_H is selected from among any of SEQ ID NOS: 239-272.

24. The human combinatorial antibody library of any of claims 1-23, wherein the J_H is selected from among IGHJ1, IGHJ2, IGHJ3, IGHJ4, IGHJ5 and IGHJ6 and genes and alleles thereof.

25. The human combinatorial antibody library of claim 24, wherein the J_H is selected from among any of SEQ ID NOS: 273-285.

26. The human combinatorial antibody library of any of claims 1-25, wherein the sequence of the V_H has one nucleotide added or removed at the V-D joint to maintain the reading frame of the VH chain.

27. The human combinatorial antibody library of claim 26, wherein a nucleotide from the 3' end of a V_H nucleotide sequence is deleted.

28. The human combinatorial antibody library of claim 27, wherein a nucleotide is inserted at the 3' end of a V_H nucleotide sequence to add a nucleotide between the V_H and D_H.

29. The human combinatorial antibody library of claim 28, wherein the nucleotide is a guanine (G).

30. The human combinatorial antibody library of any of claims 1-29, wherein the sequence of the D_H has one nucleotide inserted or deleted at the V-D joint and/or the D-J joint to maintain the reading frame of the VH chain.

31. The human combinatorial antibody library of claim 30, wherein the nucleotide insertion or deletion is chosen to maximize the hydrophilicity of the D_H.

32. The human combinatorial antibody library of claim 30 or claim 31, wherein a nucleotide from the 5' end of a D_H is deleted.

33. The human combinatorial antibody library of any of claims 30-32, wherein a nucleotide from the 3' end of a D_H is deleted.

34. The human combinatorial antibody library of any of claims 30-32, wherein a nucleotide is inserted at the 3' end of a D_H sequence to add a nucleotide been the D_H and J_H.

35. The human combinatorial antibody library of claim 34, wherein the nucleotide is a guanine (G).

36. The human combinatorial antibody library of any of claims 1-35, wherein the sequence of the J_H has one nucleotide inserted or deleted at the D-J joint to maintain the reading frame of the VH chain.

37. The human combinatorial antibody library of claim 31, wherein the nucleotide insertion or deletion is chosen to maintain the reading frame of the J_H.

38. The human combinatorial antibody library of claim 31 or claim 32, wherein a nucleotide from the 5' end of the J_H is deleted.

39. The human combinatorial antibody library of any of claims 20-33, wherein a nucleotide from the 3' end of the J_H is deleted.

40. The human combinatorial antibody library of any of claims 1-39, wherein the V_κ is selected from among an IGKV1, IGKV2, IGKV3, IGKV4, IGKV5 and IGKV6, and genes and alleles thereof.

41. The human combinatorial antibody library of claim 40, wherein the V_κ is selected from among any of SEQ ID NOS: 286-355 and 868.

42. The human combinatorial antibody library of any of claims 1-41, wherein the J_κ is selected from among IGKJ1, IGKJ2, IGKJ3, IGKJ4 and IGKJ5 and genes and alleles thereof.

43. The human combinatorial antibody library of claim 42, wherein the J_κ is selected from among any of SEQ ID NOS: 356-364.

44. The human combinatorial antibody library of any of claims 1-43, wherein the sequence of the V_κ has one nucleotide inserted or deleted at the V-J joint to maintain the reading frame of the VL chain.

45. The human combinatorial antibody library of claim 44, wherein a nucleotide from the 3' end of a V_κ nucleotide sequence is deleted.

46. The human combinatorial antibody library of claim 44, wherein a nucleotide is inserted at the 3' end of a V_κ nucleotide sequence to add a nucleotide between the V_κ and J_κ.

47. The human combinatorial antibody library of claim 46, wherein the nucleotide is a guanine (G).

48. The human combinatorial antibody library of any of claims 1-47, wherein the sequence of the J_κ has one nucleotide inserted or deleted at the V-J joint to maintain the reading frame of the VL chain.

49. The human combinatorial antibody library of claim 48, wherein the nucleotide insertion or deletion is chosen to maintain the reading frame of the J_κ.

50. The human combinatorial antibody library of claim 48 or claim 49, wherein a nucleotide from the 5' end of the J_κ is deleted.

51. The human combinatorial antibody library of any of claims 1-39, wherein the V_λ is selected from among an IGLV1, IGLV2, IGLV3, IGLV4, IGLV5, IGLV6, IGLV7, IGLV8, IGLV9, IGLV10 and IGLV11 and genes and alleles thereof.

52. The human combinatorial antibody library of claim 51, wherein the V_λ is selected from among any of SEQ ID NOS: 365-441.

53. The human combinatorial antibody library of any of claims 1-39, 51 and 52, wherein the J_λ is selected from among an IGLJ1, IGLJ2, IGLJ3, IGLJ4, IGLJ5, IGLJ6 and IGLJ7 and genes and alleles thereof.

54. The human combinatorial antibody library of claim 53, wherein the J_λ is selected from among any of SEQ ID NOS: 442-451.

55. The human combinatorial antibody library of any of claims 1-34 and 51-54, wherein the sequence of the V_λ has one nucleotide inserted or deleted at the V-J joint to maintain the reading frame of the VL chain.

56. The human combinatorial antibody library of claim 55, wherein a nucleotide from the 3' end of a V_λ nucleotide sequence is deleted.

57. The human combinatorial antibody library of claim 55, wherein a nucleotide is inserted at the 3' end of a V_λ nucleotide sequence to add a nucleotide between the V_λ and J_λ.

58. The human combinatorial antibody library of claim 57, wherein the nucleotide is a guanine (G).

59. The human combinatorial antibody library of any of claims 1-39 and 51-58, wherein the sequence of the J_λ has one nucleotide inserted or deleted at the V-J joint to maintain the reading frame of the VL chain.

60. The human combinatorial antibody library of claim 59, wherein the nucleotide insertion or deletion is chosen to maintain the reading frame of the J_λ.

61. The human combinatorial antibody library of claim 54 or claim 55, wherein a nucleotide from the 5' end of the J_λ is deleted.

62. The human combinatorial antibody library of any of claims 1-61, wherein the plurality of nucleic acid molecules encoding a VH chain are generated from a subset of germline segments selected based on sequence similarities or differences, gene family, length, composition, CDR length or composition, species, functionality, specificity, group or subgroup.

63. The human combinatorial antibody library of claim 62, wherein the plurality of nucleic acid molecules encoding a VH chain are generated from a subset of germline segments selected based on CDR and the CDR is CDR3.

64. The human combinatorial antibody library of claim 62, wherein the plurality of nucleic acid molecules encoding a VH chain are selected based on gene family, whereby

one germline segment from each of a V_H, D_H, and/or J_H gene family is selected or one germline segment from a subset of a V_H, D_H, and/or J_H gene family is selected.

65. The human combinatorial antibody library of claim 64, wherein:

the V_H gene family is selected from among a IGHV1-18, IGHV1-2, IGHV1-24, IGHV1-3, IGHV1-45, IGHV1-46, IGHV1-58, IGHV1-69, IGHV1-8, IGHV2-26, IGHV2-5, IGHV2-70, IGHV3-11, IGHV3-13, IGHV3-15, IGHV3-16, IGHV3-20, IGHV3-21, IGHV3-23, IGHV3-30, IGHV3-33, IGHV3-35, IGHV3-38, IGHV3-43, IGHV3-48, IGHV3-49, IGHV3-53, IGHV3-64, IGHV3-66, IGHV3-7, IGHV3-72, IGHV3-73, IGHV3-74, IGHV3-9, IGHV4-28, IGHV4-31, IGHV4-34, IGHV4-39, IGHV4-4, IGHV4-59, IGHV4-61, IGHV5-51, IGHV6-1 and IGHV7-81;

the D_H gene family is selected from among a IGHD1-1, IGHD1-14, IGHD1-20, IGHD1-26, IGHD1-7, IGHD2-15, IGHD2-2, IGHD2-21, IGHD2-8, IGHD3-10, IGHD3-16, IGHD3-22, IGHD3-3, IGHD3-9, IGHD4-11, IGHD4-17, IGHD4-23, IGHD4-4, IGHD5-12, IGHD5-18, IGHD5-24, IGHD5-5, IGHD6-13, IGHD6-19, IGHD6-25, IGHD6-6 and IGHD7-27; and

the J_H gene family is selected from among a IGHJ1, IGHJ2, IGHJ3, IGHJ4, IGHJ5 and IGHJ6.

66. The human combinatorial antibody library of any of claims 1-65, wherein the plurality of nucleic acid molecules encoding a VL chain are generated from a subset of germline segments selected based on sequence similarities or differences, gene family, length, composition, CDR length or composition, species, functionality, specificity, group, subgroup.

67. The human combinatorial antibody library of claim 66, wherein the plurality of nucleic acid molecules encoding a VL chain are generated from a subset of germline segments selected based on CDR and the CDR is CDR3.

68. The human combinatorial antibody library of claim 66, wherein the plurality of nucleic acid molecules encoding a VH chain are selected based on gene family, whereby one germline segment from each of a V_κ and/or J_κ or V_λ and/or J_λ gene family is selected or one germline segment from a subset of a V_κ and/or J_κ or V_λ and/or J_λ gene family is selected.

69. The human combinatorial antibody library of claim 68, wherein:

the V_κ gene family is selected from among a IGKV1-12, IGKV1-12, IGKV1-16, IGKV1-17, IGKV1-27, IGKV1-33, IGKV1-37, IGKV1-39, IGKV1-5, IGKV1-6, IGKV1-8, IGKV1-9, IGKV1-NL1, IGKV1/OR2, IGKV1D-12, IGKV1D-13, IGKV1D-16, IGKV1-D-17, IGKV1D-33, IGKV1D-37, IGKV1D-39, IGKV1D-42, IGKV1D-43, IGKV1D-8, IGKV2-

24, IGKV2-28, IGKV2-29, IGKV2-30, IGKV2-30, IGKV2-40, IGKV2D-24, IGKV2D-26, IGKV2D-28, IGKV2D-29, IGKV2-D-30, IGKV2D-40, IGKV3-11, IGKV3-15, IGKV3-20, IGKV3-7, IGKV3-NL1, IGV3-NL2, IGKV3-NL3, IGKV3-NL4, IGKV3-NL5, IGKV3/OR2-268, IGKV3D-11, IGKV3D-15, IGKV3D-20, iGKV3D-7, IGKV4-1, IGKV5-2, IGKV6-21, IGKV6D-21, IGKV6D-41, and IGKV1-39;

the J_κ gene family is selected from among a IGKJ1, IGKJ2, IGKJ3, IGKJ4 and IGKJ5;

the V_λ gene family is selected from among a IGLV1-36, IGLV1-40, IGLV1-41, IGLV1-44, IGLV1-47, IGLV1-50, IGLV1-51, IGLV10-54, IGLV11-55, IGLV2-11, IGLV2-14, IGLV2-18, IGLV2-23, IGLV2-33, IGLV2-8, IGLV3-1, IGLV3-10, IGLV3-12, IGLV3-16, IGLV3-19, IGLV3-21, IGLV3-22, IGLV3-25, IGLV3-27, IGLV3-32, IGLV3-9, IGLV4-3, IGLV4-60, IGLV4-69, IGLV5-37, IGLV5-39, IGLV5-45, IGLV5-8, IGLV5-52, IGLV6-57, IGLV7-43, IGLV7-46, IGLV8-61, IGLV8-61 and IGLV9-49; and

the J_λ gene family is selected from among a IGLJ1, IGLJ2, IGLJ4, IGLJ5, IGLJ6 and IGLJ7.

70. The human combinatorial antibody library of any of claims 1-69, wherein the nucleic acid molecule encoding a VH chain is modified to remove stop codons and/or restriction enzyme sites.

71. The human combinatorial antibody library of any of claims 1-69, wherein the nucleic acid molecule encoding a VL chain is modified to remove stop codons and/or restriction enzyme sites.

72. The human combinatorial antibody library of any of claims 1-71, wherein:

the nucleic acid molecule encoding the VH chain are selected from among any of SEQ ID NOS: 1059-1410, or a subset thereof; and

the nucleic acid molecule encoding the VL chain are selected from among any of SEQ ID NOS: 1411-1422, 1424-1439 and 1441-1471, or a subset thereof.

73. The human combinatorial library of any of claims 1-72, wherein:

the VH chain has a sequence of amino acids selected from among any of SEQ ID NOS: 1475-1826 or a subset thereof; and

the VL chain has a sequence of amino acids selected from among any of SEQ ID NOS: 1827-1838, 1840-1855 and 1857-1888 or a subset thereof.

74. The human combinatorial antibody library of any of claims 1-73, wherein each member antibody in the library further comprises all or a portion of a constant region sufficient to permit association of a heavy and light chain.

75. The human combinatorial antibody library of any of claims 1-74, wherein each member antibody in the library is selected from among a full length antibody, or a fragment or portion thereof sufficient to form an antigen binding site.

76. The human combinatorial antibody library of claim 75, wherein the fragment o portion thereof is selected from among a Fab, Fab', $F(ab')_2$, single-chain Fvs (scFv), Fv, dsFv, diabody, Fd and Fd' fragments, Fab fragments, Fd fragments, scFv fragments, and scFab fragments.

77. The human combinatorial antibody library of any of claims 1-76, wherein each member antibody in the library is a Fab.

78. The human combinatorial antibody library of any of claims 1-77, comprising about or 50, 10^2, 10^3, 10^4, 2×10^4, 3×10^4, 4×10^4, 5×10^4, 6×10^4, 7×10^4, 8×10^4, 9×10^4, 10^5, 10^6, 10^7, 10^8, 10^9 or more different members.

79. The human combinatorial antibody library of any of claims 1-78, comprising 10^3, 2×10^3, 3×10^3, 4×10^3, 5×10^3, 6×10^3, 7×10^3, 8×10^3, 9×10^3, 10^4, 2×10^4, 3×10^4, 4×10^4, 5×10^4, 6×10^4, 7×10^4, 8×10^4, 9×10^4 or more different members.

80. The human combinatorial antibody library of any of claims 1-79, wherein the addressable antibodies are arranged in a spatial array.

81. The human combinatorial antibody library of claim 80, wherein the spatial array is a multiwell plate, wherein each individual locus of the plate corresponds to a different antibody member.

82. The human combinatorial antibody library of claim 81, wherein the different antibody members are immobilized to the surface of the wells of the plate.

83. The human combinatorial antibody library of claim 76, wherein the different antibody members are present in solution.

84. The human combinatorial antibody library of any of claims 1-79, wherein the addressable antibodies are attached to a solid support.

85. The human combinatorial antibody library of claim 84, wherein the solid support is a filter, chip, slide, bead or cellulose, and the different antibody members are immobilized to the surface thereof.

86. The human combinatorial antibody library of claim 85, wherein the solid support is a biacore chip.

87. The human combinatorial antibody library of any of claims 80-86, wherein the antibodies are identifiably labeled.

88. The human combinatorial antibody library of claim 87, wherein the label is colored, chromogenic, luminescent, chemical, fluorescent or electronic.

89. A library of nucleic acid molecules, comprising a plurality of addressable nucleic acid molecules encoding a variable light (VL) chain, wherein:

each VL chain is encoded by a nucleic acid molecule that comprises a V_κ and a J_κ human germline segment or a V_λ and a J_λ human germline segment linked in-frame; and

the nucleic acid molecule within each address is the same and is different from the nucleic acid molecules at all other addresses.

90. The library of nucleic acid molecules of claim 89, wherein the V_κ and J_κ or V_λ and J_λ germline segments of the nucleic acid molecule encoding a VL chain are linked such that the V_κ segment is 5' to the J_κ segment or the V_λ segment is 5' to the J_λ segment.

91. The library of nucleic acid molecules of claim 90, wherein all or a subset of germline V_κ segments are linked with all or a subset of germline J_κ segments, or all or a subset of germline V_λ segments are linked to all or a subset of germline J_λ segments to generate a plurality of nucleic acid molecules encoding a VL chain.

92. The library of nucleic acid molecules of any of claims 89-91, wherein the V_κ is selected from among an IGKV1, IGKV2, IGKV3, IGKV4, IGKV5 and IGKV6, and genes and alleles thereof.

93. The library of nucleic acid molecules of claim 92, wherein the V_κ is selected from among any of SEQ ID NOS: 286-355 and 868.

94. The library of nucleic acid molecules of any of claims 89-93, wherein the sequence of the V_κ has one nucleotide inserted or deleted at the V-J joint to maintain the reading frame of the VL chain.

95. The library of nucleic acid molecules of claim 94, wherein a nucleotide from the 3' end of a V_κ nucleotide sequence is deleted.

96. The library of nucleic acid molecules of claim 94, wherein a nucleotide is inserted at the 3' end of a V_κ nucleotide sequence to add a nucleotide between the V_κ and J_κ.

97. The library of nucleic acid molecules of claim 96, wherein the nucleotide is a guanine (G).

98. The library of nucleic acid molecules of any of claims 89-97, wherein the J_κ is selected from among IGKJ1, IGKJ2, IGKJ3, IGKJ4 and IGKJ5 and genes and alleles thereof.

99. The library of nucleic acid molecules of claim 98, wherein the J_κ is selected from among any of SEQ ID NOS: 356-364.

100. The library of nucleic acid molecules of any of claims 89-99, wherein the sequence of the J_κ has one nucleotide inserted or deleted at the V-J joint to maintain the reading frame of the VL chain.

101. The library of nucleic acid molecules of claim 100, wherein the nucleotide insertion or deletion is chosen to maintain the reading frame of the J_κ.

102. The library of nucleic acid molecules of claim 100 or claim 101, wherein a nucleotide from the 5' end of the J_κ is deleted.

103. The library of nucleic acid molecules of any of claims 89-91, wherein the V_λ is selected from among an IGLV1, IGLV2, IGLV3, IGLV4, IGLV5, IGLV6, IGLV7, IGLV8, IGLV9, IGLV10 and IGLV11 and genes and alleles thereof.

104. The library of nucleic acid molecules of claim 98, wherein the V_λ is selected from among any of SEQ ID NOS: 365-441.

105. The library of nucleic acid molecules of any of claims 89-91 and 103-104, wherein the sequence of the V_λ has one nucleotide inserted or deleted at the V-J joint to maintain the reading frame of the VL chain.

106. The library of nucleic acid molecules of claim 105, wherein a nucleotide from the 3' end of a V_λ nucleotide sequence is deleted.

107. The library of nucleic acid molecules of claim 105, wherein a nucleotide is inserted at the 3' end of a V_λ nucleotide sequence to add a nucleotide between the V_λ and J_λ.

108. The library of nucleic acid molecules of claim 107, wherein the nucleotide is a guanine (G).

109. The library of nucleic acid molecules of any of claims 89-91 and 105-108, wherein the J_λ is selected from among an IGLJ1, IGLJ2, IGLJ3, IGLJ4, IGLJ5, IGLJ6 and IGLJ7 and genes and alleles thereof.

110. The library of nucleic acid molecules of claim 109, wherein the J_λ is selected from among any of SEQ ID NOS: 442-451.

111. The library of nucleic acid molecules of any of claims 89-91 and 105-110, wherein the sequence of the J_λ has one nucleotide inserted or deleted at the V-J joint to maintain the reading frame of the VL chain.

112. The library of nucleic acid molecules of claim 111, wherein the nucleotide insertion or deletion is chosen to maintain the reading frame of the J_λ.

113. The library of nucleic acid molecules of claim 111 or claim 107, wherein a nucleotide from the 5' end of the J_λ is deleted.

114. The library of nucleic acid molecules of any of claims 89-113, wherein the plurality of nucleic acid molecules encoding a VL chain are generated from a subset of germline segments selected based on sequence similarities or differences, gene family, length, composition, CDR length or composition, species, functionality, specificity, group, subgroup.

115. The library of nucleic acid molecules of claim 114, wherein the plurality of nucleic acid molecules encoding a VL chain are generated from a subset of germline segments selected based on CDR and the CDR is CDR3.

116. The library of nucleic acid molecules of claim 114, wherein the plurality of nucleic acid molecules encoding a VL chain are selected based on gene family, whereby one germline segment from each of a V_κ and/or J_κ or V_λ and/or J_λ gene family is selected or one germline segment from a subset of a V_κ and/or J_κ or V_λ and/or J_λ gene family is selected.

117. The library of nucleic acid molecules of claim 116, wherein:

the V_κ gene family is selected from among a IGKV1-12, IGKV1-12, IGKV1-16, IGKV1-17, IGKV1-27, IGKV1-33, IGKV1-37, IGKV1-39, IGKV1-5, IGKV1-6, IGKV1-8, IGKV1-9, IGKV1-NL1, IGKV1/OR2, IGKV1D-12, IGKV1D-13, IGKV1D-16, IGKV1-D-17, IGKV1D-33, IGKV1D-37, IGKV1D-39, IGKV1D-42, IGKV1D-43, IGKV1D-8, IGKV2-24, IGKV2-28, IGKV2-29, IGKV2-30, IGKV2-30, IGKV2-40, IGKV2D-24, IGKV2D-26, IGKV2D-28, IGKV2D-29, IGKV2-D-30, IGKV2D-40, IGKV3-11, IGKV3-15, IGKV3-20, IGKV3-7, IGKV3-NL1, IGV3-NL2, IGKV3-NL3, IGKV3-NL4, IGKV3-NL5, IGKV3/OR2-268, IGKV3D-11, IGKV3D-15, IGKV3D-20, iGKV3D-7, IGKV4-1, IGKV5-2, IGKV6-21, IGKV6D-21, IGKV6D-41, and IGKV1-39;

the J_κ gene family is selected from among a IGKJ1, IGKJ2, IGKJ3, IGKJ4 and IGKJ5;

the V_λ gene family is selected from among a IGLV1-36, IGLV1-40, IGLV1-41, IGLV1-44, IGLV1-47, IGLV1-50, IGLV1-51, IGLV10-54, IGLV11-55, IGLV2-11, IGLV2-14, IGLV2-18, IGLV2-23, IGLV2-33, IGLV2-8, IGLV3-1, IGLV3-10, IGLV3-12, IGLV3-16, IGLV3-19, IGLV3-21, IGLV3-22, IGLV3-25, IGLV3-27, IGLV3-32, IGLV3-9, IGLV4-3, IGLV4-60, IGLV4-69, IGLV5-37, IGLV5-39, IGLV5-45, IGLV5-8, IGLV5-52, IGLV6-57, IGLV7-43, IGLV7-46, IGLV8-61, IGLV8-61 and IGLV9-49; and

the J_λ gene family is selected from among a IGLJ1, IGLJ2, IGLJ4, IGLJ5, IGLJ6 and IGLJ7.

118. The library of nucleic acid molecules of any of claims 89-117, wherein the nucleic acid molecule encoding a VL chain is modified to remove stop codons and/or restriction enzyme sites.

119. The library of nucleic acid molecules of any of claims 89-118, wherein the nucleic acid molecules encoding the VL chain are selected from among any of SEQ ID NOS:1411-1422, 1424-1439 and 1441-1471, or a subset thereof.

120. A library of addressable vectors, comprising the nucleic acid molecules of any of claims 89-119, wherein each vector in the library contains a different nucleic acid molecule.

121. A library of addressable cells, comprising vectors of claim 120, wherein each cell in the library contains a different vector.

122. A library of nucleic acid molecules, comprising a plurality of addressable nucleic acid molecules encoding a variable heavy (VH) chain, wherein:

each VH chain is encoded by a nucleic acid molecule that comprises a V_H, a D_H and a J_H human germline segment linked in-frame; and

the nucleic acid molecule within each address is the same and is different from the nucleic acid molecules at all other addresses.

123. The library of nucleic acid molecules of claim 122, wherein the V_H, D_H and J_H germline segments of the nucleic acid molecule encoding a VH chain are linked such that the V_H segment is 5' to the D_H segment which is 5' to the J_H segment.

124. The library of nucleic acid molecules of claim 123, wherein all or a subset of germline V_H segment are linked with all or a subset of germline D_H segments which are linked with all or a subset of germline J_H segments to generate the plurality of nucleic acid molecules encoding a VH chain.

125. The library of nucleic acid molecules of any of claims 122-124, wherein the V_H is selected from among an IGHV1, IGHV2, IGHV3, IGHV4, IGHV5, IGHV6 and IGHV7 and genes and alleles thereof.

126. The library of nucleic acid molecules of claim 125, wherein the V_H is selected from among any of SEQ ID NOS: 10-238.

127. The library of nucleic acid molecules of any of claims 122-126, wherein the sequence of the V_H has one nucleotide added or removed at the V-D joint to maintain the reading frame of the VH chain.

128. The library of nucleic acid molecules of claim 127, wherein a nucleotide from the 3' end of a V_H nucleotide sequence is deleted.

129. The library of nucleic acid molecule of claim 127, wherein a nucleotide is inserted at the 3' end of a V_H nucleotide sequence to add a nucleotide between the V_H and D_H.

130. The library of nucleic acid molecules of claim 129, wherein the nucleotide is a guanine (G).

131. The library of nucleic acid molecules of any of claims 122-130, wherein the D_H is selected from among IGHD1, IGHD2, IGHD3, IGHD4, IGHD5, IGHD6, and IGHD7 and genes and alleles thereof.

132. The library of nucleic acid molecules of claim 131, wherein the D_H is selected from among any of SEQ ID NOS: 239-272.

133. The library of nucleic acid molecules of any of claims 122-132, wherein the sequence of the D_H has one nucleotide inserted or deleted at the V-D joint and/or the D-J joint to maintain the reading frame of the VH chain.

134. The library of nucleic acid molecules of claim 133, wherein the nucleotide insertion or deletion is chosen to maximize the hydrophilicity of the D_H.

135. The library of nucleic acid molecules of claim 133 or claim 134, wherein a nucleotide from the 5' end of a D_H is deleted.

136. The library of nucleic acid molecules of any of claims 133-135, wherein a nucleotide from the 3' end of a D_H is deleted.

137. The library of nucleic acid molecules of any of claims 133-136, wherein a nucleotide is inserted at the 3' end of a D_H sequence to add a nucleotide been the D_H and J_H.

138. The library of nucleic acid molecules of claim 137, wherein the nucleotide is a guanine (G).

139. The library of nucleic acid molecules of any of claims 122-139, wherein the J_H is selected from among IGHJ1, IGHJ2, IGHJ3, IGHJ4, IGHJ5, and IGHJ6 and genes and alleles thereof.

140. The library of nucleic acid molecules of claim 139, wherein the J_H is selected from among any of SEQ ID NOS: 273-285.

141. The library of nucleic acid molecules of any of claims 122-140, wherein the sequence of the J_H has one nucleotide inserted or deleted at the D-J joint to maintain the reading frame of the VH chain.

142. The library of nucleic acid molecules of claim 141, wherein the nucleotide insertion or deletion is chosen to maintain the reading frame of the J_H.

143. The library of nucleic acid molecules of claim 141 or claim 142, wherein a nucleotide from the 5' end of the J_H is deleted.

144. The library of nucleic acid molecules of any of claims 141-143, wherein a nucleotide from the 3' end of the J_H is deleted.

145. The library of nucleic acid molecules of any of claims 122-145, wherein the plurality of nucleic acid molecules encoding a VH chain are generated from a subset of germline segments selected based on sequence similarities or differences, gene family, length, composition, CDR length or composition, species, functionality, specificity, group or subgroup.

146. The library of nucleic acid molecules of claim 145, wherein the plurality of nucleic acid molecules encoding a VH chain are generated from a subset of germline segments selected based on CDR and the CDR is CDR3.

147. The library of nucleic acid molecules of claim 145, wherein the plurality of nucleic acid molecules encoding a VH chain are selected based on gene family, whereby one germline segment from each of a V_H, D_H, and/or J_H gene family is selected or one germline segment from a subset of a V_H, D_H, and/or J_H gene family is selected.

148. The library of nucleic acid molecules of claim 147, wherein:

the V_H gene family is selected from among a IGHV1-18, IGHV1-2, IGHV1-24, IGHV1-3, IGHV1-45, IGHV1-46, IGHV1-58, IGHV1-69, IGHV1-8, IGHV2-26, IGHV2-5, IGHV2-70, IGHV3-11, IGHV3-13, IGHV3-15, IGHV3-16, IGHV3-20, IGHV3-21, IGHV3-23, IGHV3-30, IGHV3-33, IGHV3-35, IGHV3-38, IGHV3-43, IGHV3-48, IGHV3-49, IGHV3-53, IGHV3-64, IGHV3-66, IGHV3-7, IGHV3-72, IGHV3-73, IGHV3-74, IGHV3-9, IGHV4-28, IGHV4-31, IGHV4-34, IGHV4-39, IGHV4-4, IGHV4-59, IGHV4-61, IGHV5-51, IGHV6-1 and IGHV7-81;

the D_H gene family is selected from among a IGHD1-1, IGHD1-14, IGHD1-20, IGHD1-26, IGHD1-7, IGHD2-15, IGHD2-2, IGHD2-21, IGHD2-8, IGHD3-10, IGHD3-16, IGHD3-22, IGHD3-3, IGHD3-9, IGHD4-11, IGHD4-17, IGHD4-23, IGHD4-4, IGHD5-12, IGHD5-18, IGHD5-24, IGHD5-5, IGHD6-13, IGHD6-19, IGHD6-25, IGHD6-6 and IGHD7-27; and

the J_H gene family is selected from among a IGHJ1, IGHJ2, IGHJ3, IGHJ4, IGHJ5 and IGHJ6.

149. The library of nucleic acid molecules of any of claims 122-149, wherein the nucleic acid molecule encoding a VH chain is modified to remove stop codons and/or restriction enzyme sites.

150. The library of nucleic acid molecules of any of claims 122-149, wherein:

the plurality of nucleic acid molecule encoding a VH chain are selected from among any of SEQ ID NOS: 1059-1410, or a subset thereof.

151. A library of addressable vectors, comprising the nucleic acid molecules of any of claims 122-150, wherein each vector in the library contains a different nucleic acid molecule.

152. A library of addressable cells, comprising vectors of claim 151, wherein each cell in the library contains a different vector.

153. A library of nucleic acid molecules, comprising a plurality of addressable nucleic acid molecules encoding a variable light (VL) chain and a plurality of addressable nucleic acid molecules encoding a variable heavy (VH) chain, wherein:

each VL chain is encoded by a nucleic acid molecule that comprises a V_κ and a J_κ human germline segments or V_λ and J_λ germline segments linked in-frame;

each VH chain is encoded by a nucleic acid molecule that comprises a V_H, a D_H and a J_H human germline segment;

each locus contains a nucleic acid molecule encoding a VH chain and a nucleic acid molecule encoding a VL chain; and

the combination of VH nucleic acid molecules and VL nucleic acid molecules within each address is different from the combination of nucleic acid molecules at all other addresses.

154. A method of generating a human combinatorial antibody library, comprising:

a) combining a V_H, a D_H and a J_H human germline segment or portion thereof in frame to generate a sequence of a nucleic acid molecule encoding a VH chain or a portion thereof;

b) combining a V_κ and a J_κ human germline segment or portion thereof, or a V_λ and a J_λ germline segment or portion thereof in frame to generate a sequence of a nucleic acid molecule encoding a VL chain or a portion thereof, wherein:

in step a) and b) each of the portions of the V_H, D_H, J_H, V_κ , J_κ, V_λ or J_λ are sufficient to produce an antibody or portion thereof containing a VH or VL or portion thereof that forms a sufficient antigen binding site;

c) repeating step a) and b) a plurality of times to generate sequences of a plurality of different nucleic acid molecules;

d) synthesizing the nucleic acid molecules to produce two libraries, wherein:

the first library comprises nucleic acid molecules encoding a VH chain or a portion thereof; and

the second library comprises nucleic acid molecules encoding a VL chain or a portion thereof;

e) introducing a nucleic acid molecule from the first library and from the second library into a cell and repeating this a plurality of times to produce a library of cells, wherein each cell contains nucleic acid molecules encoding a different combination of VH and VL from every other cell in the library of cells; and

f) growing the cells to express the antibodies or portions thereof in each cell, thereby producing a plurality of antibodies or portion thereof , wherein each antibody or portion thereof in the library comprises a different combination of a VH and a VL chain or a sufficient portion thereof to form an antigen binding site from all other antibodies or portions thereof in the library.

155. The method of generating a human combinatorial antibody library of claim 154, wherein the library is an addressable library, whereby:

in step d) the synthesized nucleic acid sequences are individually addressed, thereby generating a first addressed nucleic acid library and a second addressed nucleic acid library;

in step e) the cells are addressed, wherein each locus comprises a cell that contains nucleic acid molecules encoding a different combination of a VH and a VL from every other cell in the addressed library of cells; and

in step f) the plurality of antibodies or portions thereof are addressed, wherein:

the antibodies or portions thereof at each locus in the library is the same antibody and is different from those at each and every other locus; and

the identity of the antibody or portion thereof is known by its address.

156. The method of generating a human combinatorial antibody library of claim 154 or claim 155, wherein

in step a) the V_H, D_H and J_H germline segments or portions thereof of the nucleic acid molecule encoding a VH chain are combined such that the V_H segment is 5' to the D_H segment which is 5' to the J_H segment; and

in step b) the V_κ and J_κ or V_λ and J_λ germline segments or portions thereof of the nucleic acid molecule encoding a VL chain are linked such that the V_κ segment is 5' to the J_κ segment or the V_λ segment is 5' to the J_λ segment.

157. The method of generating a human combinatorial antibody library of any of claims 154-156, wherein steps a)-b) are performed by a computer programmed to carry out an algorithm(s).

158. The method of generating a human combinatorial antibody library of any of claims 154-157, wherein step a) comprises:

i) selecting a V_H, a D_H and a J_H germline segment or portion thereof;

ii) generating a V-D joint by modifying the germline sequence of the V_H and/or D_H by insertion or deletion of one or more nucleotides in order to maximize the hydrophilicity of the D_H germline segment;

iii) generating a D-J joint by modifying the germline sequence of the D_H and/or J_H by insertion or deletion of one or more nucleotides to maintain the reading frame of the J_H; and

iv) combining the resulting V_H, D_H, and J_H, to generate a sequence of a nucleic acid molecule encoding a VH chain.

159. The method of generating a human combinatorial antibody library of claim 158, wherein the V-D joint is generated by deleting a nucleotide from the 5' end of the D_H.

160. The method of generating a human combinatorial antibody library of claim 158, wherein the V-D joint is generated by deleting a nucleotide from the 3' end of the V_H.

161. The method of generating a human combinatorial antibody library of claim 158, wherein the V-D joint is generated by inserting a nucleotide at the 5' end of the D_H.

162. The method of claim 161, wherein the nucleotide is a guanine (G).

163. The method of generating a human combinatorial antibody library of claim 158, wherein the D-J joint is generated by deleting a nucleotide from the 5' end of the J_H.

164. The method of generating a human combinatorial antibody library of claim 158, wherein the D-J joint is generated by deleting a nucleotide from the 3' end of the D_H.

165. The method of generating a human combinatorial antibody library of claim 158, wherein the D-J joint is generated by inserting a nucleotide at the 5' end of the D_H.

166. The method of generating a human combinatorial antibody library of claim 165, wherein the nucleotide is a guanine (G).

167. The method of generating a human combinatorial antibody library of any of claims 154-157, wherein step b) comprises:

i) selecting a V_κ and J_κ or V_λ and J_λ germline segment or portion thereof;

ii) generating a V-J joint by modifying the germline sequence of the V_κ or J_κ by insertion or deletion of one or more nucleotides to maintain the reading frame of the J_κ, or by modifying the germline sequence of the V_λ or J_λ by insertion or deletion of one or more nucleotides to maintain the reading frame of the J_λ; and

iv) combining the resulting V_κ and J_κ or V_λ and J_λ to generate a sequence of a nucleic acid molecule encoding a VL chain.

168. The method of generating a human combinatorial antibody library of claim 167, wherein the V-J joint is generated by deleting a nucleotide from the 5' end of the J_κ or J_λ

169. The method of generating a human combinatorial antibody library of claim 167, wherein the V-J joint is generated by deleting a nucleotide from the 3' end of the V_κ or V_λ.

170. The method of generating a human combinatorial antibody library of claim 167, wherein the V-J joint is generated by inserting a nucleotide at the 5' end of the J_κ or J_λ.

171. The method of claim 170, wherein the nucleotide is a guanine (G).

172. The method of generating a human combinatorial antibody library of any of claims 154-171, wherein repeating step a) a plurality of times comprises:

selecting N1 different V_H germline segments;

selecting N2 different D_H germline segments,

selecting N3 different J_H sequences, wherein:

N1, N2 and N3 are a number of germline segments that can be all or a subset of V_H, D_H or J_H germline segments; and

N1, N2 and N3 can be the same or different; and

combining all possible V_H, D_H and J_H combinations to generate N1 x N2 x N3 different nucleic acid sequences encoding a VH chain.

173. The method of generating a human combinatorial antibody library of any of claims 157-172, wherein a V_H germline segment is selected from among all or a subset of an IGHV1, IGHV2, IGHV3, IGHV4, IGHV5, IGHV6 and IGHV7 and genes and alleles thereof.

174. The method of generating a human combinatorial antibody library of claim 173, wherein a V_H germline segment is selected from among all or a subset of SEQ ID NOS: 10-238.

175. The method of generating a human combinatorial antibody library of any of claims 157-172, wherein a D_H germline segment is selected from among all or a subset of an IGHD1, IGHD2, IGHD3, IGHD4, IGHD5, IGHD6, and IGHD7 and genes and alleles thereof.

176. The method of generating a human combinatorial antibody library of claim 175, wherein a D_H germline segment is selected from among any of SEQ ID NOS: 239-272.

177. The method of generating a human combinatorial antibody library of any of claims 157-172, wherein a J_H germline segment is selected from among all or a subset of IGHJ1, IGHJ2, IGHJ3, IGHJ4, IGHJ5, and IGHJ6 and genes and alleles thereof.

178. The method of generating a human combinatorial antibody library of claim 177, wherein a J_H germline segment is selected from among any of SEQ ID NOS: 273-285.

179. The human combinatorial antibody library of any of claims 172-178, wherein the subset of germline segments are selected based on sequence similarities or differences, gene family, length, composition, CDR length or composition, species, functionality, specificity, group or subgroup.

180. The human combinatorial antibody library of claim 179, wherein the subset of germline segments are selected based on gene family.

181. The human combinatorial antibody library of claim 180, wherein one germline segment from each of a V_H, D_H, and/or J_H gene family is selected or one germline segment from a subset of a V_H, D_H, and/or J_H gene family is selected, wherein:

the V_H gene family is selected from among a IGHV1-18, IGHV1-2, IGHV1-24, IGHV1-3, IGHV1-45, IGHV1-46, IGHV1-58, IGHV1-69, IGHV1-8, IGHV2-26, IGHV2-5, IGHV2-70, IGHV3-11, IGHV3-13, IGHV3-15, IGHV3-16, IGHV3-20, IGHV3-21, IGHV3-23, IGHV3-30, IGHV3-33, IGHV3-35, IGHV3-38, IGHV3-43, IGHV3-48, IGHV3-49, IGHV3-53, IGHV3-64, IGHV3-66, IGHV3-7, IGHV3-72, IGHV3-73, IGHV3-74, IGHV3-9, IGHV4-28, IGHV4-31, IGHV4-34, IGHV4-39, IGHV4-4, IGHV4-59, IGHV4-61, IGHV5-51, IGHV6-1 and IGHV7-81;

the D_H gene family is selected from among a IGHD1-1, IGHD1-14, IGHD1-20, IGHD1-26, IGHD1-7, IGHD2-15, IGHD2-2, IGHD2-21, IGHD2-8, IGHD3-10, IGHD3-16, IGHD3-22, IGHD3-3, IGHD3-9, IGHD4-11, IGHD4-17, IGHD4-23, IGHD4-4, IGHD5-12, IGHD5-18, IGHD5-24, IGHD5-5, IGHD6-13, IGHD6-19, IGHD6-25, IGHD6-6 and IGHD7-27; and

the J_H gene family is selected from among a IGHJ1, IGHJ2, IGHJ3, IGHJ4, IGHJ5 and IGHJ6.

182. The method of generating a human combinatorial antibody library of any of claims 154-171, wherein repeating step b) a plurality of times comprises:

selecting N1 (number) different V_λ germline segments and selecting N2 different J_λ germline segments; or

selecting N3 different V_κ germline segments and selecting N4 different J_κ germline segments, wherein:

N1, N2, N3 and N4 are a number of germline segments that can be all or a subset of V_λ, J_λ, V_κ, J_κ germline segments; and

N1, N2, N3 and N4 can be the same or different; and

combining all possible V_λ or J_λ combinations to generate N1 x N2 different nucleic acid molecules encoding a VL chain, or combining all possible V_κ and J_κ to generate N3 x N4 different nucleic acid molecules encoding a VL chain.

183. The method of generating a human combinatorial antibody library of any of claims 157-171 and 182, wherein a V_λ germline segment is selected from among all or a subset of an IGLV1, IGLV2, IGLV3, IGLV4, IGLV5, IGLV6, IGLV7, IGLV8, IGLV9, IGLV10 and IGLV11 and genes and alleles thereof.

184. The method of generating a human combinatorial antibody library of claim 183, wherein a V_λ germline segment is selected from among all or a subset of SEQ ID NOS: 365-441.

185. The method of generating a human combinatorial antibody library of any of claims 157-171 and 182, wherein a J_λ germline segment is selected from among all or a subset of an IGLJ1, IGLJ2, IGLJ3, IGLJ4, IGLJ5, IGLJ6 and IGLJ7 and genes and alleles thereof.

186. The method of generating a human combinatorial antibody library of claim 185, wherein a J_λ germline segment is selected from among all or a subset of SEQ ID NOS: 442-451.

187. The method of generating a human combinatorial antibody library of any of claims 157-171 and 182, wherein a V_κ germline segment is selected from among all or a subset of an IGKV1, IGKV2, IGKV3, IGKV4, IGKV5 and IGKV6, and genes and alleles thereof.

188. The method of generating a human combinatorial antibody library of claim 187, wherein a V_κ germline segment is selected from among all or a subset of SEQ ID NOS: 286-355 and 868.

189. The method of generating a human combinatorial antibody library of any of claims 157-171 and 182, wherein a J_κ germline segment is selected from among all or a subset of IGKJ1, IGKJ2, IGKJ3, IGKJ4 and IGKJ5 and genes and alleles thereof.

190. The method of generating a human combinatorial antibody library of claim 189, wherein a J_κ germline segment is selected from among all or a subset of SEQ ID NOS: 356-364.

191. The method of generating a human combinatorial antibody library of any of claims 182-190, wherein the subset of germline segments are selected based on sequence

similarities or differences, gene family, length, composition, CDR length or composition, species, functionality, specificity, group or subgroup.

192. The method of generating a human combinatorial antibody library of claim 191, wherein germline segments are selected based on gene family, whereby one germline segment from each of a V_κ and/or J_κ or V_λ and/or J_λ gene family is selected or one germline segment from a subset of a V_κ and/or J_κ or V_λ and/or J_λ gene family is selected, wherein:

the V_κ gene family is selected from among a IGKV1-12, IGKV1-12, IGKV1-16, IGKV1-17, IGKV1-27, IGKV1-33, IGKV1-37, IGKV1-39, IGKV1-5, IGKV1-6, IGKV1-8, IGKV1-9, IGKV1-NL1, IGKV1/OR2, IGKV1D-12, IGKV1D-13, IGKV1D-16, IGKV1-D-17, IGKV1D-33, IGKV1D-37, IGKV1D-39, IGKV1D-42, IGKV1D-43, IGKV1D-8, IGKV2-24, IGKV2-28, IGKV2-29, IGKV2-30, IGKV2-30, IGKV2-40, IGKV2D-24, IGKV2D-26, IGKV2D-28, IGKV2D-29, IGKV2-D-30, IGKV2D-40, IGKV3-11, IGKV3-15, IGKV3-20, IGKV3-7, IGKV3-NL1, IGV3-NL2, IGKV3-NL3, IGKV3-NL4, IGKV3-NL5, IGKV3/OR2-268, IGKV3D-11, IGKV3D-15, IGKV3D-20, IGKV3D-7, IGKV4-1, IGKV5-2, IGKV6-21, IGKV6D-21, IGKV6D-41, and IGKV1-39;

the J_κ gene family is selected from among a IGKJ1, IGKJ2, IGKJ3, IGKJ4 and IGKJ5;

the V_λ gene family is selected from among a IGLV1-36, IGLV1-40, IGLV1-41, IGLV1-44, IGLV1-47, IGLV1-50, IGLV1-51, IGLV10-54, IGLV11-55, IGLV2-11, IGLV2-14, IGLV2-18, IGLV2-23, IGLV2-33, IGLV2-8, IGLV3-1, IGLV3-10, IGLV3-12, IGLV3-16, IGLV3-19, IGLV3-21, IGLV3-22, IGLV3-25, IGLV3-27, IGLV3-32, IGLV3-9, IGLV4-3, IGLV4-60, IGLV4-69, IGLV5-37, IGLV5-39, IGLV5-45, IGLV5-8, IGLV5-52, IGLV6-57, IGLV7-43, IGLV7-46, IGLV8-61, IGLV8-61 and IGLV9-49; and

the J_λ gene family is selected from among a IGLJ1, IGLJ2, IGLJ4, IGLJ5, IGLJ6 and IGLJ7.

193. The method of generating a human combinatorial antibody library of any of claims 154-192 wherein the germline segments are set forth in a user-created database.

194. The method of generating a human combinatorial antibody library of claim 193, wherein the sequences of the J_H, J_κ, and J_λ germline segment in the database are set forth in their correct reading frame.

195. The method of generating a human combinatorial antibody library of any of claims 154-194, further comprising in step a) and/or step b) modifying the nucleic acid molecule encoding a VH chain or a portion thereof and/or a VL chain or portion thereof by removing any stop codons.

196. The method of generating a human combinatorial antibody library of claim 195, wherein the stop codon TAA is modified to TAT, the stop codon TAG is modified to TAT, and the stop codon TGA is modified to TCA.

197. The method of generating a human combinatorial antibody library of any of claims 154-196, further comprising in step a) and/or step b) modifying the nucleic acid molecule encoding a VH chain or a portion thereof and/or a VL chain or portion thereof by removing any restriction sites.

198. The method of generating a human combinatorial antibody library of claim 197, wherein the restriction sites are modified to maximize codon usage in *E. coli* K12.

199. The method of generating a human combinatorial antibody library of any of claims 154-198, further comprising determining the sequence similarity between and among the plurality of different nucleic acid molecules encoding a VH chain and/or the sequence similarity between and among the plurality of different nucleic acid molecules encoding a VL chain.

200. The method of generating a human combinatorial antibody library of claim 199, wherein, based on sequence similarity, selecting a subset of nucleic acid sequences encoding a VH chain and/or a subset of nucleic acid sequences encoding a VL chain that are the most similar or that are the most different.

201. The method of generating a human combinatorial antibody library of any of claims 154-200, wherein the synthesized nucleic acid sequences in the libraries are contained in vectors.

202. The method of generating a human combinatorial antibody library of claim 201, wherein the vector further contains all or a portion of a constant region sufficient to permit association of a heavy and light chain.

203. The method of generating a human combinatorial antibody library of any of claims 154 -202, wherein the cells are prokaryotic cells or eukaryotic cells.

204. The method of generating a human combinatorial antibody library of any of claims 154-203, wherein the cells are *E. coli* cells.

205. The method of generating a human combinatorial antibody library of any of claims 155-204, wherein the addressed cells are arranged in a spatial array.

206. The method of generating a human combinatorial antibody library of claim 205, wherein the spatial array is a multiwell plate, wherein each individual locus of the plate corresponds to a cell that contains nucleic acid molecules encoding a different combination of VH and VL from every other cell in the addressed library of cells.

207. The method of generating a human combinatorial antibody library of any of claims 154-206, wherein the expressed antibody is a full length antibody, or a fragment or portion thereof sufficient to form an antigen binding site.

208. The method of generating a human combinatorial antibody library of any of claims 154-206, wherein the expressed antibody is a Fab.

209. The method of generating a human combinatorial antibody library of any of claims 154-208, further purifying the antibodies or portions thereof.

210. The method of generating a human combinatorial antibody library of claim 209, wherein the purified antibodies or portions thereof in the library are 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% pure.

211. The method of generating a human combinatorial antibody library of claim 209 or claim 210, wherein:

the purified antibodies or portions thereof are addressed; and

the antibody within each address is the same antibody and is different from the antibodies at all other addresses.

212. A human combinatorial antibody library produced by the method of any of claims 154-211.

213. The human combinatorial antibody library of claim 212, wherein:

the VH chain has a sequence of amino acids selected from among any of SEQ ID NOS: 1475-1826 or a subset thereof; and

the VL chain has a sequence of amino acids selected from among any of SEQ ID NOS: 1827-1838, 1840-1855 and 1857-1888 or a subset thereof.

214. A method of screening a human combinatorial antibody library for binding or activity against a target protein, comprising:

a) providing a human combinatorial antibody library of any of claims 1-88, 212 or 213;

b) contacting an antibody or portion thereof in the library with a target protein;

c) assessing binding of the antibody or portion thereof with the target protein and/or whether the antibody or portion thereof modulates a functional activity of the target protein; and

d) identifying an antibody or portion thereof that binds to the target protein and/or modulates an activity of the target protein, wherein the identified antibody or portion thereof is a HIT.

215. The method of claim 214, wherein the human combinatorial antibody library is an addressable library and contacting is performed in an addressable array such that the identity of the HIT is known by its address.

216. The method of claim 214 or claim 215, wherein the target protein is a membrane-bound protein, cell surface receptor (CSR), or a CSR ligand.

217. The method of claim 216, wherein the membrane-bound protein or CSR is selected from among a cytokine receptor, a receptor kinase, a receptor phosphatase, a receptor involved in cell-cell interactions, and a cellular adhesion molecule.

218. The method of any of claims 214-217, wherein the target protein is selected from among a VEGFR-1, VEGFR-2, VEGFR-3, a epidermal growth factor receptor (EGFR), ErbB-2, ErbB-3, IGF-R1, C-Met, TNF-R1, TNF-R2, BTLA, HVEM, LT-βR, CD20, CD3, CD25, NOTCH, DLL4, G-CSF-R, GM-CSF-R, EPO-R, a cadherin, an integrin, CD52 and CD44, a VEGF-A, VEGF-B, VEGF-C, VEGF-D, PIGF, EGF, HGF, TNF-α, LIGHT, lymphotoxin (LT), IgE, G-CSF, GM-CSF and EPO.

219. The method of any of claims 213-218, comprising assessing the binding of an antibody or portion thereof to the target protein.

220. The method of claim 213-218, comprising assessing whether the antibody or portion thereof modulates a functional activity of the target protein.

221. The method of claim 220, wherein the functional activity is selected from among cellular proliferation, lymphoma apoptosis, chemotaxis, cancer cell invasion, matrigel, endothelial proliferation, tube formation and signal transduction.

222. The method of any of claims 214-221, wherein:

binding is assessed on cells and/or a functional activity is assessed in a cell-based assay; and

the cells express the target protein.

223. The method of claim 222, wherein the cells are transiently or stably expressed with a nucleic acid molecule encoding the target protein.

224. The method of any of any of claims 214-223, further comprising:

providing a second combinatorial antibody library based on the identified HIT(s), wherein the second library is generated by a method comprising:

a) selecting V_H, D_H and J_H human germline segments that are related by sequence similarity to the germline segments of the identified HIT(s), and combining all possible V_H, D_H and J_H human germline segments or portions thereof in frame to generate a

plurality of sequences of nucleic acid molecules each encoding a different VH chain or a portion thereof;

b) selecting V_κ and a J_κ or V_λ and a J_λ human germline segments that are related by sequence similarity to the germline segments of the identified HIT(s), and combining all possible V_κ and a J_κ human germline segments or portions thereof, or all possible V_λ and a J_λ germline segment or portions thereof in frame to generate a plurality of sequences of nucleic acid molecule each encoding a different VL chain or a portion thereof, wherein:

in step a) and b) each of the portions of the V_H, D_H, J_H, V_κ , J_κ, V_λ or J_λ are sufficient to produce an antibody containing a VH or VL or portion thereof that is sufficient to bind to an antigen;

c) synthesizing the nucleic acid molecules to produce two libraries, wherein:

the first library comprises nucleic acid molecules encoding a VH chain or a portion thereof; and

the second library comprises nucleic acid molecules encoding a VL chain or a portion thereof;

d) introducing a nucleic acid molecule from the first library and from the second library into a cell and repeating this a plurality of times to produce a library of cells, wherein each cell contains nucleic acid molecules encoding a different combination of VH and VL from every other cell in the library of cells; and

e) growing the cells to express the antibodies in each cell, thereby producing a plurality of antibodies or portions thereof wherein the antibody or portion thereof in the library comprises a different combination of a VH and a VL chain or a sufficient portion thereof to form an antigen binding site from all other antibodies or portions thereof in the library; and

f) further purifying the antibodies or portions thereof to generate a second human combinatorial antibody library;

contacting an antibody or portion thereof in the library with a target protein;

assessing binding of the antibody or portion thereof with the target protein and/or whether the antibody or portion thereof modulates a functional activity of the target protein; and

identifying an antibody or portion thereof that binds to the target protein and/or modulates an activity of the target protein, wherein the identified antibody or portion thereof is a further HIT.

225. The method of claim 224, wherein the sequence similarity is or is about 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more.

226. The method of any of claims 214-223, further comprising:

providing a second combinatorial antibody library based on the identified HIT(s), wherein the second library is generated by a method comprising:

a) selecting a plurality of nucleic acid molecules encoding a VH chain that contain a V_H, a D_H or a J_H human germline segment that is the same as contained in the nucleic acid molecule encoding the identified HIT;

b) selecting a plurality of nucleic acid molecules encoding a VL chain that contains a V_κ and a J_κ or a V_λ and a J_λ human germline segment that is the same as contained in the nucleic acid molecule encoding the identified HIT;

c) introducing a nucleic acid molecule from the plurality of nucleic acid molecules encoding a VH and a nucleic acid molecule from the plurality of nucleic acid molecules encoding a VL into a cell and repeating this a plurality of times to produce a library of cells, wherein each cell contains nucleic acid molecules encoding a different combination of VH and VL from every other cell in the library of cells; and

d) growing the cells to express the antibodies in each cell, thereby producing an a plurality of antibodies or portions thereof wherein each antibody or portion thereof in the library comprises a different combination of a VH and a VL chain or a sufficient portion thereof to form an antigen binding site from all other antibodies or portions thereof in the library; and

f) further purifying the antibodies or portions thereof;

contacting an antibody or portion thereof in the library with a target protein;

assessing binding of the antibody or portion thereof with the target protein and/or whether the antibody or portion thereof modulates a functional activity of the target protein; and

identifying an antibody or portion thereof that binds to the target protein and/or modulates an activity of the target protein, wherein the identified antibody or portion thereof is a further HIT.

227. The method of anyof claims 224-226, wherein:

the second human combinatorial library is an addressable library, whereby the purified antibodies or portion thereof are addressed and the purified antibody within each address is the same antibody and is different from the antibodies at all other addresses;

contacting is performed in an addressable array; and

the identity of the further HIT is known by its address.

228. The method of any of claims 214-223, further comprising:

providing a second combinatorial antibody library based on the identified HIT(s), wherein the second library is generated by introducing amino acid mutations into the "HIT" to generate a plurality of antibodies or portions thereof, wherein each antibody member or portion thereof of the second combinatorial antibody library differs from the identified "HIT" by one or more amino acid mutations in its primary sequence;

contacting an antibody or portion thereof in the library with a target protein;

assessing binding of the antibody or portion thereof with the target protein and/or whether the antibody or portion thereof modulates a functional activity of the target protein; and

identifying an antibody or portion thereof that binds to the target protein and/or modulates an activity of the target protein, wherein the identified antibody or portion thereof is a further HIT.

229. The method of claim 228, wherein the amino acid mutations are in the complementarity determining regions (CDRs) of the identified HIT.

230. The method of any of claims 224-229 that is repeated iteratively until a further "HIT" is identified having an optimized binding affinity for a target protein and/or having an activity that is optimized against a target protein compared to previous "HITS" in earlier iterations of the method.

231. A computer system or a computer readable medium, comprising computer-readable instructions executable by a computer device for performing a method of combining human germline segments, wherein the method comprises the steps of:

(a) accessing a user-created *in silico* database of all available human antibody germline segments (V_H, D_H, J_H, V_κ, J_κ, V_λ and J_λ);

(b) applying an algorithm to generate a collection of every possible recombined full length nucleic acid sequence encoding a heavy chain (5'-V_H-D_H-J_H-3');

(c) applying an algorithm to generate a collection of every possible recombined full length nucleic acid sequence encoding a kappa light chains (5'-V_κ-J_κ-3') and/or every

possible recombined full length nucleic acid sequence encoding a lambda light chains (5'-V_λ-J_λ-3');

(d) applying an algorithm to modify nucleotides at the V-D and/or D-J joints of the nucleic acid sequences of (b) and at the V-J joints of the nucleic acid sequences of (c) so that the resulting nucleic acids sequences are in frame;

(e) modifying the nucleic acid sequences of (d) to remove any inadvertently generated stop codons;

(f) assigning each recombined nucleic acid sequence to a unique locus of an addressable format; and

(g) generating an output file that identifies the address of each recombined nucleic acid sequences.

232. The computer system or computer readable medium of claim 231, wherein the method further comprises the steps of:

(h) after step (e) adding nucleotides at the 5' and 3' termini of the recombined nucleic acid sequences comprising a sequence recognized by a restriction enzyme; and

(i) modifying the recombined nucleic acid sequence by nucleotide replacement to remove internal nucleotides that are recognized by a restriction enzyme.

233. The computer system or computer readable medium of claim 231 or claim 232, wherein the method further comprises modifying the recombined nucleic acid sequence to optimize codon usage for bacterial expression.

234. The computer system or computer readable medium of any of claims 231-233, wherein:

before step (f) the method selects recombined nucleic acid sequence(s) from the library of recombined nucleic acid sequences based on sequence similarities or differences; and

the selected sequences are assigned in step (f).

235. A method, comprising execution of computer-readable instructions for performing a method of combining human germline segment by a computer device, wherein the method of combining human germline segments comprises the steps of:

(a) accessing a user-created *in silico* database of all available human antibody germline segments (V_H, D_H, J_H, V_κ, J_κ, V_λ and J_λ);

(b) applying an algorithm to generate a collection of every possible recombined full length nucleic acid sequence encoding a heavy chain (5'-V_H-D_H-J_H-3');

(c) applying an algorithm to generate a collection of every possible recombined full length nucleic acid sequence encoding a kappa light chains (5'-V_κ-J_κ-3') and/or every possible recombined full length nucleic acid sequence encoding a lambda light chains (5'-V_λ-J_λ-3');

(d) applying an algorithm to modify nucleotides at the V-D and/or D-J joints of the nucleic acid sequences of (b) and at the V-J joints of the nucleic acid sequences of (c) so that the resulting nucleic acids sequences are in frame;

(e) modifying the nucleic acid sequences of (d) to remove any inadvertently generated stop codons;

(f) assigning each recombined nucleic acid sequence to a unique locus of an addressable format; and

(g) generating an output file that identifies the address of each recombined nucleic acid sequences.

236. The method of claim 235, further comprising synthesizing the recombined nucleic acid sequences encoding a heavy chain, encoding a kappa light chain, and/or encoding a lambda light chain, or a subset of recombined nucleic acid sequences encoding a heavy chain, encoding a kappa light chain, and/or encoding a lambda light chain.

237. A human combinatorial antibody library, comprising a plurality of antibodies, wherein:

a) each member antibody contains a variable light (VL) chain and a variable heavy (VH) chain or a sufficient portion thereof to form an antigen binding site; wherein;

i) each VL chain is encoded by a nucleic acid molecule that comprises a V_κ and a J_κ human germline segment or degenerate codons thereof or modified forms thereof, or a V_λ and a J_λ human germline segment or degenerate codons thereof or modified forms thereof , whereby the segments are linked in-frame;

ii) each VH chain is encoded by a nucleic acid molecule that comprises a human V_H and a human J_H germline segment or degenerate codons thereof or modified forms thereof and any sequence of nucleotides between the V_H and a J_H germline segments, whereby the segments are linked in-frame; and

b) the library comprises at least about or 50 or 100 or more different members.

238. The human combinatorial antibody library of claim 237, wherein:

the V_H germline segment, the sequence of nucleotides between the V_H and J_H and the J_H germline segment of the nucleic acid molecule encoding a VH chain are linked directly or

indirectly such that the V_H segment is 5' to the sequence of nucleotides between the V_H and J_H which is 5' to the J_H segment; and

the V_κ and J_κ or V_λ and J_λ germline segments of the nucleic acid molecule encoding a VL chain are linked directly or indirectly such that the V_κ segment is 5' to the J_κ segment or the V_λ segment is 5' to the J_λ segment.

239. The human combinatorial antibody library of claim 238, wherein the sequence of nucleotides between the V_H and J_H and the J_H germline segment are linked indirectly via a peptide linker at the D-J joint.

240. The human combinatorial antibody library of claim 239, wherein the peptide linker is an SY.

241. The human combinatorial antibody library of any of claims 237-240, wherein the V_H germline segment is an IGHV3-23*01 or degenerate codon thereof.

242. The human combinatorial antibody of any of claims 237-241, wherein the sequence of nucleotides between the V_H and J_H germline segments is a D_H germline segment or degenerate codons thereof or is an inverted D_H germline segment.

243. The human combinatorial antibody library of claim 242, wherein the D_H germline segments are selected from among any of SEQ ID NOS:239-272.

244. The human combinatorial antibody library of claim 242, wherein the inverted D_H germline segments are selected from among any of SEQ ID NOS: 3462-3488.

245. The human combinatorial antibody library of any of claims 237-244, wherein the D_H germline segment or inverted D_H germline segment has one or more nucleotides added or removed at the V-D or D-J joint to maintain the reading frame of the VH chain.

246. The human combinatorial antibody library of any of claims 237-245, wherein the J_H germline segment comprises one or more nucleotide modifications.

247. The human combinatorial antibody library of claim 246, wherein the modified J_H germline segment has a sequence of nucleotides set forth in any of SEQ ID NOS: 3450-3455.

248. The human combinatorial antibody library of any of claims 237-247, wherein:

the nucleic acid molecule encoding the VH chain is selected from among any of SEQ ID NOS: 2070-2759, or a subset thereof; and

the nucleic acid molecule encoding the VL chain are selected from among any of SEQ ID NOS: 1411-1422, 1424-1439 and 1441-1471 or a subset thereof.

249. The human combinatorial antibody library of any of claims 237-248, wherein:

the VH chain has a sequence of amino acids selected from among any of SEQ ID NOS: 2760-3449, or a subset thereof; and

the VL chain has a sequence of amino acids selected from among any of SEQ ID NOS: 1827-1838, 1840-1855 and 1857-1888 or a subset thereof.

250. The human combinatorial antibody library of any of claims 237-249, wherein the each member antibody in the library further comprises all or a portion of a constant region sufficient to permit association of a heavy and light chain.

251. The human combinatorial antibody library of any of claims 237-250, wherein each member antibody in the library is selected from among a full length antibody, or a fragment or portion thereof sufficient to form an antigen binding site.

252. The human combinatorial antibody library of claim 251, wherein the fragment o portion thereof is selected from among a Fab, Fab', $F(ab')_2$, single-chain Fvs (scFv), Fv, dsFv, diabody, Fd and Fd' fragments, Fab fragments, Fd fragments, scFv fragments, and scFab fragments.

253. The human combinatorial antibody library of any of claims 237-252, wherein each member antibody in the library is a Fab.

254. The human combinatorial antibody library of any of claims 237-253, comprising about or 50, 10^2, 10^3, 10^4, 2×10^4, 3×10^4, 4×10^4, 5×10^4, 6×10^4, 7×10^4, 8×10^4, 9×10^4, 10^5, 10^6, 10^7, 10^8, 10^9 or more different members.

255. The human combinatorial antibody library of any of claims 237-254, comprising 10^3, 2×10^3, 3×10^3, 4×10^3, 5×10^3, 6×10^3, 4×10^3, 7×10^3, 8×10^3, 9×10^3, 10^4, 2×10^4, 3×10^4, 4×10^4, 5×10^4, 6×10^4, 7×10^4, 8×10^4, 9×10^4 or more different members.

256. The human combinatorial antibody library of any of claims 237-255, wherein antibody library is addressable.

257. A library of nucleic acid molecules, comprising a plurality of addressable nucleic acid molecules encoding a variable heavy (VH) chain, wherein:

each VH chain is encoded by a nucleic acid molecule that comprises a human V_H and a human J_H germline segment or degenerate codons thereof or modified forms thereof and any sequence of nucleotides between the V_H and a J_H germline segments, linked in-frame; and

the nucleic acid molecule within each address is the same and is different from the nucleic acid molecules at all other addresses.

258. The library of nucleic acid molecules of claim 257, wherein the V_H germline segment, the sequence of nucleotides between the V_H and J_H and the J_H germline segment of the nucleic acid molecule encoding a VH chain are linked directly or indirectly such that the V_H segment is 5' to the sequence of nucleotides between the V_H and J_H which is 5' to the J_H segment.

259. The library of nucleic acid molecules of claim 257 or claim 258, wherein the sequence of nucleotides between the V_H and J_H and the J_H germline segment are linked indirectly by nucleotides encoding a peptide linker at the D-J joint.

260. The library of nucleic acid molecules of claim 259, wherein the nucleotides encode a peptide linker that is SY.

261. The library of nucleic acid molecules of any of claims 257-260, wherein the V_H germline segment is an IGHV3-23*01 or degenerate codon thereof.

262. The library of nucleic acid molecules of any of claims 257-261, wherein the sequence of nucleotides between the V_H and J_H germline segments is a D_H germline segment or degenerate codons thereof or is an inverted D_H germline segment.

263. The library of nucleic acid molecules of any of claims 257-262, wherein the D_H germline segments are selected from among any of SEQ ID NOS:239-272.

264. The library of nucleic acid molecules of any of claims 257-263, wherein the inverted D_H germline segments are selected from among any of SEQ ID NOS: 3462-3488.

265. The library of nucleic acid molecules of any of claims 257-264, wherein the D_H germline segment or inverted D_H germline segment has one or more nucleotides added or removed at the V-D or D-J joint to maintain the reading frame of the VH chain.

266. The library of nucleic acid molecules of any of claims 257-265, wherein the J_H germline segment comprises one or more nucleotide modifications.

267. The library of nucleic acid molecules of claim 266, wherein the modified J_H germline segment has a sequence of nucleotides set forth in any of SEQ ID NOS: 3450-3455.

268. The library of nucleic acid molecules of any of claims 257-267, comprising a plurality of nucleic acid molecule encoding the VH chain selected from among any of SEQ ID NOS: 2070-2759, or a subset thereof.

269. A library of addressable vectors, comprising the nucleic acid molecules of any of claims 257-268, wherein each vector in the library contains a different nucleic acid molecule.

270. A library of addressable cells, comprising vectors of claim 269, wherein each cell in the library contains a different vector.

271. A method of generating a human combinatorial antibody library, comprising:

a) combining a human V_H and a human J_H germline segment or portions thereof, degenerate codons thereof or modified forms thereof and any sequence of nucleotides between the V_H and a J_H germline segments in frame to generate a sequence of a nucleic acid molecule encoding a VH chain or a portion thereof;

b) combining a V_κ and a J_κ human germline segment or portions thereof, degenerate codons thereof or modified forms thereof; or a V_λ and a J_λ germline segment or portions thereof, degenerate codons thereof or modified forms thereof in frame to generate a sequence of a nucleic acid molecule encoding a VL chain or a portion thereof, wherein:

in step a) and b) each of the portions of the V_H, any sequence of nucleotides between the V_H and a J_H germline segments, J_H, V_κ , J_κ, V_λ or J_λ are sufficient to produce an antibody or portion thereof containing a VH or VL or portion thereof that forms a sufficient antigen binding site; and

the segments are combined directly or indirectly such that the V_H germline segment, the sequence of nucleotides between the V_H and J_H and the J_H germline segment of the nucleic acid molecule encoding a VH chain are linked directly or indirectly such that the V_H segment is 5' to the sequence of nucleotides between the V_H and J_H which is 5' to the J_H segment;

c) repeating step a) and b) a plurality of times to generate sequences of a plurality of different nucleic acid molecules;

d) generating two addressable libraries, wherein:

the first library comprises nucleic acid molecules encoding a VH chain or a portion thereof; and

the second library comprises nucleic acid molecules encoding a VL chain or a portion thereof;

e) introducing a nucleic acid molecule from the first library and from the second library into addressed cells, and repeating this a plurality of times to produce a library of addressed cells, wherein each cell contains nucleic acid molecules encoding a different combination of VH and VL from every other cell in the library of cells; and

f) growing the cells to express the antibodies or portions thereof in each cell, thereby producing a plurality of antibodies or portion thereof , wherein:

each antibody or portion thereof in the library comprises a different combination of a VH and a VL chain or a sufficient portion thereof to form an antigen binding site from all other antibodies or portions thereof in the library;

the plurality of antibodies or portions thereof are addressed; and

the antibodies or portions thereof at each locus is the same antibody and is different from those at each and every other locus;

the identity of the antibody or portion thereof is known by its address.

272. The method of generating a human combinatorial antibody library of claim 271, wherein the V_H and the sequence of nucleotides between the V_H and J_H, and/or the sequence of nucleotides between the V_H and J_H and the J_H germline segment are linked indirectly by nucleotides encoding a peptide linker at the V-D and/or D-J joint.

273. The method of generating a human combinatorial antibody library of claim 271 or claim 272, wherein the V_H and the sequence of nucleotides between the V_H and J_H, and/or the sequence of nucleotides between the V_H and J_H and the J_H germline segment modified to remove stop codons.

274. The method of generating a human combinatorial antibody library of claim 271-273, wherein the V_H germline segment is selected from among all or a subset of SEQ ID NOS: 10-238 or is a portions thereof, degenerate codons thereof or modified forms thereof.

275. The method of generating a human combinatorial library of claim 274, wherein the V_H germline segment is IGHV3-23*01, or is a portions thereof, degenerate codons thereof or modified forms thereof

276. The method of generating a human combinatorial library of any of claims 271-275, wherein the sequence of nucleotides between the V_H and J_H is a D_H germline segment or degenerate codons thereof or is an inverted D_H germline segment.

277. The method of generating a human combinatorial antibody libary of any of claims 271-276, wherein the D_H germline segments are selected from among any of SEQ ID NOS:239-272 or is a portions thereof, degenerate codons thereof or modified forms thereof or is an inverted D_H germline segments thereof.

278. The method of generating a human combinatorial antibody library of any of claims 271-277, wherein the inverted D_H germline segments are selected from among any of SEQ ID NOS: 3462-3488.

279. The method of generating a human combinatorial antibody library of any of claims 271-278, wherein the D_H germline segment or inverted D_H germline segment has one or more nucleotides added or removed at the V-D or D-J joint to maintain the reading frame of the VH chain.

280. The method of generating a human combinatorial antibody library of any of claims 271-279, wherein the J_H germline segment is selected from among any of SEQ ID NOS: 273-285 or is a portion thereof, degenerate codons thereof or modified forms thereof.

281. The method of generating a human combinatorial antibody library of claim 280, wherein the J_H germline segment comprises one or more nucleotide modifications.

282. The method of generating a human combinatorial antibody library of claim 281, wherein the modified J_H germline segment has a sequence of nucleotides set forth in any of SEQ ID NOS: 3450-3455.

283. The method of generating a human combinatorial antibody library of any of claims 271-282, wherein the a V_λ germline segment is selected from among all or a subset of SEQ ID NOS: 365-441 or is a portion thereof, degenerate codons thereof or modified forms thereof.

284. The method of generating a human combinatorial antibody library of any of claims 271-283, wherein the J_λ germline segment is selected from among all or a subset of SEQ ID NOS: 442-451 or is portion thereof, degenerate codons thereof or modified forms thereof.

285. The method of generating a human combinatorial antibody library of any of claims 271-284, wherein the V_κ germline segment is selected from among all or a subset of SEQ ID NOS: 286-355 and 868 or is portion thereof, degenerate codons thereof or modified forms thereof.

286. The method of generating a human combinatorial antibody library of any of claims 271-285, wherein the J_κ germline segment is selected from among all or a subset of SEQ ID NOS: 356-364 or is portion thereof, degenerate codons thereof or modified forms thereof.

287. The method of generating a human combinatorial antibody library of any of claims 271-286, wherein:

the nucleic acid molecules encoding a VH chain or a portion thereof in the first library are contained in an expression vector, wherein each nucleic acid molecule is contained in a separate expression vector; and

the nucleic acid molecules encoding a VL chain or portion thereof in the second library are contained in an expression vector, wherein each nucleic acid molecule is contained in a separate expression vector.

288. The method of generating a human combinatorial antibody library of claim 287, wherein the vectors further contains all or a portion of a constant region sufficient to permit association of a heavy and light chain.

289. The method of generating a human combinatorial antibody library of any of claims 271-288, wherein the cells are prokaryotic cells or eukaryotic cells.

290. The method of generating a human combinatorial antibody library of any of claims 271-289, wherein the cells are *E. coli* cells.

291. The method of generating a human combinatorial antibody library of any of claims 271-290, wherein the addressed cells are arranged in a spatial array.

292. The method of generating a human combinatorial antibody library of claim 291, wherein the spatial array is a multiwell plate, wherein each individual locus of the plate corresponds to a cell that contains nucleic acid molecules encoding a different combination of VH and VL from every other cell in the addressed library of cells.

293. The method of generating a human combinatorial antibody library of any of claims 271-292, wherein the expressed antibody is a full length antibody, or a fragment or portion thereof sufficient to form an antigen binding site.

294. The method of generating a human combinatorial antibody library of any of claims 3271-293, wherein the expressed antibody is a Fab.

295. The method of generating a human combinatorial antibody library of any of claims 271-294, further purifying the antibodies or portions thereof.

296. The method of generating a human combinatorial antibody library of claim 295, wherein the purified antibodies or portions thereof in the library are 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% pure.

297. A human combinatorial antibody library produced by the method of any of claims 271-296.

298. A method of screening a human combinatorial antibody library for binding or activity against a target protein, comprising:

a) providing a human combinatorial antibody library of any of claims 237-256 or claim 297;

b) contacting an antibody or portion thereof in the library with a cell or a target protein;

c) assessing binding of the antibody or portion thereof with the cell or target protein and/or whether the antibody or portion thereof modulates a functional activity of the cell or target protein; and

d) identifying an antibody or portion thereof that binds to the cell or target protein and/or modulates an activity of the cell or target protein, wherein the identified antibody or portion thereof is a HIT.

299. The method of claim 298, wherein the human combinatorial antibody library is an addressable library and contacting is performed in an addressable array such that the identity of the HIT is known by its address.

300. The method of claim 298 or claim 299, wherein the target protein is a membrane-bound protein, cell surface receptor (CSR), or a CSR ligand.

301. The method of claim 300, wherein the membrane-bound protein or CSR is selected from among a cytokine receptor, a receptor kinase, a receptor phosphatase, a receptor involved in cell-cell interactions, and a cellular adhesion molecule.

302. The method of any of claims 298-301, wherein the target protein is selected from among a VEGFR-1, VEGFR-2, VEGFR-3, a epidermal growth factor receptor (EGFR), ErbB-2, ErbB-3, IGF-R1, C-Met, TNF-R1, TNF-R2, BTLA, HVEM, LT-βR, CD20, CD3, CD25, NOTCH, DLL4, G-CSF-R, GM-CSF-R, EPO-R, a cadherin, an integrin, CD52 and CD44, a VEGF-A, VEGF-B, VEGF-C, VEGF-D, PIGF, EGF, HGF, TNF-α, LIGHT, lymphotoxin (LT), IgE, G-CSF, GM-CSF and EPO.

303. The method of any of claims 298-302, comprising assessing the binding of an antibody or portion thereof to the target protein or to a cell.

304. The method of any of claims 298-303, comprising assessing whether the antibody or portion thereof modulates a functional activity of the cell or target protein.

305. The method of claim 304, wherein the functional activity is selected from among cellular proliferation, lymphoma apoptosis, chemotaxis, cancer cell invasion, matrigel, endothelial proliferation, tube formation and signal transduction.

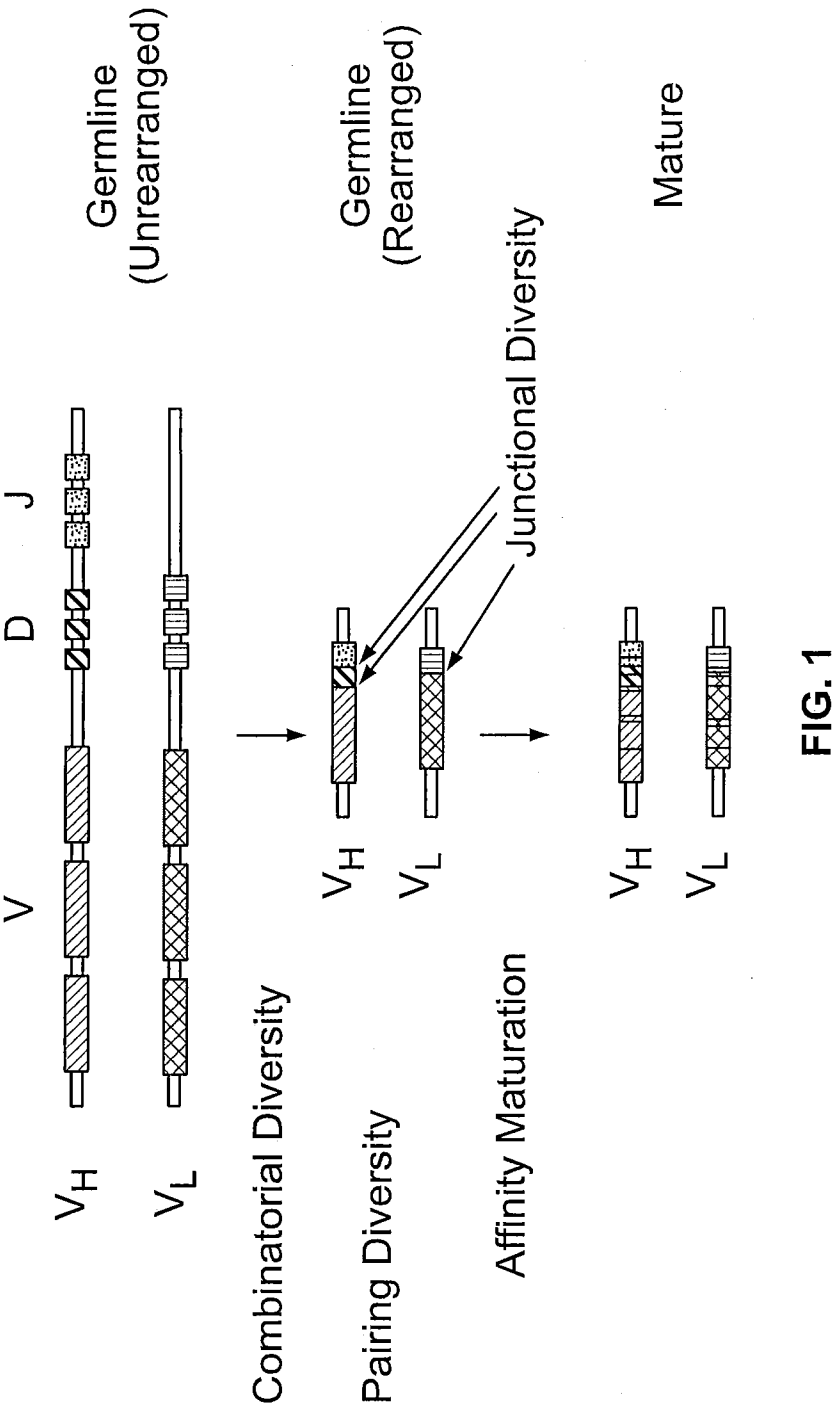

Germline
(Unrearranged)
V
D
J
V_H
V_L
Combinatorial Diversity
Germline
(Rearranged)
Junctional Diversity
Pairing Diversity
V_H
V_L
Affinity Maturation
Mature
V_H
V_L

FIG. 1

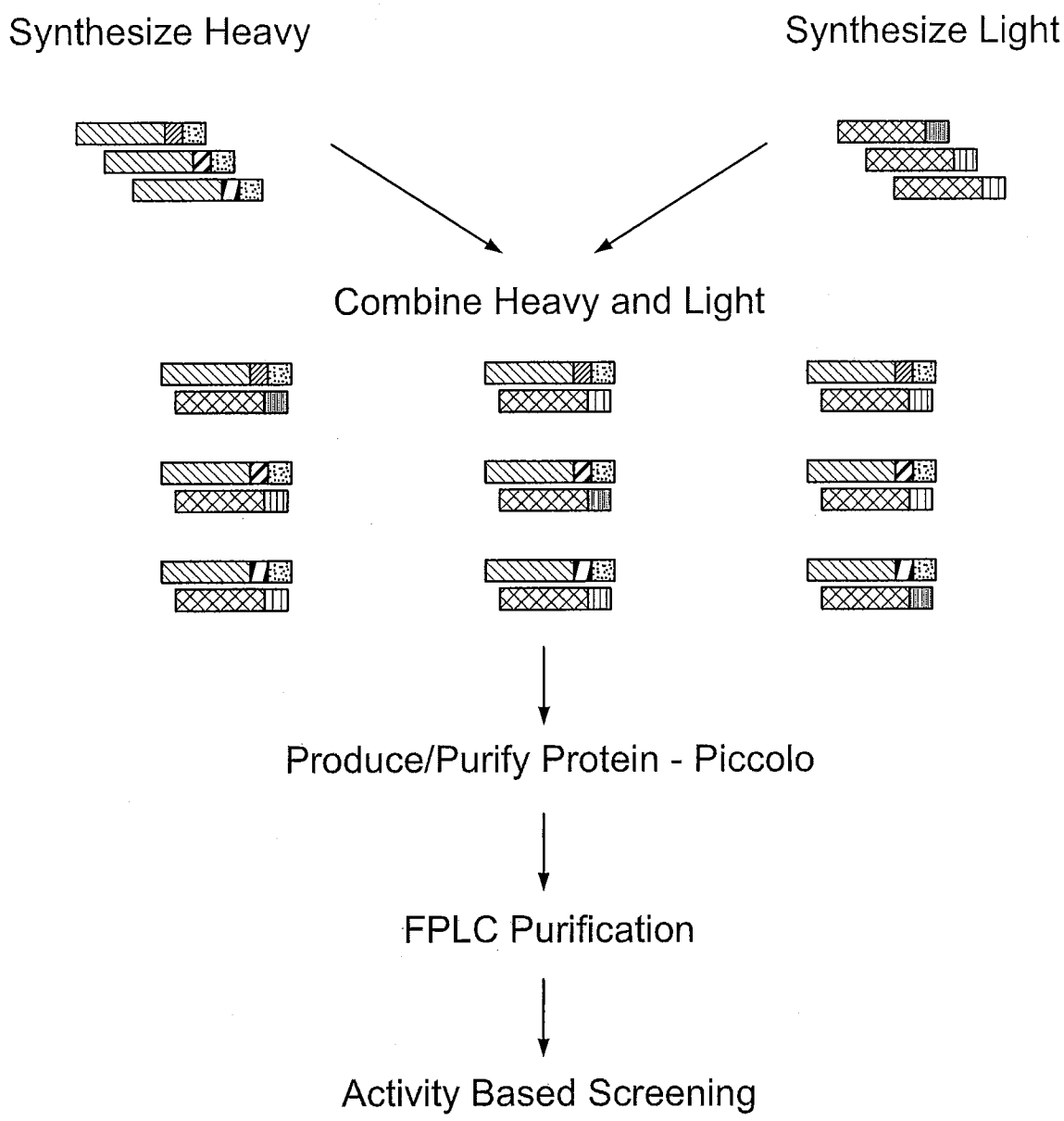

Synthesize Heavy
Synthesize Light
Combine Heavy and Light
Produce/Purify Protein - Piccolo
FPLC Purification
Activity Based Screening

FIG. 2A

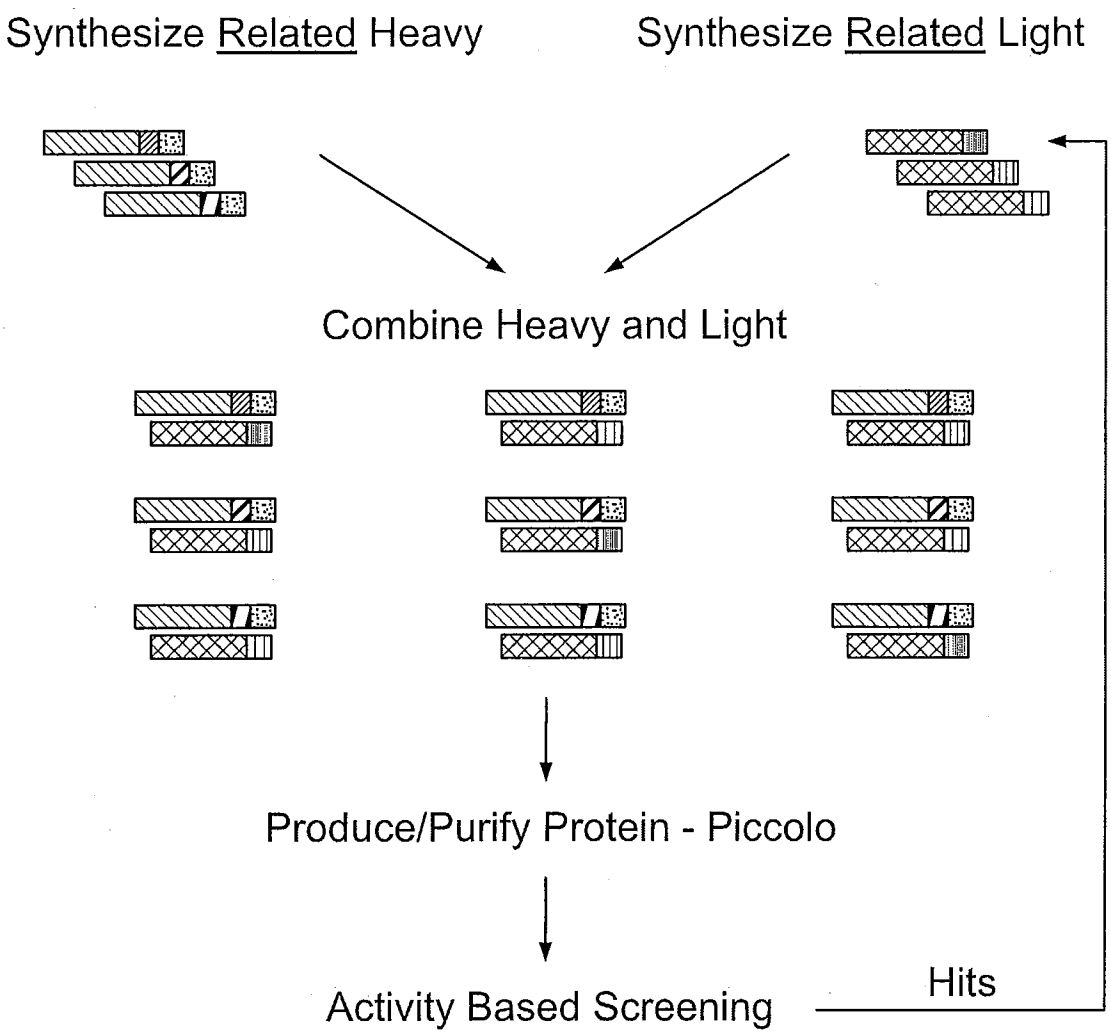

Synthesize Related Heavy
Synthesize Related Light
Combine Heavy and Light
Produce/Purify Protein - Piccolo
Activity Based Screening
Hits

FIG. 2B

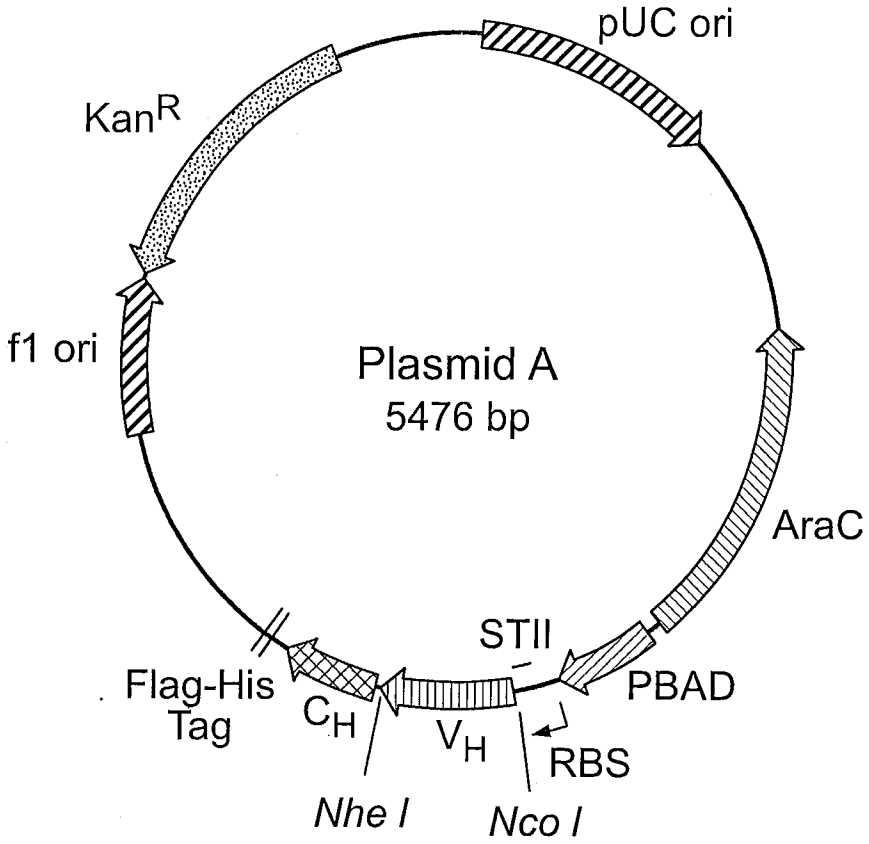
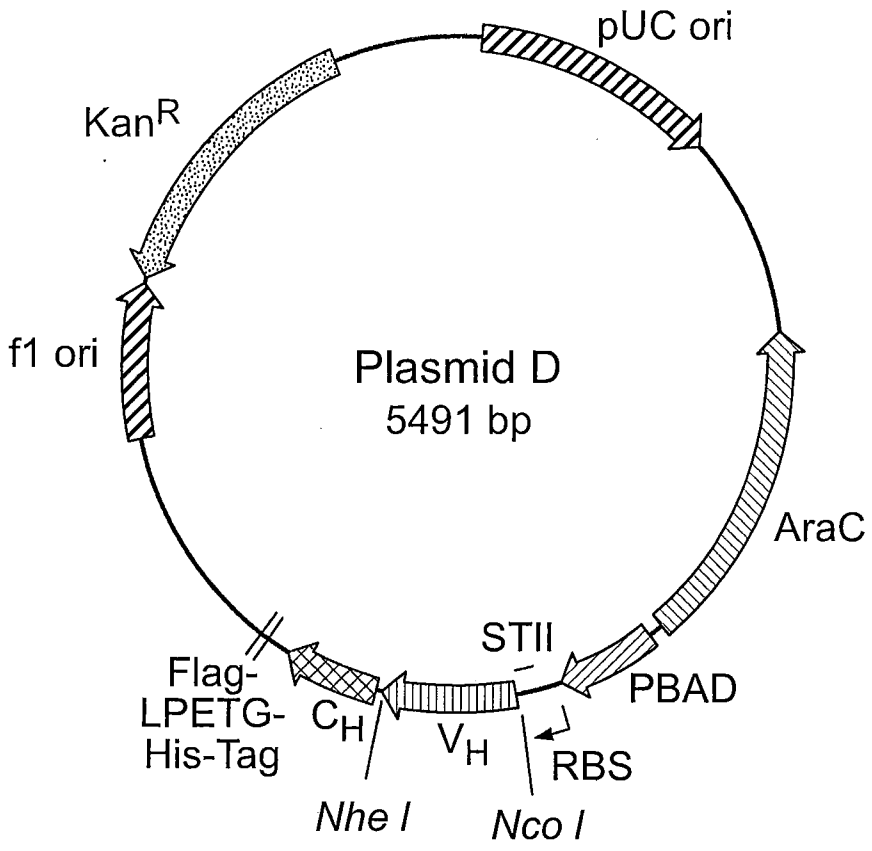

pUC ori
Kan^R
f1 ori
Plasmid A
5476 bp
AraC
STII
PBAD
Flag-His
Tag
C_H
V_H
RBS
Nhe I
Nco I

FIG. 3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Kan^R
f1 ori
Plasmid D
5491 bp
AraC
STII
PBAD
Flag-
LPETG-
His-Tag
C_H
V_H
RBS
Nhe I
Nco I

FIG. 4

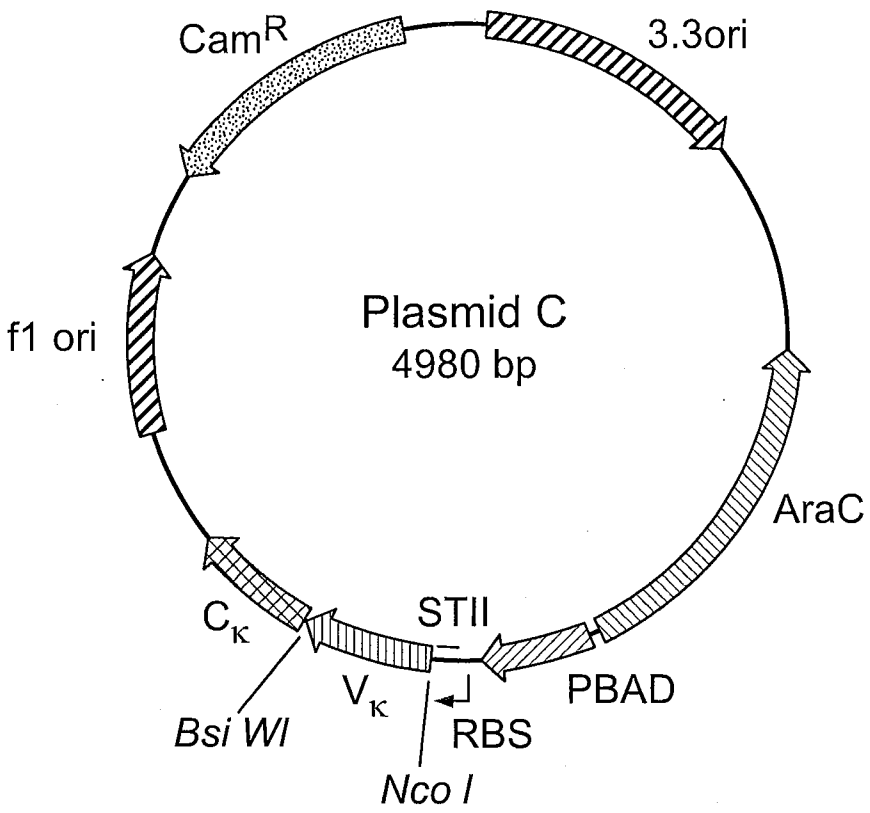

Cam^R
3.3ori
Plasmid C
4980 bp
f1 ori
AraC
C_κ
STII
V_κ
PBAD
RBS
Bsi WI
Nco I

FIG. 5

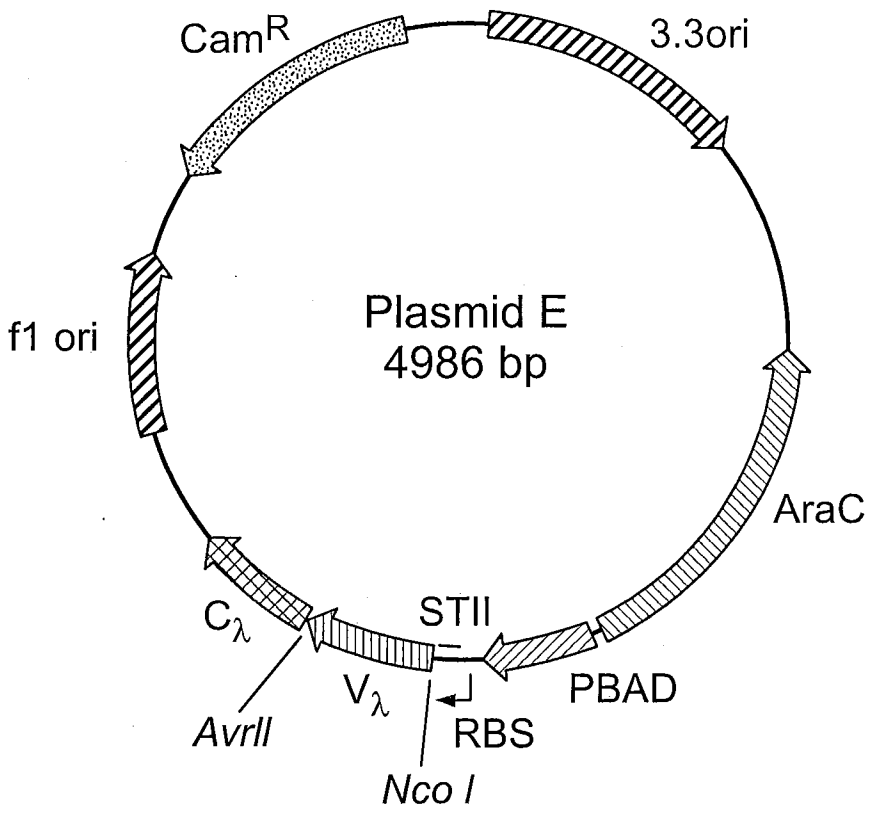

Cam^R
3.3ori
Plasmid E
4986 bp
f1 ori
AraC
STII
Cλ
Vλ
PBAD
AvrII
RBS
Nco I

FIG. 6

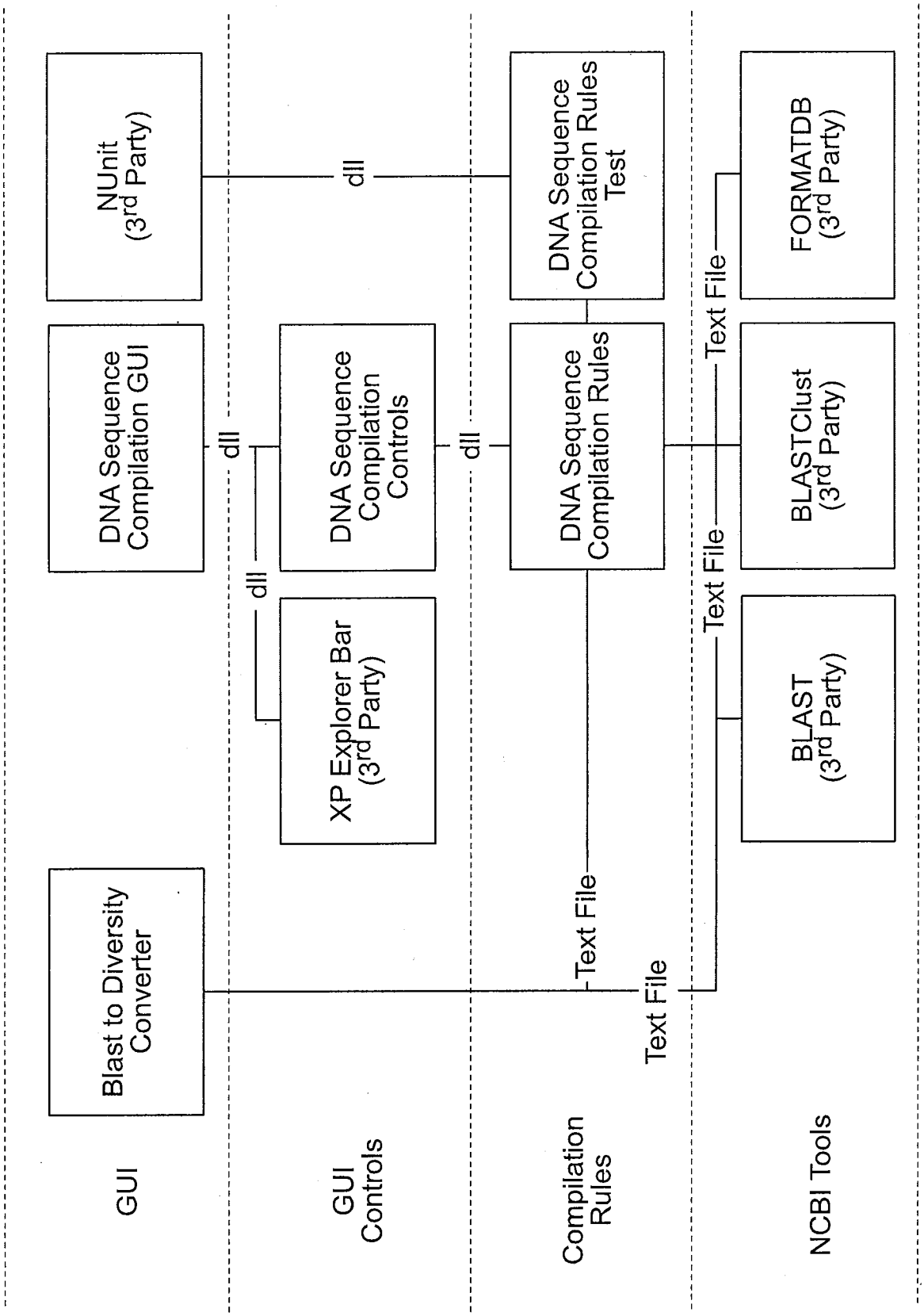

GUI
GUI Controls
Compilation Rules
NCBI Tools
Blast to Diversity Converter
DNA Sequence Compilation GUI
XP Explorer Bar (3rd Party)
DNA Sequence Compilation Controls
DNA Sequence Compilation Rules
DNA Sequence Compilation Rules Test
NUnit (3rd Party)
BLAST (3rd Party)
BLASTClust (3rd Party)
FORMATDB (3rd Party)
dll
dll
dll
dll
Text File
Text File
Text File
Text File

FIG. 7

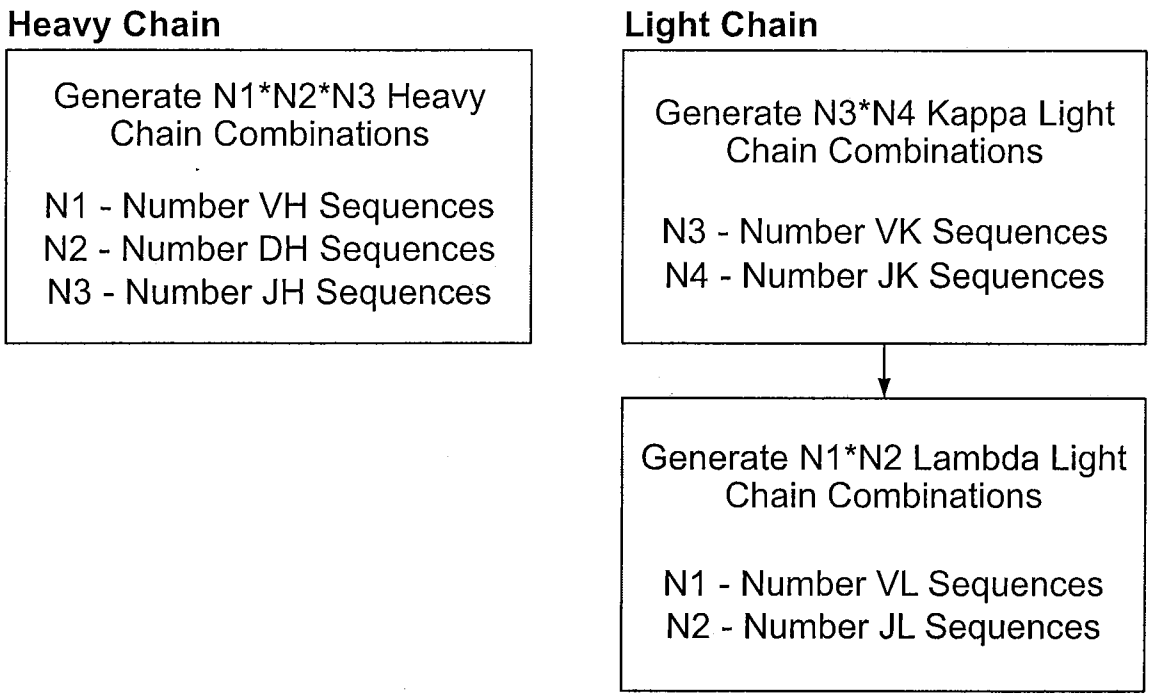

Heavy Chain
Generate N1*N2*N3 Heavy Chain Combinations
N1 - Number VH Sequences
N2 - Number DH Sequences
N3 - Number JH Sequences
Light Chain
Generate N3*N4 Kappa Light Chain Combinations
N3 - Number VK Sequences
N4 - Number JK Sequences
Generate N1*N2 Lambda Light Chain Combinations
N1 - Number VL Sequences
N2 - Number JL Sequences

FIG. 8

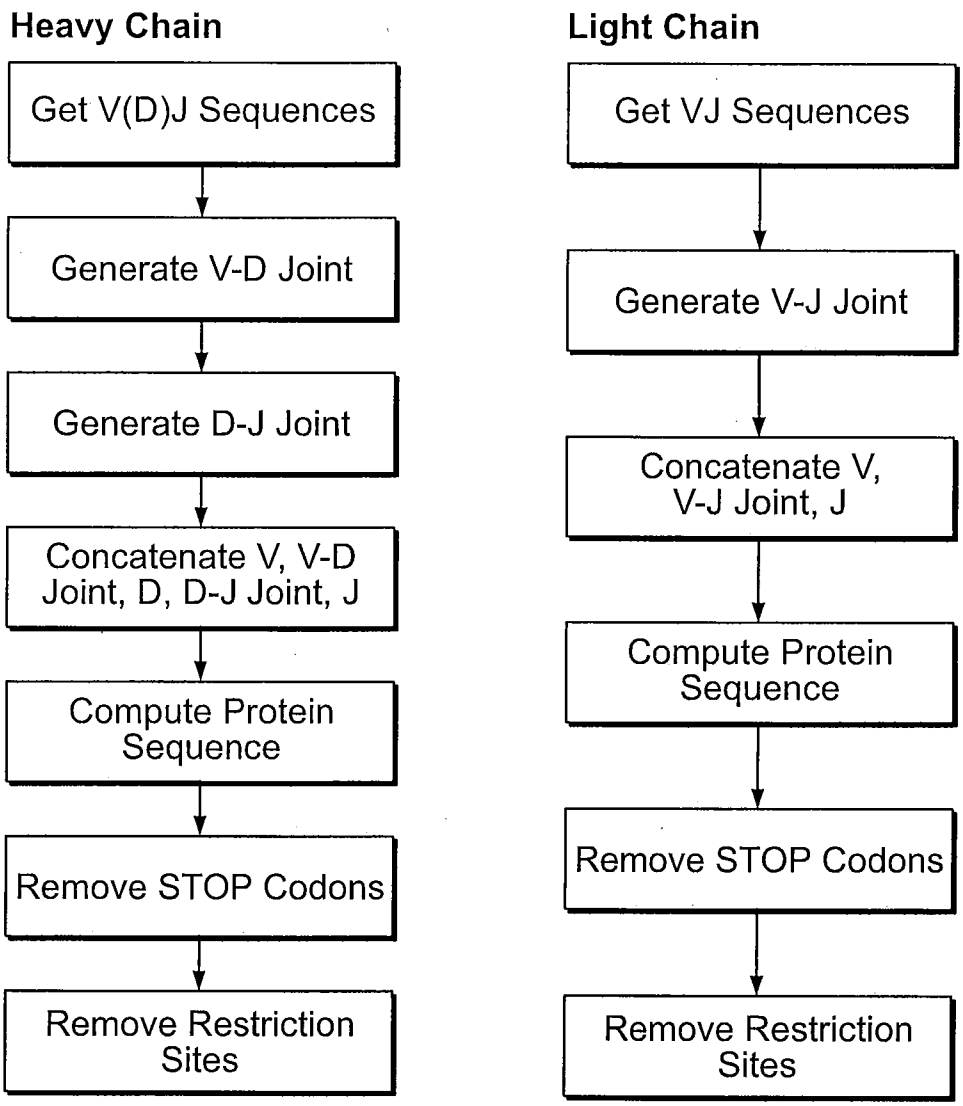

Heavy Chain
Get V(D)J Sequences
Generate V-D Joint
Generate D-J Joint
Concatenate V, V-D Joint, D, D-J Joint, J
Compute Protein Sequence
Remove STOP Codons
Remove Restriction Sites
Light Chain
Get VJ Sequences
Generate V-J Joint
Concatenate V, V-J Joint, J
Compute Protein Sequence
Remove STOP Codons
Remove Restriction Sites

FIG. 9

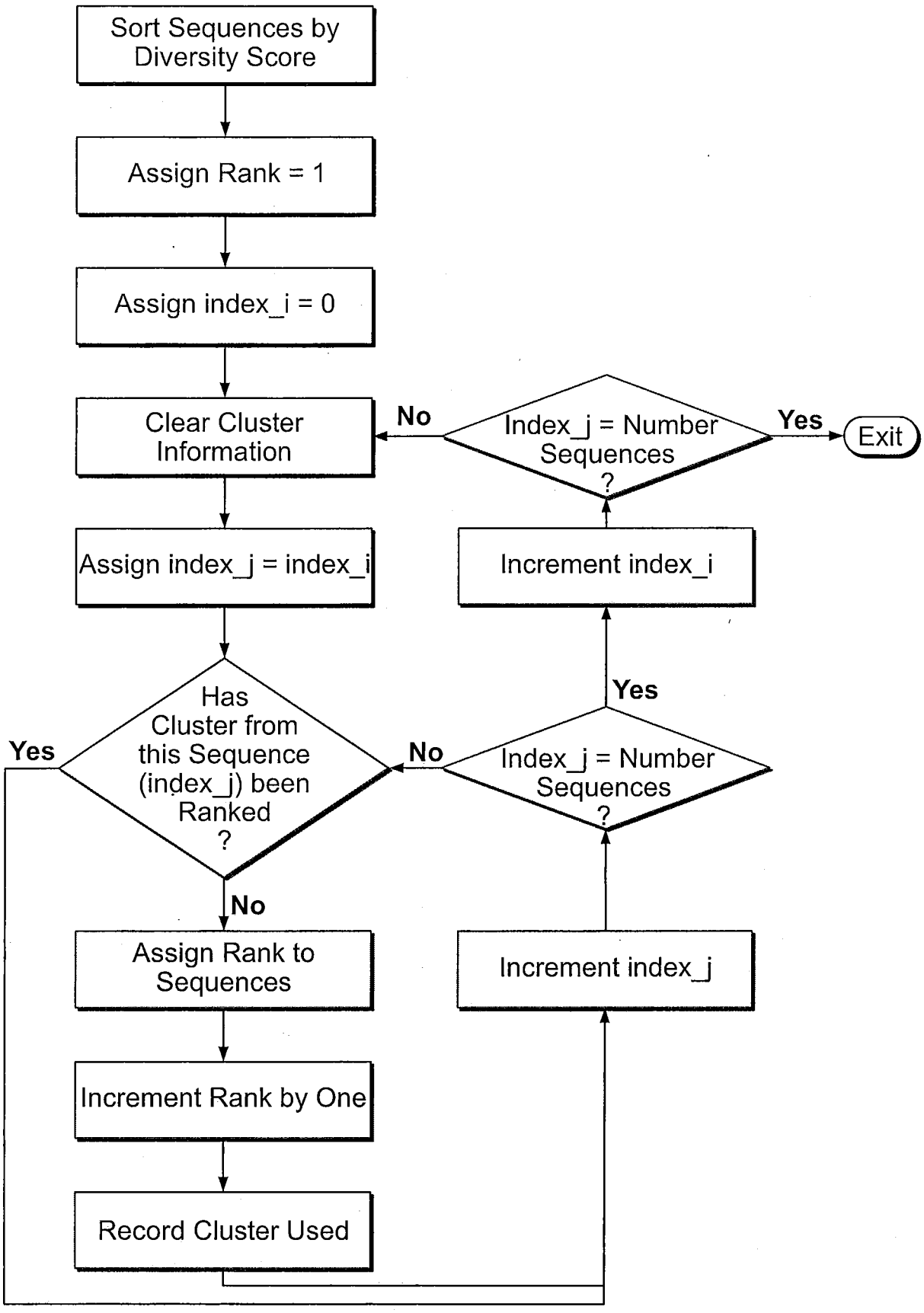

Sort Sequences by Diversity Score
Assign Rank = 1
Assign index_i = 0
Clear Cluster Information
Assign index_j = index_i
Has Cluster from this Sequence (index_j) been Ranked ?
Yes
No
Assign Rank to Sequences
Increment Rank by One
Record Cluster Used
Index_j = Number Sequences ?
No
Yes
Increment index_j
Index_j = Number Sequences ?
Yes
Exit
Increment index_i

FIG. 10

V(D)J SEQUENCES FILE FORMAT

```
//************************************************************
//
// V, D, J Sequences
//
// IMPORTANT: a blank line must be present between two sequences
//
//************************************************************
[VH]
>VH1-18
CAGGTTCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGAAGGTC
TCCTGCAAGGCTTCTGGTTACACCTTTACCAGCTATGGTATCAGCTGGGTGCGACAGGCC
CCTGGACAAGGGCTTGAGTGGATGGGATGGATCAGCGCTTACAATGGTAACACAAACTAT
GCACAGAAGCTCCAGGGCAGAGTCACCATGACCACAGACACATCCACGAGCACAGCCTAC
ATGGAGCTGAGGAGCCTGAGATCTGACGACACGGCCGTGTATTACTGTGCGAGAGA
>VH1-2
CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGAAGGTC
TCCTGCAAGGCTTCTGGATACACCTTCACCGGCTACTATATGCACTGGGTGCGACAGGCC
CCTGGACAAGGGCTTGAGTGGATGGGATGGATCAACCCTAACAGTGGTGGCACAAACTAT
GCACAGAAGTTTCAGGGCAGGGTCACCATGACCAGGGACACGTCCATCAGCACAGCCTAC
ATGGAGCTGAGCAGGCTGAGATCTGACGACACGGCCGTGTATTACTGTGCGAGAGA
//************************************************************
// Heavy Chain D sequences
//************************************************************
[DH]
>IGHD1-1*01
GGTACAACTGGAACGAC
//************************************************************
// Heavy Chain J sequences
//************************************************************
[JH]
>IGHJ1*01
GCT GAA TAC TTC CAG CAC TGG GGC CAG GGC ACC CTG GTC ACC GTC TCC TCA G
//************************************************************
// Light Chain Vk sequences
//************************************************************
[VK]
>A1
GATGTTGTGATGACTCAGTCTCCACTCTCCCTGCCCGTCACCCTTGGACAGCCGGCCTCC
ATCTCCTGCAGGTCTAGTCAAAGCCTCGTATACAGTGATGGAAACACCTACTTGAATTGG
TTTCAGCAGAGGCCAGGCCAATCTCCAAGGCGCCTAATTTATAAGGTTTCTAACTGGGAC
TCTGGGGTCCCAGACAGATTCAGCGGCAGTGGGTCAGGCACTGATTTCACACTGAAAATC
AGCAGGGTGGAGGCTGAGGATGTTGGGGTTTATTACTGCATGCAAGGTACACACTGGCCT
CC
>A10
GAAATTGTGCTGACTCAGTCTCCAGACTTTCAGTCTGTGACTCCAAAGGAGAAAGTCACC
ATCACCTGCCGGGCCAGTCAGAGCATTGGTAGTAGCTTACACTGGTACCAGCAGAAACCA
GATCAGTCTCCAAAGCTCCTCATCAAGTATGCTTCCCAGTCCTTCTCAGGGGTCCCCTCG
AGGTTCAGTGGCAGTGGATCTGGGACAGATTTCACCCTCACCATCAATAGCCTGGAAGCT
GAAGATGCTGCAACGTATTACTGTCATCAGAGTAGTAGTTTACCTCA
//************************************************************
// Light Chain Jk sequences
//************************************************************
[JK]
>IGKJ1*01
G TGG ACG TTC GGC CAA GGG ACC AAG GTG GAA ATC AAA C
//************************************************************
// Light Chain VL sequences
//************************************************************
[VL]
>V1-11
CAGTCTGTGCTGACGCAGCCGCCCTCGGTGTCTGAAGCCCCCAGGCAGAGGGTCACCATC
TCCTGTTCTGGAAGCAGCTCCAACATCGGAAATAATGCTGTAAACTGGTACCAGCAGCTC
CCAGGAAAGGCTCCCAAACTCCTCATCTATTATGATGATCTGCTGCCCTCAGGGGTCTCT
GACCGATTCTCTGGCTCCAAGTCTGGCACCTCAGCCTCCCTGGCCATCAGTGGGCTCCAG
TCTGAGGATGAGGCTGATTATTACTGTGCAGCATGGGATGACAGCCTGAATGGTCC
>V1-13
CAGTCTGTGCTGACGCAGCCGCCCTCAGTGTCTGGGGCCCCAGGGCAGAGGGTCACCATC
TCCTGCACTGGGAGCAGCTCCAACATCGGGGCAGGTTATGATGTACACTGGTACCAGCAG
CTTCCAGGAACAGCCCCCAAACTCCTCATCTATGGTAACAGCAATCGGCCCTCAGGGGTC
CCTGACCGATTCTCTGGCTCCAAGTCTGGCACCTCAGCCTCCCTGGCCATCACTGGGCTC
CAGGCTGAGGATGAGGCTGATTATTACTGCCAGTCCTATGACAGCAGCCTGAGTGGTTC
//************************************************************
// Light Chain JL sequences
//************************************************************
[JL]
>IGLJ1*01
T TAT GTC TTC GGA ACT GGG ACC AAG GTC ACC GTC CTA G
>IGLJ2*01
T GTG GTA TTC GGC GGA GGG ACC AAG CTG ACC GTC CTA G
//************************************************************
// Restriction Sites
//************************************************************
[Restriction Sites]
>Mfe I
CAATTG
```

FIG. 11

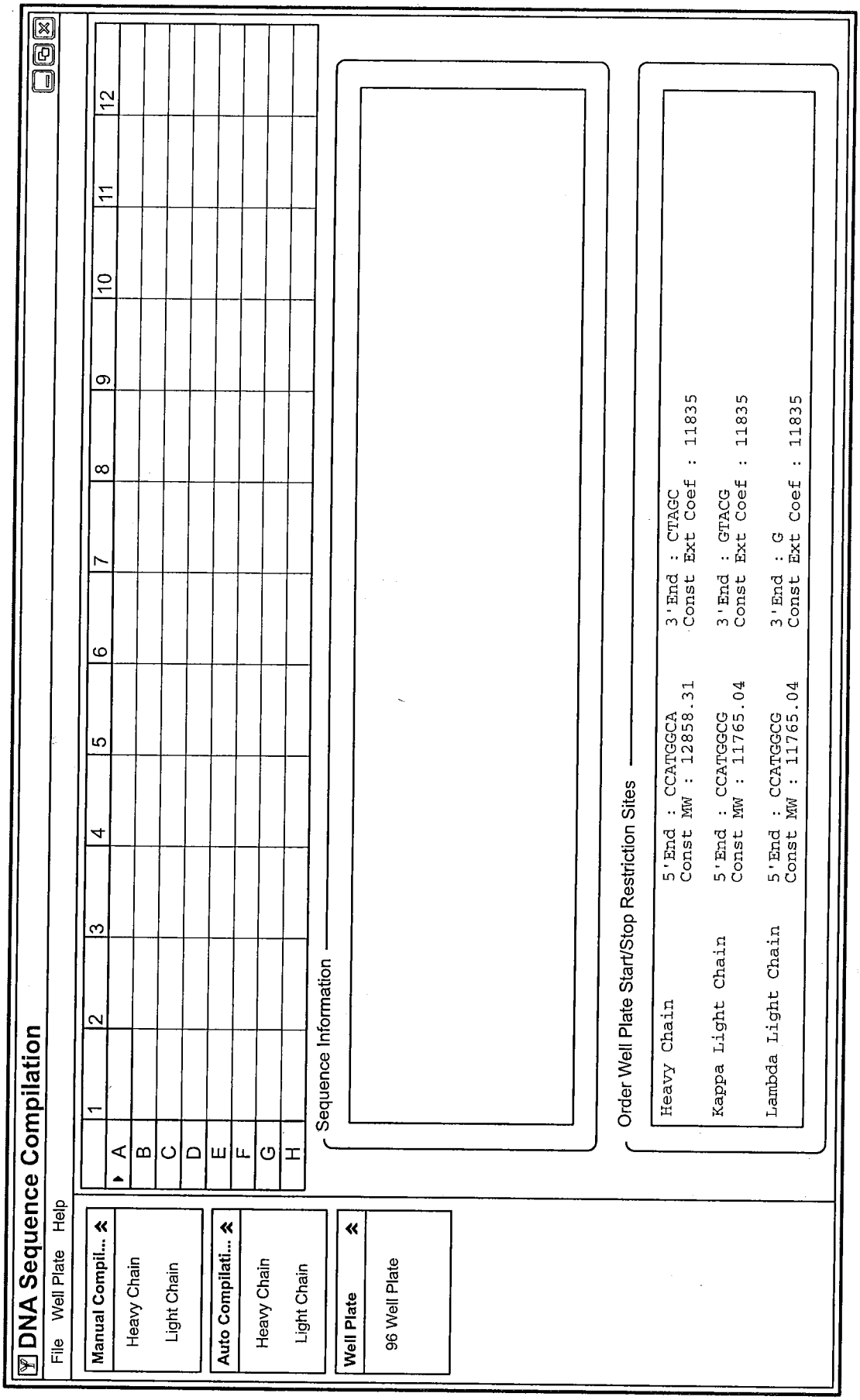

DNA Sequence Compilation
File Well Plate Help
Manual Compil...
Heavy Chain
Light Chain
Auto Compilati...
Heavy Chain
Light Chain
Well Plate
96 Well Plate
1 2 3 4 5 6 7 8 9 10 11 12
A B C D E F G H
Sequence Information
Order Well Plate Start/Stop Restriction Sites
Heavy Chain
5'End : CCATGGCA
Const MW : 12858.31
3'End : CTAGC
Const Ext Coef : 11835
Kappa Light Chain
5'End : CCATGGCG
Const MW : 11765.04
3'End : GTACG
Const Ext Coef : 11835
Lambda Light Chain
5'End : CCATGGCG
Const MW : 11765.04
3'End : G
Const Ext Coef : 11835

FIG. 12

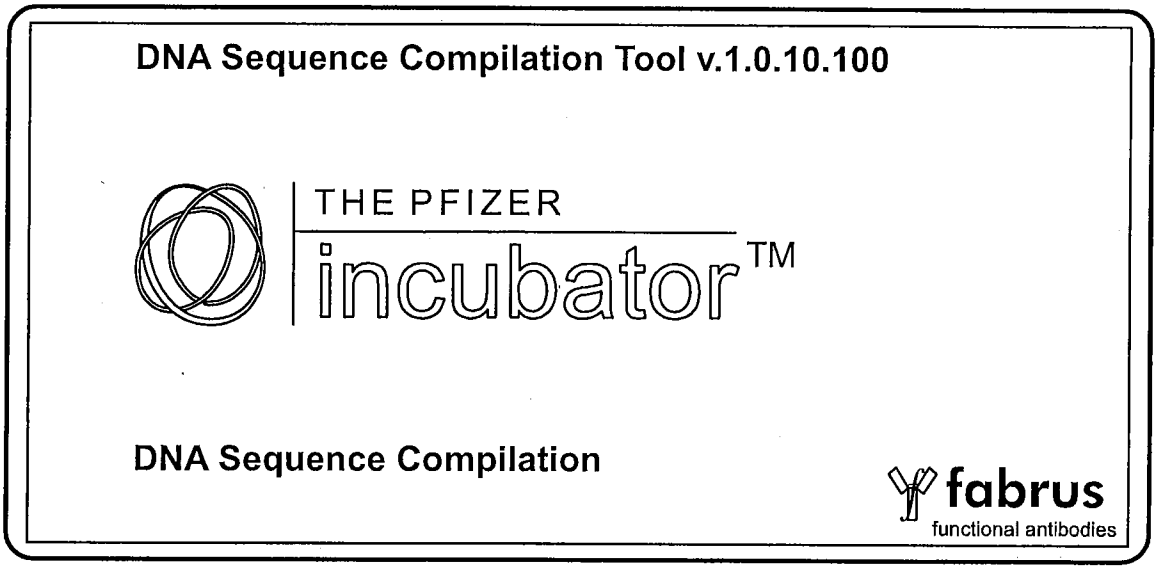

DNA Sequence Compilation Tool v.1.0.10.100
THE PFIZER
incubator™
DNA Sequence Compilation
fabrus
functional antibodies

FIG. 13

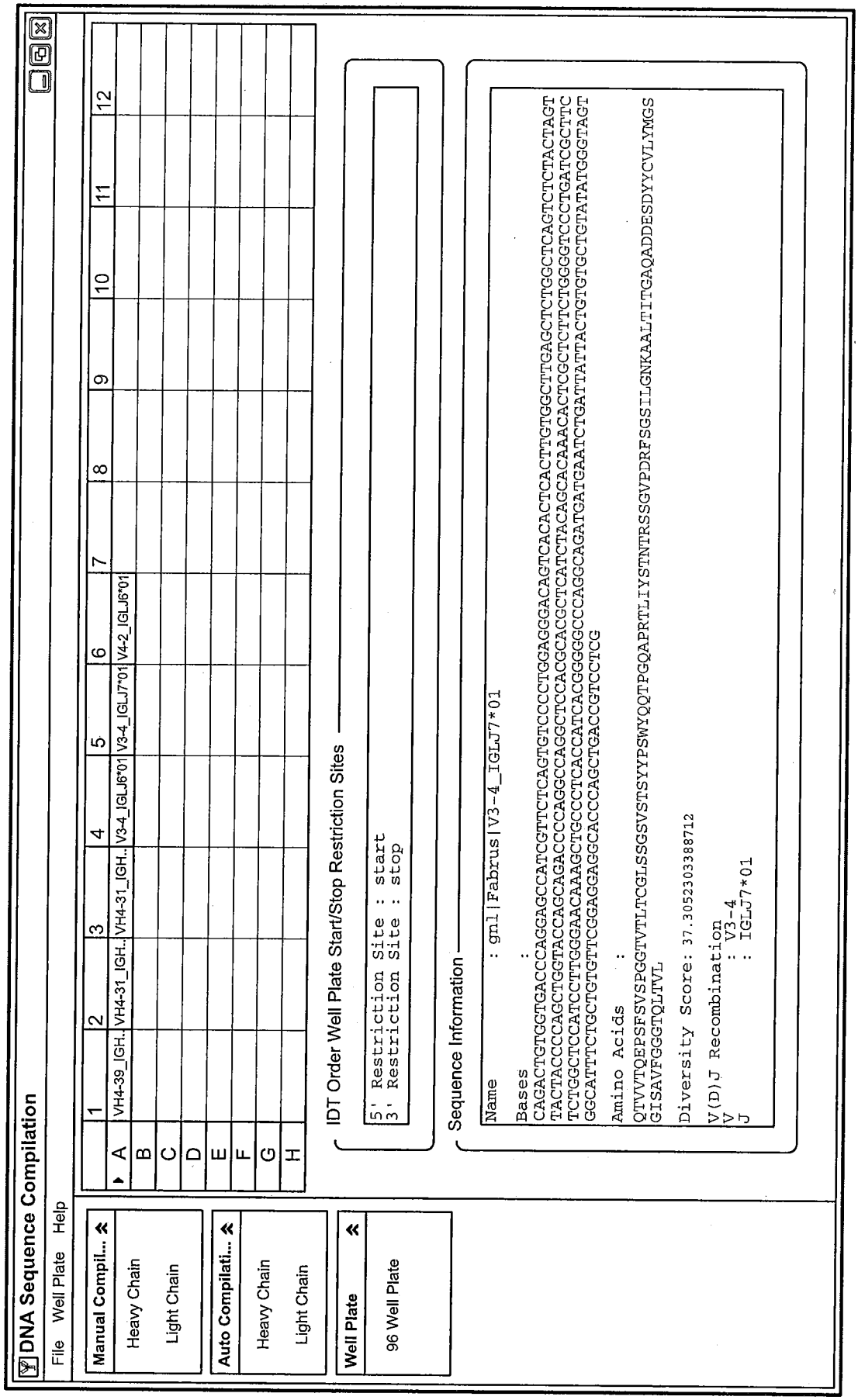

DNA Sequence Compilation
File Well Plate Help
Manual Compil...
Heavy Chain
Light Chain
Auto Compilati...
Heavy Chain
Light Chain
Well Plate
96 Well Plate
1 2 3 4 5 6 7 8 9 10 11 12
A VH4-39_IGH.. VH4-31_IGH.. VH4-31_IGH.. V3-4_IGLJ6*01 V3-4_IGLJ7*01 V4-2_IGLJ6*01
B
C
D
E
F
G
H
IDT Order Well Plate Start/Stop Restriction Sites
5' Restriction Site : start
3' Restriction Site : stop
Sequence Information
Name : gnl|Fabrus|V3-4_IGLJ7*01
Bases :
CAGACTGTGGTGACCCAGGAGCCATCGTTCTCAGTGTCCCCTGGAGGGACAGTCACACTCACTTGTGGCTTGAGCTCTGGCTCAGTCTCTACTAGT
TACTACCCCAGCTGGTACCAGCAGACCCCAGGCCAGGCTCCACGCACGCTCATCTACAGCACAAACACTCGCTCTTCTGGGTCCCTGATCGCTTC
TCTGGCTCCATCCTTGGAACAAAGCTGCCCTCACCATCACGGGGGCCCAGGCAGATGATGAATCTGATTATTACTGTGTGCTGTATATGGGTAGT
GGCATTTCTGCTGTGTTCGGAGGAGGCACCCAGCTGACCGTCCTCG
Amino Acids :
QTVVTQEPSFSVSPGGTVTLTCGLSSGSVSTSYYPSWYQQTPGQAPRTLIYSTNTRSSGVPDRFSGSILGNKAALTITGAQADDESDYYCVLYMGS
GISAVFGGGTQLTVL
Diversity Score: 37.3052303388712
V(D)J Recombination
V : V3-4
J : IGLJ7*01

FIG. 14

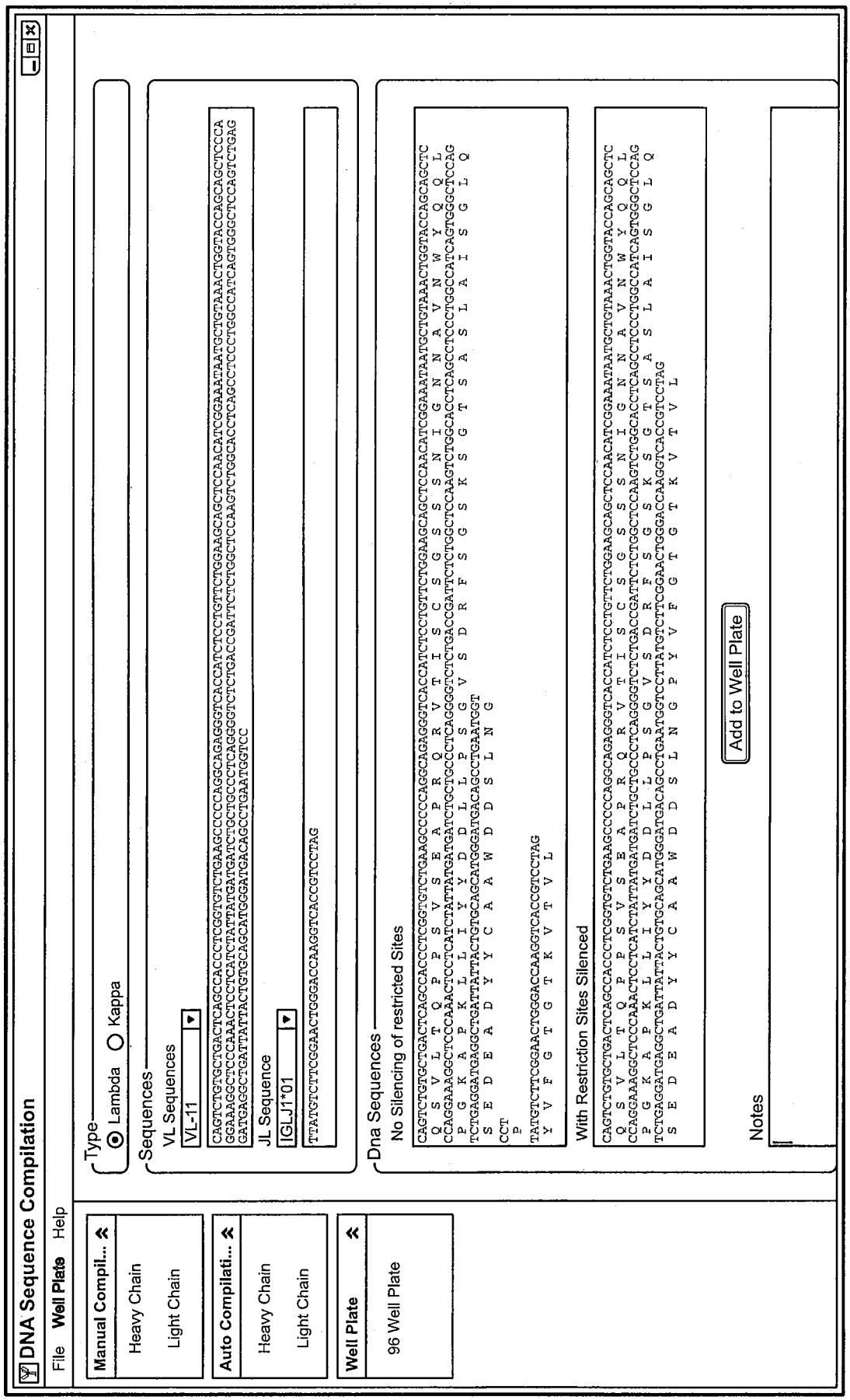

DNA Sequence Compilation
File Well Plate Help
Manual Compil...
Heavy Chain
Light Chain
Auto Compilati...
Heavy Chain
Light Chain
Well Plate
96 Well Plate
Type
Lambda
Kappa
Sequences
VL Sequences
VL-11
JL Sequence
IGLJ1*01
Dna Sequences
No Silencing of restricted Sites
With Restriction Sites Silenced
Add to Well Plate
Notes

FIG. 15

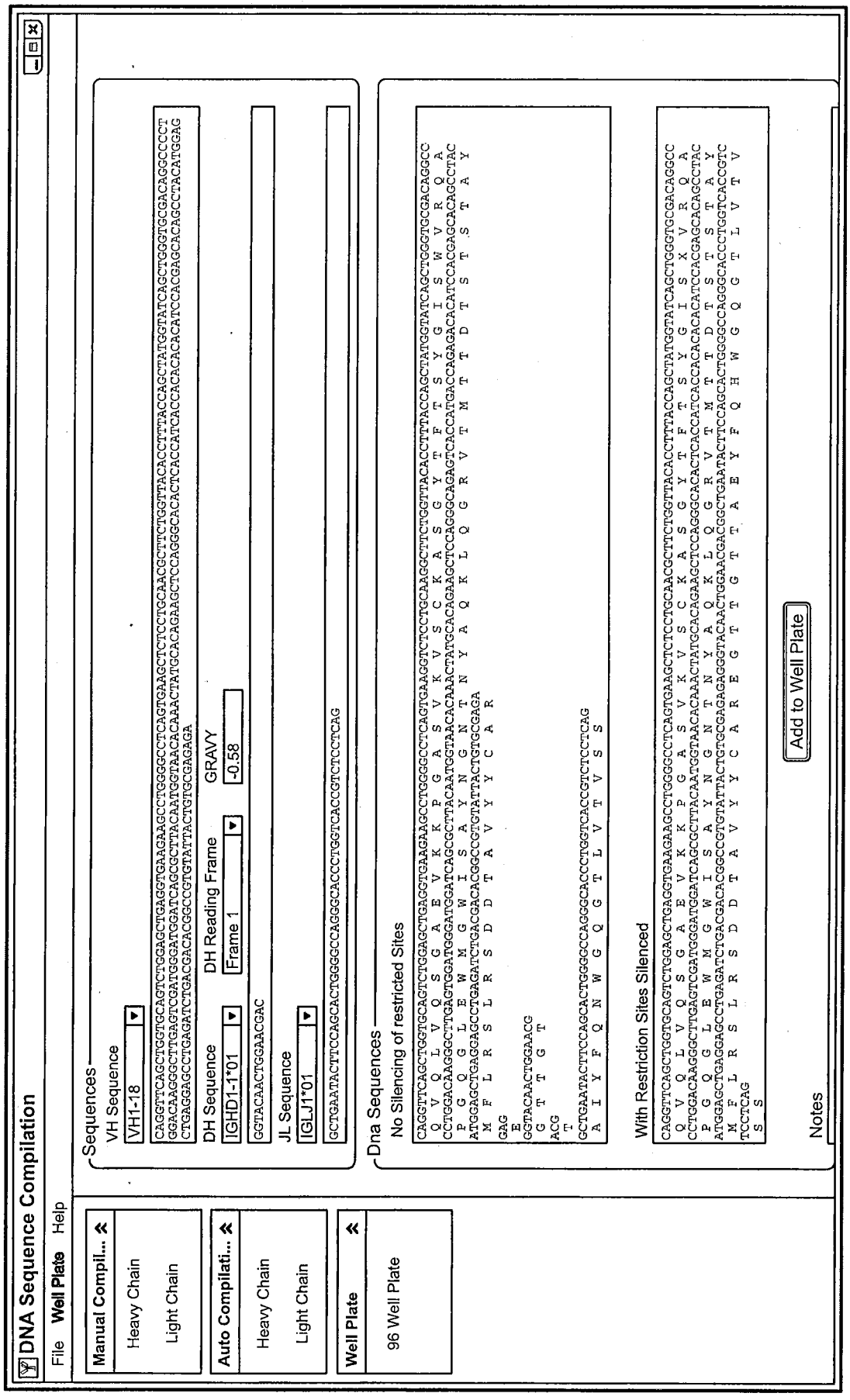
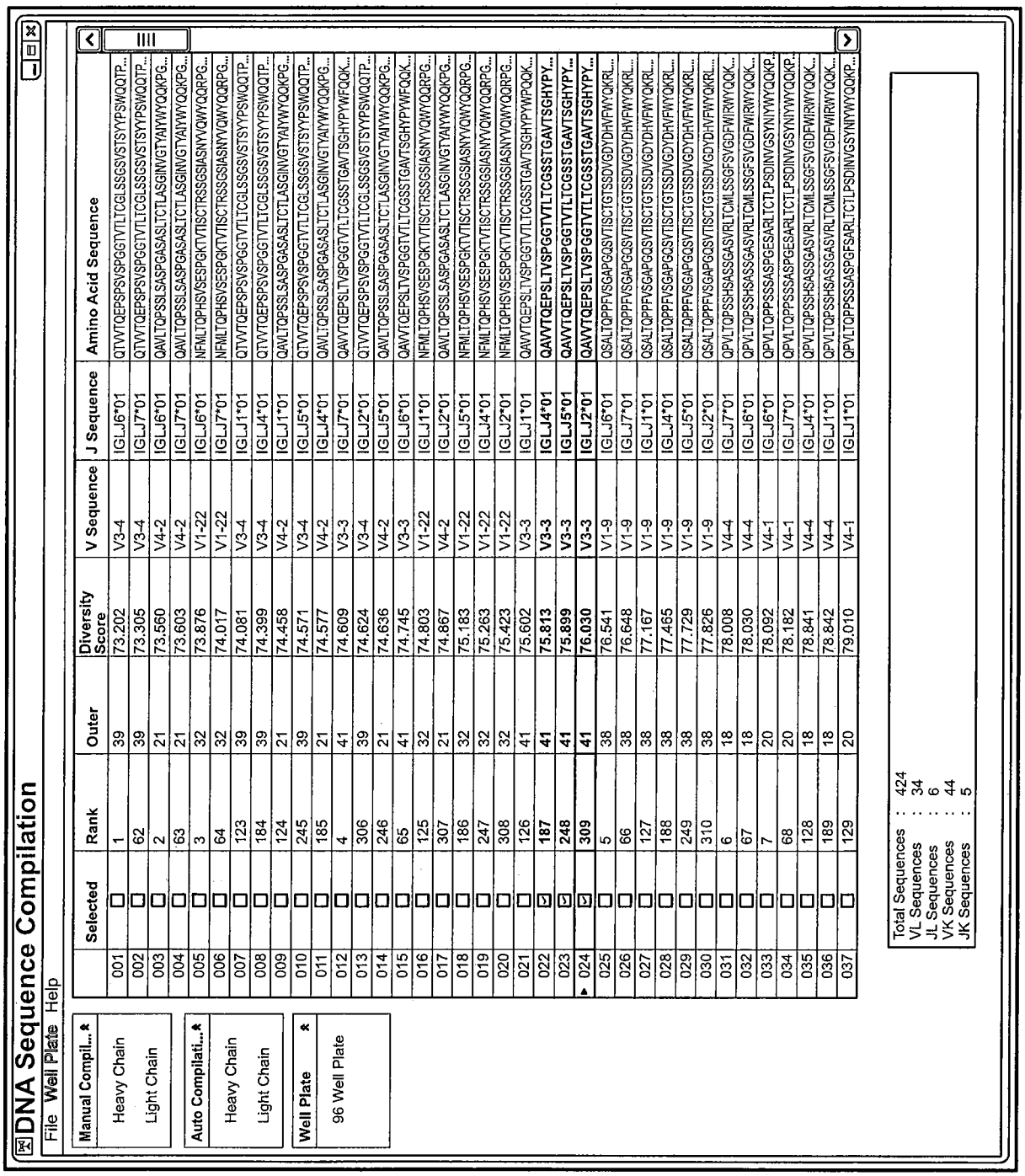

DNA Sequence Compilation
File Well Plate Help
Manual Compil...
Heavy Chain
Light Chain
Auto Compilati...
Heavy Chain
Light Chain
Well Plate
96 Well Plate
Sequences
VH Sequence
VH1-18
CAGGTTCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAACGCTTCTGGTTACACCTTTACCAGCTATGGTATCAGCTGGGTGCGACAGGCCCCT
GGACAAGGGCTTGAGTGGATGGGATCAGCGCTTACAATGGTAACACAAACTATGCACAGAAGCTCCAGGGCACACTCACCATCACCACACACATCCACGAGCACAGCCTACATGGAG
CTGAGGAGCCTGAGATCTGACGACACGGCCGTGTATTACTGTGCGAGAGA
DH Sequence
IGHD1-1*01
DH Reading Frame
Frame 1
GRAVY
-0.58
GGTACAACTGGAACGAC
JL Sequence
IGLJ1*01
GCTGAATACTTCCAGCACTGGGGCCAGGGCACCCTGGTCACCGTCTCCTCAG
Dna Sequences
No Silencing of restricted Sites
CAGGTTCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGGCTTCTGGTTACACCTTTACCAGCTATGGTATCAGCTGGGTGCGACAGGCC
Q V Q L V Q S G A E V K K P G A S V K V S C K A S G Y T F T S Y G I S W V R Q A
CCTGGACAAGGGCTTGAGTGGATGGGATCAGCGCTTACAATGGTAACACAAACTATGCACAGAAGCTCCAGGGCAGAGTCACCATGACCAGAGACACATCCACGAGCACAGCCTAC
P G Q G L E W M G W I S A Y N G N T N Y A Q K L Q G R V T M T T D T S T S T A Y
ATGGAGCTGAGGAGCCTGAGATCTGACGACACGGCCGTGTATTACTGTGCGAGA
M F L R S L R S D D T A V Y Y C A R
GAG
E
GGTACAACTGGAACG
G T T G T
ACG
T
GCTGAATACTTCCAGCACTGGGGCCAGGGCACCCTGGTCACCGTCTCCTCAG
A I Y F Q N W G Q G T L V T V S S
With Restriction Sites Silenced
CAGGTTCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAACGCTTCTGGTTACACCTTTACCAGCTATGGTATCAGCTGGGTGCGACAGGCC
Q V Q L V Q S G A E V K K P G A S V K V S C K A S G Y T F T S Y G I S W V R Q A
CCTGGACAAGGGCTTGAGTGGATGGGATCAGCGCTTACAATGGTAACACAAACTATGCACAGAAGCTCCAGGGCACACTCACCATCACCACACACATCCACGAGCACAGCCTAC
P G Q G L E W M G W I S A Y N G N T N Y A Q K L Q G R V T M T T D T S T S T A Y
ATGGAGCTGAGGAGCCTGAGATCTGACGACACGGCCGTGTATTACTGTGCGAGAGGGTACAACTGGAACGACGGCTGAATACTTCCAGCACTGGGGCCAGGGCACCCTGGTCACCGTC
M F L R S L R S D D T A V Y Y C A R E G T T G T T A E Y F Q H W G Q G T L V T V
TCCTCAG
S S
Add to Well Plate
Notes

FIG. 16



	Selected	Rank	Outer	Diversity Score	V Sequence	J Sequence	Amino Acid Sequence
001	☐	1	39	73.202	V3-4	IGLJ6*01	QTVVTQEPSPSVSPGGTVTLTCGLSSGSVSTSYYPSWQQTP...
002	☐	62	39	73.305	V3-4	IGLJ7*01	QTVVTQEPSPSVSPGGTVTLTCGLSSGSVSTSYYPSWQQTP...
003	☐	2	21	73.560	V4-2	IGLJ6*01	QAVLTQPSSLSASPGASASLTCTLASGINVGTYAIYWYQQKPG...
004	☐	63	21	73.603	V4-2	IGLJ7*01	QAVLTQPSSLSASPGASASLTCTLASGINVGTYAIYWYQQKPG...
005	☐	3	32	73.876	V1-22	IGLJ6*01	NFMLTQPHSVSESPGKTVTISCTRSSGSIASNYVQWYQQRPG...
006	☐	64	32	74.017	V1-22	IGLJ7*01	NFMLTQPHSVSESPGKTVTISCTRSSGSIASNYVQWYQQRPG...
007	☐	123	39	74.081	V3-4	IGLJ1*01	QTVVTQEPSPSVSPGGTVTLTCGLSSGSVSTSYYPSWQQTP...
008	☐	184	39	74.399	V3-4	IGLJ4*01	QTVVTQEPSPSVSPGGTVTLTCGLSSGSVSTSYYPSWQQTP...
009	☐	124	21	74.458	V4-2	IGLJ1*01	QAVLTQPSSLSASPGASASLTCTLASGINVGTYAIYWYQQKPG...
010	☐	245	39	74.571	V3-4	IGLJ5*01	QTVVTQEPSPSVSPGGTVTLTCGLSSGSVSTSYYPSWQQTP...
011	☐	185	21	74.577	V4-2	IGLJ4*01	QAVLTQPSSLSASPGASASLTCTLASGINVGTYAIYWYQQKPG...
012	☐	4	41	74.609	V3-3	IGLJ7*01	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGHYPYWFQQK...
013	☐	306	39	74.624	V3-4	IGLJ2*01	QTVVTQEPSPSVSPGGTVTLTCGLSSGSVSTSYYPSWQQTP...
014	☐	246	21	74.636	V4-2	IGLJ5*01	QAVLTQPSSLSASPGASASLTCTLASGINVGTYAIYWYQQKPG...
015	☐	65	41	74.745	V3-3	IGLJ6*01	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGHYPYWFQQK...
016	☐	125	32	74.803	V1-22	IGLJ1*01	NFMLTQPHSVSESPGKTVTISCTRSSGSIASNYVQWYQQRPG...
017	☐	307	21	74.867	V4-2	IGLJ2*01	QAVLTQPSSLSASPGASASLTCTLASGINVGTYAIYWYQQKPG...
018	☐	186	32	75.183	V1-22	IGLJ5*01	NFMLTQPHSVSESPGKTVTISCTRSSGSIASNYVQWYQQRPG...
019	☐	247	32	75.263	V1-22	IGLJ4*01	NFMLTQPHSVSESPGKTVTISCTRSSGSIASNYVQWYQQRPG...
020	☐	308	32	75.423	V1-22	IGLJ2*01	NFMLTQPHSVSESPGKTVTISCTRSSGSIASNYVQWYQQRPG...
021	☐	126	41	75.602	V3-3	IGLJ1*01	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGHYPYWPQQK...
022	☑	**187**	**41**	**75.813**	**V3-3**	**IGLJ4*01**	**QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGHYPY...**
023	☑	**248**	**41**	**75.899**	**V3-3**	**IGLJ5*01**	**QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGHYPY...**
▸ 024	☑	**309**	**41**	**76.030**	**V3-3**	**IGLJ2*01**	**QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGHYPY...**
025	☐	5	38	76.541	V1-9	IGLJ6*01	QSALTQPPFVSGAPGQSVTISCTGTSSDVGDYDHVFWYQKRL...
026	☐	66	38	76.648	V1-9	IGLJ7*01	QSALTQPPFVSGAPGQSVTISCTGTSSDVGDYDHVFWYQKRL...
027	☐	127	38	77.167	V1-9	IGLJ1*01	QSALTQPPFVSGAPGQSVTISCTGTSSDVGDYDHVFWYQKRL...
028	☐	188	38	77.465	V1-9	IGLJ4*01	QSALTQPPFVSGAPGQSVTISCTGTSSDVGDYDHVFWYQKRL...
029	☐	249	38	77.729	V1-9	IGLJ5*01	QSALTQPPFVSGAPGQSVTISCTGTSSDVGDYDHVFWYQKRL...
030	☐	310	38	77.826	V1-9	IGLJ2*01	QSALTQPPFVSGAPGQSVTISCTGTSSDVGDYDHVFWYQKRL...
031	☐	6	18	78.008	V4-4	IGLJ7*01	QPVLTQPSSHSASSGASVRLTCMLSSGFSVGDFWIRWYQQK...
032	☐	67	18	78.030	V4-4	IGLJ6*01	QPVLTQPSSHSASSGASVRLTCMLSSGFSVGDFWIRWYQQK...
033	☐	7	20	78.092	V4-1	IGLJ6*01	QPVLTQPPSSASPGESARLTCTLPSDINVGSYNIYWYQQKP...
034	☐	68	20	78.182	V4-1	IGLJ7*01	QPVLTQPPSSASPGESARLTCTLPSDINVGSYNIYWYQQKP...
035	☐	128	18	78.841	V4-4	IGLJ4*01	QPVLTQPSSHSASSGASVRLTCMLSSGFSVGDFWIRWYQQK...
036	☐	189	18	78.842	V4-4	IGLJ1*01	QPVLTQPSSHSASSGASVRLTCMLSSGFSVGDFWIRWYQQK...
037	☐	129	20	79.010	V4-1	IGLJ1*01	QPVLTQPPSSASPGFSARLTCTLPSDINVGSYNIYWYQQKP...

FIG. 17

BLAST [gnl|Fabrus|V4-2_IGLJ2*01 Protein]

	Selected	Rank	Cluster	BLAST Bit Score	V Sequence	J Sequence	Amino Acid Sequence
▸ 001	☑	1	39	71.2	V3-4	IGLJ6*01	QTVVTQEPSFSVSPGGTVTLCGLSSGSVSTSYYPSWYQQTPGQA...
002	☐	62	39	73.9	V3-4	IGLJ7*01	QTVVTQEPSFSVSPGGTVTLCGLSSGSVSTSYYPSWYQQTPGQA...
003	☐	2	21	180	V4-2	IGLJ6*01	QAVLTQPSSLSASPGASASLTCTLRSGINVGTYRIYWYQQKPGSPP...
004	☐	63	21	182	V4-2	IGLJ7*01	QAVLTQPSSLSASPGASASLTCTLRSGINVGTYRIYWYQQKPGSPP...
005	☐	3	32	77	V1-22	IGLJ6*01	NFMLTQPHSVSESPGKTVTISCTRSSGSIASNYVQWYQQRPGSSPT...
006	☐	64	32	79.7	V1-22	IGLJ7*01	NFMLTQPHSVSESPGKTVTISCTRSSGSIASNYVQWYQQRPGSSPT...
007	☐	123	39	71.2	V3-4	IGLJ1*01	QTVVTQEPSFSVSPGGTVTLTCGLSSGSVSTSYYPSWYQQTPGQA...
008	☐	184	39	72.4	V3-4	IGLJ4*01	QTVVTQEPSFSVSPGGTVTLTCGLSSGSVSTSYYPSWYQQTPGQA...
009	☐	124	21	180	V4-2	IGLJ1*01	QAVLTQPSSLSASPGASASLTCTLRSGINVGTYRIYWYQQKPGSPP...
010	☐	245	39	70.9	V3-4	IGLJ5*01	QTVVTQEPSFSVSPGGTVTLTCGLSSGSVSTSYYPSWYQQTPGQA...
011	☐	185	21	181	V4-2	IGLJ4*01	QAVLTQPSSLSASPGASASLTCTLRSGINVGTYRIYWYQQKPGSPP...
012	☐	4	41	73.2	V3-3	IGLJ7*01	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGHYPYWFQQKPGQA...
013	☐	306	39	77	V3-4	IGLJ2*01	QTVVTQEPSFSVSPGGTVTLTCGLSSGSVSTSYYPSWYQQTPGQA...
014	☐	246	21	180	V4-2	IGLJ5*01	QAVLTQPSSLSASPGASASLTCTLRSGINVGTYRIYWYQQKPGSPP...
015	☐	65	41	70.5	V3-3	IGLJ6*01	QAVLTQPSSLASAPGASASLTCTLRSGINVGTYRIYWYQQKPGSPP...
016	☐	125	32	77	V1-22	IGLJ1*01	NFMLTQPHSVSESPGKTVISCTRSSGSIASNYVQWYQQRPGSSPT...
017	☐	307	21	186	V4-2	IGLJ2*01	QAVLTQPSSLSASPGASASLTCTLRSGINVGTYRIYWYQQKPGSPP...
018	☐	186	32	76.6	V1-22	IGLJ5*01	NFMLTQPHSVSESPGKTVTISCTRSSGSIASNYVQWYQQRPGSSPT...
019	☐	247	32	77.8	V1-22	IGLJ4*01	NFMLTQPHSVSESPGKTVTISCTRSSGSIASNYVQWYQQRPGSSPT...
020	☐	308	32	83.2	V1-22	IGLJ2*01	NFMLTQPHSVSESPGKTVTISCTRSSGSIASNYVQWYQQRPGSSPT...
021	☐	126	41	70.5	V3-3	IGLJ1*01	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGHYPWFQQKPGQA...
022	☐	187	41	71.6	V3-3	IGLJ4*01	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGHYPWFQQKPGQA...
023	☐	248	41	70.1	V3-3	IGLJ5*01	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGHYPWFQQKPGQA...
024	☐	309	41	76.6	V3-3	IGLJ2*01	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGHYPWFQQKPGQA...
025	☐	5	38	55.8	V1-9	IGLJ6*01	QSALTQPPFVSGAPGQSVTISCTGTSSDVGDYDHVFWYQKRLSTTS...
026	☐	66	38	57.8	V1-9	IGLJ7*01	QSALTQPPFVSGAPGQSVTISCTGTSSDVGDYDHVFWYQKRLSTTS...
027	☐	127	38	55.1	V1-9	IGLJ1*01	QSALTQPPFVSGAPGQSVTISCTGTSSDVGDYDHVFWYQKRLSTTS...
028	☐	188	38	56.2	V1-9	IGLJ4*01	QSALTQPPFVSGAPGQSVTISCTGTSSDVGDYDHVFWYQKRLSTTS...
029	☐	249	38	55.5	V1-9	IGLJ5*01	QSALTQPPFVSGAPGQSVTISCTGTSSDVGDYDHVFWYQKRLSTTS...
030	☐	310	38	60.8	V1-9	IGLJ2*01	QSALTQPPFVSGAPGQSVTISCTGTSSDVGDYDHVFWYQKRLSTTS...
031	☐	6	18	140	V4-4	IGLJ7*01	QPVLTQPSSHSASSGASVRLTCMLSSGFSVGDFWIRWYQQKPGNP...
032	☐	67	18	139	V4-4	IGLJ6*01	QPVLTQPSSHSASSGASVRLTCMLSSGFSVGDFWIRWYQQKPGNP...
033	☐	7	20	157	V4-1	IGLJ6*01	QPVLTQPPSSSASPGESARLTCTLPSDINVGSYNIYWYQQKPGSPP...
034	☐	68	20	159	V4-1	IGLJ7*01	QPVLTQPPSSSASPGESARLTCTLPSDINVGSYNIYWYQQKPGSPP...
035	☐	128	18	139	V4-4	IGLJ4*01	QPVLTQPSSHSASSGASVRLTCMLSSGFSVGDFWIRWYQQKPGNP...
036	☐	189	18	137	V4-4	IGLJ1*01	QPVLTQPSSHSASSGASVRLTCMLSSGFSVGDFWIRWYQQKPGNP...

FIG. 18

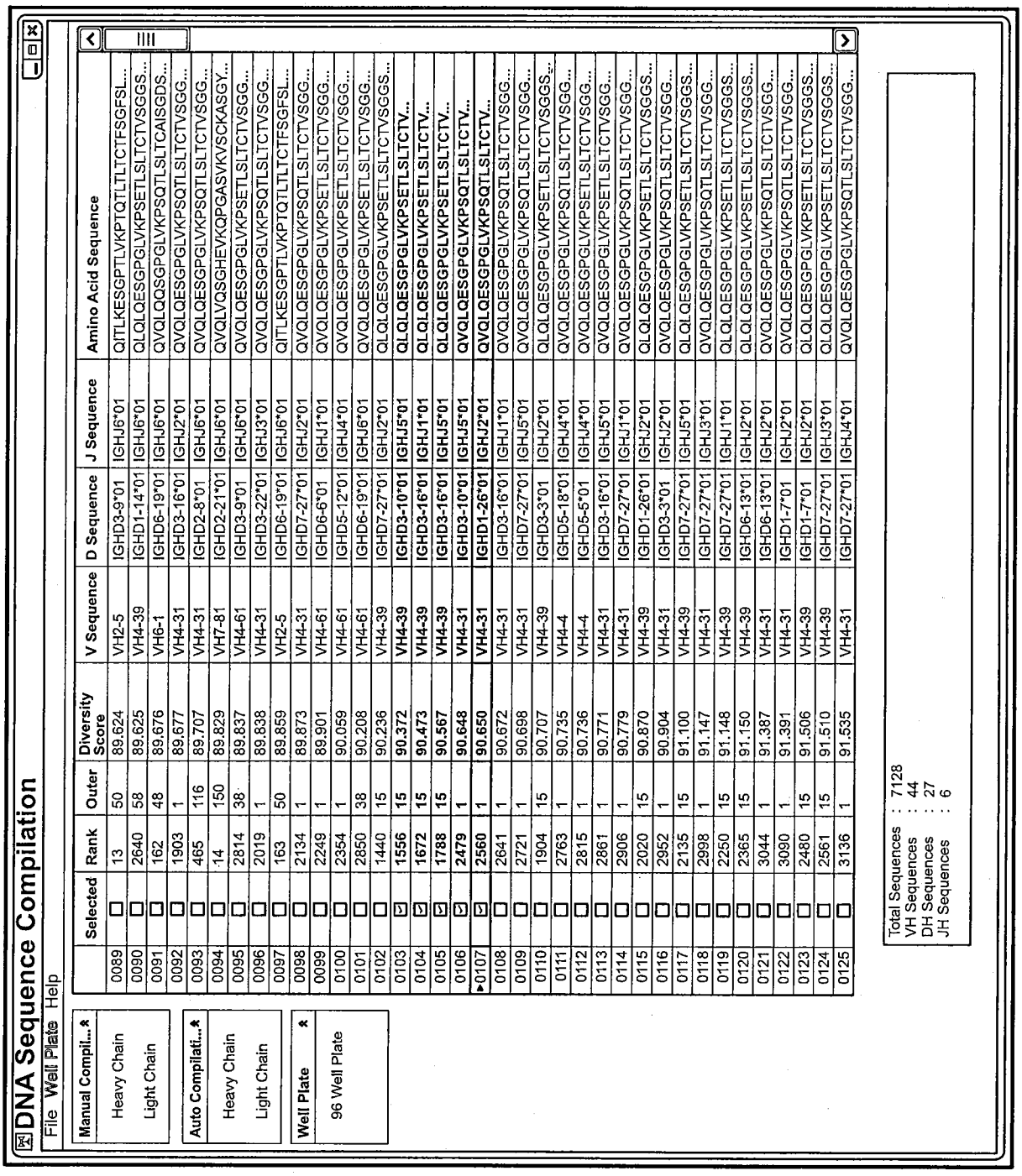

DNA Sequence Compilation
File Well Plate Help
Manual Compil...
Heavy Chain
Light Chain
Auto Compilati...
Heavy Chain
Light Chain
Well Plate
96 Well Plate
Selected
Rank
Outer
Diversity Score
V Sequence
D Sequence
J Sequence
Amino Acid Sequence
0089 13 50 89.624 VH2-5 IGHD3-9*01 IGHJ6*01 QITLKESGPTLVKPTQTLTLTCTFSGFSL...
0090 2640 58 89.625 VH4-39 IGHD1-14*01 IGHJ6*01 QLQLQESGPGLVKPSETLSLTCTVSGGS...
0091 162 48 89.676 VH6-1 IGHD6-19*01 IGHJ6*01 QVQLQQSGPGLVKPSQTLSLTCAISGDS...
0092 1903 1 89.677 VH4-31 IGHD3-16*01 IGHJ2*01 QVQLQESGPGLVKPSQTLSLTCTVSGG...
0093 465 116 89.707 VH4-31 IGHD2-8*01 IGHJ6*01 QVQLQESGPGLVKPSQTLSLTCTVSGG...
0094 14 150 89.829 VH7-81 IGHD2-21*01 IGHJ6*01 QVQLVQSGHEVKQPGASVKVSCKASGY...
0095 2814 38 89.837 VH4-61 IGHD3-9*01 IGHJ6*01 QVQLQESGPGLVKPSETLSLTCTVSGG...
0096 2019 1 89.838 VH4-31 IGHD3-22*01 IGHJ3*01 QVQLQESGPGLVKPSQTLSLTCTVSGG...
0097 163 50 89.859 VH2-5 IGHD6-19*01 IGHJ6*01 QITLKESGPTLVKPTQTLTLTCTFSGFSL...
0098 2134 1 89.873 VH4-31 IGHD7-27*01 IGHJ2*01 QVQLQESGPGLVKPSQTLSLTCTVSGG...
0099 2249 1 89.901 VH4-61 IGHD6-6*01 IGHJ1*01 QVQLQESGPGLVKPSETLSLTCTVSGG...
0100 2354 1 90.059 VH4-61 IGHD5-12*01 IGHJ4*01 QVQLQESGPGLVKPSETLSLTCTVSGG...
0101 2850 38 90.208 VH4-61 IGHD6-19*01 IGHJ6*01 QVQLQESGPGLVKPSETLSLTCTVSGG...
0102 1440 15 90.236 VH4-39 IGHD7-27*01 IGHJ2*01 QLQLQESGPGLVKPSETLSLTCTVSGGS...
0103 1556 15 90.372 VH4-39 IGHD3-10*01 IGHJ5*01 QLQLQESGPGLVKPSETLSLTCTV...
0104 1672 15 90.473 VH4-39 IGHD3-16*01 IGHJ1*01 QLQLQESGPGLVKPSETLSLTCTV...
0105 1788 15 90.567 VH4-39 IGHD3-16*01 IGHJ5*01 QLQLQESGPGLVKPSETLSLTCTV...
0106 2479 1 90.648 VH4-31 IGHD3-10*01 IGHJ5*01 QVQLQESGPGLVKPSQTLSLTCTV...
0107 2560 1 90.650 VH4-31 IGHD1-26*01 IGHJ2*01 QVQLQESGPGLVKPSQTLSLTCTV...
0108 2641 1 90.672 VH4-31 IGHD3-16*01 IGHJ1*01 QVQLQESGPGLVKPSQTLSLTCTVSGG...
0109 2721 1 90.698 VH4-31 IGHD7-27*01 IGHJ5*01 QVQLQESGPGLVKPSQTLSLTCTVSGG...
0110 1904 15 90.707 VH4-39 IGHD3-3*01 IGHJ2*01 QLQLQESGPGLVKPSETLSLTCTVSGGS...
0111 2763 1 90.735 VH4-4 IGHD5-18*01 IGHJ4*01 QVQLQESGPGLVKPSQTLSLTCTVSGG...
0112 2815 1 90.736 VH4-4 IGHD5-5*01 IGHJ4*01 QVQLQESGPGLVKPSETLSLTCTVSGG...
0113 2861 1 90.771 VH4-31 IGHD3-16*01 IGHJ5*01 QVQLQESGPGLVKPSETLSLTCTVSGG...
0114 2906 1 90.779 VH4-31 IGHD7-27*01 IGHJ1*01 QVQLQESGPGLVKPSQTLSLTCTVSGG...
0115 2020 15 90.870 VH4-39 IGHD1-26*01 IGHJ2*01 QLQLQESGPGLVKPSETLSLTCTVSGGS...
0116 2952 1 90.904 VH4-31 IGHD3-3*01 IGHJ2*01 QVQLQESGPGLVKPSQTLSLTCTVSGG...
0117 2135 15 91.100 VH4-39 IGHD7-27*01 IGHJ5*01 QLQLQESGPGLVKPSETLSLTCTVSGGS...
0118 2998 1 91.147 VH4-31 IGHD7-27*01 IGHJ3*01 QVQLQESGPGLVKPSQTLSLTCTVSGG...
0119 2250 15 91.148 VH4-39 IGHD7-27*01 IGHJ1*01 QLQLQESGPGLVKPSETLSLTCTVSGGS...
0120 2365 15 91.150 VH4-39 IGHD6-13*01 IGHJ2*01 QLQLQESGPGLVKPSETLSLTCTVSGGS...
0121 3044 1 91.387 VH4-31 IGHD6-13*01 IGHJ2*01 QVQLQESGPGLVKPSQTLSLTCTVSGG...
0122 3090 1 91.391 VH4-31 IGHD1-7*01 IGHJ2*01 QVQLQESGPGLVKPSQTLSLTCTVSGG...
0123 2480 15 91.506 VH4-39 IGHD1-7*01 IGHJ2*01 QLQLQESGPGLVKPSETLSLTCTVSGGS...
0124 2561 15 91.510 VH4-39 IGHD7-27*01 IGHJ3*01 QLQLQESGPGLVKPSETLSLTCTVSGGS...
0125 3136 1 91.535 VH4-31 IGHD7-27*01 IGHJ4*01 QVQLQESGPGLVKPSQTLSLTCTVSGG...
Total Sequences : 7128
VH Sequences : 44
DH Sequences : 27
JH Sequences : 6

FIG. 19

BLAST [gnl|Fabrus|VH4-39_IGHD5-24*01_IGHJ6*01]

	Selected	Rank	Cluster	BLAST Bit Score	V Sequence	D Sequence	J Sequence	Amino Acid Sequence
0995	☐	1918	20	41.2	VH1-45	IGHD3-16*01	IGHJ4*01	QMQLVQSGAEVKKTGSSVKVSCKASGYTFTYRYLHWVRQAPGQ...
0996	☐	2866	40	120	VH4-4	IGHD2-2*01	IGHJ5*01	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPAGKG...
0997	☐	6906	1	124	VH4-59	IGHD3-22*01	IGHJ3*01	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGKG...
0998	☐	1571	110	121	VH4-28	IGHD2-8*01	IGHJ5*01	QVQLQESGPGLVKPSDTLSLTCAVSGYSISSSNWWGWIRQPPG...
0999	☐	194	23	58.9 -	VH1-69	IGHD5-12*01	IGHJ4*01	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQG...
1000	☐	195	66	63.5	VH1-69	IGHD6-19*01	IGHJ6*01	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQG...
1001	☐	2490	7	94	VH2-5	IGHD7-27*01	IGHJ3*01	QITLKESGPTLVKPTQTLTLTCTFSGFSLSTSGGVGVGWIRQPPGK...
1002	☐	6907	1	125	VH4-61	IGHD1-26*01	IGHJ5*01	QVQLQESGPGLVKPSETLSLTCTVSGGSVSSGGYYWSWIRQPP...
1003	☐	196	24	49.7	VH1-8	IGHD4-17*01	IGHJ4*01	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYDINWVRQATGQ...
1004	☐	3094	5	97.1	VH6-1	IGHD6-6*01	IGHJ2*01	QVQLQQSGPGLVKPSQTLSLTCAISGDSVSSNSAAWNWIRQSPS...
1005	☐	1110	8	89.4	VH2-70	IGHD3-22*01	IGHJ5*01	QVTLRESGPALVKPTQTLTLTCTFSGFSLSTSGMCVSWIRQPPG...
1006	☐	6908	1	119	VH4-4	IGHD1-1*01	IGHJ4*01	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPAGKG...
1007	☐	6909	1	119	VH4-4	IGHD1-20*01	IGHJ4*01	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPAGKG...
1008	☐	3140	5	97.4	VH6-1	IGHD5-18*01	IGHJ2*01	QVQLQQSGPGLVKPSQTLSLTCAISGDSVSSNSAAWNWIRQSPS...
1009	☐	3186	5	97.4	VH6-1	IGHD5-5*01	IGHJ2*01	QVQLQQSGPGLVKPSQTLSLTCAISGDSVSSNSAAWNWIRQSPS...
1010	☐	6910	1	122	VH4-59	IGHD7-27*01	IGHJ2*01	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGKG...
1011	☐	6911	1	116	VH4-4	IGHD4-23*01	IGHJ1*01	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPAGKG...
1012	☐	3232	5	100	VH6-1	IGHD3-3*01	IGHJ1*01	QVQLQQSGPGLVKPSQTLSLTCAISGDSVSSNSAAWNWIRQSPS...
1013	☐	3278	5	97.8	VH6-1	IGHD1-1*01	IGHJ2*01	QVQLQQSGPGLVKPSQTLSLTCAISGDSVSSNSAAWNWIRQSPS...
1014	☐	3324	5	97.8	VH6-1	IGHD1-20*01	IGHJ2*01	QVQLQQSGPGLVKPSQTLSLTCAISGDSVSSNSAAWNWIRQSPS...
1015	☐	1687	110	119	VH4-28	IGHD2-15*01	IGHJ3*01	QVQLQESGPGLVKPSDTLSLTCAVSGYSISSSNWWGWIRQPPG...
1016	☐	3370	5	101	VH6-1	IGHD3-16*01	IGHJ3*01	QVQLQQSGPGLVKPSQTLSLTCAISGDSVSSNSAAWNWIRQSPS...
1017	☐	6912	1	125	VH4-61	IGHD6-19*01	IGHJ2*01	QVQLQESGPGLVKPSETLSLTCTVSGGSVSSGGYYWSWIRQPP...
1018	☐	1803	110	120	VH4-28	IGHD2-21*01	IGHJ3*01	QVQLQESGPGLVKPSDTLSLTCAVSGYSISSSNWWGWIRQPPG...

FIG. 20

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2009/063299

A. CLASSIFICATION OF SUBJECT MATTER
INV. C40B40/08

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C40B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WEAVER-FELDHAUS J M ET AL: "Yeast mating for combinatorial Fab library generation and surface display" FEBS LETTERS, ELSEVIER, AMSTERDAM, NL, vol. 564, no. 1-2, 23 April 2004 (2004-04-23), pages 24-34, XP004503587 ISSN: 0014-5793 page 26, column 1, paragraph 2; figure 1 ----- -/--	1

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
17 February 2010	24/02/2010

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Fax: (+31–70) 340–3016	Aslund, Fredrik

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2009/063299

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DE WILDT RUUD M T ET AL: "Antibody arrays for high-throughput screening of antibody-antigen interactions" NATURE BIOTECHNOLOGY, NATURE PUBLISHING GROUP, NEW YORK, NY, US, vol. 18, no. 9, 1 September 2000 (2000-09-01), pages 989-994, XP002162316 ISSN: 1087-0156 page 993, column 1, last paragraph	1
X	SCHOFIELD DARREN J ET AL: "Application of phage display to high throughput antibody generation and characterization" GENOME BIOLOGY, BIOMED CENTRAL LTD., LONDON, GB, vol. 8, no. 11, 29 November 2007 (2007-11-29), page R254, XP021041520 ISSN: 1465-6906 figure 1	1
X	RAUCHENBERGER R ET AL: "Human combinatorial Fab library yielding specific and functional antibodies against the human fibroblast growth factor receptor 3" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOCHEMICAL BIOLOGISTS, BIRMINGHAM, US, vol. 278, no. 40, 3 July 2003 (2003-07-03) , pages 38194-38205, XP002404703 ISSN: 0021-9258 figure 1	1
A	ARNAOUT RAMY A: "Specificity and overlap in gene segment-defined antibody repertoires" BMC GENOMICS, BIOMED CENTRAL, LONDON, GB, vol. 6, no. 1, 28 October 2005 (2005-10-28), page 148, XP021002241 ISSN: 1471-2164	1

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2009/063299

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 2-305
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 2-305

The present application contains 305 claims. There are so many claims, and they are drafted in such a way that the claims as a whole are not in compliance with the provisions of clarity and conciseness of Article 6 PCT, as they erect a smoke screen in front of the skilled reader when assessing what should be the subject-matter to search. The non-compliance with the substantive provisions is to such an extent, that the search was performed taking into consideration the non-compliance in determining the extent of the search (PCT Guidelines 9.19). The extent of the search was consequently limited to claim 1 taking into account the disclosure of the invention in the Examples.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.2), should the problems which led to the Article 17(2) declaration be overcome.