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(54) **Title:** ANTI-DLL3 CHIMERIC ANTIGEN RECEPTORS AND METHODS OF USE

(57) **Abstract:** Provided herein are novel anti-DLL3 chimeric antigen receptors and methods of using the same to treat proliferative disorders.



ANTI-DLL3 CHIMERIC ANTIGEN RECEPTORS AND METHODS OF USE

CROSS REFERENCED APPLICATIONS

This claims the benefit of U.S. Provisional Application No. 62/119,793 filed on 23 February
5 2015, U.S. Provisional Application No. 62/241,662 filed on 14 October 2015, and U.S.
Provisional Application No. 62/296,560 filed on 17 February 2016, each of which is incorporated
herein by reference in its entirety.

SEQUENCE LISTING

10 This application contains a sequence listing which has been submitted in ASCII format via
EFS-Web and is hereby incorporated by reference in its entirety. Said ASCII copy, created on
February 19, 2016, is named S69697_1250WO_sc1605pct_ST25.txt and is 612 KB (626,688
bytes) in size.

15 FIELD OF THE INVENTION

The present invention generally relates to adoptive immunotherapy comprising the use of
novel chimeric antigen receptors incorporating a DLL3 binding domain. In preferred
embodiments the disclosed chimeric antigen receptors are useful for the treatment or
prophylaxis of proliferative disorders and any recurrence or metastasis thereof.

20

BACKGROUND OF THE INVENTION

Differentiation and proliferation of stem cells and progenitor cells are normal ongoing
processes that act in concert to support tissue growth during organogenesis, cell repair and cell
replacement. The system is tightly regulated to ensure that only appropriate signals are
25 generated based on the needs of the organism. Cell proliferation and differentiation normally
occur only as necessary for the replacement of damaged or dying cells or for growth. However,
disruption of these processes can be triggered by many factors including the under- or
overabundance of various signaling chemicals, the presence of altered microenvironments,

genetic mutations or a combination thereof. Disruption of normal cellular proliferation and/or differentiation can lead to various disorders including proliferative diseases such as cancer.

Conventional therapeutic treatments for cancer include chemotherapy, radiotherapy and immunotherapy. Often these treatments are ineffective and surgical resection may not provide a viable clinical alternative. Limitations in the current standard of care are particularly evident in those cases where patients undergo first line treatments and subsequently relapse. In such cases refractory tumors, often aggressive and incurable, frequently arise. The overall survival rates for many solid tumors have remained largely unchanged over the years due, at least in part, to the failure of existing therapies to prevent relapse, tumor recurrence and metastasis. There remains therefore a great need to develop more targeted and potent therapies for proliferative disorders. The current invention addresses this need.

SUMMARY OF THE INVENTION

In a broad aspect the present invention provides novel chimeric antigen receptors (CARs) comprising a DLL3 binding domain that specifically binds to human DLL3 protein (DLL3 CARs). In certain embodiments the DLL3 protein is expressed on tumor initiating cells. Through genetic modification (e.g., transduction) the DLL3 CAR are expressed on cytotoxic lymphocytes (preferably autologous) to provide DLL3 sensitive lymphocytes that are used to target and kill DLL3 positive tumor cells. As will be discussed extensively herein the CARs of the instant invention generally comprise an extracellular domain comprising a DLL3 binding domain (which may be derived from an anti-DLL3 antibody), a transmembrane domain and an intracellular signaling domain that activates certain lymphocytes and generates an immune response directed to DLL3 positive tumor cells. Selected embodiments of the invention comprise immunoactive host cells expressing the disclosed CARs and various polynucleotide sequences and vectors encoding the DLL3 CARs of the invention. Yet other aspects include methods of enhancing T lymphocyte or natural killer (NK) cell activity in an individual and treating an individual suffering from cancer by introducing into the individual host cells expressing DLL3 CAR molecules. Such aspects specifically include the treatment of lung cancer (e.g., small cell lung cancer), melanoma, breast cancer, prostate cancer, colon cancer, renal cell carcinoma, ovarian cancer, neuroblastoma, rhabdomyosarcoma, leukemia and lymphoma.

As discussed in more detail below, the term "antibody" as used herein shall be held to mean intact antibodies (e.g., IgG or IgM) as well as any immunoreactive fragments (e.g., Fab

fragments) or immunoreactive constructs or derivatives thereof (e.g., scFv). In certain embodiments the DLL3 binding domains (and DLL3 CARs) of the instant invention will comprise scFv constructs and, in preferred embodiments, will comprise scFv constructs that compete for binding with antibodies comprising heavy and light chain variable regions as disclosed herein.

5 In other preferred embodiments the DLL3 binding domains (and DLL3 CARs) of the invention will comprise scFv constructs comprising heavy and light chain variable regions disclosed herein or fragments thereof. As such, for the purposes of the instant disclosure the term "antibody" shall be used generally and will expressly be held to include immunoreactive fragments, constructs or derivatives thereof unless otherwise contextually dictated.

10 In selected aspects of the invention the CAR binding domain binds specifically to hDLL3 and will be derived from, comprise or compete for binding with an antibody or antibody fragment comprising: a light chain variable region (VL) of SEQ ID NO: 21 and a heavy chain variable region (VH) of SEQ ID NO: 23; or a VL of SEQ ID NO: 25 and a VH of SEQ ID NO: 27; or a VL of SEQ ID NO: 29 and a VH of SEQ ID NO: 31; or a VL of SEQ ID NO: 33 and a VH of SEQ ID NO: 35; or a VL of SEQ ID NO: 37 and a VH of SEQ ID NO: 39; or a VL of SEQ ID NO: 41 and a VH of SEQ ID NO: 43; or a VL of SEQ ID NO: 45 and a VH of SEQ ID NO: 47; or a VL of SEQ ID NO: 49 and a VH of SEQ ID NO: 51; or a VL of SEQ ID NO: 53 and a VH of SEQ ID NO: 55; or a VL of SEQ ID NO: 57 and a VH of SEQ ID NO: 59; or a VL of SEQ ID NO: 61 and a VH of SEQ ID NO: 63; or a VL of SEQ ID NO: 65 and a VH of SEQ ID NO: 67; or a VL of SEQ ID NO: 69 and a VH of SEQ ID NO: 71; or a VL of SEQ ID NO: 73 and a VH of SEQ ID NO: 75; or a VL of SEQ ID NO: 77 and a VH of SEQ ID NO: 79; or a VL of SEQ ID NO: 81 and a VH of SEQ ID NO: 83; or a VL of SEQ ID NO: 85 and a VH of SEQ ID NO: 87; or a VL of SEQ ID NO: 89 and a VH of SEQ ID NO: 91; or a VL of SEQ ID NO: 93 and a VH of SEQ ID NO: 95; or a VL of SEQ ID NO: 97 and a VH of SEQ ID NO: 99; or a VL of SEQ ID NO: 101 and a VH of SEQ ID NO: 103; or a VL of SEQ ID NO: 105 and a VH of SEQ ID NO: 107; or a VL of SEQ ID NO: 109 and a VH of SEQ ID NO: 111; or a VL of SEQ ID NO: 113 and a VH of SEQ ID NO: 115; or a VL of SEQ ID NO: 117 and a VH of SEQ ID NO: 119; or a VL of SEQ ID NO: 121 and a VH of SEQ ID NO: 123; or a VL of SEQ ID NO: 125 and a VH of SEQ ID NO: 127; or a VL of SEQ ID NO: 129 and a VH of SEQ ID NO: 131; or a VL of SEQ ID NO: 133 and a VH of SEQ ID NO: 135; or a VL of SEQ ID NO: 137 and a VH of SEQ ID NO: 139; or a VL of SEQ ID NO: 141 and a VH of SEQ ID NO: 143; or a VL of SEQ ID NO: 145 and a VH of SEQ ID NO: 147; or a VL of SEQ ID NO: 149 and a VH of SEQ ID NO: 151; or a VL of SEQ ID NO: 153 and a VH of SEQ ID NO: 155; or a VL of SEQ ID NO: 157 and a VH of SEQ ID NO: 159; or a

VL of SEQ ID NO: 161 and a VH of SEQ ID NO: 163; or a VL of SEQ ID NO: 165 and a VH of
SEQ ID NO: 167; or a VL of SEQ ID NO: 169 and a VH of SEQ ID NO: 171; or a VL of SEQ ID
NO: 173 and a VH of SEQ ID NO: 175; or a VL of SEQ ID NO: 177 and a VH of SEQ ID NO:
179; or a VL of SEQ ID NO: 181 and a VH of SEQ ID NO: 183; or a VL of SEQ ID NO: 185 and
5 a VH of SEQ ID NO: 187; or a VL of SEQ ID NO: 189 and a VH of SEQ ID NO: 191; or a VL of
SEQ ID NO: 193 and a VH of SEQ ID NO: 195; or a VL of SEQ ID NO: 197 and a VH of SEQ
ID NO: 199; or a VL of SEQ ID NO: 201 and a VH of SEQ ID NO: 203; or a VL of SEQ ID NO:
205 and a VH of SEQ ID NO: 207; or a VL of SEQ ID NO: 209 and a VH of SEQ ID NO: 211; or
a VL of SEQ ID NO: 213 and a VH of SEQ ID NO: 215; or a VL of SEQ ID NO: 217 and a VH of
10 SEQ ID NO: 219; or a VL of SEQ ID NO: 221 and a VH of SEQ ID NO: 223; or a VL of SEQ ID
NO: 225 and a VH of SEQ ID NO: 227; or a VL of SEQ ID NO: 229 and a VH of SEQ ID NO:
231; or a VL of SEQ ID NO: 233 and a VH of SEQ ID NO: 235; or a VL of SEQ ID NO: 237 and
a VH of SEQ ID NO: 239; or a VL of SEQ ID NO: 241 and a VH of SEQ ID NO: 243; or a VL of
SEQ ID NO: 245 and a VH of SEQ ID NO: 247; or a VL of SEQ ID NO: 249 and a VH of SEQ
15 ID NO: 251; or a VL of SEQ ID NO: 253 and a VH of SEQ ID NO: 255; or a VL of SEQ ID NO:
257 and a VH of SEQ ID NO: 259; or a VL of SEQ ID NO: 261 and a VH of SEQ ID NO: 263;
or a VL of SEQ ID NO: 265 and a VH of SEQ ID NO: 267; or a VL of SEQ ID NO: 269 and a VH
of SEQ ID NO: 271; or a VL of SEQ ID NO: 273 and a VH of SEQ ID NO: 275; or a VL of SEQ
ID NO: 277 and a VH of SEQ ID NO: 279; or a VL of SEQ ID NO: 281 and a VH of SEQ ID NO:
20 283; or a VL of SEQ ID NO: 285 and a VH of SEQ ID NO: 287; or a VL of SEQ ID NO: 289 and
a VH of SEQ ID NO: 291; or a VL of SEQ ID NO: 293 and a VH of SEQ ID NO: 295; or a VL of
SEQ ID NO: 297 and a VH of SEQ ID NO: 299; or a VL of SEQ ID NO: 301 and a VH of SEQ
ID NO: 303; or a VL of SEQ ID NO: 305 and a VH of SEQ ID NO: 307; or a VL of SEQ ID NO:
309 and a VH of SEQ ID NO: 311; or a VL of SEQ ID NO: 313 and a VH of SEQ ID NO: 315; or
25 a VL of SEQ ID NO: 317 and a VH of SEQ ID NO: 319; or a VL of SEQ ID NO: 321 and a VH of
SEQ ID NO: 323; or a VL of SEQ ID NO: 325 and a VH of SEQ ID NO: 327; or a VL of SEQ ID
NO: 329 and a VH of SEQ ID NO: 331; or a VL of SEQ ID NO: 333 and a VH of SEQ ID NO:
335; or a VL of SEQ ID NO: 337 and a VH of SEQ ID NO: 339; or a VL of SEQ ID NO: 341 and
a VH of SEQ ID NO: 343; or a VL of SEQ ID NO: 345 and a VH of SEQ ID NO: 347; or a VL of
30 SEQ ID NO: 349 and a VH of SEQ ID NO: 351; or a VL of SEQ ID NO: 353 and a VH of SEQ
ID NO: 355; or a VL of SEQ ID NO: 357 and a VH of SEQ ID NO: 359; or a VL of SEQ ID NO:
361 and a VH of SEQ ID NO: 363; or a VL of SEQ ID NO: 365 and a VH of SEQ ID NO: 367;
or a VL of SEQ ID NO: 369 and a VH of SEQ ID NO: 371; or a VL of SEQ ID NO: 373 and a VH

of SEQ ID NO: 375; or a VL of SEQ ID NO: 377 and a VH of SEQ ID NO: 379; or a VL of SEQ ID NO: 381 and a VH of SEQ ID NO: 383; or a VL of SEQ ID NO: 385 and a VH of SEQ ID NO: 387; or a VL of SEQ ID NO: 389 and a VH of SEQ ID NO: 391; or a VL of SEQ ID NO: 393 and a VH of SEQ ID NO: 395; or a VL of SEQ ID NO: 397 and a VH of SEQ ID NO: 399; or a VL of SEQ ID NO: 401 and a VH of SEQ ID NO: 403; or a VL of SEQ ID NO: 405 and a VH of SEQ ID NO: 407. In particularly preferred embodiments the DLL3 binding domain will comprise a scFv construct comprising the aforementioned VL and VH sequences or fragments thereof. In some aspects of the invention the CAR binding domain comprises a chimeric, CDR grafted, humanized or human antibody or an immunoreactive fragment thereof. In other aspects of the invention the CAR binding domain comprising the aforementioned sequences is an internalizing antibody.

Yet other preferred DLL3 CARs of the instant invention will comprise CDR grafted or humanized antibodies, or fragments or constructs thereof, comprising one or more heavy (CDRH1, CDRH2, CDRH3) or light (CDRL1, CDRL2, CDRL3) chain CDRs as set forth in FIGS. 1A or 1B wherein the CDRs are derived as per Kabat et al.

In yet other compatible embodiments the CARs of the instant invention will comprise the binding region (e.g., in the form of a scFv) derived from one of the CDR grafted or humanized DLL3 antibodies hSC16.13, hSC16.15, hSC16.25, hSC16.34 and hSC16.56 or fragments thereof.

Other embodiments are directed to CARs comprising an antibody or antibody fragment or construct thereof wherein said antibody comprises:

an antibody light chain comprising a light chain variable region CDR1 comprising SEQ ID NO: 408, a light chain variable region CDR2 comprising SEQ ID NO: 409 and a light chain variable region CDR3 comprising SEQ ID NO: 410; and

an antibody heavy chain comprising a heavy chain variable region CDR1 comprising SEQ ID NO: 411, a heavy chain variable region CDR2 comprising SEQ ID NO: 412 and a heavy chain variable region CDR3 comprising SEQ ID NO: 413.

In another embodiment the invention is directed to CARs comprising an antibody or antibody fragment or construct thereof wherein said antibody comprises:

an antibody light chain comprising a light chain variable region CDR1 comprising SEQ ID NO: 414, a light chain variable region CDR2 comprising SEQ ID NO: 415 and a light chain variable region CDR3 comprising SEQ ID NO: 416; and

an antibody heavy chain comprising a heavy chain variable region CDR1 comprising SEQ ID NO: 417, a heavy chain variable region CDR2 comprising SEQ ID NO: 418 and a heavy chain variable region CDR3 comprising SEQ ID NO: 419.

5 In another embodiment the invention is directed to CARs comprising an antibody or antibody fragment or construct thereof wherein said antibody comprises:

an antibody light chain comprising a light chain variable region CDR1 comprising SEQ ID NO: 420, a light chain variable region CDR2 comprising SEQ ID NO: 421 and a light chain variable region CDR3 comprising SEQ ID NO: 422; and

10 an antibody heavy chain comprising a heavy chain variable region CDR1 comprising SEQ ID NO: 423, a heavy chain variable region CDR2 comprising SEQ ID NO: 424 and a heavy chain variable region CDR3 comprising SEQ ID NO: 425.

In another embodiment the invention is directed to CARs comprising an antibody or antibody fragment or construct thereof wherein said antibody comprises:

15 an antibody light chain comprising a light chain variable region CDR1 comprising SEQ ID NO: 426, a light chain variable region CDR2 comprising SEQ ID NO: 427 and a light chain variable region CDR3 comprising SEQ ID NO: 428; and

an antibody heavy chain comprising a heavy chain variable region CDR1 comprising SEQ ID NO: 429, a heavy chain variable region CDR2 comprising SEQ ID NO: 430 and a heavy chain variable region CDR3 comprising SEQ ID NO: 431.

20 In another embodiment the invention is directed to CARs comprising an antibody or antibody fragment or construct thereof wherein said antibody comprises:

an antibody light chain comprising a light chain variable region CDR1 comprising SEQ ID NO: 432, a light chain variable region CDR2 comprising SEQ ID NO: 433 and a light chain variable region CDR3 comprising SEQ ID NO: 434; and

25 an antibody heavy chain comprising a heavy chain variable region CDR1 comprising SEQ ID NO: 435, a heavy chain variable region CDR2 comprising SEQ ID NO: 436 and a heavy chain variable region CDR3 comprising SEQ ID NO: 437.

30 In certain preferred embodiments each of the aforementioned antibodies comprises humanized antibodies. Moreover, as described herein nucleic acid sequences encoding such exemplary murine and humanized heavy and light chain variable regions are set forth in the attached sequence listing.

In other embodiments the CARs of the present invention comprise an antibody or antibody fragment or construct thereof residing in a bin defined by a reference antibody selected

from the group consisting of SC16.3, SC16.4, SC16.5, SC16.7, SC16.8, SC16.10, SC16.11, SC16.13, SC16.15, SC16.18, SC16.19, SC16.20, SC16.21, SC16.22, SC16.23, SC16.25, SC16.26, SC16.29, SC16.30, SC16.31, SC16.34, SC16.35, SC16.36, SC16.38, SC16.41, SC16.42, SC16.45, SC16.47, SC16.49, SC16.50, SC16.52, SC16.55, SC16.56, SC16.57, SC16.58, SC16.61, SC16.62, SC16.63, SC16.65, SC16.67, SC16.68, SC16.72, SC16.73, SC16.78, SC16.79, SC16.80, SC16.81, SC16.84, SC16.88, SC16.101, SC16.103, SC16.104, SC16.105, SC16.106, SC16.107, SC16.108, SC16.109, SC16.110, SC16.111, SC16.113, SC16.114, SC16.115, SC16.116, SC16.117, SC16.118, SC16.120, SC16.121, SC16.122, SC16.123, SC16.124, SC16.125, SC16.126, SC16.129, SC16.130, SC16.131, SC16.132, SC16.133, SC16.134, SC16.135, SC16.136, SC16.137, SC16.138, SC16.139, SC16.140, SC16.141, SC16.142, SC16.143, SC16.144, SC16.147, SC16.148, SC16.149 and SC16.150.

In still other embodiments the CARs of the invention will comprise antibodies (or antibody fragments) from bin A, antibodies from bin B, antibodies from bin C, antibodies from bin D, antibodies from bin E, antibodies from bin F, antibodies from bin G, antibodies from bin H or antibodies from bin I. Yet other preferred embodiments will comprise a reference antibody and any antibody that competes with the reference antibody.

The term “compete” or “competing antibody” when used in the context of the disclosed binding domains means binding competition between antibodies as determined by an assay in which a reference antibody or immunoreactive fragment thereof substantially prevents or inhibits (e.g., greater than 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85% or 90%.) specific binding of a test antibody to a common antigen. Compatible methods for determining such competition comprise art known techniques such as, for example, bio-layer interferometry, surface plasmon resonance, flow cytometry, competitive ELISA, etc.

In certain embodiments the invention is directed to a nucleic acid encoding the heavy or light chain amino acid sequence (or constructs or derivatives thereof) of any one of the anti-DLL3 binding domains disclosed herein. Compatible anti-DLL3 heavy and light chain variable region nucleic acid sequences are set forth in the appended sequence listing. In preferred embodiments the nucleic acid encoding the binding domain or CAR are incorporated in a plasmid or vector. In yet other embodiments the vector will comprise a viral vector.

In another embodiment the present invention provides methods of treating cancer such as, for example, pancreatic cancer, colorectal cancer, prostate cancer, small cell and non-small cell lung cancer, breast cancer, ovarian cancer and gastric cancer, comprising administering a

pharmaceutical composition comprising a host cell expressing an anti-DLL3 CAR as disclosed herein.

In some embodiments, the invention provides methods of treating cancer comprising administering a pharmaceutical composition comprising a host cell expressing an anti-DLL3
5 CAR as disclosed herein and further comprising administering to the subject at least one additional therapeutic moiety. In preferred embodiments the host cell will comprise a sensitized lymphocyte.

The present invention further provides a method of reducing tumor initiating cells in a tumor cell population, wherein the method comprises contacting a tumor cell population
10 comprising tumor initiating cells and tumor cells other than tumor initiating cells, with a host cell expressing an anti-DLL3 CAR; whereby the frequency of tumor initiating cells is reduced.

In yet other preferred embodiments the present invention also provides kits or devices and associated methods that are useful in the treatment of DLL3 associated disorders such as cancer. To this end the present invention preferably provides an article of manufacture useful
15 for generating DLL3 sensitized lymphocytes for treating DLL3 associated disorders comprising, for example, a container or receptacle containing vectors (e.g., viral vectors) encoding the disclosed CARs and instructional materials for generating DLL3 sensitized lymphocytes. In selected embodiments the kits will comprise additional reagents and receptacles to effectively transduce the lymphocytes. In other selected embodiments such kits comprise allogeneic DLL3
20 sensitized lymphocytes that may be directly administered to the patient to generate the desired immune response. In still other embodiments such articles of manufacture will comprise a container or receptacle comprising a liquid formulation of DLL3 sensitized lymphocytes. In such embodiments the DLL3 sensitized lymphocytes may comprise allogenic or autologous host cells and in other embodiments the liquid formulation may comprise a pharmaceutically acceptable
25 carrier.

The foregoing is a summary and thus contains, by necessity, simplifications, generalizations, and omissions of detail; consequently, those skilled in the art will appreciate that the summary is illustrative only and is not intended to be in any way limiting. Other aspects, features, and advantages of the methods, compositions and/or devices and/or other subject
30 matter described herein will become apparent in the teachings set forth herein. The summary is provided to introduce a selection of concepts in a simplified form that are further described below in the Detailed Description. This summary is not intended to identify key features or

essential features of the claimed subject matter, nor is it intended to be used as an aid in determining the scope of the claimed subject matter.

BRIEF DESCRIPTION OF THE FIGURES

FIGS. 1A and 1B provide, in a tabular form, contiguous amino acid sequences (SEQ ID NOS: 21-407, odd numbers) of light and heavy chain variable regions of a number of murine and humanized exemplary DLL3 antibodies compatible with the disclosed DLL3 CARs as isolated, cloned and engineered as described in the Examples herein;

FIG. 2 depicts, in schematic form, the results of domain level mapping analysis of exemplary DLL3 antibodies isolated, cloned and engineered as described in the Examples herein;

FIG. 3 provides a schematic representation of an exemplary DLL3 CAR construct illustrating the various components thereof;

FIGS. 4A – 4C provide nucleic acid sequences and amino acid sequences for three exemplary DLL3 CARs (SCT1-h16.15, SCT1-h16.13 and SCT1-h16.25 respectively) compatible with the instant invention;

FIG. 5 provides a schematic representation illustrating a process for producing DLL3 sensitized lymphocytes and their subsequent use to generate an immune response directed to DLL3 positive tumor cells;

FIGS. 6A and 6B demonstrate the expression of exemplary DLL3 CARs (SCT1-h16.13, SCT1-h16.15 and SCT1-h16.25) on transduced Jurkat cells (FIG. 6A) and the expression of hDLL3 on engineered HEK-293T control cells (FIG. 6B) each as measured using flow cytometry;

FIGS. 7A and 7B depict the induction of an immune response in SCT1-h16.15 transduced Jurkat cells at various ratios of lymphocyte to target cells as measured by IL-2 production (FIG. 7A) and the induction of an immune response (again as measured by IL2 levels) generated using three different exemplary DLL3 CAR cells at the same lymphocyte to target cell ratio (FIG. 7B);

FIG. 8 demonstrates that human primary lymphocytes may be engineered to effectively express exemplary anti-DLL3 CARs in accordance with the teachings herein;

FIGS. 9A and 9B provide DLL3 surface expression profiles for a 293T cell line engineered to express DLL3 (FIG. 9A) and a small cell lung cancer patient derived xenograft ("PDX") cell line (FIG. 9B) as evidenced by flow cytometry;

FIG. 10 shows the ability of DLL3 sensitized primary lymphocytes comprising three different DLL3 CARs (SCT1-h16.13, SCT1-h16.15 and SCT1-h16.25) to eliminate engineered 293T cells expressing DLL3;

FIG. 11 demonstrates that primary human lymphocytes from two individuals may be engineered to effectively express an anti-DLL3 CAR in accordance with the teachings herein;

FIGS. 12A and 12B demonstrate the ability of DLL3 sensitized lymphocytes comprising host cells from two individuals to provoke an immune response (as measured by the induction of TNF α) when exposed to engineered 293T cells (FIG. 12A) or PDX tumor cells (FIG. 12B);

FIGS. 13A and 13B demonstrate the ability of DLL3 sensitized lymphocytes comprising host cells from two individuals to provoke an immune response (as measured by the induction of INF γ) when exposed to engineered 293T cells (FIG. 13A) or PDX tumor cells (FIG. 13B); and

FIGS. 14A and 14B show the ability of DLL3 sensitized lymphocytes comprising host cells from two individuals to eliminate engineered 293T cells (FIG. 14A) or PDX tumor cells (FIG. 14B) upon exposure.

DETAILED DESCRIPTION OF THE INVENTION

The invention may be embodied in many different forms. Disclosed herein are non-limiting, illustrative embodiments of the invention that exemplify the principles thereof. Any section headings used herein are for organizational purposes only and are not to be construed as limiting the subject matter described. For the purposes of the instant disclosure all identifying sequence accession numbers may be found in the NCBI Reference Sequence (RefSeq) database and/or the NCBI GenBank[®] archival sequence database unless otherwise noted.

Recent advances in adoptive transfer immunotherapy have provided a promising approach for the treatment of various neoplasia and a chance to improve patient experiences, particularly with regard to solid tumors. In this regard the present invention is directed to the use of novel chimeric antigen receptors ("CARs") comprising an extracellular binding or targeting domain that associates or reacts with delta-like ligand 3 ("DLL3"). As will be discussed extensively herein, DLL3 is a particularly effective tumor marker that is expressed on a number of different cancers and, significantly, has been found to be associated with cancer stem cells.

Thus, when the anti-DLL3 binding domains of the instant invention are incorporated in a chimeric antigen receptor expressed on lymphocytes, the resulting “DLL3 sensitized lymphocytes” (e.g., natural killer cells or T cells that immunospecifically recognize a DLL3 determinant) are able to effectively mount an immune response directed to aberrant DLL3 positive cells including cancer stem cells. This ability to effectively eliminate tumorigenic “seed” cells is often critical in reducing the possibility of tumor recurrence or metastasis. To this end it will be appreciated that the anti-DLL3 CAR lymphocytes of the instant invention may be used in combination with other therapeutic agents (including anti-DLL3 antibody drug conjugates) or as part of a maintenance regimen following standard of care treatments.

More generally a chimeric antigen receptor is an artificially constructed hybrid protein or polypeptide containing or comprising an antigen binding domain of an antibody linked to a signaling domain (e.g., T-cell signaling or T-cell activation domains). The CARs of the instant invention have the ability to redirect the specificity and reactivity of sensitized lymphocytes (e.g., T-cells) toward DLL3 positive target cells in a non-MHC-restricted manner by exploiting the antigen-binding properties of monoclonal antibodies. The non-MHC-restricted antigen recognition gives T-cells expressing DLL3 CARs the ability to recognize tumorigenic DLL3 independent of antigen processing, thus bypassing a major mechanism of tumor escape. Moreover, when expressed in T-cells, CARs advantageously do not dimerize with endogenous T cell receptor (TCR) alpha and beta chains.

Accordingly, the present invention is generally directed to chimeric antigen receptors comprising a DLL3 binding domain that immunospecifically associates with DLL3 on target cells and stimulates an immune response. In preferred embodiments the DLL3 binding domain of the CAR may comprise a scFv derived from the heavy and light chain antibody variable regions disclosed herein. More specifically an “anti-DLL3 CAR” or simply “DLL3 CAR” of the instant invention shall comprise a chimeric protein incorporating an extracellular DLL3 binding domain, a transmembrane domain and an intracellular signaling domain (see FIG. 3). Typically a nucleotide sequence encoding the desired DLL3 CAR will be synthesized or engineered and inserted into an expression vector or system (e.g. lentiviral, retroviral, etc.). In preferred embodiments lymphocytes, including T-lymphocytes, natural killer cells (“NK cells”) and dendritic cells, obtained from a patient or donor are then exposed to (e.g., transduced) the selected DLL3 CAR vector to provide engineered lymphocytes that express the CAR protein with the extracellular DLL3 binding domain (i.e., “DLL3 sensitized lymphocytes”). Following optional expansion, these DLL3 sensitized lymphocytes may be infused into a patient to mount

an immunospecific response to DLL3 positive tumor cells (see generally FIG. 5). In this regard the DLL3 sensitized lymphocytes will be activated upon contacting a target cell expressing a DLL3 determinant. To "activate the sensitized lymphocytes" (e.g., T cells and NK cells) means to induce a change in their biologic state by which the cells express activation markers, produce
5 cytokines, proliferate and/or become cytotoxic to target cells. All these changes can be produced by primary stimulatory signals. Costimulatory signals amplify the magnitude of the primary signals and suppress cell death following initial stimulation resulting in a more durable activation state and thus a higher cytotoxic capacity.

Thus, it will further be appreciated that, besides the DLL3 binding domain, CARs of the
10 invention will comprise an intracellular or cytoplasmic domain that initiates a primary cytoplasmic signaling sequence (e.g., a sequence for initiating antigen-dependent primary activation via a T-cell receptor complex). Compatible intracellular domains may, for example, be derived from CD3 ζ , FcR γ , FcR β , CD3 γ , CD3 δ , CD3 ϵ , CD5, CD22, CD79a, CD79b, and CD66d. In other preferred embodiments, the CARs of the invention will comprise an
15 intracellular domain that initiates a secondary or co-stimulating signal. Compatible co-stimulatory domains may comprise, for example, intracellular domains derived from CD2, CD4, CD5, CD8 α , CD8 β , CD28, CD134, CD137, ICOS, CD154, 4-1BB and glucocorticoid-induced tumor necrosis factor receptor (see U.S.P.N. US/2014/0242701). Additionally, in preferred
20 embodiments the disclosed CARs will comprise a transmembrane (and optionally a spacer) domain interposed between the extracellular DLL3 binding domain and the intracellular signaling domain. As discussed in more detail below the transmembrane domain may comprise, for example, part of an antibody constant (Fc) region, human CD8a or artificially produced spacers known in the art. Essentially, any amino acid sequence that anchors the CAR in the cell membrane and allows for effective association of the DLL3 binding domain and
25 transmission of appropriate signaling from the intracellular domain is compatible with the invention.

With respect to the novel DLL3 CARs of the invention, it will be appreciated that the selection of DLL3 as the tumor target is integral in generating an effective anti-tumor immune response. More specifically it has been found that DLL3 phenotypic determinants are clinically
30 associated with various proliferative disorders, including neoplasia exhibiting neuroendocrine features, and that DLL3 protein and variants or isoforms thereof provide useful tumor markers which may be exploited in the treatment of related diseases. In this regard the present invention provides a number of chimeric antigen receptors that comprise an anti-DLL3 binding domain in

addition to any signaling component. As discussed in more detail below, the disclosed DLL3 CARs are particularly effective at eliminating tumorigenic cells and therefore useful for the treatment and prophylaxis of certain proliferative disorders or the progression or recurrence thereof.

Moreover, as shown in the instant application it has been found that DLL3 markers or determinants such as cell surface DLL3 protein are therapeutically associated with cancer stem cells (also known as tumor perpetuating cells) and may be effectively leveraged to eliminate or silence the same. The ability to selectively reduce or eliminate cancer stem cells through the use of DLL3 CARs as disclosed herein is surprising in that such cells are known to generally be resistant to many conventional treatments. That is, the effectiveness of traditional, as well as more recent targeted treatment methods, is often limited by the existence and/or emergence of resistant cancer stem cells that are capable of perpetuating tumor growth even in face of diverse treatment methods. Further, determinants associated with cancer stem cells often make poor therapeutic targets due to low or inconsistent expression, failure to remain associated with the tumorigenic cell or failure to present at the cell surface. In sharp contrast to the teachings of the prior art, the instantly disclosed DLL3 CARs and associated methods effectively overcome this inherent resistance to specifically eliminate, deplete, silence or promote the differentiation of such cancer stem cells thereby negating their ability to sustain or, significantly, re-induce underlying tumor growth. Moreover, as expression of DLL3 protein has largely been associated with intracellular locations such as the Golgi, it was uncertain that such phenotypic determinants could be successfully exploited as a therapeutic target for the specific DLL3 CARs as taught herein.

Thus, it is particularly remarkable that DLL3 CARs such as those disclosed herein may advantageously be used in the treatment and/or prevention of selected proliferative (e.g., neoplastic) disorders or progression or recurrence thereof. It will be appreciated that, while preferred embodiments of the invention will be discussed extensively below, particularly in terms of exemplary signaling or costimulatory domains or regions or in the context of cancer stem cells or tumors comprising neuroendocrine features and their interactions with the disclosed DLL3 CARs, those skilled in the art will appreciate that the scope of the instant invention is not limited by such exemplary embodiments. Rather, the most expansive embodiments of the present invention and the appended claims are broadly and expressly directed to any chimeric antigen receptor comprising a binding domain that immunospecifically associates or binds to DLL3 and their use in the treatment and/or prevention of a variety of DLL3 associated or

mediated disorders, including neoplastic or cell proliferative disorders, regardless of any particular mechanism of action, CAR construct or specifically targeted tumor, cellular or molecular component.

To that end, and as demonstrated in the instant application, it has unexpectedly been
5 found that the disclosed DLL3 CARs can effectively be used to target and eliminate or otherwise incapacitate proliferative or tumorigenic cells and treat DLL3 associated disorders (e.g., neoplasia). As used herein a "DLL3 associated disorder" shall be held to mean any disorder or disease (including proliferative disorders) that is marked, diagnosed, detected or identified by a phenotypic aberration of DLL3 genetic components or expression ("DLL3 determinant") during
10 the course or etiology of the disease or disorder. In this regard a DLL3 phenotypic aberration or determinant may, for example, comprise elevated or depressed levels of DLL3 protein expression, abnormal DLL3 protein expression on certain definable cell populations or abnormal DLL3 protein expression at an inappropriate phase or stage of a cell lifecycle. Of course, it will be appreciated that similar expression patterns of genotypic determinants (e.g., mRNA
15 transcription levels) of DLL3 may also be used to classify, detect or treat DLL3 disorders.

I. DLL3 Physiology

It has been found that DLL3 phenotypic determinants are clinically associated with various proliferative disorders, including neoplasia exhibiting neuroendocrine features, and that DLL3 protein and variants or isoforms thereof provide useful tumor markers which may be exploited in
20 the treatment of related diseases. In this regard the present invention provides a number of DLL3 CAR constructs comprising an engineered anti-DLL3 binding or targeting agent operably associated with one or more signaling domain(s) capable of inducing an immune response in a lymphocyte. As discussed in more detail below and set forth in the appended Examples, the disclosed anti-DLL3 CARs are particularly effective at eliminating tumorigenic cells and
25 therefore useful for the treatment and prophylaxis of certain proliferative disorders or the progression or recurrence thereof.

Moreover, it has been found that DLL3 markers or determinants such as cell surface DLL3 protein are therapeutically associated with cancer stem cells (also known as tumor perpetuating cells) and may be effectively exploited to eliminate or silence the same. The ability to
30 selectively reduce or eliminate cancer stem cells through the use of DLL3 CARs as disclosed herein is surprising in that such cells are known to generally be resistant to many conventional treatments. That is, the effectiveness of traditional, as well as more recent targeted treatment

methods, is often limited by the existence and/or emergence of resistant cancer stem cells that are capable of perpetuating tumor growth even in face of these diverse treatment methods. Further, determinants associated with cancer stem cells often make poor therapeutic targets due to low or inconsistent expression, failure to remain associated with the tumorigenic cell or failure to present at the cell surface. In sharp contrast to the teachings of the prior art, the instantly disclosed CARs and methods effectively overcome this inherent resistance and to specifically eliminate, deplete, silence or promote the differentiation of such cancer stem cells thereby negating their ability to sustain or re-induce the underlying tumor growth.

In *Drosophila*, Notch signaling is mediated primarily by one Notch receptor gene and two ligand genes, known as Serrate and Delta (Wharton et al, 1985; Rebay et al., 1991). In humans, there are four known Notch receptors and five DSL (Delta-Serrate LAG2) ligands -- two homologs of Serrate, known as Jagged1 and Jagged 2, and three homologs of Delta, termed delta-like ligands or DLL1, DLL3 and DLL4. In general, Notch receptors on the surface of the signal-receiving cell are activated by interactions with ligands expressed on the surface of an opposing, signal-sending cell (termed a trans-interaction). These trans-interactions lead to a sequence of protease mediated cleavages of the Notch receptor. In consequence, the Notch receptor intracellular domain is free to translocate from the membrane to the nucleus, where it partners with the CSL family of transcription factors (RBPJ in humans) and converts them from transcriptional repressors into activators of Notch responsive genes.

Of the human Notch ligands, DLL3 is different in that it seems incapable of activating the Notch receptor via trans-interactions (Ladi et al., 2005). Notch ligands may also interact with Notch receptors in cis (on the same cell) leading to inhibition of the Notch signal, although the exact mechanisms of cis-inhibition remain unclear and may vary depending upon the ligand (for instance, see Klein et al., 1997; Ladi et al., 2005; Glittenberg et al., 2006). Two hypothesized modes of inhibition include modulating Notch signaling at the cell surface by preventing trans-interactions, or by reducing the amount of Notch receptor on the surface of the cell by perturbing the processing of the receptor or by physically causing retention of the receptor in the endoplasmic reticulum or Golgi (Sakamoto et al., 2002; Dunwoodie, 2009). It is clear, however, that stochastic differences in expression of Notch receptors and ligands on neighboring cells can be amplified through both transcriptional and non-transcriptional processes, and subtle balances of cis- and trans-interactions can result in a fine tuning of the Notch mediated delineation of divergent cell fates in neighboring tissues (Sprinzak et al., 2010).

DLL3 is a member of the Delta-like family of Notch DSL ligands. Representative DLL3 protein orthologs include, but are not limited to, human (Accession Nos. NP_058637 and NP_982353), chimpanzee (Accession No. XP_003316395), mouse (Accession No. NP_031892), and rat (Accession No. NP_446118). In humans, the DLL3 gene consists of 8
5 exons spanning 9.5 kbp located on chromosome 19q13. Alternate splicing within the last exon gives rise to two processed transcripts, one of 2389 bases (Accession No. NM_016941) and one of 2052 bases (Accession No. NM_203486). The former transcript encodes a 618 amino acid protein (Accession No. NP_058637; SEQ ID NO: 1), whereas the latter encodes a 587 amino acid protein (Accession No. NP_982353; SEQ ID NO: 2). These two protein isoforms of
10 DLL3 share overall 100% identity across their extracellular domains and their transmembrane domains, differing only in that the longer isoform contains an extended cytoplasmic tail containing 32 additional residues at the carboxy terminus of the protein. The biological relevance of the isoforms is unclear, although both isoforms can be detected in tumor cells.

As shown schematically in FIG. 2 the extracellular region of the DLL3 protein, comprises
15 six EGF-like domains, the single DSL domain and the N-terminal domain. Generally, the EGF domains are recognized as occurring at about amino acid residues 216-249 (domain 1), 274-310 (domain 2), 312-351 (domain 3), 353-389 (domain 4), 391-427 (domain 5) and 429-465 (domain 6), with the DSL domain at about amino acid residues 176-215 and the N-terminal domain at about amino acid residues 27-175 of hDLL3 (SEQ ID NOS: 1 and 2). As discussed in
20 more detail herein and shown in the Examples below, each of the EGF-like domains, the DSL domain and the N-terminal domain comprise part of the DLL3 protein as defined by a distinct amino acid sequence. Note that, for the purposes of the instant disclosure the respective EGF-like domains may be termed EGF1 to EGF6 with EGF1 being closest to the N-terminal portion of the protein. In regard to the structural composition of the protein one significant aspect of the
25 instant invention is that the disclosed DLL3 modulators may be generated, fabricated, engineered or selected so as to react with a selected domain, motif or epitope. In certain cases such site-specific modulators may provide enhanced reactivity and/or efficacy depending on their primary mode of action. In particularly preferred embodiments the DLL3 CAR will bind to the DSL domain and, in even more preferred embodiments, will bind to an epitope comprising
30 G203, R205, P206 (SEQ ID NO: 4) within the DSL domain.

II. Cancer Stem Cells

As alluded to above it has surprisingly been discovered that aberrant DLL3 expression

(genotypic and/or phenotypic) is associated with various tumorigenic cell subpopulations. In this respect the present invention provides DLL3 CAR mediated therapeutic regimens that may be particularly useful for targeting such cells (e.g., cancer stem cells), thereby facilitating the treatment, management or prevention of neoplastic disorders. Thus, in preferred embodiments the disclosed DLL3 CAR may be advantageously be used to reduce tumor initiating cell frequency in accordance with the present teachings and thereby facilitate the treatment or management of proliferative disorders.

According to the current models, a tumor comprises non-tumorigenic cells and tumorigenic cells. Non-tumorigenic cells do not have the capacity to self-renew and are incapable of reproducibly forming tumors, even when transplanted into immunocompromised mice in excess cell numbers. Tumorigenic cells, also referred to herein as "tumor initiating cells" (TICs), which make up 0.1-40% (more typically 0.1-10%) of a tumor's cell population, have the ability to form tumors. Tumorigenic cells encompass both tumor perpetuating cells (TPCs), referred to interchangeably as cancer stem cells (CSCs) and tumor progenitor cells (TProgs).

CSCs, like normal stem cells that support cellular hierarchies in normal tissue, are able to self-replicate indefinitely while maintaining the capacity for multilineage differentiation. CSCs are able to generate both tumorigenic progeny and non-tumorigenic progeny and are able to completely recapitulate the heterogeneous cellular composition of the parental tumor as demonstrated by serial isolation and transplantation of low numbers of isolated CSCs into immunocompromised mice.

Tprogs, like CSCs have the ability to fuel tumor growth in a primary transplant. However, unlike CSCs, they are not able to recapitulate the cellular heterogeneity of the parental tumor and are less efficient at reinitiating tumorigenesis in subsequent transplants because Tprogs are typically only capable of a finite number of cell divisions as demonstrated by serial transplantation of low numbers of highly purified Tprog into immunocompromised mice. Tprogs may further be divided into early Tprogs and late Tprogs, which may be distinguished by phenotype (e.g., cell surface markers) and their different capacities to recapitulate tumor cell architecture. While neither can recapitulate a tumor to the same extent as CSCs, early Tprogs have a greater capacity to recapitulate the parental tumor's characteristics than late Tprogs. Notwithstanding the foregoing distinctions, it has been shown that some Tprog populations can, on rare occasion, gain self-renewal capabilities normally attributed to CSCs and can themselves become CSCs.

CSCs exhibit higher tumorigenicity and are relatively more quiescent than: (i) Tprogs (both

early and late Tprogs); and (ii) non-tumorigenic cells such as tumor-infiltrating cells, for example, fibroblasts/stroma, endothelial and hematopoietic cells that may be derived from CSCs and typically comprise the bulk of a tumor. Given that conventional therapies and regimens have, in large part, been designed to debulk tumors and attack rapidly proliferating cells, CSCs are more resistant to conventional therapies and regimens than the faster proliferating Tprogs and other bulk tumor cell populations such as non-tumorigenic cells. Other characteristics that may make CSCs relatively chemoresistant to conventional therapies are increased expression of multi-drug resistance transporters, enhanced DNA repair mechanisms and anti-apoptotic gene expression. These properties in CSCs constitute a key reason for the failure of standard oncology treatment regimens to ensure long-term benefit for most patients with advanced stage neoplasia because standard chemotherapy does not target the CSCs that actually fuel continued tumor growth and recurrence.

It has surprisingly been discovered that DLL3 expression is associated with various tumorigenic cell populations. The invention provides DLL3 CARs that may be particularly useful for targeting tumorigenic cells and may be used to silence, sensitize, neutralize, reduce the frequency, block, abrogate, interfere with, decrease, hinder, restrain, control, deplete, moderate, mediate, diminish, reprogram, eliminate, or otherwise inhibit (collectively, "inhibit") tumorigenic cells, thereby facilitating the treatment, management and/or prevention of proliferative disorders (e.g. cancer). Advantageously, the novel DLL3 CARs of the invention may be selected so they preferably reduce the frequency or tumorigenicity of tumorigenic cells upon administration to a subject regardless of the form of the DLL3 determinant (e.g., isotype a or b). The reduction in tumorigenic cell frequency may occur as a result of (i) inhibition or eradication of tumorigenic cells; (ii) controlling the growth, expansion or recurrence of tumorigenic cells; (iii) interrupting the initiation, propagation, maintenance, or proliferation of tumorigenic cells; or (iv) by otherwise hindering the survival, regeneration and/or metastasis of the tumorigenic cells. In some embodiments, the inhibition of tumorigenic cells may occur as a result of a change in one or more physiological pathways. The change in the pathway, whether by inhibition of the tumorigenic cells, modification of their potential (for example, by induced differentiation or niche disruption) or otherwise interfering with the ability of tumorigenic cells to influence the tumor environment or other cells, allows for the more effective treatment of DLL3 associated disorders by inhibiting tumorigenesis, tumor maintenance and/or metastasis and recurrence.

Methods that can be used to assess the reduction in the frequency of tumorigenic cells, include but are not limited to, cytometric or immunohistochemical analysis, preferably by *in vitro*

or *in vivo* limiting dilution analysis (Dylla *et al.* 2008, PMID: PMC2413402 and Hoey *et al.* 2009, PMID: 19664991).

Flow cytometry and immunohistochemistry may also be used to determine tumorigenic cell frequency. Both techniques employ one or more antibodies or reagents that bind art
5 recognized cell surface proteins or markers known to enrich for tumorigenic cells (see WO 2012/031280). As known in the art, flow cytometry (e.g. florescence activated cell sorting (FACS)) can also be used to characterize, isolate, purify, enrich or sort for various cell populations including tumorigenic cells. Flow cytometry measures tumorigenic cell levels by passing a stream of fluid, in which a mixed population of cells is suspended, through an
10 electronic detection apparatus which is able to measure the physical and/or chemical characteristics of up to thousands of particles per second. Immunohistochemistry provides additional information in that it enables visualization of tumorigenic cells *in situ* (e.g., in a tissue section) by staining the tissue sample with labeled antibodies or reagents which bind to tumorigenic cell markers.

15 Listed below are markers that have been associated with CSC populations and have been used to isolate or characterize CSCs: ABCA1, ABCA3, ABCG2, DLL3, ADCY9, ADORA2A, AFP, AXIN1, B7H3, BCL9, Bmi-1, BMP-4, C20orf52, C4.4A, carboxypeptidase M, CAV1, CAV2, CD105, CD133, CD14, CD16, CD166, CD16a, CD16b, CD2, CD20, CD24, CD29, CD3, CD31, CD324, CD325, CD34, CD38, CD44, CD45, CD46, CD49b, CD49f, CD56, CD64, CD74, CD9,
20 CD90, CEACAM6, CELSR1, CPD, CRIM1, CX3CL1, CXCR4, DAF, decorin, easyh1, easyh2, EDG3, eed, EGFR, ENPP1, EPCAM, EPHA1, EPHA2, FLJ10052, FLVCR, FZD1, FZD10, FZD2, FZD3, FZD4, FZD6, FZD7, FZD8, FZD9, GD2, GJA1, GLI1, GLI2, GPNMB, GPR54, GPRC5B, IL1R1, IL1RAP, JAM3, Lgr5, Lgr6, LRP3, LY6E, MCP, mf2, mlt3, MPZL1, MUC1, MUC16, MYC, N33, Nanog, NB84, nestin, NID2, NMA, NPC1, oncostatin M, OCT4, OPN3,
25 PCDH7, PCDHA10, PCDHB2, PPAP2C, PTPN3, PTS, RARRES1, SEMA4B, SLC19A2, SLC1A1, SLC39A1, SLC4A11, SLC6A14, SLC7A8, smarcA3, smarcD3, smarcE1, smarcA5, Sox1, STAT3, STEAP, TCF4, TEM8, TGFB3, TMEPAI, TMPRSS4, transferrin receptor, TrkA, WNT10B, WNT16, WNT2, WNT2B, WNT3, WNT5A, YY1 and β -catenin. See, for example, Schulenburg *et al.*, 2010, PMID: 20185329, U.S.P.N. 7,632,678 and U.S.P.N.s. 2007/0292414,
30 2008/0175870, 2010/0275280, 2010/0162416 and 2011/0020221.

Similarly, non-limiting examples of cell surface phenotypes associated with CSCs of certain tumor types include $CD44^{hi}CD24^{low}$, $ALDH^{+}$, $CD133^{+}$, $CD123^{+}$, $CD34^{+}CD38^{-}$, $CD44^{+}CD24^{-}$, $CD46^{hi}CD324^{+}CD66c^{-}$, $CD133^{+}CD34^{+}CD10^{-}CD19^{-}$, $CD138^{-}CD34^{-}CD19^{+}$,

CD133⁺RC2⁺, CD44⁺ $\alpha_2\beta_1$ ^{hi}CD133⁺, CD44⁺CD24⁺ESA⁺, CD271⁺, ABCB5⁺ as well as other CSC surface phenotypes that are known in the art. See, for example, Schulenburg *et al.*, 2010, supra, Visvader *et al.*, 2008, PMID: 18784658 and U.S.P.N. 2008/0138313. Of particular interest with respect to the instant invention are CSC preparations comprising CD46^{hi}CD324⁺ phenotypes.

“Positive,” “low” and “negative” expression levels as they apply to markers or marker phenotypes are defined as follows. Cells with negative expression (i.e. “-”) are herein defined as those cells expressing less than, or equal to, the 95th percentile of expression observed with an isotype control antibody in the channel of fluorescence in the presence of the complete antibody staining cocktail labeling for other proteins of interest in additional channels of fluorescence emission. Those skilled in the art will appreciate that this procedure for defining negative events is referred to as “fluorescence minus one”, or “FMO”, staining. Cells with expression greater than the 95th percentile of expression observed with an isotype control antibody using the FMO staining procedure described above are herein defined as “positive” (i.e. “+”). As defined herein there are various populations of cells broadly defined as “positive.” A cell is defined as positive if the mean observed expression of the antigen is above the 95th percentile determined using FMO staining with an isotype control antibody as described above. The positive cells may be termed cells with low expression (i.e. “lo”) if the mean observed expression is above the 95th percentile determined by FMO staining and is within one standard deviation of the 95th percentile. Alternatively, the positive cells may be termed cells with high expression (i.e. “hi”) if the mean observed expression is above the 95th percentile determined by FMO staining and greater than one standard deviation above the 95th percentile. In other embodiments the 99th percentile may preferably be used as a demarcation point between negative and positive FMO staining and in particularly preferred embodiments the percentile may be greater than 99%.

The CD46^{hi}CD324⁺marker phenotype and those exemplified immediately above may be used in conjunction with standard flow cytometric analysis and cell sorting techniques to characterize, isolate, purify or enrich TIC and/or TPC cells or cell populations for further analysis.

The ability of the CARs of the current invention to reduce the frequency of tumorigenic cells can therefore be determined using the techniques and markers described above. In some instances DLL3 CAR may reduce the frequency of tumorigenic cells by 10%, 15%, 20%, 25%, 30% or even by 35%. In other embodiments, the reduction in frequency of tumorigenic cells may be in the order of 40%, 45%, 50%, 55%, 60% or 65%. In certain embodiments, the disclosed

adoptive immunotherapy may reduce the frequency of tumorigenic cells by 70%, 75%, 80%, 85%, 90% or even 95%. It will be appreciated that any reduction of the frequency of tumorigenic cells is likely to result in a corresponding reduction in the tumorigenicity, persistence, recurrence and aggressiveness of the neoplasia.

5 III. Chimeric Antigen Receptor Therapy

Cancer immunotherapies aim to harness the power of the human immune system to eradicate tumors via the activity of cytotoxic lymphocytes (comprising both cytotoxic T-lymphocytes and NK cells). That cytotoxic lymphocyte-mediated immune responses could lead to the eradication of residual tumor cells was inferred from studies that compared relapse rates
10 in leukemia patients that had undergone various types of transplantation: a significant reduction in relapse rates was observed for patients receiving non-T-cell depleted marrow in allogeneic transplants from HLA identical siblings versus those receiving syngenic transplants, and this effect could be attributed to other T-cell mediated actions beyond graft-versus-host disease responses. However, clinically effective adoptive transfer of anti-tumor T-cells has been
15 hampered by the fact that most tumor antigens are self-antigens, and therefore are poorly immunogenic. More specifically negative selection of T-cells bearing high-affinity T-cell receptors (TCRs) recognizing self-antigens takes place in the thymus during development, resulting in central tolerance and selection for T-cells having low-avidity recognition of the tumor/self-antigen. These lower avidity T-cells then have consequent weak activation of anti-
20 tumor T-cell function and limited persistence. Genetically engineered cytotoxic lymphocytes are being deployed in two major approaches to circumvent this tolerance/low avidity block to strong anti-tumor T-cell activation. In the first approach, affinity-enhanced TCR recognizing tumor antigens are artificially introduced into T-cells using molecular genetic engineering techniques. This approach is limited by several factors, including difficulty in expressing the affinity-
25 enhanced TCR at levels approaching wild-type TCR expression, the potential for mispairing of TCR chains which arises when introducing additional sets of TCR genes into a native T-cell, and the ability of tumor cells to evade MHC-restricted TCR recognition by down-regulating MHC molecules.

A second approach to the genetic engineering of cytotoxic lymphocytes is introduction of
30 an artificial, non-MHC-restricted chimeric antigen receptor (CAR) into various lymphocyte populations. This is most typically achieved by harvesting bulk lymphocyte populations which are cultured, stimulated and expanded *ex vivo* prior to transduction with retroviral or lentiviral

vectors encoding the CAR molecule. Like a native TCR, the CAR must possess the ability to specifically and selectively recognize a target antigen, and then upon binding to this antigen, transduce the appropriate signals to the lymphocyte to stimulate effector functions and/or the cytokine production necessary for a sustained anti-tumor immunological response. The concept of CAR-modified T-cells arose from studies in which it was observed that the cytoplasmic ITAM domain of the CD3 ζ chain could activate T-cells when expressed independently from the TCR:CD3 protein complex, particularly when the CD3 ζ ITAM domain was fused to a heterologous extracellular and transmembrane domain. A first-generation CD4-CD3 ζ CAR was transduced into T-cells and tested in HIV patients. Follow up studies showed these engineered CAR-T cells persisted for up to a decade after infusion, indicative of some proliferation and persistence of the engineered cells. Subsequently, anti-tumor CARs were constructed by combining in a single recombinant molecule a scFv domain and a transmembrane domain with the cytoplasmic domain of the CD3 ζ chain, and it could be shown the antigen recognition of these engineered CAR-T cells was redirected to reflect the specificity of the scFv (U.S.P.N. 7,446,179). These first generation scFv-directed CAR-T cells were capable of acting as non-MHC restricted cytotoxic lymphocytes, recognizing native tumor antigen rather than processed peptides, and promoting lysis of tumor cells expressing the native antigen.

While many of the first generation scFv-directed CAR-T cells showed expected effects *in vitro*, *in vivo* studies in cancer patients were disappointing for their lack of anti-tumor effects and lack of CAR-T persistence. As T-cell biology has become better understood, it has become clear that T-cell populations are comprised of short lived effector cells, longer-lived central and peripheral memory T-cells, as well as regulatory T-cells (Tregs) that interact with the other T-cell subpopulations. Central to function of these populations are the role of costimulatory signals in inducing persistent activation of resting naïve or memory T-cells via cytokine production, as well as the role co-stimulation provides in preventing anergy, a state of T-cell non-responsiveness that may potentially arise from exclusive TCR:CD3 ζ signaling in the absence of costimulatory signals. In particular, various costimulatory signals from proteins such as CD28, OX40, CD27, CD137/4-1BB, CD2, CD3, CD11a/CD18, CD54 and CD58 may be beneficial for optimal levels of cytokine production, proliferation and clonal expansion, and induction of cytolytic activity. Of these, CD28 is perhaps the best understood costimulatory signal, and CD28 co-stimulation has been shown to augment cytokine release by antigen activated CAR-T cells. Similarly, costimulatory signaling through CD137/4-1BB has been shown to enhance native T-cell proliferation, and may contribute to longer persistence of CAR-T *in vivo*. Therefore, so called

second generation CAR constructs have been designed in which various additional signaling domains from these molecules have been added in tandem to the CD3 ζ domain (U.S.P.N.s. 5,686,281 and 8,399,645). So called third generation CAR molecules including three or more signaling domains (e.g., CD3 ζ and two costimulatory signaling domains) are also reportedly under development.

Several second generation CAR-T cells directed to the CD19 antigen have been shown to have strong antitumor effects, as well as substantial persistence, in patients with hematological malignancies. To date, the effectiveness of CAR-T therapies with respect to the treatment of solid tumors remains to be conclusively demonstrated. With respect to the instant invention it has surprisingly been discovered that anti-DLL3 binding domains may be advantageously integrated with each of the aforementioned chimeric antigen receptors and adoptive immunotherapies to provide effective antineoplastic treatments that overcome some of the previous limitations.

IV. Chimeric Antigen Receptors

As alluded to above the CARs of the instant invention generally comprise an extracellular domain comprising a DLL3 binding domain, a transmembrane domain and an intracellular signaling domain that activates certain lymphocytes and generates an immune response directed to DLL3 positive tumor cells. More generally, the disclosed chimeric antigen receptors comprise an ectodomain and an endodomain each as defined by the host cell wall. In this regard the terms "ectodomain" or "extracellular domain" will refer to the portion of the CAR polypeptide outside of the cell or exterior to the membranous lipid bilayer, which may comprise the antigen recognition (e.g., DLL3) binding domains, an optional hinge region, and any spacer domains exterior the to the amino acid residues physically spanning the membrane. Conversely the terms "endodomain" or "intracellular domain" will refer to the portion of the CAR polypeptide inside the cell or interior to the membranous lipid bilayer, which may comprise any spacer domains interior to the amino acid residues physically spanning the membrane, as well as the intracellular signaling domain.

A. DLL3 Binding Domains

1. Binding domain structure

As discussed extensively throughout the instant disclosure, chimeric antigen receptors

comprising an anti-DLL3 binding domain may advantageously be used to provide targeted therapies for various proliferative disorders. It will be appreciated that compatible anti-DLL3 binding domains may comprise anti-DLL3 antibodies or immunoreactive fragments or constructs or derivatives thereof. In certain embodiments intact antibodies or antibodies comprising at least some portion of the fc or constant domain comprise the DLL3 binding domain (see, for example, U.S.P.N. 2015/0139943). In other preferred embodiments, and as demonstrated in the Examples appended hereto, the anti-DLL3 binding domain may comprise a scFv derived from a monoclonal antibody (including humanized or CDR grafted monoclonal antibodies) that binds to DLL3. Compatible antibodies that may be used to provide DLL3 binding domains consistent with the instant invention are discussed in more detail immediately below. For the purposes of the instant application the terms "binding domain" and "antibody" may be used interchangeably unless otherwise contextually dictated.

Antibodies and variants and derivatives thereof, including accepted nomenclature and numbering systems, have been extensively described, for example, in Abbas *et al.* (2010), *Cellular and Molecular Immunology* (6th Ed.), W.B. Saunders Company; or Murphey *et al.* (2011), *Janeway's Immunobiology* (8th Ed.), Garland Science.

An "intact antibody" typically comprises a Y-shaped tetrameric protein comprising two heavy (H) and two light (L) polypeptide chains held together by covalent disulfide bonds and non-covalent interactions. Each light chain is composed of one variable domain (VL) and one constant domain (CL). Each heavy chain comprises one variable domain (VH) and a constant region, which in the case of IgG, IgA, and IgD antibodies, comprises three domains termed CH1, CH2, and CH3 (IgM and IgE have a fourth domain, CH4). In IgG, IgA, and IgD classes the CH1 and CH2 domains are separated by a flexible hinge region, which is a proline and cysteine rich segment of variable length (from about 10 to about 60 amino acids in various IgG subclasses). The variable domains in both the light and heavy chains are joined to the constant domains by a "J" region of about 12 or more amino acids and the heavy chain also has a "D" region of about 10 additional amino acids. Each class of antibody further comprises inter-chain and intra-chain disulfide bonds formed by paired cysteine residues.

As alluded to above the term "antibody" should be construed generally and includes polyclonal antibodies, monoclonal antibodies, chimeric antibodies, humanized and primatized antibodies, CDR grafted antibodies, human antibodies, recombinantly produced antibodies, intrabodies, multispecific antibodies, bispecific antibodies, monovalent antibodies, multivalent antibodies, anti-idiotypic antibodies, synthetic antibodies, including muteins and variants

thereof, immunospecific antibody fragments such as Fd, Fab, F(ab')₂, F(ab') fragments, single-chain fragments (e.g. scFv and ScFvFc); and derivatives thereof including Fc fusions and other modifications, and any other immunoreactive immunoglobulin molecule so long as it exhibits preferential association or binding with a DLL3 determinant. Moreover, unless dictated otherwise by contextual constraints the term further comprises all classes of antibodies (i.e. IgA, IgD, IgE, IgG, and IgM) and all subclasses (i.e., IgG1, IgG2, IgG3, IgG4, IgA1, and IgA2) and all immunoreactive fragments thereof. Heavy-chain constant domains that correspond to the different classes of antibodies are typically denoted by the corresponding lower case Greek letter α , δ , ϵ , γ , and μ , respectively. Light chains of the antibodies from any vertebrate species can be assigned to one of two clearly distinct types, called kappa (κ) and lambda (λ), based on the amino acid sequences of their constant domains. In short, any such antibody that binds to or associates with human DLL3 is compatible with the teachings herein and may be used as the binding domain component for the disclosed chimeric antigen receptors.

The variable domains of antibodies show considerable variation in amino acid composition from one antibody to another and are primarily responsible for antigen recognition and binding. Variable regions of each light/heavy chain pair form the antibody binding site such that an intact IgG antibody has two binding sites (i.e. it is bivalent). VH and VL domains comprise three regions of extreme variability, which are termed hypervariable regions, or more commonly, complementarity-determining regions (CDRs), framed and separated by four less variable regions known as framework regions (FRs). The non-covalent association between the VH and the VL region forms the Fv fragment (for "fragment variable") which contains one of the two antigen-binding sites of an intact antibody. Of particular interest scFv constructs (for single chain fragment variable), which can be obtained by genetic engineering as discussed more extensively below, join VH and the VL regions (preferably from the same antibody), though a peptide linker. Depending on the desired conformation it will be appreciated that the peptide linker may be of various lengths.

As used herein, the assignment of amino acids to each domain, framework region and CDR may be in accordance with one of the numbering schemes provided by Kabat *et al.* (1991) *Sequences of Proteins of Immunological Interest* (5th Ed.), US Dept. of Health and Human Services, PHS, NIH, NIH Publication no. 91-3242; Chothia *et al.*, 1987, PMID: 3681981; Chothia *et al.*, 1989, PMID: 2687698; MacCallum *et al.*, 1996, PMID: 8876650; or Dubel, Ed. (2007) *Handbook of Therapeutic Antibodies*, 3rd Ed., Wiley-VCH Verlag GmbH and Co or AbM (Oxford Molecular/MSI Pharmacopia) unless otherwise noted. The amino acid

residues which comprise CDRs as defined by Kabat, Chothia, MacCallum (also known as Contact) and AbM schemes, as obtained from the Abysis website database (infra.), are set out below.

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Table 1

	Kabat	Chothia	MacCallum	AbM
VH CDR1	31-35	26-32	30-35	26-35
VH CDR2	50-65	52-56	47-58	50-58
VH CDR3	95-102	95-102	93-101	95-102
VL CDR1	24-34	24-34	30-36	24-34
VL CDR2	50-56	50-56	46-55	50-56
VL CDR3	89-97	89-97	89-96	89-97

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Variable regions and CDRs in an antibody sequence can be identified according to general rules that have been developed in the art (as set out above, such as, for example, the Kabat numbering system) or by aligning the sequences against a database of known variable regions. Methods for identifying these regions are described in Kontermann and Dubel, eds., *Antibody Engineering*, Springer, New York, NY, 2001 and Dinarello *et al.*, *Current Protocols in Immunology*, John Wiley and Sons Inc., Hoboken, NJ, 2000. Exemplary databases of antibody sequences are described in, and can be accessed through, the "Abysis" website at www.bioinf.org.uk/abs (maintained by A.C. Martin in the Department of Biochemistry & Molecular Biology University College London, London, England) and the VBASE2 website at www.vbase2.org, as described in Retter *et al.*, *Nucl. Acids Res.*, 33 (Database issue): D671 - D674 (2005). Preferably antibody sequences are analyzed using the Abysis database, which integrates sequence data from Kabat, IMGT and the Protein Data Bank (PDB) with structural data from the PDB. See Dr. Andrew C. R. Martin's book chapter *Protein Sequence and Structure Analysis of Antibody Variable Domains*. In: *Antibody Engineering Lab Manual* (Ed.: Duebel, S. and Kontermann, R., Springer-Verlag, Heidelberg, ISBN-13: 978-3540413547, also available on the website bioinforg.uk/abs). The Abysis database website further includes general rules that have been developed for identifying CDRs which can be used in accordance

with the teachings herein. Unless otherwise indicated, all CDRs set forth herein are derived according to the Abysis database website as per Kabat *et al.*

For heavy chain constant region amino acid positions discussed in the invention, numbering is according to the Eu index first described in Edelman *et al.*, 1969, Proc. Natl. Acad. Sci. USA 63(1): 78-85 describing the amino acid sequence of myeloma protein Eu, which reportedly was the first human IgG1 sequenced. The EU index of Edelman is also set forth in Kabat *et al.*, 1991 (*supra.*). Thus, the terms "EU index as set forth in Kabat" or "EU index of Kabat" or "EU index" in the context of the heavy chain refers to the residue numbering system based on the human IgG1 Eu antibody of Edelman *et al.* as set forth in Kabat *et al.*, 1991 (*supra.*) The numbering system used for the light chain constant region amino acid sequence is similarly set forth in Kabat *et al.*, (*supra.*) An exemplary kappa light chain constant region amino acid sequence compatible with the present invention is set forth immediately below:

RTVAAPSVFIFPPSDEQLKSGTASVVCLLNFPREAKVQWKVDNALQSGNSQESVTEQDSK
DSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 5).

Similarly, an exemplary IgG1 heavy chain constant region amino acid sequence compatible with the present invention is set forth immediately below:

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL
YSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFL
FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVS
VLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTC
LVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPG (SEQ ID NO: 6).

The disclosed constant region sequences, or variations or derivatives thereof, may be operably associated with the disclosed heavy and light chain variable regions using standard molecular biology techniques to provide antibodies (full length or immunoreactive fragments comprising partial fc regions) that may be used as such or incorporated in DLL3 CARs of the invention (preferably as part of the transmembrane domain).

More generally, the anti-DLL3 binding domain component of compatible CARs may be generated from any antibody that specifically recognizes or associates with a DLL3

determinant. As used herein “determinant” or “target” means any detectable trait, property, marker or factor that is identifiably associated with, or specifically found in or on a particular cell, cell population or tissue. Determinants or targets may be morphological, functional or biochemical in nature and are preferably phenotypic. In certain preferred embodiments a determinant is a protein that is differentially expressed (over- or under-expressed) by specific cell types or by cells under certain conditions (e.g., during specific points of the cell cycle or cells in a particular niche). For the purposes of the instant invention a determinant preferably is differentially expressed on aberrant cancer cells and may comprise a DLL3 protein, or any of its splice variants, isoforms, homologs or family members, or specific domains, regions or epitopes thereof. An “antigen”, “immunogenic determinant”, “antigenic determinant” or “immunogen” means any protein or any fragment, region or domain thereof that can stimulate an immune response when introduced into an immunocompetent animal and is recognized by the antibodies produced from the immune response. The presence or absence of the DLL3 determinants contemplated herein may be used to identify a cell, cell subpopulation or tissue (e.g., tumors, tumorigenic cells or CSCs).

2. Antibody generation and production

Antibodies compatible with the invention can be produced using a variety of methods known in the art and any such antibodies may be further modified to provide the binding domain of the anti-DLL3 chimeric antigen receptors of the instant invention.

a. Generation of polyclonal antibodies in host animals

The production of polyclonal antibodies in various host animals is well known in the art (see for example, Harlow and Lane (Eds.) (1988) *Antibodies: A Laboratory Manual*, CSH Press; and Harlow *et al.* (1989) *Antibodies*, NY, Cold Spring Harbor Press). In order to generate polyclonal antibodies, an immunocompetent animal (e.g., mouse, rat, rabbit, goat, non-human primate, etc.) is immunized with an antigenic protein or cells or preparations comprising an antigenic protein. After a period of time, polyclonal antibody-containing serum is obtained by bleeding or sacrificing the animal. The serum may be used in the form obtained from the animal or the antibodies may be partially or fully purified to provide immunoglobulin fractions or isolated antibody preparations.

Any form of antigen, or cells or preparations containing the antigen, can be used to generate an antibody that is specific for a determinant. The term “antigen” is used in a broad

sense and may comprise any immunogenic fragment or determinant of the selected target including a single epitope, multiple epitopes, single or multiple domains or the entire extracellular domain (ECD). The antigen may be an isolated full-length protein, a cell surface protein (e.g., immunizing with cells expressing at least a portion of the antigen on their surface),
5 or a soluble protein (e.g., immunizing with only the ECD portion of the protein). The antigen may be produced in a genetically modified cell. Any of the aforementioned antigens may be used alone or in combination with one or more immunogenicity enhancing adjuvants known in the art. The DNA encoding the antigen may be genomic or non-genomic (e.g., cDNA) and may encode at least a portion of the ECD, sufficient to elicit an immunogenic response. Any vectors may be
10 employed to transform the cells in which the antigen is expressed, including but not limited to adenoviral vectors, lentiviral vectors, plasmids, and non-viral vectors, such as cationic lipids.

b. Monoclonal antibodies

In selected embodiments, the invention contemplates use of monoclonal antibodies. The term "monoclonal antibody" or "mAb" refers to an antibody obtained from a population of
15 substantially homogeneous antibodies, i.e., the individual antibodies comprising the population are identical except for possible mutations (e.g., naturally occurring mutations), that may be present in minor amounts.

Monoclonal antibodies can be prepared using a wide variety of techniques including hybridoma techniques, recombinant techniques, phage display technologies, transgenic animals
20 (e.g., a XenoMouse®) or some combination thereof. For example, in preferred embodiments monoclonal antibodies can be produced using hybridoma and biochemical and genetic engineering techniques such as described in more detail in An, Zhigiang (ed.) *Therapeutic Monoclonal Antibodies: From Bench to Clinic*, John Wiley and Sons, 1st ed. 2009; Shire et. al. (eds.) *Current Trends in Monoclonal Antibody Development and Manufacturing*, Springer
25 Science + Business Media LLC, 1st ed. 2010; Harlow et al., *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory Press, 2nd ed. 1988; Hammerling, et al., in: *Monoclonal Antibodies and T-Cell Hybridomas* 563-681 (Elsevier, N.Y., 1981). Following generation of a number of monoclonal antibodies that bind specifically to a determinant, particularly suitable antibodies may be selected through various screening processes, based on, for example,
30 affinity for the determinant or rate of internalization. In particularly preferred embodiments monoclonal antibodies produced as described herein may be used as "source" antibodies and further modified to provide effective DLL3 binding domains that may be associated with the

disclosed CARs. For example the source antibody may be manipulated to provide scFvs or other fragments, improve affinity for the target, improve its production in cell culture, reduce immunogenicity *in vivo*, create multispecific constructs, etc. A more detailed description of monoclonal antibody production and screening is set out below and in the appended Examples.

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c. Human antibodies

Antibodies compatible with the instant invention may comprise fully human antibodies. The term "human antibody" refers to an antibody (preferably a monoclonal antibody) which possesses an amino acid sequence that corresponds to that of an antibody produced by a human and/or has been made using any of the techniques for making human antibodies described below.

In one embodiment, recombinant human antibodies may be isolated by screening a recombinant combinatorial antibody library prepared using phage display. In one embodiment, the library is a scFv phage or yeast display library, generated using human VL and VH cDNAs prepared from mRNA isolated from B-cells.

Human antibodies can also be made by introducing human immunoglobulin loci into transgenic animals, e.g., mice in which the endogenous immunoglobulin genes have been partially or completely inactivated and human immunoglobulin genes have been introduced. Upon challenge antibody generation is observed which closely resembles that seen in humans in all respects, including gene rearrangement, assembly and fully human antibody repertoire. This approach is described, for example, in U.S.P.Ns. 5,545,807; 5,545,806; 5,569,825; 5,625,126; 5,633,425; 5,661,016, and U.S.P.Ns. 6,075,181 and 6,150,584 regarding XenoMouse[®] technology; and Lonberg and Huszar, 1995, PMID: 7494109). Alternatively, a human antibody may be prepared via immortalization of human B lymphocytes producing an antibody directed against a target antigen (such B lymphocytes may be recovered from an individual suffering from a neoplastic disorder or may have been immunized *in vitro*). See, e.g., Cole *et al.*, *Monoclonal Antibodies and Cancer Therapy*, Alan R. Liss, p. 77 (1985); Boerner *et al.*, 1991, PMID: 2051030; and U.S.P.N. 5,750,373. As with other monoclonal antibodies such human antibodies may be used as source antibodies.

d. Antibody production and engineering

Antibodies and fragments thereof may be produced or modified using genetic material

obtained from antibody producing cells and recombinant technology (see, for example, Berger and Kimmel, Guide to Molecular Cloning Techniques, *Methods in Enzymology* vol. 152 Academic Press, Inc., San Diego, CA; Sambrook and Russell (Eds.) (2000) *Molecular Cloning: A Laboratory Manual* (3rd Ed.), NY, Cold Spring Harbor Laboratory Press; Ausubel *et al.* (2002) *Short Protocols in Molecular Biology: A Compendium of Methods from Current Protocols in Molecular Biology*, Wiley, John & Sons, Inc.; and U.S.P.N. 7,709,611).

As will be discussed in more detail below another aspect of the invention pertains to nucleic acid molecules that encode the DLL3 binding domains and CARs of the invention. The nucleic acids may be present in whole cells, in a cell lysate, or in a partially purified or substantially pure form. A nucleic acid is "isolated" or rendered substantially pure when separated from other cellular components or other contaminants, e.g., other cellular nucleic acids or proteins, by standard techniques, including alkaline/SDS treatment, CsCl banding, column chromatography, agarose gel electrophoresis and others well known in the art. A nucleic acid of the invention can be, for example, DNA (e.g. genomic DNA, cDNA), RNA and artificial variants thereof (e.g., peptide nucleic acids), whether single-stranded or double-stranded or RNA, RNA and may or may not contain introns. In a preferred embodiment, the nucleic acid is a cDNA molecule.

Nucleic acids of the invention can be obtained and manipulated using standard molecular biology techniques. For antibodies expressed by hybridomas (e.g., hybridomas prepared as set forth in the Examples below), cDNAs encoding the light and heavy chains of the antibody can be obtained by standard PCR amplification or cDNA cloning techniques. For antibodies obtained from an immunoglobulin gene library (e.g., using phage display techniques), nucleic acid encoding the antibody can be recovered from the library.

DNA fragments encoding VH and VL segments can be further manipulated by standard recombinant DNA techniques, for example to convert the variable region genes to full-length antibody chain genes, to Fab fragment genes or preferably to a nucleotide sequence encoding a DLL3 specific scFv. In these manipulations, a VL- or VH-encoding DNA fragment is operatively linked to another DNA fragment encoding another protein, such as an antibody constant region or a flexible linker. The term "operatively linked" or "operably linked", as used in this context, means that the two DNA fragments are joined such that the amino acid sequences encoded by the two DNA fragments remain in-frame.

The isolated DNA encoding the VH region can be converted to a full-length heavy chain gene by operatively linking the VH-encoding DNA to another DNA molecule encoding heavy

chain constant regions (CH1, CH2 and CH3). The sequences of human heavy chain constant region genes are known in the art (see e.g., Kabat, et al. (1991) (*supra*)) and DNA fragments encompassing these regions can be obtained by standard PCR amplification. The heavy chain constant region can be an IgG1, IgG2, IgG3, IgG4, IgA, IgE, IgM or IgD constant region, but
5 most preferably is an IgG1 or IgG4 constant region. An exemplary IgG1 constant region is set forth in SEQ ID NO: 6. For a Fab fragment heavy chain gene, the VH-encoding DNA can be operatively linked to another DNA molecule encoding only the heavy chain CH1 constant region.

The isolated DNA encoding the VL region can be converted to a full-length light chain
10 gene (as well as a Fab light chain gene) by operatively linking the VL-encoding DNA to another DNA molecule encoding the light chain constant region, CL. The sequences of human light chain constant region genes are known in the art (see e.g., Kabat, et al. (1991) (*supra*)) and DNA fragments encompassing these regions can be obtained by standard PCR amplification. The light chain constant region can be a kappa or lambda constant region, but most preferably
15 is a kappa constant region. In this respect an exemplary compatible kappa light chain constant region is set forth in SEQ ID NO: 5.

Contemplated herein are certain polypeptides (e.g. antibody variable regions) that exhibit "sequence identity", sequence similarity" or "sequence homology" to the polypeptides of the invention. A "homologous" polypeptide may exhibit 65%, 70%, 75%, 80%, 85%, or 90%
20 sequence identity. In other embodiments a "homologous" polypeptides may exhibit 93%, 95% or 98% sequence identity. As used herein, the percent homology between two amino acid sequences is equivalent to the percent identity between the two sequences. The percent identity between the two sequences is a function of the number of identical positions shared by the sequences (i.e., % homology= # of identical positions/total # of positions×100), taking into
25 account the number of gaps, and the length of each gap, which need to be introduced for optimal alignment of the two sequences. The comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm, as described in the non-limiting examples below.

The percent identity between two amino acid sequences can be determined using the
30 algorithm of E. Meyers and W. Miller (*Comput. Appl. Biosci.*,4:11-17 (1988)) which has been incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4. In addition, the percent identity between two amino acid sequences can be determined using the Needleman and Wunsch (*J. Mol. Biol.* 48:444-453

(1970)) algorithm which has been incorporated into the GAP program in the GCG software package (available at www.gcg.com), using either a Blossum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6.

Additionally or alternatively, the protein sequences of the present invention can further be used as a “query sequence” to perform a search against public databases to, for example, identify related sequences. Such searches can be performed using the XBLAST program (version 2.0) of Altschul, et al. (1990) *J. Mol. Biol.* 215:403-10. BLAST protein searches can be performed with the XBLAST program, score=50, wordlength=3 to obtain amino acid sequences homologous to the antibody molecules of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al., (1997) *Nucleic Acids Res.* 25(17):3389-3402. When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) can be used.

Residue positions which are not identical may differ by conservative amino acid substitutions or by non-conservative amino acid substitutions. A “conservative amino acid substitution” is one in which an amino acid residue is substituted by another amino acid residue having a side chain with similar chemical properties (e.g., charge or hydrophobicity). In general, a conservative amino acid substitution will not substantially change the functional properties of a protein. In cases where two or more amino acid sequences differ from each other by conservative substitutions, the percent sequence identity or degree of similarity may be adjusted upwards to correct for the conservative nature of the substitution. In cases where there is a substitution with a non-conservative amino acid, in preferred embodiments the polypeptide exhibiting sequence identity will retain the desired function or activity of the polypeptide of the invention (e.g., antibody.)

Also contemplated herein are nucleic acids that that exhibit “sequence identity”, sequence similarity” or “sequence homology” to the nucleic acids of the invention. A “homologous sequence” means a sequence of nucleic acid molecules exhibiting at least about 65%, 70%, 75%, 80%, 85%, or 90% sequence identity. In other embodiments, a “homologous sequence” of nucleic acids may exhibit 93%, 95% or 98% sequence identity to the reference nucleic acid cells or CSCs).

3. Derived antibodies as DLL3 binding domains

Once the source antibodies have been generated, selected and isolated as described above, they may be further altered to provide anti-DLL3 CAR binding domain components compatible with the teachings herein. Preferably the source antibodies are modified or altered using known molecular engineering techniques to provide derived binding domain components having the desired therapeutic properties.

a. Chimeric and humanized antibodies

As discussed above selected embodiments of the invention comprise murine monoclonal antibodies that immunospecifically bind to DLL3 and, for the purposes of the instant disclosure, may be considered "source" antibodies for DLL3 binding domains. In selected embodiments, DLL3 binding domains compatible with the invention can be derived from such source antibodies through optional modification of the constant region and/or the antigen binding amino acid sequences of the source antibody. In certain embodiments an antibody is derived from a source antibody if selected amino acids in the source antibody are altered through deletion, mutation, substitution, integration or combination. In another embodiment, a "derived" antibody is one in which fragments of the source antibody (e.g., one or more CDRs or the entire heavy and light chain variable regions) are combined with or incorporated into an acceptor binding domain construct to provide the derivative DLL3 binding domain (e.g. chimeric or humanized binding domains). These derived binding domains can be generated using standard molecular biological techniques as described below, such as, for example, to provide an scFv; to improve affinity for the determinant; to improve antibody stability; to improve expression; to reduce immunogenicity *in vivo*; to reduce toxicity or to facilitate transmission of a signal. Such antibodies may also be derived from source antibodies through modification of the mature molecule (e.g., glycosylation patterns or pegylation) by chemical means or post-translational modification.

In one embodiment, the chimeric binding regions of the invention are derived from protein segments from at least two different species or class of antibodies that have been covalently joined. The term "chimeric" antibody is directed to constructs in which a portion of the heavy and/or light chain is identical or homologous to corresponding sequences in antibodies from a particular species or belonging to a particular antibody class or subclass, while the remainder of the chain(s) is identical or homologous to corresponding sequences in antibodies from another species or belonging to another antibody class or subclass, as well as fragments of such

antibodies (U.S. P.N. 4,816,567; Morrison *et al.*, 1984, PMID: 6436822). In some preferred embodiments chimeric antibodies of the instant invention may comprise all or most of the selected murine heavy and light chain variable regions operably linked to all or part of human light and heavy chain constant regions. In other particularly preferred embodiments, DLL3
5 binding domains may be “derived” from the mouse antibodies disclosed herein.

In other embodiments, the chimeric binding domains of the invention are “CDR grafted” where the CDRs (as defined using Kabat, Chothia, McCallum, etc.) are derived from a particular species or belonging to a particular antibody class or subclass, while the remainder of the binding region is derived from an antibody from another species or belonging to another
10 antibody class or subclass. For use in humans, one or more selected rodent CDRs (e.g., mouse CDRs) may be grafted into a human acceptor binding domain (i.e., with human framework regions), replacing one or more of the naturally occurring CDRs of the human antibody. These constructs generally have the advantages of providing effective binding while reducing unwanted immune responses to the binding domain by the subject. In particularly preferred
15 embodiments the CDR grafted binding domains will comprise one or more CDRs obtained from a mouse incorporated in a human framework sequence.

Similar to the CDR-grafted binding domain is a “humanized” binding domain. As used herein, a “humanized” binding domain is a human binding domain (acceptor domain generally comprising human framework regions) comprising one or more amino acid sequences (e.g.
20 CDR sequences) derived from one or more non-human antibodies (a donor or source antibody). In certain embodiments, “back mutations” can be introduced into the humanized binding domain, in which residues in one or more FRs of the variable region of the recipient human binding domain are replaced by corresponding residues from the non-human species donor antibody. Such back mutations may to help maintain the appropriate three-dimensional
25 configuration of the grafted CDR(s) and thereby improve affinity and binding domain stability. Antibodies from various donor species may be used including, without limitation, mouse, rat, rabbit, or non-human primate. Furthermore, humanized antibodies or fragments may comprise new residues that are not found in the recipient antibody or in the donor antibody to, for example, further refine antibody performance. CDR grafted and humanized antibodies (and
30 related DLL3 binding domains) compatible with the instant invention and comprising the source murine antibodies set forth in the Examples below may therefor readily be provided without undue experimentation using the prior art techniques as set forth herein.

Various art-recognized techniques can further be used to determine which human sequences to use as acceptor antibodies to provide humanized constructs in accordance with the instant invention. Compilations of compatible human germline sequences and methods of determining their suitability as acceptor sequences are disclosed, for example, in Tomlinson, I. A. *et al.* (1992) *J. Mol. Biol.* 227:776-798; Cook, G. P. *et al.* (1995) *Immunol. Today* 16: 237-242; Chothia, D. *et al.* (1992) *J. Mol. Biol.* 227:799-817; and Tomlinson *et al.* (1995) *EMBO J* 14:4628-4638 each of which is incorporated herein in its entirety. The V-BASE directory (VBASE2 – Retter *et al.*, *Nucleic Acid Res.* 33; 671-674, 2005) which provides a comprehensive directory of human immunoglobulin variable region sequences (compiled by Tomlinson, I. A. *et al.* MRC Centre for Protein Engineering, Cambridge, UK) may also be used to identify compatible acceptor sequences. Additionally, consensus human framework sequences described, for example, in U.S.P.N. 6,300,064 may also prove to be compatible acceptor sequences and can be used in accordance with the instant teachings. In general, human framework acceptor sequences are selected based on homology with the murine source framework sequences along with an analysis of the CDR canonical structures of the source and acceptor antibodies. The derived sequences of the heavy and light chain variable regions of the derived antibody (or binding domain) may then be synthesized using art recognized techniques.

By way of example CDR grafted and humanized antibodies, and associated methods, are described in U.S.P.Ns. 6,180,370 and 5,693,762. For further details, see, e.g., Jones *et al.*, 1986, PMID: 3713831; and U.S.P.Ns. 6,982,321 and 7,087,409.

The sequence identity or homology of the CDR grafted or humanized antibody variable region to the human acceptor variable region may be determined as discussed herein and, when measured as such, will preferably share at least 60% or 65% sequence identity, more preferably at least 70%, 75%, 80%, 85%, or 90% sequence identity, even more preferably at least 93%, 95%, 98% or 99% sequence identity. Preferably, residue positions which are not identical differ by conservative amino acid substitutions. A “conservative amino acid substitution” is one in which an amino acid residue is substituted by another amino acid residue having a side chain (R group) with similar chemical properties (e.g., charge or hydrophobicity). In general, a conservative amino acid substitution will not substantially change the functional properties of a protein. In cases where two or more amino acid sequences differ from each other by conservative substitutions, the percent sequence identity or degree of similarity may be adjusted upwards to correct for the conservative nature of the substitution.

It will be appreciated that the annotated CDRs and framework sequences as provided in the appended FIGS. 1A and 1B are defined as per Kabat et al. using a proprietary Abysis database. However, as discussed herein one skilled in the art could readily identify CDRs in accordance with definitions provided by Chothia et al., ABM or MacCallum et al as well as Kabat et al. As such, anti-DLL3 humanized antibodies comprising one or more CDRs derived according to any of the aforementioned systems are explicitly held to be within the scope of the instant invention.

b. Antibody fragments, derivatives or constructs

In particularly preferred embodiments the DLL3 binding domain will comprise an antibody fragment, derivative or construct. More particularly, regardless of which form of antibody (e.g. chimeric, humanized, etc.) is selected to practice the invention it will be appreciated that immunoreactive fragments of the same may be used, as part of a DLL3 CAR, in accordance with the teachings herein. In a broad sense an "antibody fragment" comprises at least an immunoreactive portion of an intact antibody. That is, as used herein, the term "antibody fragment" includes at least an antigen-binding fragment or portion of an intact antibody and the term "antigen-binding fragment" refers to a polypeptide fragment of an immunoglobulin or antibody that immunospecifically binds or reacts with an immunogenic determinant of DLL3 or competes with the intact antibody from which the fragments were derived for specific antigen binding. Moreover, for the purposes of the instant invention an "antibody construct" or "antibody derivative" shall be held to mean any molecular structure comprising an antibody fragment. Preferably such derivatives or constructs shall be non-natural and will be fabricated to impart beneficial molecular properties while maintaining the immunoreactive (or immunospecific) nature of the antibody.

Exemplary compatible antibody fragments, constructs or derivatives include: variable light chain fragments (VL), variable heavy chain fragments (VH), scFv, F(ab')₂ fragment, Fab fragment, Fd fragment, Fv fragment, single domain antibody fragments, diabodies, linear antibodies, single-chain antibody molecules and multispecific antibodies formed or derived from antibody fragments. In other embodiments the DLL3 binding domain of the instant invention may comprise an intact antibody, a scFv-Fc construct, a minibody, a diabody, a scFv construct, a Fab-scFv₂ construct, a Fab-scFv construct or a peptibody. In certain aspects the DLL3 binding domain will be covalently linked (e.g., by using art-recognized genetic engineering techniques) to the transmembrane and intracellular domains of the CAR. In other embodiments

the DLL3 binding domain may be non-covalently linked (e.g., via an Fc portion of the binding domain as set forth in U.S.P.N. 2015/0139943) to the transmembrane and intracellular domains of the CAR. Each form of binding domain attachment is compatible with the instant invention as long as the sensitized lymphocytes are able to induce the desired immune response.

5 In particularly preferred embodiments, and as shown in the appended Examples, the DLL3 binding domain will comprise a scFv construct. As used herein, a “single chain variable fragment (scFv)” means a single chain polypeptide derived from an antibody which retains the ability to bind to an antigen. An example of the scFv includes an antibody polypeptide which is formed by a recombinant DNA technique and in which Fv regions of immunoglobulin heavy chain and light chain fragments are linked via a spacer sequence. Various methods for preparing an scFv are known, and include methods described in U.S.P.N. 4,694,778.

10 In other embodiments, the DLL3 binding domain is one that comprises an Fc region and that retains at least one of the biological functions normally associated with the Fc region when present in an intact antibody, such as FcRn binding, antibody half-life modulation, ADCC function and complement binding. In one embodiment, an antibody fragment is a monovalent antibody that has an *in vivo* half-life substantially similar to an intact antibody. For example, such a binding domain may comprise an immunoreactive region linked to an Fc sequence comprising at least one free cysteine capable of conferring *in vivo* stability to the fragment. In other embodiments the Fc region may be modified using art-recognized techniques to modify the pharmacokinetics or pharmacodynamics of the disclosed CARs and sensitized lymphocytes.

20 Where the DLL3 binding domain comprises an Fc portion it may be non-covalently linked or joined with the remaining portions of the CAR via an extracellular Fc receptor or binding molecule (“Fc binder”) that is operably associated with the transmembrane and intracellular domains. As used herein the term “Fc binder” is held to mean any molecule or portion thereof that binds to, or associates with, the Fc portion of an antibody (e.g., an Fc receptor). Such constructs (i.e., a “proto-CAR” comprising an Fc binder, transmembrane domain and intracellular signaling domain) may be fabricated using standard molecular biology techniques and associated with the selected lymphocytes (autologous or allogeneic) as described herein (e.g., via transduction) to generate “primed lymphocytes”. At some point prior to introduction into the patient, the primed lymphocytes may then be exposed to selected DLL3 binding domain(s) comprising at least an Fc portion under conditions that allow association of the DLL3 binding domain(s) with the proto-CAR. The non-covalent association of the binding domain with the proto-CAR provide the DLL3 sensitized lymphocytes of the instant invention and may be

used to inhibit tumorigenic cell proliferation as described herein (see generally U.S.P.N. 2015/0139943 which is incorporated herein in its entirety).

In those embodiments comprising a proto-CAR the Fc binder may comprise an Fc receptor such as an Fc-gamma receptor, an Fc-alpha receptor or an Fc-epsilon receptor. In certain selected embodiments the Fc receptor may comprise the ligand binding domain of CD16 (e.g., CD16A or CD16B), CD32 (e.g., CD32A or CD32B) or CD64 (e.g., CD64A, CD64B or CD64C). In certain other embodiments the Fc binder will not be an Fc receptor. For example the Fc binder may comprise all or part of protein A or protein G as long as the proto-CAR has the ability to associate with the DLL3 binding domain. In other embodiments the Fc binder may comprise an immunoreactive antibody or fragment or construct or derivative thereof that binds the Fc portion of an immunoglobulin. As to such embodiments the Fc binder may, for example comprise an scFv, a nanobody or a minibody. Similarly DLL3 binding domains compatible with such embodiments include any molecule that is capable of being bound by the Fc binder and immunospecifically reacting with DLL3. In some embodiments the DLL3 binding domain will comprise intact DLL3 monoclonal antibodies or mixtures of intact DLL3 monoclonal antibodies. In other embodiments the DLL3 binding domain may comprise intact polyclonal DLL3 antibodies (preferably fully human). In yet other embodiments the DLL3 binding domain may comprise a scFv-Fc construct. More generally, those of skill in the art will readily be able to identify proto-CAR compatible DLL3 binding regions based on the teachings of the instant disclosure.

Moreover, as would be readily recognized by those skilled in the art, the disclosed fragments, construct or derivatives can be obtained by molecular engineering or via chemical or enzymatic treatment (such as papain or pepsin) of an intact or complete antibody or antibody chain or by recombinant means. See, e.g., Fundamental Immunology, W. E. Paul, ed., Raven Press, N.Y. (1999), for a more detailed description of antibody fragments.

c. Post-production selection

No matter how obtained, antibody-producing cells (e.g., hybridomas, yeast colonies, etc.) may be selected, cloned and further screened for desirable characteristics including, for example, high affinity for DLL3. Hybridomas can be expanded *in vitro* in cell culture or *in vivo* in syngeneic immunocompromised animals. Methods of selecting, cloning and expanding hybridomas and/or colonies are well known to those of ordinary skill in the art. Once the desired antibodies are identified the relevant genetic material may be isolated, manipulated and expressed using common, art-recognized molecular biology and biochemical techniques.

The antibodies produced by naïve libraries (either natural or synthetic) may be of moderate affinity (K_a of about 10^6 to 10^7 M^{-1}). To enhance affinity, affinity maturation may be mimicked *in vitro* by constructing antibody libraries (e.g., by introducing random mutations *in vitro* by using error-prone polymerase) and reselecting antibodies with high affinity for the antigen from those secondary libraries (e.g. by using phage or yeast display). WO 9607754 describes a method for inducing mutagenesis in a CDR of an immunoglobulin light chain to create a library of light chain genes.

Various techniques can be used to select antibodies, including but not limited to, phage or yeast display in which a library of human combinatorial antibodies or scFv fragments is synthesized on phages or yeast, the library is screened with the antigen of interest or an antibody-binding portion thereof, and the phage or yeast that binds the antigen is isolated, from which one may obtain the antibodies or immunoreactive fragments (Vaughan *et al.*, 1996, PMID: 9630891; Sheets *et al.*, 1998, PMID: 9600934; Boder *et al.*, 1997, PMID: 9181578; Pepper *et al.*, 2008, PMID: 18336206). Kits for generating phage or yeast display libraries are commercially available. There also are other methods and reagents that can be used in generating and screening antibody display libraries (see U.S.P.N. 5,223,409; WO 92/18619, WO 91/17271, WO 92/20791, WO 92/15679, WO 93/01288, WO 92/01047, WO 92/09690; and Barbas *et al.*, 1991, PMID: 1896445). Such techniques advantageously allow for the screening of large numbers of candidate antibodies and provide for relatively easy manipulation of sequences (e.g., by recombinant shuffling).

4. Characteristics of DLL3 binding domains

In selected embodiments, antibody-producing cells (e.g., hybridomas or yeast colonies) may be selected, cloned and further screened for favorable properties including, for example, robust growth, high antibody production and, as discussed in more detail below, desirable binding domain characteristics. In other cases characteristics of the antibody may be imparted by selecting a particular antigen (e.g., a specific DLL3 domain) or immunoreactive fragment of the target antigen for inoculation of the animal. In still other embodiments the selected antibodies may be engineered as described above to enhance or refine immunochemical characteristics such as affinity or pharmacokinetics fragments.

a. Binding domain affinity

Disclosed herein are antibodies that have a high binding affinity for a specific determinant

e.g. DLL3. The terms "immunospecifically binds" "specific binding," "selective binding," "selectively binds," and "specifically binds," refer to antibody binding to an epitope on a predetermined antigen. Typically, the antibody binds with an affinity (K_D) of approximately less than 10^{-7} M, such as approximately less than 10^{-8} M, 10^{-9} M or 10^{-10} M or even lower. The term
 5 "K_D" refers to the dissociation constant or apparent affinity of a particular antibody-antigen interaction.

More specifically an antibody of the invention can immunospecifically bind its target antigen when the dissociation constant K_D (k_{off}/k_{on}) is $\leq 10^{-7}$ M. The antibody specifically binds antigen with high affinity when the K_D is $\leq 5 \times 10^{-9}$ M, and with very high affinity when the K_D is $\leq 5 \times 10^{-10}$ M. In one embodiment of the invention, the antibody has a K_D of $\leq 10^{-9}$ M and an off-rate of about 1×10^{-4} /sec. In one embodiment of the invention, the off-rate is $< 1 \times 10^{-5}$ /sec. In other
 10 embodiments of the invention, the antibodies will bind to a determinant with a K_D of between about 10^{-7} M and 10^{-10} M, and in yet another embodiment it will bind with a $K_D \leq 2 \times 10^{-10}$ M. Still other selected embodiments of the invention comprise antibodies that have a K_D (k_{off}/k_{on}) of less
 15 than 10^{-6} M, less than 5×10^{-6} M, less than 10^{-7} M, less than 5×10^{-7} M, less than 10^{-8} M, less than 5×10^{-8} M, less than 10^{-9} M, less than 5×10^{-9} M, less than 10^{-10} M, less than 5×10^{-10} M, less than 10^{-11} M, less than 5×10^{-11} M, less than 10^{-12} M, less than 5×10^{-12} M, less than 10^{-13} M, less than 5×10^{-13} M, less than 10^{-14} M, less than 5×10^{-14} M, less than 10^{-15} M or less than 5×10^{-15} M.

In certain embodiments, an antibody of the invention that immunospecifically binds to a
 20 determinant e.g. DLL3 may have an association rate constant or k_{on} (or k_a) rate (antibody + antigen (Ag) $^k_{on} \leftarrow$ antibody-Ag) of at least 10^5 M⁻¹s⁻¹, at least 2×10^5 M⁻¹s⁻¹, at least 5×10^5 M⁻¹s⁻¹, at least 10^6 M⁻¹s⁻¹, at least 5×10^6 M⁻¹s⁻¹, at least 10^7 M⁻¹s⁻¹, at least 5×10^7 M⁻¹s⁻¹, or at least 10^8 M⁻¹s⁻¹.

In another embodiment, an antibody of the invention that immunospecifically binds to a
 25 determinant e.g. DLL3 may have a disassociation rate constant or k_{off} (or k_d) rate (antibody + antigen (Ag) $^k_{off} \leftarrow$ antibody-Ag) of less than 10^{-1} s⁻¹, less than 5×10^{-1} s⁻¹, less than 10^{-2} s⁻¹, less than 5×10^{-2} s⁻¹, less than 10^{-3} s⁻¹, less than 5×10^{-3} s⁻¹, less than 10^{-4} s⁻¹, less than 5×10^{-4} s⁻¹, less than 10^{-5} s⁻¹, less than 5×10^{-5} s⁻¹, less than 10^{-6} s⁻¹, less than 5×10^{-6} s⁻¹, less than 10^{-7} s⁻¹, less than 5×10^{-7} s⁻¹, less than 10^{-8} s⁻¹, less than 5×10^{-8} s⁻¹, less than 10^{-9} s⁻¹, less than 5×10^{-9} s⁻¹ or less than 10^{-10} s⁻¹.

Binding affinity may be determined using various techniques known in the art, for
 30 example, surface plasmon resonance, bio-layer interferometry, dual polarization interferometry, static light scattering, dynamic light scattering, isothermal titration calorimetry, ELISA, analytical ultracentrifugation, and flow cytometry.

b. Binning and epitope mapping

As used herein, the term “binning” refers to methods used to group antibodies (or binding domains) into “bins” based on their antigen binding characteristics and whether they compete with each other. The initial determination of bins may be further refined and confirmed by epitope mapping and other techniques as described herein. However it will be appreciated that empirical assignment of antibodies to individual bins provides information that may be indicative of the therapeutic potential of the disclosed antibodies.

More specifically, one can determine whether a selected reference antibody (or fragment thereof) competes for binding with a second test antibody (i.e., is in the same bin) by using methods known in the art and set forth in the Examples herein. In one embodiment, a reference antibody is associated with DLL3 antigen under saturating conditions and then the ability of a secondary or test antibody to bind to DLL3 is determined using standard immunochemical techniques. If the test antibody is able to substantially bind to DLL3 at the same time as the reference anti-DLL3 antibody, then the secondary or test antibody binds to a different epitope than the primary or reference antibody. However, if the test antibody is not able to substantially bind to DLL3 at the same time, then the test antibody binds to the same epitope, an overlapping epitope, or an epitope that is in close proximity (at least sterically) to the epitope bound by the primary antibody. That is, the test antibody competes for antigen binding and is in the same bin as the reference antibody.

The term “compete” or “competing antibody” when used in the context of the disclosed antibodies means competition between antibodies as determined by an assay in which a test antibody or immunologically functional fragment being tested inhibits specific binding of a reference antibody to a common antigen. Typically, such an assay involves the use of purified antigen (e.g., DLL3 or a domain or fragment thereof) bound to a solid surface or cells, an unlabeled test antibody and a labeled reference antibody. Competitive inhibition is measured by determining the amount of label bound to the solid surface or cells in the presence of the test antibody. Usually the test antibody is present in excess and/or allowed to bind first. Additional details regarding methods for determining competitive binding are provided in the Examples herein. Usually, when a competing antibody is present in excess, it will inhibit specific binding of a reference antibody to a common antigen by at least 30%, 40%, 45%, 50%, 55%, 60%, 65%, 70% or 75%. In some instance, binding is inhibited by at least 80%, 85%, 90%, 95%, or 97% or more.

Conversely, when the reference antibody is bound it will preferably inhibit binding of a

subsequently added test antibody (i.e., a DLL3 antibody) by at least 30%, 40%, 45%, 50%, 55%, 60%, 65%, 70% or 75%. In some instance, binding of the test antibody is inhibited by at least 80%, 85%, 90%, 95%, or 97% or more.

Generally binning or competitive binding may be determined using various art-recognized techniques, such as, for example, immunoassays such as western blots, radioimmunoassays, enzyme linked immunosorbent assay (ELISA), “sandwich” immunoassays, immunoprecipitation assays, precipitin reactions, gel diffusion precipitin reactions, immunodiffusion assays, agglutination assays, complement-fixation assays, immunoradiometric assays, fluorescent immunoassays and protein A immunoassays. Such immunoassays are routine and well known in the art (see, Ausubel et al, eds, (1994) *Current Protocols in Molecular Biology*, Vol. 1, John Wiley & Sons, Inc., New York). Additionally, cross-blocking assays may be used (see, for example, WO 2003/48731; and Harlow *et al.* (1988) *Antibodies, A Laboratory Manual*, Cold Spring Harbor Laboratory, Ed Harlow and David Lane).

Other technologies used to determine competitive inhibition (and hence “bins”), include: surface plasmon resonance using, for example, the BIAcore™ 2000 system (GE Healthcare); bio-layer interferometry using, for example, a ForteBio® Octet RED (ForteBio); or flow cytometry bead arrays using, for example, a FACSCanto II (BD Biosciences) or a multiplex LUMINEX™ detection assay (Luminex).

Luminex is a bead-based immunoassay platform that enables large scale multiplexed antibody pairing. The assay compares the simultaneous binding patterns of antibody pairs to the target antigen. One antibody of the pair (capture mAb) is bound to Luminex beads, wherein each capture mAb is bound to a bead of a different color. The other antibody (detector mAb) is bound to a fluorescent signal (e.g. phycoerythrin (PE)). The assay analyzes the simultaneous binding (pairing) of antibodies to an antigen and groups together antibodies with similar pairing profiles. Similar profiles of a detector mAb and a capture mAb indicates that the two antibodies bind to the same or closely related epitopes. In one embodiment, pairing profiles can be determined using Pearson correlation coefficients to identify the antibodies which most closely correlate to any particular antibody on the panel of antibodies that are tested. In preferred embodiments a test/detector mAb will be determined to be in the same bin as a reference/capture mAb if the Pearson’s correlation coefficient of the antibody pair is at least 0.9. In other embodiments the Pearson’s correlation coefficient is at least 0.8, 0.85, 0.87 or 0.89. In further embodiments, the Pearson’s correlation coefficient is at least 0.91, 0.92, 0.93, 0.94, 0.95, 0.96, 0.97, 0.98, 0.99 or 1. Other methods of analyzing the data obtained from the

Luminex assay are described in U.S.P.N. 8,568,992. The ability of Luminex to analyze 100 different types of beads (or more) simultaneously provides almost unlimited antigen and/or antibody surfaces, resulting in improved throughput and resolution in antibody epitope profiling over a biosensor assay (Miller, et al., 2011, PMID: 21223970).

5 “Surface plasmon resonance,” refers to an optical phenomenon that allows for the analysis of real-time specific interactions by detection of alterations in protein concentrations within a biosensor matrix.

In other embodiments, a technique that can be used to determine whether a test antibody “competes” for binding with a reference antibody is “bio-layer interferometry”, an optical
10 analytical technique that analyzes the interference pattern of white light reflected from two surfaces: a layer of immobilized protein on a biosensor tip, and an internal reference layer. Any change in the number of molecules bound to the biosensor tip causes a shift in the interference pattern that can be measured in real-time. Such biolayer interferometry assays may be conducted using a ForteBio® Octet RED machine as follows. A reference antibody (Ab1) is
15 captured onto an anti-mouse capture chip, a high concentration of non-binding antibody is then used to block the chip and a baseline is collected. Monomeric, recombinant target protein is then captured by the specific antibody (Ab1) and the tip is dipped into a well with either the same antibody (Ab1) as a control or into a well with a different test antibody (Ab2). If no further binding occurs, as determined by comparing binding levels with the control Ab1, then Ab1 and
20 Ab2 are determined to be “competing” antibodies. If additional binding is observed with Ab2, then Ab1 and Ab2 are determined not to compete with each other. This process can be expanded to screen large libraries of unique antibodies using a full row of antibodies in a 96-well plate representing unique bins. In preferred embodiments a test antibody will compete with a reference antibody if the reference antibody inhibits specific binding of the test antibody to a
25 common antigen by at least 40%, 45%, 50%, 55%, 60%, 65%, 70% or 75%. In other embodiments, binding is inhibited by at least 80%, 85%, 90%, 95%, or 97% or more.

Once a bin, encompassing a group of competing antibodies, has been defined further characterization can be carried out to determine the specific domain or epitope on the antigen to which the antibodies in a bin bind. Domain-level epitope mapping may be performed using a
30 modification of the protocol described by Cochran *et al.*, 2004, PMID: 15099763. Fine epitope mapping is the process of determining the specific amino acids on the antigen that comprise the epitope of a determinant to which the antibody binds. The term “epitope” is used in its common biochemical sense and refers to that portion of the target antigen capable of being recognized

and specifically bound by a particular antibody. In certain embodiments, epitopes or immunogenic determinants include chemically active surface groupings of molecules such as amino acids, sugar side chains, phosphoryl groups, or sulfonyl groups, and, in certain
5 charge characteristics. In certain embodiments, an antibody is said to specifically bind an antigen when it preferentially recognizes its target antigen in a complex mixture of proteins and/or macromolecules.

When the antigen is a polypeptide such as DLL3, epitopes may generally be formed from both contiguous amino acids and noncontiguous amino acids juxtaposed by tertiary folding of a
10 protein ("conformational epitopes"). In such conformational epitopes the points of interaction occur across amino acid residues on the protein that are linearly separated from one another. Epitopes formed from contiguous amino acids (sometimes referred to as "linear" or "continuous" epitopes) are typically retained upon protein denaturing, whereas epitopes formed by tertiary folding are typically lost upon protein denaturing. An antibody epitope typically includes at least
15 3, and more usually, at least 5 or 8-10 amino acids in a unique spatial conformation. Methods of epitope determination or "epitope mapping" are well known in the art and may be used in conjunction with the instant disclosure to identify epitopes on DLL3 bound by the disclosed antibodies.

Compatible epitope mapping techniques include alanine scanning mutants, peptide blots
20 (Reineke (2004) Methods Mol Biol 248:443-63), or peptide cleavage analysis. In addition, methods such as epitope excision, epitope extraction and chemical modification of antigens can be employed (Tomer (2000) Protein Science 9: 487-496). Other compatible methods comprise yeast display methods. In other embodiments Modification-Assisted Profiling (MAP), also known as Antigen Structure-based Antibody Profiling (ASAP) provides a method that
25 categorizes large numbers of monoclonal antibodies directed against the same antigen according to the similarities of the binding profile of each antibody to chemically or enzymatically modified antigen surfaces (U.S.P.N. 2004/0101920). This technology allows rapid filtering of genetically identical antibodies, such that characterization can be focused on genetically distinct antibodies. It will be appreciated that MAP may be used to sort the DLL3 antibodies of the
30 invention into groups of antibodies binding different epitopes.

Once a desired epitope on an antigen is determined, it is possible to generate antibodies to that epitope, e.g., by immunizing with a peptide comprising the epitope using techniques described in the present invention. Alternatively, during the discovery process, the generation

and characterization of antibodies may elucidate information about desirable epitopes located in specific domains or motifs. From this information, it is then possible to competitively screen antibodies for binding to the same epitope. An approach to achieve this is to conduct competition studies to find antibodies that compete for binding to the antigen. A high throughput process for binning antibodies based upon their cross-competition is described in WO 03/48731. Other methods of binning or domain level or epitope mapping comprising antibody competition or antigen fragment expression on yeast are well known in the art.

B. Optional hinge region

As used herein, the term "hinge region" refers to a flexible polypeptide connector region (also referred to herein as "hinge") that may be included within the CAR ectodomain (or extracellular domain) providing structural flexibility to flanking polypeptide regions. The hinge region may consist of natural or synthetic polypeptides. It will be appreciated by those skilled in the art that hinge regions may improve the function of the CAR by promoting optimal positioning of the DLL3 binding domain in relationship to the portion of the antigen recognized by the same. It will be appreciated that, in some embodiments, the hinge region may not be required for optimal CAR activity. In other embodiments a beneficial hinge region comprising a short sequence of amino acids promotes CAR activity by facilitating flexibility of the antigen binding domain or antibody. The sequence encoding the hinge region may be positioned between the antigen recognition moiety (e.g., an anti-DLL3 scFv) and the transmembrane domains. The hinge sequence can be any moiety or sequence derived or obtained from any suitable molecule. In one embodiment, for example, the hinge sequence is derived from the human CD8 α molecule or a CD28 molecule. A "hinge region" derived from an immunoglobulin (e.g., IgG1) is generally defined as stretching from Glu216 to Pro230 of human IgG1. Hinge regions of other IgG isotypes may be aligned with the IgG1 sequence by placing the first and last cysteine residues forming inter-heavy chain disulfide (S-S) bonds in the same positions. In other embodiments the hinge region may be of natural occurrence or non-natural occurrence, including but not limited to an altered hinge region as described in U.S.P.N. 5,677,425. Of course, when certain binding domains such as (Fab')₂ or an intact antibody are used in the CAR it will naturally follow that the corresponding hinge region will be included.

In other selected embodiments the hinge region can include complete hinge region derived from an antibody of a different class or subclass from that of the CH1 domain. The term "hinge region" can also include regions derived from human CD8 α (aka CD8a) molecule or a

CD28 molecule and any other receptors that provide a similar function in providing flexibility to flanking regions. The hinge region can have a length of from about 4 amino acids to about 50 amino acids, e.g., from about 4 aa to about 10 aa, from about 10 aa to about 15 aa, from about 15 aa to about 20 aa, from about 20 aa to about 25 aa, from about 25 aa to about 30 aa, from about 30 aa to about 40 aa, or from about 40 aa to about 50 aa. Suitable hinge regions can be readily selected and can be of any of a number of suitable lengths, such as from 1 amino acid (e.g., Gly) to 20 amino acids, from 2 amino acids to 15 amino acids, from 3 amino acids to 12 amino acids, including 4 amino acids to 10 amino acids, 5 amino acids to 9 amino acids, 6 amino acids to 8 amino acids, or 7 amino acids to 8 amino acids, and can be 1, 2, 3, 4, 5, 6, or 7 amino acids.

Those skilled in the art will appreciate that compatible hinge regions are well known and, as such, operable embodiments may readily be selected and incorporated in the DLL3 CARs of the instant invention.

C. Transmembrane/spacer domain

As alluded to above, the DLL3 CARs of the instant invention preferably comprise a transmembrane domain that is interposed between the extracellular DLL3 binding domain and/or hinge region, and the intracellular or cytoplasmic signaling domain. For the purposes of the instant discussion the term “transmembrane domain” will be used with the understanding that while it always includes amino acid residues that are physically buried in the lipid bilayer of a cellular membrane, it may include support or “spacer domains” that can extend beyond either side of the cell membrane. Those of skill in the art can readily distinguish between the functional aspects of the CAR components and easily determine what constitutes a compatible transmembrane domain in view of the instant disclosure.

It will be appreciated that the transmembrane domain may be derived from a natural polypeptide, or may be artificially designed. Compatible transmembrane domains may be derived from any membrane-binding or transmembrane protein which may be modified or truncated as necessary. For example, transmembrane domains derived from a T cell receptor α or β chain, a Fc region of an IgG (such as IgG4), a CD3 ζ chain, CD28, CD3 ϵ , CD45, CD4, CD5, CD8 (e.g. CD8a aka CD8 α), CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD137, ICOS, CD154 or a GITR are all compatible with various embodiments of the disclosed DLL3 CAR constructs. In certain embodiments it is preferred to employ the transmembrane domain of CD8 ζ , FcR η , Fc ϵ R1- γ and - β , MB1 (Ig α), B29 or CD3- γ , ζ , or ϵ , in order to retain

physical association with other members of the receptor complex. Compatible artificial transmembrane domains may comprise various polypeptide sequences incorporating high levels of hydrophobic residues such as leucine and valine. In other preferred embodiments the transmembrane domain may comprise a triplet of phenylalanine, tryptophan and valine which is
5 located at each end of the synthetic transmembrane domain.

Certain embodiments of the invention will comprise transmembrane domains having a spacer. In the DLL3 CARs of the present invention, a "spacer domain" or "spacer region" is an amino acid sequence that can be arranged between an extracellular functional domain (e.g., the antigen binding domain or the hinge region if included) and the transmembrane domain, or
10 between the intracellular signaling domain and the transmembrane domain. The spacer domain means any oligopeptide or polypeptide that serves to link the transmembrane domain with the extracellular domain and/or the transmembrane domain with the intracellular domain, with the intent to optimally position these elements within the CAR polypeptide for efficient CAR function. The spacer domain comprises up to 300 amino acids, preferably 10 to 100 amino acids, and
15 most preferably 25 to 50 amino acids. The spacer domain preferably has a sequence that promotes binding of the DLL3 CAR with DLL3 and enhances transmembrane signaling into a cell. Examples of amino acids that are expected to promote the binding include cysteine, a charged amino acid, and serine and threonine in a potential glycosylation site, and these amino acids can be used as an amino acid constituting the spacer domain. In preferred embodiments
20 the spacer may comprise all or part of an antibody constant region (e.g., IgG1 CH or CL) which may optionally dimerize.

Other compatible spacers include glycine polymers (G)_n, glycine-serine polymers, glycine-alanine polymers, alanine-serine polymers, and other flexible spacers known in the art. Glycine and glycine-serine polymers can be used; both Gly and Ser are relatively unstructured,
25 and therefore can serve as a neutral tether between components. Glycine polymers can be used; glycine accesses significantly more phi-psi space than even alanine, and is much less restricted than residues with longer side chains.

Those skilled in the art will appreciate that compatible transmembrane domains are well known in the art and, as such, operable embodiments may readily be selected and incorporated
30 in the DLL3 CARs of the instant invention.

D. Intracellular signaling domain

In addition to the extracellular DLL3 binding domain and the transmembrane domain, the DLL3 CARs of the instant invention will incorporate an intracellular or cytoplasmic domain comprising at least one signaling and/or T cell activating moiety. The intracellular signaling domain used in the present invention is a molecule that can transmit one or more signals into a cell when the extracellular domain present within (or non-covalently associated with) the same molecule binds to (interacts with) DLL3. The binding of DLL3 triggers a signal that passes along the CAR and is transmitted intracellularly to activate the sensitized lymphocyte. This lymphocyte activation triggers the desired immune response that results in the elimination of the target cell.

The two signal theory of T-lymphocyte activation proposes that two signals are required to efficiently activate T-cells: first, antigenic peptides presented in the context of an MHC molecule interact with the alpha:beta chain heterodimer of the TCR, leading to conformational changes that result in activation of a signal from the cytoplasmic domains found in protein components of the TCR complex; and second, transmission of a signal from the cytoplasmic domain of a single or several costimulatory molecules as they interact with their cognate ligands on the cell presenting the peptide:MHC complex. More specifically it is known that a signal generated only via a TCR complex may be insufficient to activate a T cell, and a secondary or costimulating signal is also required to avoid a state of T-cell inactivity known as anergy. Natural T cell-activation is transmitted by two different kinds of cytoplasmic signaling sequences, that is, a sequence for initiating antigen-dependent primary activation via a TCR complex (primary cytoplasmic signaling sequence) and a sequence for acting antigen-independently to provide a secondary or costimulating signal (secondary cytoplasmic signaling sequence). In a preferable aspect, the DLL3 CAR of the present invention comprises the primary cytoplasmic signaling sequence and/or the secondary cytoplasmic signaling sequence as the CAR endodomain.

In general, signaling motifs found in the cytoplasmic domains of immune system receptors may be activating or inhibitory. The primary cytoplasmic signaling sequence that stimulates the activation may comprise a signal transduction motif known as an immunoreceptor tyrosine-based activation motif (ITAM) [Nature, vol. 338, pp. 383-384 (1989)]. On the other hand, the primary cytoplasmic signaling sequence that acts in an inhibitory way comprises a signal transduction motif known as an immunoreceptor tyrosine-based inhibition motif (ITIM). In the present invention, an intracellular domain having an ITAM or an ITIM can be used.

The primary cytoplasmic signaling sequence that transmits the first stimulating signal for T-cell activation from the native TCR complex is an ITAM found in the CD3 ζ chain, but it is

known that other ITAMs may also be employed to transmit positive primary activating signal. Examples of the intracellular domain having an ITAM that can be used in the present invention include intracellular domains having ITAM derived from CD3 ζ , FcR γ , FcR β , CD3 γ , CD3 δ , CD3 ϵ , CD5, CD22, CD79a, CD79b, and CD66d. Specifically, examples of the ITAM include

5 peptides having sequences of amino acid numbers 51 to 164 of CD3 ζ (NCBI RefSeq: NP_932170.1), amino acid numbers 45 to 86 of Fc ϵ R γ (NCBI RefSeq: NP_004097.1), amino acid numbers 201 to 244 of Fc ϵ R β (NCBI RefSeq: NP_000130.1), amino acid numbers 139 to 182 of CD3 γ (NCBI RefSeq: NP_000064.1), amino acid numbers 128 to 171 of CD3 δ (NCBI RefSeq: NP_000723.1), amino acid numbers 153 to 207 of CD3 ϵ (NCBI RefSeq: NP_000724.1), amino acid numbers 402 to 495 of CD5 (NCBI RefSeq: NP_055022.2), amino acid numbers 707 to 847 of CD22 (NCBI RefSeq: NP_001762.2), amino acid numbers 166 to 226 of CD79a (NCBI RefSeq: NP_001774.1), amino acid numbers 182 to 229 of CD79b (NCBI RefSeq: NP_000617.1), and amino acid numbers 177 to 252 of CD66d (NCBI RefSeq: NP_001806.2), and their variants having the same function as these peptides have. The amino acid

10 number based on amino acid sequence information of NCBI RefSeq ID or GenBank described herein is numbered based on the full length of the precursor (comprising a signal peptide sequence etc.) of each protein.

The secondary, costimulatory signal may come from the cytoplasmic domain of a variety of costimulatory molecules, the best characterized of which is CD28. CD28 is expressed on T-

20 cells and is the receptor for CD80 (B7.1) and CD86 (B7.2). However, other costimulatory molecules include, but are not limited to the CD27 molecule, the CD137/4-1BB molecule, the CD134/OX40 molecule, and other intracellular signaling molecules known in the art. CD134/OX40 is known to enhance T-cell clonal expansion, likely by suppressing apoptosis, and may play a role in the establishment of memory cells. 4-1BB, also known as CD137, transmits

25 a potent costimulatory signal to T-cells, promoting differentiation and enhancing long-term survival of T lymphocytes. As each of these costimulatory molecules activates different intracellular signaling pathways and may have differing effects in different populations of T-lymphocytes, domains from, one, several, or each may be included in the endodomain of the CAR in order to maximize T-cell activation and other desired properties of the CAR. In a

30 preferred embodiment, the CD28, CD27, 4-1BB, and OX40 molecules are human. Examples of the intracellular domain comprising a secondary cytoplasmic signaling sequence that can be used in the present invention include sequences derived from CD2, CD4, CD5, CD8 α , CD8 β , CD28, CD134, CD137 (4-1BB), ICOS, and CD154. Specific examples thereof include peptides

having sequences of amino acid numbers 236 to 351 of CD2 (NCBI RefSeq: NP-001758.2), amino acid numbers 421 to 458 of CD4 (NCBI RefSeq: NP-000607.1), amino acid numbers 402 to 495 of CD5 (NCBI RefSeq: NP-055022.2), amino acid numbers 207 to 235 of CD8 α (NCBI RefSeq: NP-001759.3), amino acid numbers 196 to 210 of CD83 (GenBank: AAA35664.1), amino acid numbers 181 to 220 (SEQ ID NO: 25) of CD28 (NCBI RefSeq: NP-006130.1), amino acid numbers 214 to 255 of CD137 (4-1BB, NCBI RefSeq: NP-001552.2), amino acid numbers 241 to 277 of CD134 (OX40, NCBI RefSeq: NP-003318.1), and amino acid numbers 166 to 199 of ICOS (NCBI RefSeq: NP-036224.1), and their variants having the same function as these peptides have.

The signaling/activating domain(s) of the DLL3 CAR encoded by the disclosed nucleic acid sequence can comprise any one of aforementioned signaling domains and any one or more of the aforementioned intercellular T-cell activating domains in any combination. For example, the inventive nucleic acid sequence can encode a CAR comprising a CD28 signaling domain and intracellular T-cell activating domains of CD28 and CD3 ζ . Alternatively, for example, the nucleic acid sequences of the invention can encode a CAR comprising a CD8 α signaling domain and T cell signaling domains of CD28, CD3 ζ , the Fc receptor gamma (FcR γ) chain, and/or 4-1BB. As shown in the Examples below selected embodiments may comprise a 4-1BB costimulatory region along with a CD3 ζ cytoplasmic region or variants thereof.

Those skilled in the art will appreciate that each of the aforementioned signaling/stimulatory domains are compatible with the instant invention and may be used effectively (alone or preferably in combination) with the disclosed DLL3 CARs. Accordingly, each of the aforementioned moieties, in any combination or configuration are expressly contemplated as being within the scope of the instant invention as components of the intracellular/cytoplasmic domain.

V. CAR nucleic acids and vectors

The invention provides an isolated or purified nucleic acid sequence encoding an anti-DLL3 chimeric antigen receptor, wherein the CAR preferably comprises an extracellular DLL3 binding domain (e.g., a scFv), a transmembrane domain and an intracellular signaling domain (e.g., a T-cell activation moiety). As used herein "nucleic acid sequence" is intended to encompass a polymer of DNA or RNA, i.e., a polynucleotide, which can be single-stranded or double-stranded and which can contain non-natural or altered nucleotides. The terms "nucleic acid" and "polynucleotide" as used herein refer to a polymeric form of nucleotides of any length,

either ribonucleotides (RNA) or deoxyribonucleotides (DNA). These terms refer to the primary structure of the molecule, and thus include double- and single-stranded DNA, and double- and single-stranded RNA. The terms include, as equivalents, analogs of either RNA or DNA made from nucleotide analogs and modified polynucleotides such as, though not limited to methylated and/or capped polynucleotides.

By "isolated" is meant the removal of a nucleic acid from its natural environment. By "purified" is meant that a given nucleic acid, whether one that has been removed from nature (including genomic DNA and mRNA) or synthesized (including cDNA) and/or amplified under laboratory conditions, has been increased in purity, wherein "purity" is a relative term, not "absolute purity." It is to be understood, however, that nucleic acids and proteins may be formulated with diluents or adjuvants and still for practical purposes be isolated. For example, nucleic acids typically are mixed with an acceptable carrier or diluent when used for introduction into cells.

As described herein and shown in the appended Examples, nucleic acid sequences compatible with the invention can be generated using methods known in the art. For example, nucleic acid sequences, polypeptides, and proteins can be recombinantly produced using standard recombinant DNA methodology (see, e.g., Sambrook et al., *Molecular Cloning: A Laboratory Manual*, 3rd ed., Cold Spring Harbor Press, Cold Spring Harbor, N.Y. 2001). Further, a synthetically produced nucleic acid sequence encoding the DLL3 CAR can be isolated and/or purified from a source, such as a CHO cell, plant, a bacterium, an insect, or a mammal, e.g., a rat, a human, etc. Methods of isolation and purification are well known in the art. Alternatively, the nucleic acid sequences described herein can be commercially synthesized. In this respect, the inventive nucleic acid sequence can be synthetic, recombinant, isolated, and/or purified.

A nucleic acid sequence of the invention can encode a DLL3 CAR of any length, i.e., the CAR can comprise any number of amino acids, provided that the CAR retains its biological activity, e.g., the ability to specifically bind to antigen and treat or prevent disease in a mammal, etc. For example, the CAR can comprise 50 or more, 60 or more, 100 or more, 250 or more, or 500 or more amino acids. Preferably, the CAR is about 50 to about 700 amino acids (e.g., about 70, about 80, about 90, about 150, about 200, about 300, about 400, about 550, or about 650 amino acids), about 100 to about 500 amino acids (e.g., about 125, about 175, about 225, about 250, about 275, about 325, about 350, about 375, about 425, about 450, or about 475 amino acids), or a range defined by any two of the foregoing values.

Included in the scope of the invention are nucleic acid sequences that encode functional

portions of the DLL3 CAR described herein. The term "functional portion," when used in reference to a CAR, refers to any part or fragment of the CAR of the invention, which part or fragment retains the biological activity of the CAR of which it is a part (the parent CAR). Functional portions encompass, for example, those parts of a CAR that retain the ability to recognize target cells or provide an immunomodulatory signal, or treat a disease, to a similar extent, the same extent, or to a higher extent, as the parent CAR. In reference to a nucleic acid sequence encoding the parent DLL3 CAR, a nucleic acid sequence encoding a functional portion of the CAR can encode a protein comprising, for example, about 10%, 25%, 30%, 50%, 68%, 80%, 90%, 95%, or more, of the parent CAR. In this regard compatible nucleic acid sequences can encode a functional portion of a CAR that contains additional amino acids at the amino or carboxy terminus of the portion, or at both termini, which additional amino acids are not found in the amino acid sequence of the parent CAR. Desirably, the additional amino acids do not interfere with the biological function of the functional portion, e.g., recognize target cells, detect cancer, treat or prevent cancer, etc. More desirably, the additional amino acids enhance the biological activity of the CAR, as compared to the biological activity of the parent CAR.

The invention also provides nucleic acid sequences encoding functional variants of the DLL3 CAR. The term "functional variant," as used herein, refers to a CAR, a polypeptide, or a protein having substantial or significant sequence identity or similarity to the CAR encoded by the disclosed nucleic acid sequences, which functional variant retains the DLL3 binding capacity of the CAR of which it is a variant. Functional variants encompass, for example, those variants of the CAR described herein (the parent CAR) that retain the ability to recognize DLL3 positive target cells to a similar extent, the same extent, or to a higher extent, as the parent CAR. In reference to a nucleic acid sequence encoding the parent CAR, a nucleic acid sequence encoding a functional variant of the CAR can be for example, about 10% identical, about 25% identical, about 30% identical, about 50% identical, about 65% identical, about 80% identical, about 90% identical, about 95% identical, or about 99% identical to the nucleic acid sequence encoding the parent CAR.

Regardless of the precise form of the DLL3 CAR it will be appreciated that the nucleic acids of the present invention may be used for *ex vivo* transformation of selected host cells (e.g., lymphocytes) or introduced directly into the subject for *in vivo* gene therapy. In each case the disclosed nucleic acids may be combined with a substance that promotes transference of a nucleic acid into a cell, for example, a reagent for introducing a nucleic acid such as a liposome or a cationic lipid, in addition to other excipients disclosed herein. In certain preferred

embodiments the nucleic acids of the instant invention will be combined with, or integrated into, a vector is suitable for *in vivo* gene therapy.

Accordingly, in conjunction with the foregoing the present invention provides compositions comprising DLL3 CAR nucleic acids which, together with a pharmaceutically acceptable carrier, may be used as an active ingredient (e.g., in *in vivo* gene therapy) or to generate sensitized lymphocytes. Suitable pharmaceutically acceptable additives are well known to a person skilled in the art. Examples of the pharmaceutically acceptable additives or excipients include phosphate buffered saline (e.g. 0.01 M phosphate, 0.138 M NaCl, 0.0027 M KCl, pH 7.4), an aqueous solution containing a mineral acid salt such as a hydrochloride, a hydrobromide, a phosphate, or a sulfate, saline, a solution of glycol or ethanol, and a salt of an organic acid such as an acetate, a propionate, a malonate or a benzoate. An adjuvant such as a wetting agent or an emulsifier, and a pH buffering agent can also be used. Compositions of the present invention can be formulated into a known form suitable for parenteral administration, for example, injection or infusion. Further, such compositions may comprise formulation additives such as a suspending agent, a preservative, a stabilizer and/or a dispersant, and a preservation agent for extending a validity term during storage. Further the composition may be in a dry form for reconstitution with an appropriate sterile liquid prior to use.

In addition to the nucleic acid sequence encoding the DLL3 CAR, compatible vectors preferably comprise expression control sequences, such as promoters, enhancers, polyadenylation signals, transcription terminators, internal ribosome entry sites (IRES), and the like, that provide for the expression of the nucleic acid sequence in a host cell. In this regard a large number of promoters, including constitutive, inducible, and repressible promoters, from a variety of different sources are well known in the art. Representative sources of promoters include for example, virus, mammal, insect, plant, yeast, and bacteria, and suitable promoters from these sources are readily available, or can be made synthetically, based on sequences publicly available, for example, from depositories such as the ATCC as well as other commercial or individual sources. Promoters can be unidirectional (i.e., initiate transcription in one direction) or bi-directional (i.e., initiate transcription in either a 3' or 5' direction). Non-limiting examples of promoters include, for example, the T7 bacterial expression system, pBAD (araA) bacterial expression system, the cytomegalovirus (CMV) promoter, the SV40 promoter, and the RSV promoter. Inducible promoters include, for example, the Tet system, the Ecdysone inducible system, the T-REX™ system (Invitrogen, Carlsbad, Calif.), LACSWITCH™ System (Stratagene, San Diego, Calif.), and the Cre-ERT tamoxifen inducible recombinase system. In

addition the DLL3 CAR may be associated with a gene that can be a marker for confirming expression of the nucleic acid (e.g. a drug resistance gene, a gene encoding a reporter enzyme, or a gene encoding a fluorescent protein).

In certain embodiments the nucleic acid encoding the DLL3 CAR, along with any control elements, can preferably be inserted into a vector that can then be introduced into a selected cell to provide the disclosed DLL3 sensitized lymphocytes. In preferred embodiments the vector can be, for example, a plasmid, a transposon, a cosmid or a viral vector (e.g., phage, retroviral, lentiviral or adenoviral). For example, a virus vector such as a retrovirus vector (including an oncoretrovirus vector, a lentivirus vector, and a pseudo type vector), an adenovirus vector, an adeno-associated virus (AAV) vector, a simian virus vector, a vaccinia virus vector or a sendai virus vector, an Epstein-Barr virus (EBV) vector, and a HSV vector can be used.

More generally the terms "vector", "cloning vector" and "expression vector" mean the vehicle by which a DNA or RNA sequence (e.g., a foreign gene encoding a DLL3 CAR) can be introduced into a host cell, so as to transform the host and promote expression (e.g. transcription and translation) of the introduced sequence. It will be appreciated that the introduced gene or sequence may include regulatory or control sequences, such as start, stop, promoter, signal, secretion, or other sequences used by a cell's genetic machinery. As described herein compatible vectors are well known in the art and include plasmids, transposons, phages, viruses, etc. The vector may then be used to transform the selected lymphocytes (autologous or allogeneic) to provide the disclosed sensitized lymphocytes. For the purposes of the instant disclosure the term "transform" or "transformation" will be used in its most general sense and shall be held to mean the introduction of a heterologous gene, DNA or RNA sequence to a host cell (prokaryotic or eukaryotic), so that the host cell will express the introduced gene or sequence to produce a desired substance, typically a protein or enzyme coded by the introduced gene or sequence. Exemplary methods of cell transformation compatible with the invention comprise transfection and transduction. As used herein the term "transfection" means the introduction of a foreign nucleic acid or gene into a cell (prokaryotic or eukaryotic) using physical or chemical means while the term "transduction" means the introduction of a foreign nucleic acid or gene into a cell (prokaryotic or eukaryotic) through use of a viral vector.

In terms of transduction phage or viral vectors can be introduced into host cells, preferably after growth of infectious particles in suitable packaging cells, many of which are commercially available. Compatible transduction methods and packaging cells are set forth in the Examples

below and would be readily discernable to the skilled artisan in view of the instant disclosure.

By way of example, when a retrovirus vector is to be used, compositions compatible with the teachings herein can be generated by selecting a suitable packaging cell based on a LTR sequence and a packaging signal sequence possessed by the vector and preparing a retrovirus particle using the packaging cell. Examples of the packaging cell include PG13 (ATCC CRL-10686), PA317 (ATCC CRL-9078), GP+E-86 and GP+envAm-12, and Psi-Crip. A retrovirus particle can also be prepared using a 293 cell or a 293T cell having high transfection efficiency. Many kinds of retrovirus vectors produced based on retroviruses and packaging cells that can be used for packaging of the retrovirus vectors are widely commercially available from many companies. Similar systems are also commercially available for the fabrication of compatible lentiviral vectors in accordance with the teachings herein. Such vectors may be used to transduce selected lymphocyte populations to provide the desired DLL3 sensitized lymphocytes.

In addition, non-viral packaging vector systems can also be used in the present invention in combination with a liposome and a condensing agent such as a cationic lipid as described in WO 96/10038, WO 97/18185, WO 97/25329, WO 97/30170 and WO 97/31934 (which are incorporated herein by reference).

Similarly, many methods of transfection are compatible with the instant invention and may be used in conjunction with the teachings herein to provide the desired compositions. As discussed, transfection typically refers to the introduction of one or more exogenous polynucleotides into a host cell by using physical or chemical methods. Many transfection techniques are known in the art and include, for example, calcium phosphate DNA co-precipitation; DEAE-dextran; electroporation; cationic liposome-mediated transfection; tungsten particle-facilitated microparticle bombardment; and strontium phosphate DNA co-precipitation. Additionally, electroporation, sonoporation, impalefection, optical transfection and hydrodynamic delivery comprise some non-chemical based gene transfection methods compatible with the instant invention.

Regardless of which methodology is selected to effect transformation, it will be appreciated that the DLL3 CAR nucleic acid constructs and vectors may be used to generate the disclosed sensitized lymphocytes.

VI. Host Cells

A vector comprising a nucleic acid encoding the DLL3 CAR can be introduced into any

host cell that is capable of carrying and/or expressing the CAR protein, including any suitable prokaryotic or eukaryotic cell. Particularly compatible methods of transformation comprise the use of lentiviral, and retroviral systems along with transposons and naked RNA. Preferred host cells are those that can be easily and reliably grown, have reasonably fast growth rates, have well characterized expression systems, and can be transformed or transfected easily and efficiently.

As used herein, the term "host cell" refers to any type of cell that can contain the expression vector. The host cell can be a eukaryotic cell (e.g., plant, animal, fungi, or algae), a prokaryotic cell (e.g., bacteria or protozoa) or a viral or retroviral vector. The host cell can be a cultured or "off-the-shelf" cell or a primary cell (i.e., isolated directly from a subject). The host cell can be an adherent cell or a suspended cell, i.e., a cell that grows in suspension. Suitable host cells are known in the art and include, for instance, DH5 α *E. coli* cells, Chinese hamster ovarian cells, monkey VERO cells, COS cells, HEK293 cells, and the like. For purposes of amplifying or replicating the recombinant expression vector, the host cell may be a prokaryotic cell, e.g., a DH5 α cell. For purposes of producing a recombinant CAR, the host cell can be a mammalian cell. The host cell preferably is a human cell. The host cell can be of any cell type, can originate from any type of tissue, and can be of any developmental stage. For example, a cell collected, isolated, purified or induced from a body fluid, a tissue or an organ such as blood (peripheral blood, umbilical cord blood etc.) or bone marrow can be used. A peripheral blood mononuclear cell (PBMC), an immune cell [a dendritic cell, a B cell, a hematopoietic stem cell, a macrophage, a monocyte, a NK cell or a hematopoietic cell (a neutrophil, a basophil)], an umbilical cord blood mononuclear cell, a fibroblast, a precursor adipocyte, a hepatocyte, a skin keratinocyte, a mesenchymal stem cell, an adipose stem cell, various cancer cell strains, or a neural stem cell can be used. In particularly preferred embodiments the host cell can be a peripheral blood lymphocyte (PBL), a peripheral blood mononuclear cell (PBMC), or a natural killer (NK) cell. In selected embodiments the host cell is a natural killer (NK) cell. In other preferred embodiments the host cell will be a T-cell. Methods for selecting suitable mammalian host cells and methods for transformation, culture, amplification, screening, and purification of cells are known in the art.

The invention provides an isolated host cell that expresses nucleic acid sequence encoding the DLL3 CARs described herein or compositions of the same. In particularly preferred embodiments the host cell comprises a lymphocyte which is transformed into a DLL3 sensitized lymphocyte upon expression of the disclosed CARs. In one embodiment, the host

cell is a T-cell. The T-cell of the invention can be any T-cell, such as a cultured T-cell (e.g., a primary T-cell, or a T-cell from a cultured T-cell line, or a T-cell obtained from a mammal). If obtained from a mammal, the T-cell can be obtained from numerous sources, including but not limited to blood, bone marrow, lymph node, the thymus, or other tissues or fluids. T-cells can also be enriched for or purified. The T-cell preferably is a human T-cell (e.g., isolated from a human). The T-cell can be of any developmental stage, including but not limited to, a CD4+/CD8+ double positive T-cell, a CD4+ helper T-cell, e.g., Th1 and Th2 cells, a CD8+ T-cell (e.g., a cytotoxic T-cell), a tumor infiltrating cell, a memory T-cell, a naïve T-cell, and the like. In one embodiment, the T-cell is a CD8+ T-cell or a CD4+ T-cell. T-cell lines are available from commercial sources (e.g., the American Type Culture Collection and the German Collection of Microorganisms and Cell Cultures) and include, for example, Jurkat cells (ATCC TIB-152), Sup-T1 cells (ATCC CRL-1942), RPMI 8402 cells (DSMZ ACC-290), Karpas 45 cells (DSMZ ACC-545), and derivatives thereof.

In another embodiment, the host cell is a natural killer (NK) cell. NK cells are a type of cytotoxic lymphocyte that plays a role in the innate immune system. NK cells are defined as large granular lymphocytes and constitute the third kind of cells differentiated from the common lymphoid progenitor which also gives rise to B and T lymphocytes (see, e.g., *Immunobiology*, 5th ed., Janeway et al., eds., Garland Publishing, New York, N.Y. (2001)). NK cells differentiate and mature in the bone marrow, lymph node, spleen, tonsils, and thymus. Following maturation, NK cells enter into the circulation as large lymphocytes with distinctive cytotoxic granules. NK cells are able to recognize and kill some abnormal cells, such as, for example, some tumor cells and virus-infected cells, and are thought to be important in the innate immune defense against intracellular pathogens. As described above with respect to T-cells, the NK cell can be any NK cell, such as a cultured NK cell, e.g., a primary NK cell, or an NK cell from a cultured NK cell line, or an NK cell obtained from a mammal. If obtained from a mammal, the NK cell can be obtained from numerous sources, including but not limited to blood, bone marrow, lymph node, the thymus, or other tissues or fluids. NK cells can also be enriched for or purified. The NK cell preferably is a human NK cell (e.g., isolated from a human). NK cell lines are available from commercial sources (e.g., the American Type Culture Collection) and include, for example, NK-92 cells (ATCC CRL-2407), NK92MI cells (ATCC CRL-2408), and derivatives thereof.

In autologous adoptive immunotherapy, a patient's circulating lymphocytes, or tumor infiltrated lymphocytes, are isolated (e.g., by apheresis) *in vitro*, preferably activated or stimulated by lymphokines such as IL-2 and then transduced with nucleic acids encoding a

DLL3 CAR construct. Following transduction the autologous sensitized lymphocytes are preferably expanded using cytokine support as known in the art and readministered to the patient. To achieve this, one would administer to an animal, or human patient, an immunologically effective amount of activated lymphocytes genetically modified to express a
5 DLL3 CAR gene as described herein. In such autologous procedures the activated lymphocytes (i.e., DLL3 sensitized lymphocytes) are the patient's own cells that most preferably were earlier isolated from a blood or tumor sample and activated and expanded *in vitro*. In some aspects of the present invention T lymphocytes or NK cells from a patient having cancer would be isolated and transduced with SCT1-h16.15 polynucleotides (e.g., see Example 10
10 below) so that the DLL3 CAR is expressed on the cell surface of the T cell or NK cell. The modified cells would then be readministered into the patient to target and kill the tumor cells (see generally FIG. 5).

Other preferred aspects of the invention comprise allogeneic transplants of DLL3 sensitized lymphocytes. In such embodiments the disclosed DLL3 CARs may be introduced
15 (e.g., through transduction) into lymphocytes obtained from a source other than the subject to be treated. Some aspects of the instant invention comprise the use of allogeneic lymphocytes obtained from a donor that has been immunologically matched with the recipient to reduce the chance of rejection. In other aspects the disclosed CARs will be introduced into "off-the-shelf" allogeneic lymphocytes (see PMID: 26183927 which is incorporated herein by reference) that
20 have been modified to facilitate transplantation and generate the appropriate immune response upon contact with the target cell. It will be appreciated that the use of such prefabricated allogeneic lymphocyte preparations may provide several advantages in terms of preparing the pharmaceutically active sensitized lymphocytes and reducing the chances of patient rejection.

It will also be appreciated that the selected host cells can be expanded *in vitro* before or
25 after transformation with the DLL3 CAR. Methods for expanding the selected cell populations are well known in the art and several commercial kits compatible with the instant invention are available. In this regard T cells and or NK cells may be expanded *in vitro* to provide more robust dosing options. For example, in accordance with the present invention NK cells may be preferentially expanded by exposure to cells that lack or poorly express major histocompatibility
30 complex I and/or II molecules and which have been genetically modified to express membrane bound IL-15 and 4-1BB ligand (CD137L). Such cell lines include, but are not necessarily limited to, K562 (ATCC, CCL 243), and the Wilms tumor cell line HFWT, the uterine endometrium tumor cell line HHUA, the melanoma cell line HMV-II, the hepatoblastoma cell line HuH-6, the

lung small cell carcinoma cell lines Lu-130 and Lu-134-A, the neuroblastoma cell lines NB 19 and N1369, the embryonal carcinoma cell line from testis NEC 14, the cervix carcinoma cell line TCO-2, and the bone marrow-metastated neuroblastoma cell line TNB 1. Preferably the cell line used lacks or poorly expresses both MHC I and II molecules, such as the K562 and HFWT cell lines. Similar techniques allow for the expansion of selected T cell populations. In this regard some processes employ anti-CD3 plus autologous or allogeneic feeder cells and high doses of IL-2. Other processes use IL-7, IL-15, IL-21 or combinations thereof for expansion and stimulation of T cells. It will be appreciated that each of the aforementioned processes, along with any process that provides the desired number of DLL3 sensitized lymphocytes, is compatible with the instant invention.

VII. Formulation and administration of DLL3 Sensitized Lymphocytes

As set forth herein the selected host cells can be expanded *in vitro* for use in adoptive cellular immunotherapy comprising autologous or allogeneic DLL3 sensitized lymphocytes. In this regard the compositions and methods of this invention can be used to generate a population of sensitized lymphocytes that preferably deliver both primary and costimulatory signals for use in the treatment of cancer and, by way of example, the treatment of lung cancer including small cell lung cancer, melanoma, breast cancer, prostate cancer, colon cancer, renal cell carcinoma, ovarian cancer, neuroblastoma, rhabdomyosarcoma, leukemia and lymphoma. The compositions and methods described in the present invention may be used in conjunction with other types of therapy for cancer, such as chemotherapy, surgery, radiation, gene therapy, and so forth.

The DLL3 sensitized lymphocytes or host cells are preferably administered to a subject in the form of a pharmaceutical composition comprising one or more pharmaceutically acceptable carriers. In particularly preferred embodiments the disclosed pharmaceutical compositions will comprise a population of T cells or NK cells (autologous or allogeneic) that express the DLL3 CAR. Besides such host cells pharmaceutical compositions of the invention can comprise other pharmaceutically active agents or drugs, such as chemotherapeutic agents (e.g., asparaginase, busulfan, carboplatin, cisplatin, daunorubicin, doxorubicin, fluorouracil, gemcitabine, hydroxyurea, methotrexate, paclitaxel, rituximab, vinblastine, vincristine, etc.) or adjuvant therapies that further stimulate the immune response. In a preferred embodiment, the pharmaceutical composition comprises isolated T cells or NK cells which express the disclosed DLL3 CARs and more preferably a population of sensitized T cells or NK cells which express

the disclosed DLL3 CARs. In addition such compositions may comprise a pharmaceutically acceptable buffers, preservatives, excipients, etc. as is well known in the art.

Alternatively, nucleic acid sequences encoding the DLL3 CAR, or vectors comprising a DLL3 CAR-encoding nucleic acid sequence, can be formulated into a pharmaceutical composition and administered directly to the patient. In such embodiments vector systems comprising viral vector host cells (e.g., lentiviral systems or retroviral systems) or directed artificial viral envelopes are preferred. Such vectors allow for the *in vivo* generation of DLL3 sensitized lymphocytes which can then induce the desired anti-tumor immune response.

In any event the DLL3 CAR host cells of the invention and any co-reagents can be formulated in various ways using art recognized techniques. In some embodiments, the therapeutic compositions of the invention can be administered neat or with a minimum of additional components while others may optionally be formulated to contain suitable pharmaceutically acceptable carriers. As used herein, "pharmaceutically acceptable carriers" comprise excipients, vehicles, adjuvants and diluents that are well known in the art and can be available from commercial sources for use in pharmaceutical preparation (see, e.g., Gennaro (2003) *Remington: The Science and Practice of Pharmacy with Facts and Comparisons: Drugfacts Plus*, 20th ed., Mack Publishing; Ansel *et al.* (2004) *Pharmaceutical Dosage Forms and Drug Delivery Systems*, 7th ed., Lippencott Williams and Wilkins; Kibbe *et al.* (2000) *Handbook of Pharmaceutical Excipients*, 3rd ed., Pharmaceutical Press.)

Suitable pharmaceutically acceptable carriers typically comprise substances that are relatively inert and can facilitate administration of the sensitized lymphocyte or host cell or can aid processing of the same into preparations that are pharmaceutically optimized for delivery to the site of action. Such pharmaceutically acceptable carriers include agents that can alter the form, consistency, viscosity, pH, tonicity, stability, osmolarity, pharmacokinetics, protein aggregation or solubility of the formulation and include buffering agents, wetting agents, emulsifying agents, diluents, encapsulating agents and skin penetration enhancers. Certain non-limiting examples of carriers include saline, buffered saline, dextrose, arginine, sucrose, water, glycerol, ethanol, sorbitol, dextran, sodium carboxymethyl cellulose and combinations thereof. Sensitized lymphocytes for systemic administration may be formulated for enteral, parenteral or topical administration. Indeed, all three types of formulation may be used simultaneously to achieve systemic administration of the active ingredient. Excipients as well as formulations for parenteral and nonparenteral drug delivery are well known in the art.

Formulations suitable for parenteral administration of DLL3 sensitized lymphocytes (e.g., by injection or infusion), include aqueous or non-aqueous, isotonic, pyrogen-free, sterile liquids (e.g., solutions, suspensions), in which the active ingredient is dissolved, suspended, or otherwise provided (e.g., in a liposome or other microparticulate). Such liquids may additionally
5 contain other pharmaceutically acceptable carriers, such as anti-oxidants, buffers, preservatives, stabilizers, bacteriostats, suspending agents, thickening agents, and solutes that render the formulation isotonic with the blood (or other relevant bodily fluid) of the intended recipient. Examples of excipients include, for example, water, alcohols, polyols, glycerol, vegetable oils, and the like. Examples of suitable isotonic pharmaceutically acceptable carriers
10 for use in such formulations include sodium chloride injection, Ringer's Solution, or Lactated Ringer's Injection.

Methods of introducing cellular components are also known in the art and include procedures such as those exemplified in U.S.P.Ns. 4,844,893 and 4,690,915. The amount of DLL3 sensitized lymphocytes (e.g., T cells or NK cells) used can vary between in vitro and in
15 vivo uses, as well as with the amount and type of the target cells. The amount administered will also vary depending on the condition of the patient and should be determined by the practitioner after considering all appropriate factors.

The particular dosage regimen of DLL3 sensitized lymphocytes, i.e., dose, timing and repetition, will depend on the particular individual, as well as empirical considerations such as
20 pharmacokinetics (e.g., half-life, clearance rate, etc.). For example, individuals may be given incremental dosages of sensitized lymphocytes produced as described herein. In selected embodiments the dosage may be gradually increased or reduced or attenuated based respectively on empirically determined or observed side effects or toxicity. Determination of the frequency of administration may be made by persons skilled in the art, such as an attending
25 physician based on considerations of the condition and severity of the condition being treated, age and general state of health of the subject being treated and the like. Frequency of administration may be adjusted over the course of therapy based on assessment of the efficacy of the selected composition and the dosing regimen. Such assessment can be made on the basis of markers of the specific disease, disorder or condition. In embodiments where the
30 individual has cancer, these include direct measurements of tumor size via palpation or visual observation; indirect measurement of tumor size by x-ray or other imaging techniques; an improvement as assessed by direct tumor biopsy and microscopic examination of a tumor sample; the measurement of an indirect tumor marker (e.g., DLL3 for SCLC) or an antigen

identified according to the methods described herein; reduction in the number of proliferative or tumorigenic cells, maintenance of the reduction of such neoplastic cells; reduction of the proliferation of neoplastic cells; or delay in the development of metastasis.

5 In view of the instant disclosure the DLL3 CAR may be administered on a specific schedule. Generally, an effective dose of the sensitized lymphocytes is administered to a subject one or more times. More particularly, an effective dose of the DLL3 CAR is administered to the subject once a month, more than once a month, or less than once a month. In certain embodiments, the effective dose of the DLL3 sensitized lymphocytes may be administered multiple times, including for periods of at least a month, at least six months, at
10 least a year, at least two years or a period of several years. In yet other embodiments, several days (2, 3, 4, 5, 6 or 7), several weeks (1, 2, 3, 4, 5, 6, 7 or 8) or several months (1, 2, 3, 4, 5, 6, 7 or 8) or even a year or several years may lapse between administration of the DLL3 sensitized lymphocytes.

In certain preferred embodiments the course of treatment involving DLL3 CAR will
15 comprise multiple doses of the selected sensitized lymphocytes over a period of weeks or months. More specifically, DLL3 sensitized lymphocytes of the instant invention may administered once every day, every two days, every four days, every week, every ten days, every two weeks, every three weeks, every month, every six weeks, every two months, every ten weeks or every three months. In this regard it will be appreciated that the dosages may be
20 altered or the interval may be adjusted based on patient response and clinical practices.

A typical amount of host cells administered to a mammal (e.g., a human) can be, for example, in the range of one million to 100 billion cells; however, amounts below or above this exemplary range are within the scope of the invention. For example, the daily dose of inventive host cells can be about 1 million to about 50 billion cells (e.g., about 5 million cells, about 25
25 million cells, about 500 million cells, about 1 billion cells, about 5 billion cells, about 20 billion cells, about 30 billion cells, about 40 billion cells, or a range defined by any two of the foregoing values), preferably about 10 million to about 100 billion cells (e.g., about 20 million cells, about 30 million cells, about 40 million cells, about 60 million cells, about 70 million cells, about 80 million cells, about 90 million cells, about 10 billion cells, about 25 billion cells, about 50 billion
30 cells, about 75 billion cells, about 90 billion cells, or a range defined by any two of the foregoing values), more preferably about 100 million cells to about 50 billion cells (e.g., about 120 million cells, about 250 million cells, about 350 million cells, about 450 million cells, about 650 million cells, about 800 million cells, about 900 million cells, about 3 billion cells, about 30 billion cells,

about 45 billion cells, or a range defined by any two of the foregoing values). In preferred embodiments about 0.5 billion, 1.0 billion, 1.5 billion, 2 billion, 2.5 billion, 3 billion, 3.5 billion, 4 billion, 4.5 billion, 5 billion, 5.5 billion, 6 billion, 6.5 billion, 7 billion, 7.5 billion, 8 billion, 8.5 billion, 9 billion, 9.5 billion or 10 billion cells are administered to the patient in one or more doses.

5 Therapeutic or prophylactic efficacy can be monitored by periodic assessment of treated patients. For repeated administrations over several days or longer, depending on the condition, the treatment is repeated until a desired suppression of disease symptoms occurs. However, other dosage regimens may be useful and are within the scope of the invention. The desired dosage can be delivered by a single bolus administration of the composition, by multiple bolus
10 administrations of the composition, or by continuous infusion administration of the composition.

As discussed above compositions comprising sensitized the host cells expressing the DLL3 CAR can be administered to a mammal using standard administration techniques, including intravenous, intraperitoneal, subcutaneous, pulmonary, transdermal, intramuscular or intranasal. The composition preferably is suitable for parenteral administration. The term
15 “parenteral,” as used herein, includes intravenous, intramuscular, subcutaneous, rectal, vaginal, and intraperitoneal administration. More preferably, the composition is administered to a mammal using peripheral systemic delivery by intravenous, intraperitoneal, or subcutaneous injection.

Moreover host cells expressing the DLL3 CAR nucleic acid sequence, or a vector
20 comprising the CAR-encoding nucleic acid sequence, can be administered with one or more additional therapeutic agents, which can be coadministered to the mammal. By “coadministering” is meant administering one or more additional therapeutic agents and the composition comprising the inventive host cells or the inventive vector sufficiently close in time such that the DLL3 CAR can enhance the effect of one or more additional therapeutic agents, or
25 vice versa. In this regard, the composition comprising the sensitized lymphocytes can be administered first, and the one or more additional therapeutic agents can be administered second, or vice versa. Alternatively, the composition comprising the DLL3 sensitized lymphocytes and the one or more additional therapeutic agents can be administered simultaneously.

30 In selected preferred embodiments the DLL3 sensitized lymphocytes will be administered in conjunction with lymphotoxic therapies to increase the availability of homeostatic cytokines (e.g., IL-7, IL-15, etc.) to support T cell expansion. In such protocols the lymphotoxic therapy will preferably be conducted prior to administration of the sensitized lymphocytes. More

specifically it is believed that a lymphodepleting preparative regimen may enhance the efficacy of adoptive cell therapy by reducing endogenous lymphocytes thereby leading to the accumulation of homeostatic cytokines that support expansion and persistence of the administered sensitized lymphocytes. Further, such preparative treatments may lead to a transient reduction in the number and frequency of Tregs thereby diminishing lymphocyte suppression and an induction of gut damage which may lead to the systemic release of bacterial byproducts (e.g., lipopolysaccharides) that activate the innate immune system. Taken together such mechanisms can substantially enhance the receptiveness of the immune environment for the transplanted DLL3 sensitized lymphocytes thereby promoting expansion and persistence of the same.

VIII. Indications

The present invention preferably provides for the use of DLL3 sensitized lymphocytes for the treatment, maintenance and/or prophylaxis of various disorders including neoplastic, inflammatory, angiogenic and immunologic DLL3 associated disorders. Preferred targets for treatment are neoplastic conditions comprising solid tumors and hematologic malignancies. In certain embodiments the DLL3 CAR treatments of the invention will be used to inhibit, reduce or eliminate tumors or tumorigenic cells expressing DLL3. In selected aspects the disclosed compositions may be used to inhibit tumor cell proliferation. Preferably the "subject" or "patient" to be treated will be human although, as used herein, the terms are expressly held to comprise any mammalian species.

Neoplastic conditions subject to treatment in accordance with the instant invention may be benign or malignant; solid tumors or other blood neoplasia; and may be selected from the group including, but not limited to: adrenal gland tumors, AIDS-associated cancers, alveolar soft part sarcoma, astrocytic tumors, autonomic ganglia tumors, bladder cancer (squamous cell carcinoma and transitional cell carcinoma), blastocoelic disorders, bone cancer (adamantinoma, aneurismal bone cysts, osteochondroma, osteosarcoma), brain and spinal cord cancers, metastatic brain tumors, breast cancer including triple negative breast cancer, carotid body tumors, cervical cancer, chondrosarcoma, chordoma, chromophobe renal cell carcinoma, clear cell carcinoma, colon cancer, colorectal cancer, cutaneous benign fibrous histiocytomas, desmoplastic small round cell tumors, ependymomas, epithelial disorders, Ewing's tumors, extraskeletal myxoid chondrosarcoma, fibrogenesis imperfecta ossium, fibrous dysplasia of the bone, gallbladder and bile duct cancers, gastric cancer, gastrointestinal, gestational

trophoblastic disease, germ cell tumors, glandular disorders, head and neck cancers, hypothalamic, intestinal cancer, islet cell tumors, Kaposi's Sarcoma, kidney cancer (nephroblastoma, papillary renal cell carcinoma), leukemias, lipoma/benign lipomatous tumors, liposarcoma/malignant lipomatous tumors, liver cancer (hepatoblastoma, hepatocellular carcinoma), lymphomas, lung cancers (small cell carcinoma, adenocarcinoma, squamous cell carcinoma, large cell carcinoma etc.), macrophagal disorders, medulloblastoma, melanoma, meningiomas, multiple endocrine neoplasia, multiple myeloma, myelodysplastic syndrome, neuroblastoma, neuroendocrine tumors, ovarian cancer, pancreatic cancers, papillary thyroid carcinomas, parathyroid tumors, pediatric cancers, peripheral nerve sheath tumors, phaeochromocytoma, pituitary tumors, prostate cancer, posterior uveal melanoma, rare hematologic disorders, renal metastatic cancer, rhabdoid tumor, rhabdomyosarcoma, sarcomas, skin cancer, soft-tissue sarcomas, squamous cell cancer, stomach cancer, stromal disorders, synovial sarcoma, testicular cancer, thymic carcinoma, thymoma, thyroid metastatic cancer, and uterine cancers (carcinoma of the cervix, endometrial carcinoma, and leiomyoma).

In certain embodiments the compounds and compositions of the instant invention will be used as a front line therapy and administered to subjects who have not previously been treated for the cancerous condition. In other embodiments the compounds and compositions of the present invention will be used to treat subjects that have previously been treated (with compositions of the present invention or with other anti-cancer agents) and have relapsed or determined to be refractory to the previous treatment. In selected embodiments the compounds and compositions of the instant invention may be used to treat subjects that have recurrent tumors.

In selected aspects the proliferative disorder will comprise a solid tumor including, but not limited to, adrenal, liver, kidney, bladder, breast, gastric, ovarian, cervical, uterine, esophageal, colorectal, prostate, pancreatic, lung (both small cell and non-small cell), thyroid, carcinomas, sarcomas, glioblastomas and various head and neck tumors.

In other preferred embodiments the compounds or compositions will be administered to a subject suffering from melanoma. More generally the compositions and methods disclosed herein may be used to diagnose, monitor, treat or prevent melanoma. The term "melanoma", as used herein, includes all types of melanoma including, but not limited to, primary melanoma, malignant melanoma, cutaneous melanoma, extracutaneous melanoma, superficial spreading melanoma, polypoid melanoma, melanocarcinomas, melanoepitheliomas, melanosarcomas, melanoma in situ, nodular malignant melanoma, lentigo maligna melanoma, lentiginous

melanoma, lentiginous malignant melanoma, mucosal lentiginous melanoma, mucosal melanoma, acral lentiginous melanoma, soft tissue melanoma, ocular melanoma, invasive melanoma, familial atypical mole and melanoma (FAM-M) syndrome, desmoplastic malignant melanoma or uveal melanoma.

5 In selected aspects the disclosed DLL3 CAR treatments are especially effective at treating lung cancer, including the following subtypes: small cell lung cancer, non-small cell lung cancer (e.g. squamous cell non-small cell lung cancer or squamous cell small cell lung cancer) and large cell neuroendocrine carcinoma (LCNEC). In selected embodiments the DLL3 sensitive lymphocytes can be administered to patients exhibiting limited stage disease or extensive stage
10 disease. In other preferred embodiments the disclosed conjugated antibodies will be administered to refractory patients (i.e., those whose disease recurs during or shortly after completing a course of initial therapy); sensitive patients (i.e., those whose relapse is longer than 2-3 months after primary therapy); or patients exhibiting resistance to a platinum based agent (e.g. carboplatin, cisplatin, oxaliplatin) and/or a taxane (e.g. docetaxel, paclitaxel,
15 larotaxel or cabazitaxel).

In another particularly preferred embodiment the disclosed DLL3 CAR treatments are effective at treating ovarian cancer, including ovarian-serous carcinoma and ovarian-papillary serous carcinoma.

The disclosed compositions may further be used to prevent, treat or diagnose tumors
20 with neuroendocrine features or phenotypes including neuroendocrine tumors. True or canonical neuroendocrine tumors (NETs) arising from the dispersed endocrine system are relatively rare, with an incidence of 2-5 per 100,000 people, but highly aggressive. Neuroendocrine tumors occur in the kidney, genitourinary tract (bladder, prostate, ovary, cervix, and endometrium), gastrointestinal tract (colon, stomach), thyroid (medullary thyroid cancer),
25 and lung (small cell lung carcinoma and large cell neuroendocrine carcinoma). These tumors may secrete several hormones including serotonin and/or chromogranin A that can cause debilitating symptoms known as carcinoid syndrome. Such tumors can be denoted by positive immunohistochemical markers such as neuron-specific enolase (NSE, also known as gamma enolase, gene symbol = ENO2), CD56 (or NCAM1), chromogranin A (CHGA), and
30 synaptophysin (SYP) or by genes known to exhibit elevated expression such as ASCL1. Unfortunately traditional chemotherapies have not been particularly effective in treating NETs and liver metastasis is a common outcome.

While the disclosed compositions may be advantageously used to treat neuroendocrine tumors they may also be used to treat, prevent or diagnose pseudo neuroendocrine tumors (pNETs) that genotypically or phenotypically mimic, resemble or exhibit common traits with canonical neuroendocrine tumors. Pseudo neuroendocrine tumors or tumors with neuroendocrine features are tumors that arise from cells of the diffuse neuroendocrine system or from cells in which a neuroendocrine differentiation cascade has been aberrantly reactivated during the oncogenic process. Such pNETs commonly share certain phenotypic or biochemical characteristics with traditionally defined neuroendocrine tumors, including the ability to produce subsets of biologically active amines, neurotransmitters, and peptide hormones. Histologically, such tumors (NETs and pNETs) share a common appearance often showing densely connected small cells with minimal cytoplasm of bland cytopathology and round to oval stippled nuclei. For the purposes of the instant invention commonly expressed histological markers or genetic markers that may be used to define neuroendocrine and pseudo neuroendocrine tumors include, but are not limited to, chromogranin A, CD56, synaptophysin, PGP9.5, ASCL1 and neuron-specific enolase (NSE).

Accordingly the sensitized lymphocytes of the instant invention may beneficially be used to treat both pseudo neuroendocrine tumors and canonical neuroendocrine tumors. In this regard the ADCs may be used as described herein to treat neuroendocrine tumors (both NET and pNET) arising in the kidney, genitourinary tract (bladder, prostate, ovary, cervix, and endometrium), gastrointestinal tract (colon, stomach), thyroid (medullary thyroid cancer), and lung (small cell lung carcinoma and large cell neuroendocrine carcinoma). Moreover, the compositions of the instant invention may be used to treat tumors expressing one or more markers selected from the group consisting of NSE, CD56, synaptophysin, chromogranin A, ASCL1 and PGP9.5 (UCHL1). That is, the present invention may be used to treat a subject suffering from a tumor that is NSE⁺ or CD56⁺ or PGP9.5⁺ or ASCL1⁺ or SYP⁺ or CHGA⁺ or some combination thereof.

In another preferred embodiment the DLL3 CAR treatments of the instant invention may be used in maintenance therapy to reduce or eliminate the chance of tumor recurrence following the initial presentation of the disease. Preferably the disorder will have been treated and the initial tumor mass eliminated, reduced or otherwise ameliorated so the patient is asymptomatic or in remission. At such time the subject may be administered pharmaceutically effective amounts of the disclosed DLL3 CAR treatments one or more times even though there is little or no indication of disease using standard diagnostic procedures. In some embodiments, the

modulators will be administered on a regular schedule over a period of time, such as weekly, every two weeks, monthly, every six weeks, every two months, every three months every six months or annually. Given the teachings herein, one skilled in the art could readily determine favorable dosages and dosing regimens to reduce the potential of disease recurrence. Moreover such treatments could be continued for a period of weeks, months, years or even indefinitely depending on the patient response and clinical and diagnostic parameters.

In yet another preferred embodiment the DLL3 CAR treatments of the present invention may be used to prophylactically or as an adjuvant therapy to prevent or reduce the possibility of tumor metastasis following a debulking procedure. As used in the instant disclosure a “debulking procedure” is defined broadly and shall mean any procedure, technique or method that eliminates, reduces, treats or ameliorates a tumor or tumor proliferation. Exemplary debulking procedures include, but are not limited to, surgery, radiation treatments (i.e., beam radiation), chemotherapy, immunotherapy or ablation. At appropriate times readily determined by one skilled in the art in view of the instant disclosure the disclosed DLL3 CAR treatments may be administered as suggested by clinical, diagnostic or theragnostic procedures to reduce tumor metastasis. The DLL3 sensitized lymphocytes may be administered one or more times at pharmaceutically effective dosages as determined using standard techniques. Preferably the dosing regimen will be accompanied by appropriate diagnostic or monitoring techniques that allow it to be modified.

Yet other embodiments of the invention comprise administering the disclosed DLL3 CAR treatments to subjects that are asymptomatic but at risk of developing a proliferative disorder. That is, the DLL3 CAR treatments of the instant invention may be used in a truly preventative sense and given to patients that have been examined or tested and have one or more noted risk factors (e.g., genomic indications, family history, *in vivo* or *in vitro* test results, etc.) but have not developed neoplasia. In such cases those skilled in the art would be able to determine an effective dosing regimen through empirical observation or through accepted clinical practices.

IX. Combination Therapies

As previously discussed It will be appreciated that the DLL3 CAR treatments described herein may be used in combination with other clinical oncology treatments. In general the treatments of the instant invention may be used with a therapeutic moiety or a drug such as an anti-cancer agent including, but not limited to, cytotoxic agents, cytostatic agents, anti-angiogenic agents, debulking agents, chemotherapeutic agents, radiotherapeutic agents,

targeted anti-cancer agents, biological response modifiers, cancer vaccines, cytokines, hormone therapies, anti-metastatic agents and immunotherapeutic agents.

Combination therapies may be useful in preventing or treating cancer and in preventing metastasis or recurrence of cancer. "Combination therapy", as used herein, means the administration of a combination comprising at least one DLL3 CAR treatment and at least one therapeutic moiety (e.g., anti-cancer agent) wherein the combination preferably has therapeutic synergy or improves the measurable therapeutic effects in the treatment of cancer over (i) the DLL3 CAR treatment used alone, or (ii) the therapeutic moiety used alone, or (iii) the use of the therapeutic moiety in combination with another therapeutic moiety without the addition of DLL3 CAR treatment. The terms "therapeutic synergy" or "synergy", as used herein, means the combination of an DLL3 CAR treatment and one or more therapeutic moiety(ies) having a therapeutic effect greater than the additive effect of the combination of the DLL3 CAR treatment and the one or more therapeutic moiety(ies).

Desired outcomes of the disclosed combinations are quantified by comparison to a control or baseline measurement. As used herein, relative terms such as "improve," "increase," or "reduce" indicate values relative to a control, such as a measurement in the same individual prior to initiation of treatment described herein, or a measurement in a control individual (or multiple control individuals) in the absence of DLL3 CAR treatments described herein but in the presence of other therapeutic moiety(ies) such as standard of care treatment. A representative control individual is an individual afflicted with the same form of cancer as the individual being treated, who is about the same age as the individual being treated (to ensure that the stages of the disease in the treated individual and the control individual are comparable.)

Changes or improvements in response to therapy are generally statistically significant. As used herein, the term "significance" or "significant" relates to a statistical analysis of the probability that there is a non-random association between two or more entities. To determine whether or not a relationship is "significant" or has "significance," a "p-value" can be calculated. P-values that fall below a user-defined cut-off point are regarded as significant. A p-value less than or equal to 0.1, less than 0.05, less than 0.01, less than 0.005, or less than 0.001 may be regarded as significant.

A synergistic therapeutic effect may be an effect of at least about two-fold greater than the therapeutic effect elicited by a single therapeutic moiety or DLL3 CAR treatment, or the sum of the therapeutic effects elicited by the DLL3 CAR treatment or the single therapeutic moiety(ies) of a given combination, or at least about five-fold greater, or at least about ten-fold greater, or at

least about twenty-fold greater, or at least about fifty-fold greater, or at least about one hundred-fold greater. A synergistic therapeutic effect may also be observed as an increase in therapeutic effect of at least 10% compared to the therapeutic effect elicited by a single therapeutic moiety or DLL3 CAR treatment or the sum of the therapeutic effects elicited by the DLL3 CAR
5 treatment or the single therapeutic moiety(ies) of a given combination, or at least 20%, or at least 30%, or at least 40%, or at least 50%, or at least 60%, or at least 70%, or at least 80%, or at least 90%, or at least 100%, or more. A synergistic effect is also an effect that permits reduced dosing of therapeutic agents when they are used in combination.

In practicing combination therapy, the DLL3 CAR treatment and therapeutic moiety(ies)
10 may be administered to the subject simultaneously, either in a single composition, or as two or more distinct compositions using the same or different administration routes. Alternatively, treatment with the DLL3 CAR treatment may precede or follow the therapeutic moiety treatment by, e.g., intervals ranging from minutes to weeks. In one embodiment, both the CAR therapeutic moiety and the antibody or ADC are administered within about 5 minutes to about
15 two weeks of each other. In yet other embodiments, several days (2, 3, 4, 5, 6 or 7), several weeks (1, 2, 3, 4, 5, 6, 7 or 8) or several months (1, 2, 3, 4, 5, 6, 7 or 8) may lapse between administration of the antibody and the therapeutic moiety.

The combination therapy can be administered until the condition is treated, palliated or cured on various schedules such as once, twice or three times daily, once every two days, once
20 every three days, once weekly, once every two weeks, once every month, once every two months, once every three months, once every six months, or may be administered continuously. The antibody and therapeutic moiety(ies) may be administered on alternate days or weeks; or a sequence of DLL3 CAR treatments may be given, followed by one or more treatments with the additional therapeutic moiety. In one embodiment an DLL3 CAR is administered in combination
25 with one or more therapeutic moiety(ies) for short treatment cycles. In other embodiments the combination treatment is administered for long treatment cycles. The combination therapy can be administered via any route.

In selected embodiments the compounds and compositions of the present invention may be used in conjunction with checkpoint inhibitors such as PD-1 inhibitors or PD-L1 inhibitors.
30 PD-1, together with its ligand PD-L1, are negative regulators of the antitumor T lymphocyte response. In one embodiment the combination therapy may comprise the administration of DLL3 sensitized lymphocytes together with an anti-PD-1 antibody (e.g. pembrolizumab, nivolumab, pidilizumab) and optionally one or more other therapeutic moiety(ies). In another

embodiment the combination therapy may comprise the administration of DLL3 sensitized lymphocytes together with an anti-PD-L1 antibody (e.g. avelumab, atezolizumab, durvalumab) and optionally one or more other therapeutic moiety(ies). In yet another embodiment, the combination therapy may comprise the administration of DLL3 sensitized lymphocytes together
5 with an anti PD-1 antibody or anti-PD-L1 administered to patients who continue progress following treatments with checkpoint inhibitors and/or targeted BRAF combination therapies (e.g., ipilimumab and vemurafenib or dabrafenib).

In some embodiments the sensitized lymphocytes may be used in combination with various first line cancer treatments. In one embodiment the combination therapy comprises the
10 use of the compositions of the instant invention and a cytotoxic agent such as ifosfamide, mytomyacin C, vindesine, vinblastine, etoposide, irinotecan, gemcitabine, taxanes, vinorelbine, methotrexate, and pemetrexed) and optionally one or more other therapeutic moiety(ies).

In another embodiment the combination therapy comprises the use of an DLL3 CAR treatment and a platinum-based drug (e.g. carboplatin or cisplatin) and optionally one or more
15 other therapeutic moiety(ies) (e.g. vinorelbine; gemcitabine; a taxane such as, for example, docetaxel or paclitaxel; irinotecan; or pemetrexed).

In one embodiment, for example, in the treatment of BR-ERPR, BR-ER or BR-PR cancer, the combination therapy comprises the use of an DLL3 CAR treatment and one or more therapeutic moieties described as "hormone therapy". "Hormone therapy" as used herein,
20 refers to, e.g., tamoxifen; gonadotropin or luteinizing releasing hormone (GnRH or LHRH); everolimus and exemestane; toremifene; or aromatase inhibitors (e.g. anastrozole, letrozole, exemestane or fulvestrant).

In another embodiment, for example, in the treatment of BR-HER2, the combination therapy comprises the use of an DLL3 CAR treatment and trastuzumab or ado-trastuzumab
25 emtansine and optionally one or more other therapeutic moiety(ies) (e.g. pertuzumab and/or docetaxel).

In some embodiments, for example, in the treatment of metastatic breast cancer, the combination therapy comprises the use of an DLL3 CAR treatment and a taxane (e.g. docetaxel or paclitaxel) and optionally an additional therapeutic moiety(ies), for example, an anthracycline
30 (e.g. doxorubicin or epirubicin) and/or eribulin.

In another embodiment, for example, in the treatment of metastatic or recurrent breast cancer or BRCA-mutant breast cancer, the combination therapy comprises the use of an DLL3 CAR treatment and megestrol and optionally an additional therapeutic moiety(ies).

In further embodiments, for example, in the treatment of BR-TNBC, the combination therapy comprises the use of an DLL3 CAR treatment and a poly ADP ribose polymerase (PARP) inhibitor (e.g. BMN-673, olaparib, rucaparib and veliparib) and optionally an additional therapeutic moiety(ies).

5 In another embodiment, for example, in the treatment of breast cancer, the combination therapy comprises the use of an DLL3 CAR treatment and cyclophosphamide and optionally an additional therapeutic moiety(ies) (e.g. doxorubicin, a taxane, epirubicin, 5-FU and/or methotrexate).

10 In another embodiment combination therapy for the treatment of EGFR-positive NSCLC comprises the use of an DLL3 CAR treatment and afatinib and optionally one or more other therapeutic moiety(ies) (e.g. erlotinib and/or bevacizumab).

In another embodiment combination therapy for the treatment of EGFR-positive NSCLC comprises the use of an DLL3 CAR treatment and erlotinib and optionally one or more other therapeutic moiety(ies) (e.g. bevacizumab).

15 In another embodiment combination therapy for the treatment of ALK-positive NSCLC comprises the use of an DLL3 CAR treatment and ceritinib and optionally one or more other therapeutic moiety(ies).

20 In another embodiment combination therapy for the treatment of ALK-positive NSCLC comprises the use of an DLL3 CAR treatment and crizotinib and optionally one or more other therapeutic moiety(ies).

In another embodiment the combination therapy comprises the use of an DLL3 CAR treatment and bevacizumab and optionally one or more other therapeutic moiety(ies) (e.g. a taxane such as, for example, docetaxel or paclitaxel; and/or a platinum analog).

25 In another embodiment the combination therapy comprises the use of an DLL3 CAR treatment and bevacizumab and optionally one or more other therapeutic moiety(ies) (e.g. gemcitabine and/or a platinum analog).

30 In one embodiment the combination therapy comprises the use of an DLL3 CAR treatment and a platinum-based drug (e.g. carboplatin or cisplatin) analog and optionally one or more other therapeutic moiety(ies) (e.g. a taxane such as, for example, docetaxel and paclitaxel).

In one embodiment the combination therapy comprises the use of an DLL3 CAR treatment and platinum-based drug (e.g. carboplatin or cisplatin) analog and optionally one or more other therapeutic moiety(ies) (e.g. a taxane such, for example, docetaxel and paclitaxel).

and/or gemcitabine and/or doxorubicin).

In a particular embodiment the combination therapy for the treatment of platinum-resistant tumors comprises the use of a DLL3 CAR treatment and doxorubicin and/or etoposide and/or gemcitabine and/or vinorelbine and/or ifosfamide and/or leucovorin-modulated 5-fluorouracil and/or bevacizumab and/or tamoxifen; and optionally one or more other therapeutic moiety(ies).

In another embodiment the combination therapy comprises the use of a DLL3 CAR treatment and a PARP inhibitor and optionally one or more other therapeutic moiety(ies).

In another embodiment the combination therapy comprises the use of an DLL3 CAR treatment and bevacizumab and optionally cyclophosphamide.

The combination therapy may comprise a DLL3 CAR treatment and a chemotherapeutic moiety that is effective on a tumor comprising a mutated or aberrantly expressed gene or protein (e.g. BRCA1).

More generally the DLL3 CAR treatments of the instant invention may be used in combination with a number of anti-cancer agents. The term “anti-cancer agent” or “chemotherapeutic agent” as used herein is one subset of “therapeutic moieties”, which in turn is a subset of the agents described as “pharmaceutically active moieties”. More particularly “anti-cancer agent” means any agent that can be used to treat a cell proliferative disorder such as cancer, and includes, but is not limited to, cytotoxic agents, cytostatic agents, anti-angiogenic agents, debulking agents, chemotherapeutic agents, radiotherapy and radiotherapeutic agents, targeted anti-cancer agents, biological response modifiers, therapeutic antibodies, cancer vaccines, cytokines, hormone therapy, anti-metastatic agents and immunotherapeutic agents. It will be appreciated that in selected embodiments as discussed above, such anti-cancer agents may comprise antibody drug conjugates and may be associated with antibodies prior to administration.

The term “cytotoxic agent”, which can also be an anti-cancer agent means a substance that is toxic to the cells and decreases or inhibits the function of cells and/or causes destruction of cells. Typically, the substance is a naturally occurring molecule derived from a living organism (or a synthetically prepared natural product). Examples of cytotoxic agents include, but are not limited to, small molecule toxins or enzymatically active toxins of bacteria (e.g., Diphtheria toxin, Pseudomonas endotoxin and exotoxin, Staphylococcal enterotoxin A), fungal (e.g., α -sarcin, restrictocin), plants (e.g., abrin, ricin, modeccin, viscumin, pokeweed anti-viral protein, saporin, gelonin, momoridin, trichosanthin, barley toxin, Aleurites fordii proteins, dianthin proteins, Phytolacca mericana proteins (PAPI, PAPII, and PAP-S), Momordica charantia inhibitor, curcun,

crocin, saponaria officinalis inhibitor, mitegellin, restrictocin, phenomycin, neomycin, and the tricothecenes) or animals, (e.g., cytotoxic RNases, such as extracellular pancreatic RNases; DNase I, including fragments and/or variants thereof).

An anti-cancer agent can include any chemical agent that inhibits, or is designed to inhibit, a cancerous cell or a cell likely to become cancerous or generate tumorigenic progeny (e.g., tumorigenic cells). Such chemical agents are often directed to intracellular processes necessary for cell growth or division, and are thus particularly effective against cancerous cells, which generally grow and divide rapidly. For example, vincristine depolymerizes microtubules, and thus inhibits cells from entering mitosis. Such agents are often administered, and are often most effective, in combination, e.g., in the formulation CHOP.

Examples of anti-cancer agents that may be used in combination with DLL3 CAR treatment of the invention include, but are not limited to, alkylating agents, alkyl sulfonates, anastrozole, amanitins, aziridines, ethylenimines and methylamelamines, acetogenins, a camptothecin, BEZ-235, bortezomib, bryostatin, callystatin, CC-1065, ceritinib, crizotinib, cryptophycins, dolastatin, duocarmycin, eleutherobin, erlotinib, pancratistatin, a sarcodictyin, spongistatin, nitrogen mustards, antibiotics, enediyne dynemicin, bisphosphonates, esperamicin, chromoprotein enediyne antiobiotic chromophores, aclacinomysins, actinomycin, authramycin, azaserine, bleomycins, cactinomycin, canfosfamide, carabycin, carminomycin, carzinophilin, chromomycinis, cyclophosphamide, dactinomycin, daunorubicin, detorubicin, 6-diazo-5-oxo-L-norleucine, doxorubicin, epirubicin, esorubicin, exemestane, fluorouracil, fulvestrant, gefitinib, idarubicin, lapatinib, letrozole, lonafarnib, marcellomycin, megestrol acetate, mitomycins, mycophenolic acid, nogalamycin, olivomycins, pazopanib, peplomycin, potfiromycin, puromycin, quelamycin, rapamycin, rodorubicin, sorafenib, streptonigrin, streptozocin, tamoxifen, tamoxifen citrate, temozolomide, tepodina, tipifarnib, tubercidin, ubenimex, vandetanib, vorozole, XL-147, zinostatin, zorubicin; anti-metabolites, folic acid analogues, purine analogs, androgens, anti-adrenals, folic acid replenisher such as frolinic acid, aceglatone, aldophosphamide glycoside, aminolevulinic acid, eniluracil, amsacrine, bestrabucil, bisantrene, edatraxate, defofamine, demecolcine, diaziquone, elfornithine, elliptinium acetate, epothilone, etoglucid, gallium nitrate, hydroxyurea, lentinan, lonidainine, maytansinoids, mitoguazone, mitoxantrone, mopidanmol, nitraerine, pentostatin, phenamet, pirarubicin, losoxantrone, podophyllinic acid, 2-ethylhydrazide, procarbazine, polysaccharide complex, razoxane; rhizoxin; SF-1126, sizofiran; spirogermanium; tenuazonic acid; triaziquone; 2,2',2"-trichlorotriethylamine; tricothecenes (T-2 toxin, verracurin A, roridin A and anguidine); urethan;

vindesine; dacarbazine; mannomustine; mitobronitol; mitolactol; pipobroman; gacytosine; arabinoside; cyclophosphamide; thiotepa; taxoids, chloranbucil; gemcitabine; 6-thioguanine; mercaptopurine; methotrexate; platinum analogs, vinblastine; platinum; etoposide; ifosfamide; mitoxantrone; vincristine; vinorelbine; novantrone; teniposide; edatrexate; daunomycin; aminopterin; xeloda; ibandronate; irinotecan, topoisomerase inhibitor RFS 2000; difluoromethylornithine; retinoids; capecitabine; combretastatin; leucovorin; oxaliplatin; XL518, inhibitors of PKC-alpha, Raf, H-Ras, EGFR and VEGF-A that reduce cell proliferation and pharmaceutically acceptable salts or solvates, acids or derivatives of any of the above. Also included in this definition are anti-hormonal agents that act to regulate or inhibit hormone action on tumors such as anti-estrogens and selective estrogen receptor antibodies, aromatase inhibitors that inhibit the enzyme aromatase, which regulates estrogen production in the adrenal glands, and anti-androgens; as well as troxacitabine (a 1,3- dioxolane nucleoside cytosine analog); antisense oligonucleotides, ribozymes such as a VEGF expression inhibitor and a HER2 expression inhibitor; vaccines, PROLEUKIN[®] rIL-2; LURTOTECAN[®] topoisomerase 1 inhibitor; ABARELIX[®] rmRH; Vinorelbine and Esperamicins and pharmaceutically acceptable salts or solvates, acids or derivatives of any of the above.

Particularly preferred anti-cancer agents comprise commercially or clinically available compounds such as erlotinib (TARCEVA[®], Genentech/OSI Pharm.), docetaxel (TAXOTERE[®], Sanofi-Aventis), 5-FU (fluorouracil, 5-fluorouracil, CAS No. 51-21-8), gemcitabine (GEMZAR[®], Lilly), PD-0325901 (CAS No. 391210-10-9, Pfizer), cisplatin (cis-diamine, dichloroplatinum(II), CAS No. 15663-27-1), carboplatin (CAS No. 41575-94-4), paclitaxel (TAXOL[®], Bristol-Myers Squibb Oncology, Princeton, N.J.), trastuzumab (HERCEPTIN[®], Genentech), temozolomide (4-methyl-5-oxo- 2,3,4,6,8-pentazabicyclo [4.3.0] nona-2,7,9-triene- 9-carboxamide, CAS No. 85622-93-1, TEMODAR[®], TEMODAL[®], Schering Plough), tamoxifen ((Z)-2-[4-(1,2-diphenylbut-1-enyl)phenoxy]-N,N-dimethylethanamine, NOLVADEX[®], ISTUBAL[®], VALODEX[®]), and doxorubicin (ADRIAMYCIN[®]). Additional commercially or clinically available anti-cancer agents comprise oxaliplatin (ELOXATIN[®], Sanofi), bortezomib (VELCADE[®], Millennium Pharm.), sunitinib (SUNITINIB[®], SU11248, Pfizer), letrozole (FEMARA[®], Novartis), imatinib mesylate (GLEEVEC[®], Novartis), XL-518 (Mek inhibitor, Exelixis, WO 2007/044515), ARRY-886 (Mek inhibitor, AZD6244, Array BioPharma, Astra Zeneca), SF-1126 (PI3K inhibitor, Semafore Pharmaceuticals), BEZ-235 (PI3K inhibitor, Novartis), XL-147 (PI3K inhibitor, Exelixis), PTK787/ZK 222584 (Novartis), fulvestrant (FASLODEX[®], AstraZeneca), leucovorin (folinic acid), rapamycin (sirolimus, RAPAMUNE[®], Wyeth), lapatinib (TYKERB[®], GSK572016, Glaxo

Smith Kline), lonafarnib (SARASAR™, SCH 66336, Schering Plough), sorafenib (NEXAVAR®, BAY43-9006, Bayer Labs), gefitinib (IRESSA®, AstraZeneca), irinotecan (CAMPTOSAR®, CPT-11, Pfizer), tipifarnib (ZARNESTRA™, Johnson & Johnson), ABRAXANE™ (Cremophor-free), albumin-engineered nanoparticle formulations of paclitaxel (American Pharmaceutical Partners, Schaumburg, IL), vandetanib (rINN, ZD6474, ZACTIMA®, AstraZeneca), chloranmbucil, AG1478, AG1571 (SU 5271; Sugen), temsirolimus (TORISEL®, Wyeth), pazopanib (GlaxoSmithKline), canfosfamide (TELCYTA®, Telik), thiotepa and cyclophosphamide (CYTOXAN®, NEOSAR®); vinorelbine (NAVELBINE®); capecitabine (XELODA®, Roche), tamoxifen (including NOLVADEX®; tamoxifen citrate, FARESTON® (toremifene citrate) MEGASE® (megestrol acetate), AROMASIN® (exemestane; Pfizer), formestanie, fadrozole, RIVISOR® (vorozole), FEMARA® (letrozole; Novartis), and ARIMIDEX® (anastrozole; AstraZeneca).

The term “pharmaceutically acceptable salt” or “salt” means organic or inorganic salts of a molecule or macromolecule. Acid addition salts can be formed with amino groups. Exemplary salts include, but are not limited, to sulfate, citrate, acetate, oxalate, chloride, bromide, iodide, nitrate, bisulfate, phosphate, acid phosphate, isonicotinate, lactate, salicylate, acid citrate, tartrate, oleate, tannate, pantothenate, bitartrate, ascorbate, succinate, maleate, gentisinate, fumarate, gluconate, glucuronate, saccharate, formate, benzoate, glutamate, methanesulfonate, ethanesulfonate, benzenesulfonate, p-toluenesulfonate, and pamoate (i.e., 1,1' methylene bis-(2-hydroxy 3-naphthoate)) salts. A pharmaceutically acceptable salt may involve the inclusion of another molecule such as an acetate ion, a succinate ion or other counterion. The counterion may be any organic or inorganic moiety that stabilizes the charge on the parent compound. Furthermore, a pharmaceutically acceptable salt may have more than one charged atom in its structure. Where multiple charged atoms are part of the pharmaceutically acceptable salt, the salt can have multiple counter ions. Hence, a pharmaceutically acceptable salt can have one or more charged atoms and/or one or more counterion.

“Pharmaceutically acceptable solvate” or “solvate” refers to an association of one or more solvent molecules and a molecule or macromolecule. Examples of solvents that form pharmaceutically acceptable solvates include, but are not limited to, water, isopropanol, ethanol, methanol, DMSO, ethyl acetate, acetic acid, and ethanolamine.

In other embodiments the DLL3 CAR treatments of the instant invention may be used in combination with any one of a number of antibodies (or immunotherapeutic agents) presently in clinical trials or commercially available. The disclosed antibodies may be used in combination

with an antibody selected from the group consisting of abagovomab, adecatumumab, afutuzumab, alemtuzumab, altumomab, amatuximab, anatumomab, arcitumomab, atezolizumab, avelumab, bavituximab, bectumomab, bevacizumab, bivatumumab, blinatumomab, brentuximab, cantuzumab, catumaxomab, cetuximab, citatumumab, cixutumumab, clivatuzumab, conatumumab, daratumumab, drozitumab, duligotumab, dusigitumab, detumomab, dacetuzumab, dalotuzumab, durvalumab, ecomeximab, elotuzumab, ensituximab, ertumaxomab, etaracizumab, farletuzumab, ficlatuzumab, figitumumab, flinvotumab, futuximab, ganitumab, gemtuzumab, girentuximab, glembatumumab, ibritumomab, igovomab, imgatuzumab, indatuximab, inotuzumab, intetumumab, ipilimumab, iratumumab, labetuzumab, lexatumumab, lintuzumab, lorvotuzumab, lucatumumab, mapatumumab, matuzumab, milatumumab, minretumomab, mitumomab, moxetumomab, narnatumab, naptumomab, necitumumab, nimotuzumab, nivolumab, nofetumomab, obinutuzumab, ocaratuzumab, ofatumumab, olaratumab, olaparib, onartuzumab, oportuzumab, oregovomab, panitumumab, parsatumumab, patritumab, pembrolizumab, pemtumomab, pertuzumab, pidilizumab, pintumomab, pritumumab, racotumomab, radretumab, ramucirumab, rilotumumab, rituximab, robatumumab, satumomab, selumetinib, sibrotuzumab, siltuximab, simtuzumab, solitomab, tacatumumab, taplitumomab, tenatumomab, teprotumumab, tigatumumab, tositumomab, trastuzumab, tucotuzumab, ublituximab, veltuzumab, vorsetuzumab, votumumab, zalutumumab, CC49, 3F8, MDX-1105 and combinations thereof.

Other particularly preferred embodiments comprise the use of the disclosed compositions with antibodies approved for cancer therapy including, but not limited to, rituximab, gemtuzumab, ozogamycin, alemtuzumab, ibritumomab, tiuxetan, tositumomab, bevacizumab, cetuximab, panitumumab, ofatumumab, ipilimumab and brentuximab vedotin. Those skilled in the art will be able to readily identify additional anti-cancer agents that are compatible with the teachings herein.

The present invention also provides for the combination of the DLL3 CAR treatments with radiotherapy (i.e., any mechanism for inducing DNA damage locally within tumor cells such as gamma-irradiation, X-rays, UV-irradiation, microwaves, electronic emissions and the like). Combination therapy using the directed delivery of radioisotopes to tumor cells is also contemplated, and the disclosed DLL3 CAR treatments may be used in connection with a targeted anti-cancer agent or other targeting means. Typically, radiation therapy is administered in pulses over a period of time from about 1 to about 2 weeks. The radiation therapy may be administered to subjects having head and neck cancer for about 6 to 7 weeks. Optionally, the

radiation therapy may be administered as a single dose or as multiple, sequential doses.

X. Diagnostics

The invention provides *in vitro* and *in vivo* methods for detecting, diagnosing or monitoring the efficiency of any lymphocyte transduction or the effect of any DLL3 sensitized lymphocytes on tumor cells including tumorigenic cells. Such methods include identifying an individual having cancer (e.g., a DLL3 positive tumor) for treatment or monitoring progression of a cancer, comprising interrogating the patient or a sample obtained from a patient (either *in vivo* or *in vitro*) with an antibody as described herein before during or after treatment with DLL3 sensitized lymphocytes and detecting presence or absence, or level of association, of the antibody to bound or free target molecules in the sample. In some embodiments the DLL3 antibody will comprise a detectable label or reporter molecule as described herein. In yet other embodiments (e.g., *In situ* hybridization or ISH) a nucleic acid probe that reacts with a genomic DLL3 determinant will be used in the detection, diagnosis or monitoring of the proliferative disorder.

More generally the presence and/or levels of DLL3 determinants may be measured using any of a number of techniques available to the person of ordinary skill in the art for protein or nucleic acid analysis, e.g., direct physical measurements (e.g., mass spectrometry), binding assays (e.g., immunoassays, agglutination assays, and immunochromatographic assays), Polymerase Chain Reaction (PCR, RT-PCR; RT-qPCR) technology, branched oligonucleotide technology, Northern blot technology, oligonucleotide hybridization technology and *in situ* hybridization technology. The method may also comprise measuring a signal that results from a chemical reaction, e.g., a change in optical absorbance, a change in fluorescence, the generation of chemiluminescence or electrochemiluminescence, a change in reflectivity, refractive index or light scattering, the accumulation or release of detectable labels from the surface, the oxidation or reduction or redox species, an electrical current or potential, changes in magnetic fields, etc. Suitable detection techniques may detect binding events by measuring the participation of labeled binding reagents through the measurement of the labels via their photoluminescence (e.g., via measurement of fluorescence, time-resolved fluorescence, evanescent wave fluorescence, up-converting phosphors, multi-photon fluorescence, etc.), chemiluminescence, electrochemiluminescence, light scattering, optical absorbance, radioactivity, magnetic fields, enzymatic activity (e.g., by measuring enzyme activity through enzymatic reactions that cause changes in optical absorbance or fluorescence or cause the emission of chemiluminescence). Alternatively, detection techniques may be used that do not

require the use of labels, e.g., techniques based on measuring mass (e.g., surface acoustic wave measurements), refractive index (e.g., surface plasmon resonance measurements), or the inherent luminescence of an analyte.

In some embodiments, the association of the detection agent with particular cells or cellular components in the sample indicates that the sample may contain tumorigenic cells, thereby denoting that the individual having cancer may be effectively treated with the compositions as described herein.

In certain preferred embodiments the assays may comprise immunohistochemistry (IHC) assays or variants thereof (e.g., fluorescent, chromogenic, standard ABC, standard LSAB, etc.), immunocytochemistry or variants thereof (e.g., direct, indirect, fluorescent, chromogenic, etc.) or *In situ* hybridization (ISH) or variants thereof (e.g., chromogenic in situ hybridization (CISH) or fluorescence in situ hybridization (DNA-FISH or RNA-FISH))

In this regard certain aspects of the instant invention comprise the use of labeled DLL3 for immunohistochemistry (IHC). More particularly DLL3 IHC may be used as a diagnostic tool to aid in the diagnosis of various proliferative disorders and to monitor the potential response to treatments including DLL3 antibody therapy. As discussed herein and shown in the Examples below compatible diagnostic assays may be performed on tissues that have been chemically fixed (including but not limited to: formaldehyde, glutaraldehyde, osmium tetroxide, potassium dichromate, acetic acid, alcohols, zinc salts, mercuric chloride, chromium tetroxide and picric acid) and embedded (including but not limited to: glycol methacrylate, paraffin and resins) or preserved via freezing. Such assays can be used to guide treatment decisions and determine dosing regimens and timing.

Other particularly compatible aspects of the invention involve the use of *in situ* hybridization to detect or monitor DLL3 determinants. *In situ* hybridization technology or ISH is well known to those of skill in the art. Briefly, cells are fixed and detectable probes which contain a specific nucleotide sequence are added to the fixed cells. If the cells contain complementary nucleotide sequences, the probes, which can be detected, will hybridize to them. Using the sequence information set forth herein, probes can be designed to identify cells that express genotypic DLL3 determinants. Probes preferably hybridize to a nucleotide sequence that corresponds to such determinants. Hybridization conditions can be routinely optimized to minimize background signal by non-fully complementary hybridization though preferably the probes are preferably fully complementary to the selected DLL3 determinant. In selected

embodiments the probes are labeled with fluorescent dye attached to the probes that is readily detectable by standard fluorescent methodology.

Compatible *in vivo* theragnostics or diagnostic assays may comprise art-recognized imaging or monitoring techniques such as magnetic resonance imaging, computerized tomography (e.g. CAT scan), positron tomography (e.g., PET scan) radiography, ultrasound, etc., as would be known by those skilled in the art.

In a particularly preferred embodiment the antibodies disclosed herein may be used to detect and quantify levels of a particular determinant (e.g., DLL3) in a patient sample (e.g., plasma or blood) which may, in turn, be used to detect, diagnose or monitor proliferative disorders both before and after treatment with the DLL3 sensitized lymphocytes. In related embodiments the antibodies disclosed herein may be used to detect, monitor and/or quantify circulating tumor cells either *in vivo* or *in vitro* (WO 2012/0128801) in combination with the disclosed treatments by DLL3 sensitized lymphocytes. In still other embodiments the circulating tumor cells may comprise tumorigenic cells.

In certain embodiments of the invention, the tumorigenic cells in a subject or a sample from a subject may be assessed or characterized using the disclosed antibodies prior to DLL3 CAR therapy or regimen to establish a baseline. In other examples, the tumorigenic cells can be assessed from a sample that is derived from a subject that was treated.

XI. Articles of Manufacture

The invention further includes pharmaceutical packs and kits comprising one or more containers or receptacles, wherein a container can comprise one or more transformation doses of a DLL3 CAR plasmid or vector of the invention. In certain embodiments, the pack or kit contains a vector preparation (e.g., lentiviral or retroviral) comprising a nucleic acid encoding a DLL3 CAR, with or without one or more additional reagents and optionally a means of effecting transduction. Preferably the kit will further include the means to monitor and characterize the preparation of DLL3 sensitized lymphocytes prior to administration.

Certain other embodiments will comprise a container or receptacle incorporating, containing or holding a liquid formulation (dispersion, suspension or solution) of DLL3 sensitized lymphocytes. In selected embodiments the DLL3 sensitized lymphocytes will be allogenic. In other embodiments the DLL3 sensitized lymphocytes will comprise autologous host cells. In certain other embodiments the liquid formulation will comprise a pharmaceutically acceptable carrier.

In selected aspects kits compatible with the invention would allow a user to produce the DLL3 sensitive lymphocytes, monitor transduction rates and characterize the resulting DLL3 sensitive lymphocyte population to ensure quality prior to administration. Accordingly, a kit of the invention may generally contain a pharmaceutically acceptable formulation of the CAR nucleic acid (or vector) and, optionally, one or more reagents in the same or different containers. In preferred embodiments the DLL3 CAR vectors will comprise viral vectors (e.g., lentiviral or retroviral) that allow for transduction of selected host cells to provide the disclosed sensitized lymphocytes. In certain embodiments the selected host cell will be autologous while in other embodiments the selected host cells will be allogeneic. Some aspects of the invention are directed to kits including allogeneic cells along with the DLL3 CAR vector. Yet other embodiments comprise kits or containers or receptacles incorporating a pharmaceutical composition comprising allogeneic DLL3 sensitized lymphocytes. Still other articles of manufacture comprise a container incorporating or holding a liquid formulation of autologous DLL3 sensitized lymphocytes in a pharmaceutically acceptable carrier. In all such kits the container may comprise an infusion bag, vial, syringe or bottle that would allow the DLL3 sensitized lymphocytes to be directly administered to the patient.

The kits may also contain other pharmaceutically acceptable formulations or devices, either for diagnosis or combination therapy. Examples of diagnostic devices or instruments include those that can be used to detect, monitor, quantify or profile cells or markers associated with the DLL3 sensitive lymphocytes, transformation efficiency or the proliferative disorder to be treated. In particularly preferred embodiments the devices may be used to detect, monitor and/or quantify circulating tumor cells either *in vivo* or *in vitro*. In still other preferred embodiments the circulating tumor cells may comprise tumorigenic cells.

When selected components of the kit (e.g., DLL3 sensitized lymphocytes) are provided in one or more liquid solutions, the liquid solution can be non-aqueous though an aqueous solution is preferred, with a sterile aqueous solution being particularly preferred. The formulations of the kit (e.g., a viral vector) can also be provided as dried powder(s) or in lyophilized form that can be reconstituted upon addition of an appropriate liquid. The liquid used for reconstitution can be contained in a separate container. Such liquids can comprise sterile, pharmaceutically acceptable buffer(s) or other diluent(s) such as bacteriostatic water for injection, phosphate-buffered saline, Ringer's solution or dextrose solution. Where the kit comprises the CAR plasmid or vectors of the invention in combination with additional reagents, the solution may be pre-mixed, either in a molar equivalent combination, or with one component in excess of the other.

Alternatively, the plasmids of the invention and any optional co-reagents can be maintained separately within distinct containers prior to transformation of the lymphocytes. In other preferred embodiments container(s) of the kit may comprise liquid formulations of allogeneic DLL3 sensitized lymphocytes.

5 The disclosed kits can comprise one or multiple containers and a label or package insert in, on or associated with the container(s), indicating that the enclosed composition is useful for treating a proliferative disorder or for preparing cells for treating the selected disease. Suitable containers or receptacles include, for example, bottles, vials, syringes, etc. The containers can be formed from a variety of materials such as glass or plastic. The container(s) can comprise a
10 sterile access port, for example, the container may be an intravenous solution bag or a vial having a stopper that can be pierced by a hypodermic injection needle.

 In some embodiments the kit can contain a means by which to administer the DLL3 sensitized lymphocytes and any optional components to a patient, e.g., one or more needles or syringes (pre-filled or empty), an eye dropper, pipette, or other such like apparatus, from which
15 the formulation may be injected or introduced into the subject or applied to a diseased area of the body. The kits of the invention will also typically include a means for containing the vials, or such like, and other components in close confinement for commercial sale, such as, e.g., blow-molded plastic containers into which the desired vials and other apparatus are placed and retained method.

20 XII. Miscellaneous

 Unless otherwise defined herein, scientific and technical terms used in connection with the invention shall have the meanings that are commonly understood by those of ordinary skill in the art. Further, unless otherwise required by context, singular terms shall include pluralities and plural terms shall include the singular. In addition, ranges provided in the specification and
25 appended claims include both end points and all points between the end points. Therefore, a range of 2.0 to 3.0 includes 2.0, 3.0, and all points between 2.0 and 3.0.

 Generally, techniques of cell and tissue culture, molecular biology, immunology, microbiology, genetics and chemistry described herein are those well known and commonly used in the art. The nomenclature used herein, in association with such techniques, is also
30 commonly used in the art. The methods and techniques of the invention are generally performed according to conventional methods well known in the art and as described in various references that are cited throughout the present specification unless otherwise indicated.

XIII. References

The complete disclosure of all patents, patent applications, and publications, and electronically available material (including, for example, nucleotide sequence submissions in, e.g., GenBank and RefSeq, and amino acid sequence submissions in, e.g., SwissProt, PIR, PRF, PDB, and translations from annotated coding regions in GenBank and RefSeq) cited herein are incorporated by reference, regardless of whether the phrase “incorporated by reference” is or is not used in relation to the particular reference. The foregoing detailed description and the examples that follow have been given for clarity of understanding only. No unnecessary limitations are to be understood therefrom. The invention is not limited to the exact details shown and described. Variations obvious to one skilled in the art are included in the invention defined by the claims. Any section headings used herein are for organizational purposes only and are not to be construed as limiting the subject matter described method.

XIV. Sequences

Appended to the instant application are figures and a sequence listing comprising a number of nucleic acid and amino acid sequences. The following Table 2 provides a summary of the included sequences.

TABLE 2

SEQ ID NO:	Description
1	DLL3 isoform 1 protein
2	DLL3 isoform 2 protein
3	Epitope protein - SC16.23
4	Epitope protein - SC16.34 & SC 16.56
5	Kappa constant region protein
6	IgG1 constant region protein
7	(G ₄ S) ₃ pentamer
8	h16.15 scFv protein
9	SCT1-h16.15 CAR DNA
10	SCT1-h16.15 CAR protein
11	h16.13 scFv DNA

12	h16.13 scFv protein
13	h16.25 scFv DNA
14	h16.25 scFv protein
15	h16.15 scFv DNA
16	SCT1-h16.13 CAR DNA
17	SCT1-h16.13 CAR protein
18	SCT1-h16.25 CAR DNA
19	SCT1-h16.25 CAR protein
20	SC16.3 VL DNA (aligned with encoded protein)
21	SC16.3 VL protein
22	SC16.3 VH DNA (aligned with encoded protein)
23	SC16.3 VH protein
24-387	Additional murine clones as in SEQ ID NOs: 20-23
388-407	Humanized clones as in SEQ ID NOs: 20-23
408, 409, 410	hSC16.13 CDRL1, CDRL2, CDRL3
411, 412, 413	hSC16.13 CDRH1, CDRH2, CDRH3
414, 415, 416	hSC16.15 CDRL1, CDRL2, CDRL3
417, 418, 419	hSC16.15 CDRH1, CDRH2, CDRH3
420, 421, 422	hSC16.25 CDRL1, CDRL2, CDRL3
423, 424, 425	hSC16.25 CDRH1, CDRH2, CDRH3
426, 427, 428	hSC16.34 CDRL1, CDRL2, CDRL3
429, 430, 431	hSC16.34 CDRH1, CDRH2, CDRH3
432, 433, 434	hSC16.56 CDRL1, CDRL2, CDRL3
435, 436, 437	hSC16.56 CDRH1, CDRH2, CDRH3

As discussed in Example 2 below, Table 2 above may further be used to designate SEQ ID NOS for exemplary Kabat CDRs delineated in FIGS. 1A and 1B. More particularly FIGS. 1A and 1B denote the three Kabat CDRs of each heavy (CDRH) and light (CDRL) chain variable region sequence and Table 2 above provides for assignment of a SEQ ID designation that may be applied to each CDRL1, CDRL2 and CDRL3 of the light chain and each CDRH1, CDRH2 and CDRH3 of the heavy chain. Using this methodology each unique CDR set forth in FIGS 1A and 1B may be assigned a sequential SEQ ID NO and can be used to provide the derived antibodies of the instant invention.

XV. Tumor Listing

PDX tumor cell types are denoted by an abbreviation followed by a number, which indicates the particular tumor cell line. The passage number of the tested sample is indicated by p0-p# appended to the sample designation where p0 is indicative of an unpassaged sample obtained directly from a patient tumor and p# is indicative of the number of times the tumor has been passaged through a mouse prior to testing. As used herein, the abbreviations of the tumor types and subtypes are shown in Table 3 as follows:

TABLE 3

<u>Tumor Type</u>	<u>Abbreviation</u>	<u>Tumor subtype</u>	<u>Abbreviation</u>
Breast	BR		
		estrogen receptor positive and/or progesterone receptor positive	BR-ERPR
		ERBB2/Neu positive	BR- ERBB2/Neu
		HER2 positive	BR-HER2
		triple-negative	TNBC
		claudin subtype of triple-negative	TNBC-CLDN
colorectal	CR		
endometrial	EN		
gastric	GA		
		diffuse adenocarcinoma	GA-Ad-Dif/Muc
		intestinal adenocarcinoma	GA-Ad-Int
		stromal tumors	GA-GIST
glioblastoma	GB		
head and neck	HN		
kidney	KDY		
		clear renal cell carcinoma	KDY-CC
		papillary renal cell carcinoma	KDY-PAP
		transitional cell or urothelial carcinoma	KDY-URO
		unknown	KDY-UNK
liver	LIV		
		hepatocellular carcinoma	LIV-HCC
		cholangiocarcinoma	LIV-CHOL
lymphoma	LN		
lung	LU		
		adenocarcinoma	LU-Ad

		carcinoid	LU-CAR
		large cell neuroendocrine	LU-LCC
		non-small cell	NSCLC
		squamous cell	LU-SCC
		small cell	SCLC
		spindle cell	LU-SPC
melanoma	MEL		
ovarian	OV		
		clear cell	OV-CC
		endometrioid	OV-END
		mixed subtype	OV-MIX
		malignant mixed mesodermal	OV-MMMT
		mucinous	OV-MUC
		neuroendocrine	OV-NET
		papillary serous	OV-PS
		serous	OV-S
		small cell	OV-SC
		transitional cell carcinoma	OV-TCC
pancreatic	PA		
		acinar cell carcinoma	PA-ACC
		duodenal carcinoma	PA-DC
		mucinous adenocarcinoma	PA-MAD
		neuroendocrine	PA-NET
		adenocarcinoma	PA-PAC
		adenocarcinoma exocrine type	PA-PACe
		ductal adenocarcinoma	PA-PDAC
		ampullary adenocarcinoma	PA-AAC
prostate	PR		
skin	SK		
		melanoma	MEL
		squamous cell carcinomas	SK-SCC

EXAMPLES

The invention, thus generally described above, will be understood more readily by reference to the following examples, which are provided by way of illustration and are not intended to be limiting of the instant invention. The examples are not intended to represent that the experiments below are all or the only experiments performed. Unless indicated otherwise, parts are parts by weight, molecular weight is weight average molecular weight, temperature is in degrees Centigrade, and pressure is at or near atmospheric.

Example 1

Generation of Murine Anti-DLL3 Antibodies

Anti-DLL3 murine antibodies were produced as follows. In a first immunization campaign, three mice (one from each of the following strains: Balb/c, CD-1, FVB) were inoculated with human DLL3-fc protein (hDLL3-Fc) emulsified with an equal volume of TiterMax[®] or alum adjuvant. The hDLL3-Fc fusion construct was purchased from Adipogen International (Catalog No. AG-40A-0113). An initial immunization was performed with an emulsion of 10 µg hDLL3-Fc per mouse in TiterMax. Mice were then boosted biweekly with 5 µg hDLL3-Fc per mouse in alum adjuvant. The final injection prior to fusion was with 5 µg hDLL3-Fc per mouse in PBS.

In a second immunization campaign six mice (two each of the following strains: Balb/c, CD-1, FVB), were inoculated with human DLL3-His protein (hDLL3-His), emulsified with an equal volume of TiterMax[®] or alum adjuvant. Recombinant hDLL3-His protein was purified from the supernatants of CHO-S cells engineered to overexpress hDLL3-His. The initial immunization was with an emulsion of 10 µg hDLL3-His per mouse in TiterMax. Mice were then boosted biweekly with 5 µg hDLL3-His per mouse in alum adjuvant. The final injection was with 2×10^5 HEK-293T cells engineered to overexpress hDLL3.

Solid-phase ELISA assays were used to screen mouse sera for mouse IgG antibodies specific for human DLL3. A positive signal above background was indicative of antibodies specific for DLL3. Briefly, 96 well plates (VWR International, Cat. #610744) were coated with recombinant DLL3-His at 0.5µg/ml in ELISA coating buffer overnight. After washing with PBS containing 0.02% (v/v) Tween 20, the wells were blocked with 3% (w/v) BSA in PBS, 200 µL/well for 1 hour at room temperature (RT). Mouse serum was titrated (1:100, 1:200, 1:400, and 1:800) and added to the DLL3 coated plates at 50 µL/well and incubated at RT for 1 hour. The plates are washed and then incubated with 50 µL/well HRP-labeled goat anti-mouse IgG diluted 1:10,000 in 3% BSA-PBS or 2% FCS in PBS for 1 hour at RT. Again the plates were washed and 40 µL/well of a TMB substrate solution (Thermo Scientific 34028) was added for 15 minutes at RT. After developing, an equal volume of 2N H₂SO₄ was added to stop substrate development and the plates were analyzed by spectrophotometer at OD 450.

Sera-positive immunized mice were sacrificed and draining lymph nodes (popliteal, inguinal, and medial iliac) were dissected and used as a source for antibody producing cells. Cell suspensions of B cells (approximately 229×10^6 cells from the hDLL3-Fc immunized mice,

and 510×10^6 cells from the hDLL3-His immunized mice) were fused with non-secreting P3x63Ag8.653 myeloma cells at a ratio of 1:1 by electro cell fusion using a model BTX Hybrimmune System (BTX Harvard Apparatus). Cells were re-suspended in hybridoma selection medium consisting of DMEM medium supplemented with azaserine, 15% fetal clone I serum, 10% BM Condimed (Roche Applied Sciences), 1 mM nonessential amino acids, 1 mM HEPES, 100 IU penicillin-streptomycin, and 50 μ M 2-mercaptoethanol, and were cultured in four T225 flasks in 100 mL selection medium per flask. The flasks were placed in a humidified 37°C incubator containing 5% CO₂ and 95% air for six to seven days.

On day six or seven after the fusions the hybridoma library cells were collected from the flasks and plated at one cell per well (using the FACS Aria I cell sorter) in 200 μ L of supplemented hybridoma selection medium (as described above) into 64 Falcon 96-well plates, and 48 96-well plates for the hDLL3-His immunization campaign. The rest of the library was stored in liquid nitrogen.

The hybridomas were cultured for 10 days and the supernatants were screened for antibodies specific to hDLL3 using flow cytometry performed as follows. 1×10^5 per well of HEK-293T cells engineered to overexpress human DLL3, mouse DLL3 (pre-stained with dye), or cynomolgus DLL3 (pre-stained with Dylight800) were incubated for 30 minutes with 25 μ L hybridoma supernatant. Cells were washed with PBS/2% FCS and then incubated with 25 μ L per sample DyeLight 649 labeled goat-anti-mouse IgG, Fc fragment specific secondary diluted 1:300 in PBS/2%FCS. After a 15 minute incubation cells were washed twice with PBS/2%FCS and re-suspended in PBS/2%FCS with DAPI and analyzed by flow cytometry for fluorescence exceeding that of cells stained with an isotype control antibody. Remaining unused hybridoma library cells were frozen in liquid nitrogen for future library testing and screening.

The hDLL3-His immunization campaign yielded approximately 50 murine anti-hDLL3 antibodies and the hDLL3-Fc immunization campaign yielded approximately 90 murine anti-hDLL3 antibodies.

Example 2

Sequencing of Anti-DLL3 Antibodies

Based on the foregoing, a number of exemplary distinct monoclonal antibodies that bind immobilized human DLL3 or h293-hDLL3 cells with apparently high affinity were selected for sequencing and further analysis. Sequence analysis of the light chain variable regions and heavy chain variable regions from selected monoclonal antibodies generated in Example 1

confirmed that many had novel complementarity determining regions and often displayed novel VDJ arrangements.

Initially selected hybridoma cells expressing the desired antibodies were lysed in Trizol[®] reagent (Trizol[®] Plus RNA Purification System, Life Technologies) to prepare the RNA encoding the antibodies. Between 10^4 and 10^5 cells were re-suspended in 1 mL Trizol and shaken vigorously after addition of 200 μ L chloroform. Samples were then centrifuged at 4°C for 10 minutes and the aqueous phase was transferred to a fresh microfuge tube and an equal volume of 70% ethanol was added. The sample was loaded on an RNeasy Mini spin column, placed in a 2 mL collection tube and processed according to the manufacturer's instructions. Total RNA was extracted by elution, directly to the spin column membrane with 100 μ L RNase-free water. The quality of the RNA preparations was determined by fractionating 3 μ L in a 1% agarose gel before being stored at -80°C until used.

The variable region of the Ig heavy chain of each hybridoma was amplified using a 5' primer mix comprising 32 mouse specific leader sequence primers designed to target the complete mouse VH repertoire in combination with a 3' mouse Cy primer specific for all mouse Ig isotypes. Similarly, a primer mix containing thirty two 5' Vk leader sequences designed to amplify each of the Vk mouse families was used in combination with a single reverse primer specific to the mouse kappa constant region in order to amplify and sequence the kappa light chain. For antibodies containing a lambda light chain, amplification was performed using three 5' VL leader sequences in combination with one reverse primer specific to the mouse lambda constant region. The VH and VL transcripts were amplified from 100 ng total RNA using the Qiagen One Step RT-PCR kit as follows. A total of eight RT-PCR reactions were run for each hybridoma, four for the Vk light chain and four for the Vy heavy chain. PCR reaction mixtures included 3 μ L of RNA, 0.5 μ L of 100 μ M of either heavy chain or kappa light chain primers (custom synthesized by Integrated Data Technologies), 5 μ L of 5 $\times$ RT-PCR buffer, 1 μ L dNTPs, 1 μ L of enzyme mix containing reverse transcriptase and DNA polymerase, and 0.4 μ L of ribonuclease inhibitor RNasin (1 unit). The thermal cycler program was RT step 50°C for 30 minutes, 95°C for 15 minutes followed by 30 cycles of (95°C for 30 seconds, 48°C for 30 seconds, 72°C for 1 minute). There was then a final incubation at 72°C for 10 minutes.

The extracted PCR products were sequenced using the same specific variable region primers as described above for the amplification of the variable regions. To prepare the PCR products for direct DNA sequencing, they were purified using the QIAquick[™] PCR Purification

Kit (Qiagen) according to the manufacturer's protocol. The DNA was eluted from the spin column using 50 µL of sterile water and then sequenced directly from both strands (MCLAB).

Selected nucleotide sequences were analyzed using the IMGT sequence analysis tool (http://www.imgt.org/IMGTools/sequence_analysis.html) to identify germline V, D and J gene members with the highest sequence homology. These derived sequences were compared to known germline DNA sequences of the Ig V- and J-regions by alignment of VH and VL genes to the mouse germline database using a proprietary antibody sequence database.

FIG. 1A depicts the contiguous amino acid sequences of numerous novel murine light chain variable regions from anti-DLL3 antibodies and exemplary humanized light chain variable regions derived from the variable light chains of representative murine anti-DLL3 antibodies (as per Example 3 below). FIG. 1B depicts the contiguous amino acid sequences of novel murine heavy chain variable regions from the same anti-DLL3 antibodies and humanized heavy chain variable regions derived from the same murine antibodies providing the humanized light chains (as per Example 3 below). Murine light and heavy chain variable region amino acid sequences are provided in SEQ ID NOS: 21 - 387, odd numbers while humanized light and heavy chain variable region amino acid sequences are provided in SEQ ID NOS: 389 – 407, odd numbers.

Thus, taken together FIGS. 1A and 1B provide the annotated sequences of numerous murine anti-DLL3 binding or targeting domains, termed SC16.3, SC16.4, SC16.5, SC16.7, SC16.8, SC16.10, SC16.11, SC16.13, SC16.15, SC16.18, SC16.19, SC16.20, SC16.21, SC16.22, SC16.23, SC16.25, SC16.26, SC16.29, SC16.30, SC16.31, SC16.34, SC16.35, SC16.36, SC16.38, SC16.41, SC16.42, SC16.45, SC16.47, SC16.49, SC16.50, SC16.52, SC16.55, SC16.56, SC16.57, SC16.58, SC16.61, SC16.62, SC16.63, SC16.65, SC16.67, SC16.68, SC16.72, SC16.73, SC16.78, SC16.79, SC16.80, SC16.81, SC16.84, SC16.88, SC16.101, SC16.103, SC16.104, SC16.105, SC16.106, SC16.107, SC16.108, SC16.109, SC16.110, SC16.111, SC16.113, SC16.114, SC16.115, SC16.116, SC16.117, SC16.118, SC16.120, SC16.121, SC16.122, SC16.123, SC16.124, SC16.125, SC16.126, SC16.129, SC16.130, SC16.131, SC16.132, SC16.133, SC16.134, SC16.135, SC16.136, SC16.137, SC16.138, SC16.139, SC16.140, SC16.141, SC16.142, SC16.143, SC16.144, SC16.147, SC16.148, SC16.149 and SC16.150 and humanized antibodies, termed hSC16.13, hSC16.15, hSC16.25, hSC16.34 and hSC16.56.

In particular aspects of the invention the CAR binding domain binds specifically to hDLL3 and was derived from, comprises or competes for binding with an antibody comprising: a light chain variable region (VL) of SEQ ID NO: 21 and a heavy chain variable region (VH) of SEQ ID

NO: 23; or a VL of SEQ ID NO: 25 and a VH of SEQ ID NO: 27; or a VL of SEQ ID NO: 29 and a VH of SEQ ID NO: 31; or a VL of SEQ ID NO: 33 and a VH of SEQ ID NO: 35; or a VL of SEQ ID NO: 37 and a VH of SEQ ID NO: 39; or a VL of SEQ ID NO: 41 and a VH of SEQ ID NO: 43; or a VL of SEQ ID NO: 45 and a VH of SEQ ID NO: 47; or a VL of SEQ ID NO: 49 and a VH of SEQ ID NO: 51; or a VL of SEQ ID NO: 53 and a VH of SEQ ID NO: 55; or a VL of SEQ ID NO: 57 and a VH of SEQ ID NO: 59; or a VL of SEQ ID NO: 61 and a VH of SEQ ID NO: 63; or a VL of SEQ ID NO: 65 and a VH of SEQ ID NO: 67; or a VL of SEQ ID NO: 69 and a VH of SEQ ID NO: 71; or a VL of SEQ ID NO: 73 and a VH of SEQ ID NO: 75; or a VL of SEQ ID NO: 77 and a VH of SEQ ID NO: 79; or a VL of SEQ ID NO: 81 and a VH of SEQ ID NO: 83; or a VL of SEQ ID NO: 85 and a VH of SEQ ID NO: 87; or a VL of SEQ ID NO: 89 and a VH of SEQ ID NO: 91; or a VL of SEQ ID NO: 93 and a VH of SEQ ID NO: 95; or a VL of SEQ ID NO: 97 and a VH of SEQ ID NO: 99; or a VL of SEQ ID NO: 101 and a VH of SEQ ID NO: 103; or a VL of SEQ ID NO: 105 and a VH of SEQ ID NO: 107; or a VL of SEQ ID NO: 109 and a VH of SEQ ID NO: 111; or a VL of SEQ ID NO: 113 and a VH of SEQ ID NO: 115; or a VL of SEQ ID NO: 117 and a VH of SEQ ID NO: 119; or a VL of SEQ ID NO: 121 and a VH of SEQ ID NO: 123; or a VL of SEQ ID NO: 125 and a VH of SEQ ID NO: 127; or a VL of SEQ ID NO: 129 and a VH of SEQ ID NO: 131; or a VL of SEQ ID NO: 133 and a VH of SEQ ID NO: 135; or a VL of SEQ ID NO: 137 and a VH of SEQ ID NO: 139; or a VL of SEQ ID NO: 141 and a VH of SEQ ID NO: 143; or a VL of SEQ ID NO: 145 and a VH of SEQ ID NO: 147; or a VL of SEQ ID NO: 149 and a VH of SEQ ID NO: 151; or a VL of SEQ ID NO: 153 and a VH of SEQ ID NO: 155; or a VL of SEQ ID NO: 157 and a VH of SEQ ID NO: 159; or a VL of SEQ ID NO: 161 and a VH of SEQ ID NO: 163; or a VL of SEQ ID NO: 165 and a VH of SEQ ID NO: 167; or a VL of SEQ ID NO: 169 and a VH of SEQ ID NO: 171; or a VL of SEQ ID NO: 173 and a VH of SEQ ID NO: 175; or a VL of SEQ ID NO: 177 and a VH of SEQ ID NO: 179; or a VL of SEQ ID NO: 181 and a VH of SEQ ID NO: 183; or a VL of SEQ ID NO: 185 and a VH of SEQ ID NO: 187; or a VL of SEQ ID NO: 189 and a VH of SEQ ID NO: 191; or a VL of SEQ ID NO: 193 and a VH of SEQ ID NO: 195; or a VL of SEQ ID NO: 197 and a VH of SEQ ID NO: 199; or a VL of SEQ ID NO: 201 and a VH of SEQ ID NO: 203; or a VL of SEQ ID NO: 205 and a VH of SEQ ID NO: 207; or a VL of SEQ ID NO: 209 and a VH of SEQ ID NO: 211; or a VL of SEQ ID NO: 213 and a VH of SEQ ID NO: 215; or a VL of SEQ ID NO: 217 and a VH of SEQ ID NO: 219; or a VL of SEQ ID NO: 221 and a VH of SEQ ID NO: 223; or a VL of SEQ ID NO: 225 and a VH of SEQ ID NO: 227; or a VL of SEQ ID NO: 229 and a VH of SEQ ID NO: 231; or a VL of SEQ ID NO: 233 and a VH of SEQ ID NO: 235; or a VL of SEQ ID NO: 237 and a VH of SEQ ID NO: 239; or a VL of SEQ

ID NO: 241 and a VH of SEQ ID NO: 243; or a VL of SEQ ID NO: 245 and a VH of SEQ ID NO:
 247; or a VL of SEQ ID NO: 249 and a VH of SEQ ID NO: 251; or a VL of SEQ ID NO: 253 and
 a VH of SEQ ID NO: 255; or a VL of SEQ ID NO: 257 and a VH of SEQ ID NO: 259; or a VL of
 5 ID NO: 261 and a VH of SEQ ID NO: 263; or a VL of SEQ ID NO: 265 and a VH of SEQ
 ID NO: 267; or a VL of SEQ ID NO: 269 and a VH of SEQ ID NO: 271; or a VL of SEQ ID NO:
 273 and a VH of SEQ ID NO: 275; or a VL of SEQ ID NO: 277 and a VH of SEQ ID NO: 279;
 or a VL of SEQ ID NO: 281 and a VH of SEQ ID NO: 283; or a VL of SEQ ID NO: 285 and a VH
 of SEQ ID NO: 287; or a VL of SEQ ID NO: 289 and a VH of SEQ ID NO: 291; or a VL of SEQ
 ID NO: 293 and a VH of SEQ ID NO: 295; or a VL of SEQ ID NO: 297 and a VH of SEQ ID
 10 NO: 299; or a VL of SEQ ID NO: 301 and a VH of SEQ ID NO: 303; or a VL of SEQ ID NO: 305
 and a VH of SEQ ID NO: 307; or a VL of SEQ ID NO: 309 and a VH of SEQ ID NO: 311; or a
 VL of SEQ ID NO: 313 and a VH of SEQ ID NO: 315; or a VL of SEQ ID NO: 317 and a VH of
 SEQ ID NO: 319; or a VL of SEQ ID NO: 321 and a VH of SEQ ID NO: 323; or a VL of SEQ ID
 NO: 325 and a VH of SEQ ID NO: 327; or a VL of SEQ ID NO: 329 and a VH of SEQ ID NO:
 15 331; or a VL of SEQ ID NO: 333 and a VH of SEQ ID NO: 335; or a VL of SEQ ID NO: 337 and
 a VH of SEQ ID NO: 339; or a VL of SEQ ID NO: 341 and a VH of SEQ ID NO: 343; or a VL of
 SEQ ID NO: 345 and a VH of SEQ ID NO: 347; or a VL of SEQ ID NO: 349 and a VH of SEQ
 ID NO: 351; or a VL of SEQ ID NO: 353 and a VH of SEQ ID NO: 355; or a VL of SEQ ID NO:
 357 and a VH of SEQ ID NO: 359; or a VL of SEQ ID NO: 361 and a VH of SEQ ID NO: 363;
 20 or a VL of SEQ ID NO: 365 and a VH of SEQ ID NO: 367; or a VL of SEQ ID NO: 369 and a VH
 of SEQ ID NO: 371; or a VL of SEQ ID NO: 373 and a VH of SEQ ID NO: 375; or a VL of SEQ
 ID NO: 377 and a VH of SEQ ID NO: 379; or a VL of SEQ ID NO: 381 and a VH of SEQ ID NO:
 383; or a VL of SEQ ID NO: 385 and a VH of SEQ ID NO: 387; or a VL of SEQ ID NO: 389 and
 a VH of SEQ ID NO: 391; or a VL of SEQ ID NO: 393 and a VH of SEQ ID NO: 395; or a VL of
 25 SEQ ID NO: 397 and a VH of SEQ ID NO: 399; or a VL of SEQ ID NO: 401 and a VH of SEQ
 ID NO: 403; or a VL of SEQ ID NO: 405 and a VH of SEQ ID NO: 407.

For the purposes of the instant application the SEQ ID NOS of each particular antibody
 are sequential odd numbers. Thus the monoclonal anti-DLL3 antibody, SC16.3, comprises
 amino acid SEQ ID NOS: 21 and 23 for the light and heavy chain variable regions respectively;
 30 SC16.4 comprises SEQ ID NOS: 25 and 27; SC16.5 comprises SEQ ID NOS: 29 and 31, and
 so on. A corresponding nucleic acid sequence encoding each antibody amino acid sequence is
 included in the appended sequence listing and has the SEQ ID NO immediately preceding the
 corresponding amino acid SEQ ID NO: Thus, for example, the SEQ ID NOS of the VL and VH

of the SC16.3 antibody are 21 and 23 respectively, and the SEQ ID NOS of the nucleic acid sequences encoding the VL and VH of the SC16.3 antibody are SEQ ID NOS: 20 and 22 respectively.

It should be noted that, due to sequencing anomalies, certain heavy and light chain variable region sequences were prematurely truncated during the sequencing process. This resulted in the omission of one or more amino acids in the reported FR4 sequence. In such cases compatible amino acids (determined by review of corresponding sequences from other antibody clones) have been supplied to essentially complete the variable region sequence. For example, the residues "IK" were added to the terminal end of the SC16.22 light chain sequence in FIG. 1A (SEQ ID NO: 73) to provide an operable light chain variable region with a complete framework 4. Bases encoding the added amino acids were similarly added to the corresponding nucleic acid sequence (SEQ ID NO: 72) to ensure consistency. In each such case in FIGS. 1A and 1B (but not in the appended sequence listing) the added amino acids are underlined and bolded so as to be readily identified. The CDRs in FIGS. 1A and 1B are defined as per Kabat et al. (supra) using a proprietary version of the Abysis database.

Example 3

Generation of Chimeric and Humanized Anti-DLL3 Antibodies

To provide a benchmark for humanized binding domains compatible with the instant invention five (e.g. SC16.13, SC16.15, SC16.25, SC16.34 and SC16.56) exemplary chimeric anti-DLL3 antibodies were generated using art-recognized techniques as follows. Total RNA was extracted from the hybridomas and amplified as set forth in Example 1. Data regarding V, D and J gene segments of the VH and VL chains of the murine antibodies were obtained from the derived nucleic acid sequences. Primer sets specific to the leader sequence of the VH and VL chain of the antibody were designed using the following restriction sites: AgeI and XhoI for the VH fragments, and XmaI and DraIII for the VL fragments. PCR products were purified with a QIAquick PCR purification kit (Qiagen), followed by digestion with restriction enzymes AgeI and XhoI for the VH fragments and XmaI and DraIII for the VL fragments. The VL and VH digested PCR products were purified and ligated into kappa CL (SEQ ID NO: 5) human light chain constant region expression vector or IgG1 (SEQ ID NO: 6) human heavy chain constant region expression vector, respectively.

Ligation reactions were performed in a total volume of 10 μ L with 200U T4-DNA Ligase (New England Biolabs), 7.5 μ L of digested and purified gene-specific PCR product and 25 ng

linearized vector DNA. Competent *E. coli* DH10B bacteria (Life Technologies) were transformed via heat shock at 42 °C with 3 µL ligation product and plated onto plates with ampicillin at a concentration of 100 µg/mL. Following purification and digestion of the amplified ligation products, the VH fragment was cloned into the AgeI-XhoI restriction sites of the pEE6.4HulG1 expression vector (Lonza) and the VL fragment was cloned into the XmaI-DraIII restriction sites of the pEE12.4Hu-Kappa expression vector (Lonza).

Chimeric antibodies were expressed by co-transfection of HEK-293T cells with pEE6.4HulG1 and pEE12.4Hu-Kappa expression vectors. Prior to transfection the HEK-293T cells were cultured in 150 mm plates under standard conditions in Dulbecco's Modified Eagle's Medium (DMEM) supplemented with 10% heat inactivated FCS, 100 µg/mL streptomycin and 100 U/mL penicillin G. For transient transfections cells were grown to 80% confluency. 12.5 µg each of pEE6.4HulG1 and pEE12.4Hu-Kappa vector DNA were added to 50 µL HEK-293T transfection reagent in 1.5 mL Opti-MEM. The mix was incubated for 30 minutes at room temperature and plated. Supernatants were harvested three to six days after transfection. Culture supernatants containing recombinant chimeric antibodies were cleared from cell debris by centrifugation at 800×g for 10 minutes and stored at 4 °C. Recombinant chimeric antibodies were purified by Protein A affinity chromatography.

The same murine anti-DLL3 antibodies (e.g. SC16.13, SC16.15, SC16.25, SC16.34 and SC16.56) were also used to derive CDR-grafted or humanized binding domains. The murine antibodies were humanized using a proprietary computer-aided CDR-grafting method (Abysis Database, UCL Business) and standard molecular engineering techniques as follows. Human framework regions of the variable regions were designed based on the highest homology between the framework sequences and CDR canonical structures of human germline antibody sequences and the framework sequences and CDRs of the relevant mouse antibodies. For the purpose of the analysis the assignment of amino acids to each of the CDR domains was done in accordance with Kabat *et al.* Once the variable regions were selected, they were generated from synthetic gene segments (Integrated DNA Technologies). Humanized antibodies were cloned and expressed using the molecular methods described above for chimeric antibodies.

The genetic composition for the selected human acceptor variable regions are shown in TABLE 4 immediately below for each of the humanized antibodies. The sequences depicted in TABLE 4 correspond to the contiguous variable region amino acid sequences set forth in SEQ ID NOS: 389 and 391 (hSC16.13), SEQ ID NOS: 393 and 395 (hSC16.15), SEQ ID NOS: 397 and 399 (hSC16.25), SEQ ID NOS: 401 and 403 (hSC16.34) and SEQ ID NOS: 405 and 407

(hSC16.56) in FIGS 1A and 1B. TABLE 4 shows that no framework changes or back mutations were necessary to maintain the favorable binding properties of the selected antibodies.

TABLE 4

mAb	human VH	human DH	human JH	FW changes	human VK	human JK	FW changes
hSC16.13	IGHV2-5*01	IGHD1-1	JH6	None	IGKV1-39*01	JK1	None
hSC16.15	IGHV1-46*01	IGHD2-2	JH4	None	IGKV1-13*02	JK4	None
hSC16.25	IGHV2-5*01	IGHD3-16	JH6	None	IGKV6-21*01	JK2	None
hSC16.34	IGHV1-3*02	IGHD3-22	JH4	None	IGKV1-27*01	JK1	None
hSC16.56	IGHV1-18*01	IGHD2-21	JH4	None	IGKV3-15*01	JK2	None

5 Although no residues were altered in the framework regions, in one of the humanized clones (hSC16.13) mutations were introduced into heavy chain CDR2 to address stability concerns. The binding affinity of the antibody with the modified CDR was checked to ensure that it was equivalent to either the corresponding chimeric or murine antibody.

10 Following humanization of the selected antibodies the resulting VL and VH chain amino acid sequences were analyzed to determine their homology with regard to the murine donor and human acceptor light and heavy chain variable regions. The results shown in TABLE 5, immediately below, reveal that the humanized constructs consistently exhibited a higher homology with respect to the human acceptor sequences than with the murine donor sequences. The murine heavy and light chain variable regions show a similar overall
15 percentage homology to a closest match of human germline genes (85%-93%) compared with the homology of the humanized antibodies and the donor hybridoma protein sequences (74%-83%).

TABLE 5

mAb	Homology to Human (CDR acceptor)	Homology to Murine Parent (CDR donor)
hSC16.13 HC	93%	81%
hSC16.13 LC	87%	77%
hSC16.15 HC	85%	83%
hSC16.15 LC	85%	83%
hSC16.25 HC	91%	83%
hSC16.25 LC	85%	79%
hSC16.34 HC	87%	79%
hSC16.34 LC	85%	81%
hSC16.56 HC	87%	74%
hSC16.56 LC	87%	76%

Each of the derived humanized constructs were analyzed using surface plasmon resonance, to determine if the CDR grafting process had appreciably altered their apparent affinity for DLL3 protein. The humanized constructs were compared with chimeric antibodies comprising the murine parent (or donor) heavy and light chain variable domains and a human constant region substantially equivalent to that used in the humanized constructs. The humanized anti-DLL3 antibodies exhibited binding characteristics roughly comparable to those shown by the chimeric parent antibodies (data not shown).

Example 4

Domain and Epitope Mapping of Anti-DLL3 Antibodies

In order to characterize and position the epitopes that the disclosed anti-DLL3 antibodies bind to, domain-level epitope mapping was performed using a modification of the protocol described by Cochran et al., 2004 (supra). Individual domains of DLL3 comprising specific amino acid sequences were expressed on the surface of yeast, and binding by each anti-DLL3 antibody was determined through flow cytometry.

Yeast display plasmid constructs were created for the expression of the following constructs: DLL3 extracellular domain (amino acids 27-466); DLL1-DLL3 chimera, which consists of the N-terminal region and DSL domain of DLL1 (amino acids 22-225) fused to EGF-like domains 1 through 6 of DLL3 (amino acids 220-466); DLL3-DLL1 chimera, which consists of the N-terminal region and DSL domain of DLL3 (amino acids 27-214) fused to EGF-like domains 1 through 8 of DLL1 (amino acids 222-518); EGF1 (amino acids 215-249); EGF2

(amino acids 274-310); EGF1 and EGF2 (amino acids 215-310); EGF3 (amino acids 312-351); EGF4 (amino acids 353-389); EGF5 (amino acids 391-427); and EGF6 (amino acids 429-465). For domain information see generally UniProtKB/Swiss-Prot database entry Q9NYJ7. Note that the amino acid numbering references an unprocessed DLL3 protein with a leader sequence
5 included in the sequence set forth in SEQ ID NO: 1). For analysis of the N-terminal region or the EGF domains as a whole, chimeras with the family member DLL1 (DLL1-DLL3 and DLL3-DLL1) were used as opposed to fragments to minimize potential problems with protein folding. Domain-mapped antibodies had previously been shown not to cross-react with DLL1 indicating that any binding to these constructs was occurring through association with the DLL3 portion of
10 the construct. These plasmids were transformed into yeast, which were then grown and induced as described in Cochran et al.

To test for binding to a particular construct, 200,000 induced yeast cells expressing the desired construct were washed twice in PBS + 1 mg/mL BSA (PBSA), and incubated in 50 μ L of PBSA with biotinylated anti-HA clone 3F10 (Roche Diagnostics) at 0.1 μ g/mL and either 50 nM
15 purified antibody or 1:2 dilution of unpurified supernatant from hybridomas cultured for 7 days. Cells were incubated for 90 minutes on ice, followed by two washes in PBSA. Cells were then incubated in 50 μ L PBSA with the appropriate secondary antibodies: for murine antibodies, Alexa 488 conjugated streptavidin, and Alexa 647 conjugated goat anti mouse (Life Technologies) were added at 1 μ g/mL each; and for humanized or chimeric antibodies, Alexa
20 647 conjugated streptavidin (Life Technologies) and R-phycoerythrin conjugated goat anti human (Jackson Immunoresearch) were added at 1 μ g/mL each. After a twenty minute incubation on ice, cells were washed twice with PBSA and analyzed on a FACS Canto II. Antibodies that bound to DLL3-DLL1 chimera were designated as binding to the N-terminal region + DSL. Antibodies that bound specifically to an epitope present on a particular EGF-like
25 domain were designated as binding to its respective domain (FIG. 2.)

In order to classify an epitope as conformational (e.g., discontinuous) or linear, yeast displaying the DLL3 ECD was heat treated for 30 minutes at 80°C to denature the DLL3 ECD, and then washed twice in ice-cold PBSA. The ability of anti-DLL3 antibodies to bind the denatured yeast was tested by FACS using the same staining protocol as described above.
30 Antibodies that bound to both the denatured and native yeast were classified as binding to a linear epitope, whereas antibodies that bound native yeast but not denatured yeast were classified as conformationally specific.

A schematic summary of the domain-level epitope mapping data of the antibodies tested is presented in FIG. 2, with antibodies binding a linear epitope underlined and, where determined, the corresponding bin noted in parenthesis. A review of FIG. 2 shows that the majority of anti-DLL3 antibodies tended to map to epitopes found either in the N-terminal/DSL region of DLL3 or EGF2.

Fine epitope mapping was further performed on selected antibodies using one of two methods. The first method employed the Ph.D.-12 phage display peptide library kit (New England Biolabs) which was used in accordance with the manufacturer's instructions. The antibody for epitope mapping was coated overnight at 50 µg/mL in 3mL 0.1 M sodium bicarbonate solution, pH 8, onto a Nunc MaxiSorp tube (Nunc). The tube was blocked with 3% BSA solution in bicarbonate solution. Then, 10^{11} input phage in PBS + 0.1% Tween-20 was allowed to bind, followed by ten consecutive washes with 0.1% Tween-20 to wash away non-binding phage. Remaining phage were eluted with 1 mL 0.2 M glycine for 10 minutes at room temperature with gentle agitation, followed by neutralization with 150 µL 1M Tris-HCl pH 9. Eluted phage were amplified and panned again with 10^{11} input phage, using 0.5% Tween-20 during the wash steps to increase selection stringency. DNA from 24 plaques of the eluted phage from the second round was isolated using the Qiaprep M13 Spin kit (Qiagen) and sequenced. Binding of clonal phage was confirmed using an ELISA assay, where the mapped antibody or a control antibody was coated onto an ELISA plate, blocked, and exposed to each phage clone. Phage binding was detected using horseradish peroxidase conjugated anti-M13 antibody (GE Healthcare), and the 1-Step Turbo TMB ELISA solution (Pierce). Phage peptide sequences from specifically binding phage were aligned using Vector NTI (Life Technologies) against the antigen ECD peptide sequence to determine the epitope of binding.

Alternatively, a yeast display method (Chao et al., 2007, PMID: 17406305) was used to map the epitopes of selected antibodies. Libraries of DLL3 ECD mutants were generated with error prone PCR using nucleotide analogues 8-oxo-2'-deoxyguanosine-5'-triphosphate and 2'-deoxy-p-nucleoside-5'-triphosphate (TriLink Bio) for a target mutagenesis rate of one amino acid mutation per clone. These were transformed into a yeast display format. Using the technique described above for domain-level mapping, the library was stained for HA and antibody binding at 50 nM. Using a FACS Aria (BD), clones that exhibited a loss of binding compared to wild type DLL3 ECD were sorted. These clones were re-grown, and subjected to another round of FACS sorting for loss of binding to the target antibody. Using the Zymoprep Yeast Plasmid Miniprep kit (Zymo Research), individual ECD clones were isolated and sequenced. Where

necessary, mutations were reformatted as single-mutant ECD clones using the Quikchange site directed mutagenesis kit (Agilent).

Individual ECD clones were next screened to determine whether loss of binding was due to a mutation in the epitope, or a mutation that caused misfolding. Mutations that involved cysteine, proline, and stop codons were automatically discarded due to the high likelihood of a misfolding mutation. Remaining ECD clones were then screened for binding to a non-competing, conformationally specific antibody. ECD clones that lost binding to non-competing, conformationally specific antibodies were concluded to contain misfolding mutations, whereas ECD clones that retained equivalent binding to wild type DLL3 ECD were concluded to be properly folded. Mutations in the ECD clones in the latter group were concluded to be in the epitope.

A summary of selected antibodies with their derived epitopes comprising amino acid residues that are involved in antibody binding are listed in TABLE 6 below. Antibodies SC16.34 and SC16.56 interact with common amino acid residues which is consistent with the binning information and domain mapping results shown in FIG. 2. Moreover, SC16.23 was found to interact with a distinct contiguous epitope and was found not to bin with SC16.34 or SC16.56. Note that for the purposes of the appended sequence listing SEQ ID NO: 4 comprises a placeholder amino acid at position 204.

TABLE 6

Antibody Clone	Epitope	SEQ ID NO:
SC16.23	Q93, P94, G95, A96, P97	3
SC16.34	G203, R205, P206	4
SC16.56	G203, R205, P206	4

Example 5

Generation of an Anti-DLL3 Chimeric Antigen Receptor

Fabrication of an anti-CD19 CAR

To generate a positive control CAR construct, a synthetic open reading frame encoding a second generation CAR directed towards human CD19 (see US2014/0271635) was synthesized (Life Technologies) and subcloned into the multiple cloning site (MCS) of the lentiviral expression vector pCDH-CMV-MCS-EF1-GFP-T2A-Puro (System Biosciences,

Mountain View CA). This anti-CD19 CAR open reading frame comprises nucleotides, from 5' to 3', encoding the signal leader sequence from the human CD8 alpha chain (amino acids 1 - 21, UniProt accession P01732-1), a scFv derived from a mouse monoclonal antibody recognizing human CD19 (Nicholson et al, 1997; PMID 9566763), the human CD8 alpha hinge, transmembrane domain and proximal region (amino acids 138 - 206, UniProt accession P01732-1), the intracellular costimulatory signaling region from the human 4-1BB protein (amino acids 214-255, UniProt accession Q07011-1), and the human CD3 ζ chain intracellular signaling region (amino acids 52 - 164, UniProt accession P20963-1 with a Q65K modification). When expressed on lymphocytes the resulting CD19 CAR-T exhibited the expected immunostimulatory activity.

Besides providing a positive control the anti-CD19 CAR/lentiviral expression vector was designed with restriction sites in such a way that the anti-CD19 scFv component could be easily removed and substituted with an alternative binding region component directed to any selected determinant (e.g., DLL3). As described below, this cassette system (designated SCT1-XX where XX indicates the particular DLL3 binding domain component) was used to validate various embodiments of the instant invention. Note that the SCT nomenclature may, depending on the context, refer to the expressed anti-DLL3 CAR protein, cytotoxic lymphocytes expressing the CAR protein, the anti-DLL3 CAR ORF or an expression vector (e.g., lentiviral, retroviral, plasmid, etc.) comprising the same ORF.

Fabrication of SCT1-h16.15.

To generate a novel anti-DLL3 CAR construct (SCT1-h16.15), a nucleotide sequence encoding an scFv fragment was first synthesized by operably linking anti-hSC16.15 VL (SEQ ID NO: 394) and VH (SEQ ID NO: 396) nucleotide sequences together via a nucleic acid sequence encoding a pentameric multimer GlyGlyGlyGlySer (G₄S)₃ (GGGGSGGGGSGGGGS; SEQ ID NO: 7) linker to provide a hSC16.15-scFv polynucleotide (SEQ ID NO: 15) that encodes the hSC16.15-scFv protein. Both exemplary nucleic acid and amino acid sequences are set forth immediately below:

```

AIQLTQSPSSLSASVGDRVTITCRASENIYYNLAWYQQKPGKAPKLLIYTANS
LEDVPSRFSGSGSGTDFTLTISSLQPEDFATYFCKQAYDVPPTFGGGTKLEI
KGGGGSGGGGSGGGGSQVQLVQSGAEVKKPGASVKVSCKASGYTFTRY
WIHWIRQAPGQGLEWMGYINPTVYTEFNQNFKDRVTMTRDTSTSTVYMELS
SLRSEDTAVYYCARGGSNFFDYWQGTTVTVSS

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(SEQ ID NO: 8)

and:

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5      gccatccagttgaccagctccatcctccctgtctgcatctgtaggagacagagtcaccatcacttgccggg
      caagtgagaacattactacaatttagcctggatcagcagaaaccagggaagctcctaagctcctgatct
      atactgccaatagtttgaagatgggtcccatcaagggtcagcggcagtggtatctgggacagatttactct
      caccatcagcagcctgcagcctgaagattttgcaacttattttgtaaacaggcttatgacgttcctccgacgttc
10     ggtggaggcaccaagctggaaatcaaaggcggcggaggatctggcggaggcgggaagtggcggaggg
      ggatctcaggtgcagctggtgcagctctgggctgaggtgaagaagcctggggcctcagtgaaggtttctg
      caaggcatctggatacaccttcaccagggtactggatacactggatacagcaggccctggacaagggtt
      gaggatgggatacatcaaccctacaactgtttatactgagttcaatcagaactcaaggacagagtcacc
      atgaccaggggacacgtccacgagcacagctctacatggagctgagcagcctgagatctgaggacacggc
15     cgtgtattactgtgcgagaggcggtagtaacttcttgactactggggccaaggcaccactgtcacagtctct
      cg

```

(SEQ ID NO: 15).

Using standard molecular engineering techniques the hSC16.15-scFv nucleotide sequence was subsequently cloned into the SCT1 cassette to provide a SCT1-h16.15 lentiviral expression vector comprising an anti-DLL3 CAR. In this regard the SCT1-h16.15 CAR comprises an open reading frame encoding the following elements from 5' to 3': CD8 alpha chain leader region (amino acids 1-21, UniProt P01732-1), h16.15 VL domain (as per Example 3), (G₄S)₃ synthetic linker sequence (amino acid 1-15, Huston et al., 1988), h16.15 VH domain (as per Example 3), the human CD8 alpha hinge and transmembrane domain (amino acids 138 - 206, UniProt accession P01732-1), the intracellular costimulatory signaling region from the human 4-1BB protein (amino acids 214-255, UniProt accession Q07011-1) and the human CD3 ζ chain intracellular signaling region (amino acids 52 - 164, UniProt accession P20963-1 with a Q65K modification). The CAR open reading frame was sequence confirmed. A schematic diagram of the SCT1-h16.15 CAR open reading frame is set forth in FIG. 3 with the corresponding nucleic acid (SEQ ID NO: 9) and amino acid (SEQ ID NO: 10) sequences set forth in FIG. 4A. Note that in FIG. 4A the incorporated sc16.15 scFv binding domain is underlined (corresponding to SEQ ID NO; 8).

Example 6

Generation of Additional Exemplary Anti-DLL3 Chimeric Antigen Receptors

To further demonstrate the scope and adaptability of the instant invention two DLL3 binding domains, in the form of scFv constructs compatible with the disclosed DLL3 CARs, were

fabricated and incorporated into SCT1-16 CARs substantially as set forth above. More specifically, to generate novel anti-DLL3 binding domain constructs in accordance with the instant disclosure nucleotide sequences encoding scFv fragments were synthesized by operably linking selected VL and VH nucleotide sequences together via a nucleic acid sequence encoding a pentameric multimer GlyGlyGlyGlySer (G₄S)₃ (GGGGSGGGGSGGGGS; SEQ ID NO: 7) linker. In the first case the scFv polynucleotide (scFv-hSC16.13) comprises variable light and heavy chain sequences from hSC16.13 (SEQ ID NOS: 388 and 390) while in the second case the scFv polynucleotide (scFv-hSC16.25) comprises variable light and heavy chain sequences from hSC16.25 (SEQ ID NOS: 396 and 398). The resulting nucleic acid constructs encoding scFv-hSC16.13 (SEQ ID NO: 11) and scFv-hSC16.25 (SEQ ID NO: 13) were then inserted in the SCT1 cassette using the engineered restriction sites to provide SCT1-hSC16.13 and SCT1-hSC16.25. The nucleic acid (SEQ ID NO: 16) and amino acid (SEQ ID NO: 17) sequences of SCT1-hSC16.13 are shown in FIG. 4B while the nucleic acid (SEQ ID NO: 18) and amino acid (SEQ ID NO: 19) sequences of SCT1-hSC16.25 are shown in FIG. 4C. Note that in both FIGS. the amino acid sequence corresponding to the DLL3 scFv binding domain is underlined as well as being set forth in SEQ ID NO: 12 (h16.13 scFv) and SEQ ID NO: 14 (h16.25 scFv) respectively.

The ease of fabricating these CARs using the disclosed SCT1 cassette system illustrates the versatility of the instant invention with regard to the selection and incorporation of various DLL3 binding domains and more generally demonstrates the modular nature of the constructs. As such, it will be appreciated that the concept of the DLL3 CARS set forth herein is not limited to any particular DLL3 binding domain or by the selection of any other particular component (e.g. a specific transmembrane or signaling domain) as long as the resulting DLL3 sensitized lymphocyte is immunostimulated or activated by exposure to a DLL3 expressing cell (e.g., a tumor cell).

Example 7

Generation and Characterization of Lentiviral Vector Particles

Lentiviral vector packaging of the exemplary DLL3 CARs SCT1-h16.13, SCT1-h16.15 and SCT1-h16.25 from Examples 5 and 6, were carried out as follows: 10ug of the selected SCT1-h16 plasmid, 7ug of pΔR8.74, and 4ug of pMD2.G were co-transfected into ten-million HEK-293T cells (ATCC) in the presence of polyethylenimine (Polysciences) at a DNA:PEI ratio of

1:4. Co-transfected cells were incubated at 37°C (5%CO₂) overnight, followed by media exchange the next day. Forty-eight hours post-transfection, culture media containing lentiviral particles was harvested and clarified by centrifugation at 1200rpm for 5min at 4°C to remove cell debris. To pellet lentiviral vector particles the clarified culture media was ultracentrifuged at
5 19500rpm for two hours at 4°C. After ultracentrifugation the supernatant was discarded, the viral pellet resuspended in sterile PBS, and stored at -80°C. Quantitation of recovered lentiviral vector stocks was assessed by p24 ELISA (Cell Biolabs), and gene-transfer efficiency (functional titer) was assessed by standard lentiviral vector titration methods. Typical yields of lentiviral vector stocks ranged from 7-15 ug/ml of p24 antigen, and functional titers ranged from
10 1-3 x 10^{e8} TU/ml. The SCT1-h16.13, SCT1-h16.15 and SCT1-h16.25 lentiviral vector stocks were frozen and stored until use.

As set forth in the subsequent Examples, the vector stocks may be used to induce a desired immune response as discussed in detail throughout the instant application and shown schematically in FIG. 5 appended hereto. Moreover, while SCT1-h16.13, SCT1-h16.15 and
15 SCT1-h16.25 are used as an exemplary constructs to demonstrate various facets of the instant invention (and may be called out in the FIGS), it will be appreciated that the true scope of the invention is not limited to any particular DLL3 binding domain or particular signaling domain or any exemplary construct thereof, but rather encompasses any DLL3 CAR that effects the desired immune response upon exposure to a DLL3 expressing tumor cell.

20 Example 8

Generation of Immortalized T Lymphocytes

Expressing SCT1-h16.13, SCT1-h16.15, or SCT1-h16.25 CAR Protein

DLL3 target-specific Jurkat lymphocytes expressing either SCT1-h16.13, SCT1-h16.15 or SCT1-h16.25 were generated by transducing one million Jurkat E6-1 (ATCC) T lymphocyte cells with the subject SCT1-h16 lentiviral vector from the previous Example at a multiplicity of infection (MOI) of ~4 in the presence of 10ug/ml of polybrene (EMD Millipore) to ensure efficient
25 viral transduction. The cells were allowed to incubate in the presence of lentiviral particles for seventy-two hours at 37°C (5%CO₂). Afterwards, the spent media was exchanged with fresh media containing 2ug/ml Puromycin (Life Technologies) to positively select for SCT1-h16 CAR expressing cells. Cells were allowed to incubate an additional 5 days in the presence of Puromycin prior to assessing the anti-DLL3 CAR surface expression by flow cytometry (FIG.
30 6A). Flow cytometry was also used to detect the presence of hDLL3 protein on the surface of

an engineered HEK-293T cell line overexpressing hDLL3 (FIG. 6B) that will be used to characterize CAR constructs of the instant invention.

Flow cytometry analysis of transduced Jurkat cells expressing either SCT1-h16.13, SCT1-h16.15 or SCT1-h16.25 and non-transduced Jurkat control cells was performed as follows: 10⁶ cells of each cell line were harvested and pelleted by centrifugation at 1200 rpm at 4°C for 5 minutes; supernatant was removed and the pellet was washed in cold PBS/2% FCS twice. After supernatant from the final wash was removed, the cell pellet was resuspended in 100 microliters of PBS/2% FCS containing 1 microgram of Alexa Fluor[®] 647-conjugated Affinipure Goat Anti-Human IgG, F(ab') antibody (Jackson ImmunoResearch) and incubated in the dark at 4°C for 30 minutes. After incubation, cells were washed three times in PBS/2% FCS before being re-suspended in PBS/2% FCS with DAPI (to detect living cells). The cells were then analyzed on a BD FACS Canto II flow cytometer as per the manufacturer's instructions to provide the data set forth in FIG. 6A.

Similarly, HEK-293T parental cells or HEK-293T cells overexpressing hDLL3 were harvested and isolated into single cell suspensions with Versene (Life Technologies). The isolated cells were washed as described above and incubated for 30 minutes at 4°C in the dark with 1 microgram of anti-DLL3 antibody prior to thrice washing in PBS/2% FCS. The cells were then incubated for 30 minutes with 50 µL per sample AlexaFluor-647 labeled goat-anti-mouse IgG, Fc fragment specific secondary antibody (Life Technologies) diluted 1:200 in PBS/2%FCS, washed thrice with PBS/2% FCS and re-suspended in PBS/2% FCS with DAPI (to detect living cells). The cells were then analyzed on a BD FACS Canto II flow cytometer as per the manufacturer's instructions to provide the data set forth in FIG. 6B.

FIGS. 6A and 6B, respectively, demonstrate that the subject SCT1-h16 CAR is expressed on transduced Jurkat T lymphocytes but not on non-transduced Jurkat cells, and that human DLL3 protein is expressed on the engineered HEK-293T cells but not on HEK-293T-Naïve cells.

Example 9

Jurkat-SCT1-h16.15 T Lymphocytes Induce IL-2 Production Upon Contacting hDLL3 Expressing Cells

Transduced Jurkat-SCT1-h16.13, Jurkat-SCT1-h16.15, and Jurkat-SCT1-h16.25 lymphocytes were assessed for target-specific activation by measuring IL-2 induction which is indicative of CAR mediated T-cell activation. More specifically, using transduced Jurkat lymphocytes and engineered 293T cells expressing hDLL3 from the previous Example, IL2

levels were monitored to demonstrate that the CAR expressing lymphocytes are activated and mount an immune response upon contact with cells expressing hDLL3.

In this regard Jurkat-SCT1-h16.15 lymphocytes from Example 8 were co-cultured with HEK-293T cells engineered to over-express hDLL3 antigen on the cell surface (also from Example 8) as evidenced by flow cytometry. Co-culturing of lymphocytes with target HEK-293T-hDLL3 cells was performed at the four different lymphocyte : target (L:T) ratios set forth in FIG. 7A to assess dose response and determine maximum IL-2 production conditions. Co-cultures were incubated at 37°C (5%CO₂) for 48hrs, at which time media was harvested and clarified of cell debris by centrifugation at 1200 rpm for 5 minutes. Clarified supernatant was then assessed for IL-2 production by ELISA (Thermo Scientific) per manufacturer's instructions. To assess background IL-2 production, non-transduced Jurkat cells (Jurkat-Naïve) were co-cultured with HEK-293T-hDLL3 cells. The results, in terms of IL2 induction, is shown in FIG. 7A.

Similarly three different SCT1-h16 lymphocytes (Jurkat-SCT1-h16.13, Jurkat-SCT1-h16.15, and Jurkat-SCT1-h16.25) from Example 8 were co-cultured with engineered hDLL3+ HEK-293T cells at a 3:1 L:T ratio substantially as set forth immediately above. Results, again in terms of IL2 induction, are shown in FIG. 7B.

As evidenced by the data set forth in FIG. 7A, the Jurkat-SCT1-h16.15 lymphocytes were prompted to produce IL-2 in a concentration dependent manner upon exposure to cells expressing hDLL3. Additionally, data shown in FIG. 7B demonstrates the ability of various DLL3 CAR constructs to consistently induce the production of IL2 when exposed to antigen presenting cells. More particularly it will be appreciated that such IL-2 production is indicative of T-cell activation by the SCT1 CAR upon recognition of DLL3 antigen on hDLL3 expressing cells (including hDLL3 expressing tumorigenic cells). With regard to both FIG. 7A and 7B target-specific CAR-mediated activation of Jurkat cells is further elucidated by the lack of observable IL-2 production among co-cultures containing HEK-293T-DLL3 and non-transduced Jurkat cells.

Example 10

Generation of Primary T Lymphocytes Expressing SCT1-h16.13, SCT1-h16.15, or SCT1-h16.25 CAR Protein

In order to demonstrate that the disclosed CARs may be used to provide sensitized lymphocytes primary human CD3+ T lymphocytes were isolated from a commercially available

peripheral blood mononuclear cell preparation (PBMCs: AllCells) using a human CD3 positive selection kit (Stemcell Technologies).

Following isolation from a single donor CD3⁺ T cells were cultured in RPMI media containing 10% heat-inactivated fetal bovine serum (Hyclone), 1% penicillin/streptomycin (Corning), 1% l-glutamine (Corning), and 10mM HEPES (Corning). T lymphocytes were incubated at 37°C (5%CO₂) in the presence of CD3/CD28 activation beads (Dynabeads) at a 1:5 ratio for activation. IL-2 (Peprotech) was added every other day to a final concentration of 50 IU/ml. Twenty-four hours after initial activation, DLL3 target-specific T lymphocytes expressing SCT1-h16.13, SCT1-h16.15, or SCT1-h16.25 were generated by transducing one million T cells with the CAR lentiviral vectors generated substantially as set forth in Example 7 at a multiplicity of infection (MOI) of ~5 in the presence of 10ug/ml of polybrene (EMD Millipore) to ensure efficient viral transduction. The cells were allowed to incubate in the presence of lentiviral particles for seventy-two hours at 37°C (5%CO₂) prior to assessing the anti-DLL3 CAR surface expression by flow cytometry.

Flow cytometry analysis of transduced T lymphocytes expressing SCT1-h16.13, SCT1-h16.15 or SCT1-h16.25 and non-CAR-bearing T lymphocyte control cells was performed as follows: 10⁶ cells of each sample were harvested and pelleted by centrifugation at 1200 rpm at 4°C for 5 minutes; supernatant was removed and the pellet was washed in cold PBS/2% FCS twice. After supernatant from the final wash was removed, the cell pellet was resuspended in 100 microliters of PBS/2% FCS containing 1 microgram of Alexa Fluor[®] 647-conjugated Affinipure Goat Anti-Human IgG, F(ab') antibody (Jackson ImmunoResearch) and incubated in the dark at 4°C for 30 minutes. After incubation, cells were washed thrice in PBS/2% FCS before being re-suspended in PBS/2% FCS with DAPI (to detect living cells). The cells were then analyzed on a BD FACS Canto II flow cytometer as per the manufacturer's instructions to provide the data set forth in FIG. 8.

FIG. 8 clearly shows that SCT1-h16.13, SCT1-h16.15 and SCT1-h16.25 are expressed on transduced primary T lymphocytes (i.e., sensitized lymphocytes) but not on non-transduced lymphocytes.

Example 11

Generation and Characterization of Cells Expressing DLL3 Target Antigen

As set forth in Example 8 flow cytometry was used to detect the presence of DLL3 protein on the surface of an engineered HEK-293T cell line overexpressing human DLL3. Similarly flow

cytometry was used to confirm the expression of human DLL3 on a patient-derived xenograph (PDX) tumor cell line (LU64). Both the artificially engineered 293T cell line and the derived small cell cancer cell line were used to characterize sensitized lymphocytes of the instant invention.

5 More particularly HEK-293T cells overexpressing human DLL3 (293T-DLL3) were harvested and isolated into single cell suspensions with Versene (Life Technologies). Similarly, freshly harvested LU64 PDX tumors were processed into single cell suspension using a tumor dissociation kit (Mylteni Biotec). Isolated cells were washed as described herein and incubated for 30 minutes at 4°C in the dark with 1 microgram of anti-DLL3 antibody or isotype control prior
10 to thrice washing in PBS/2% FCS. The cells were then incubated for 30 minutes with 50 microliters per sample of AlexaFluor-647 labeled goat-anti-mouse IgG, Fc fragment specific secondary antibody (Life Technologies) diluted 1:200 in PBS/2%FCS, washed thrice with PBS/2% FCS and resuspended in PBS/2% FCS with DAPI (to detect living cells). Cells were then analyzed on a BD FACS Canto II flow cytometer as per the manufacturer's instructions to
15 provide the data set forth in FIGS. 9A and 9B.

The resulting FIGS. show that human DLL3 protein is expressed both on the engineered HEK-293T cells (FIG. 9A) and LU64 PDX tumor cells (FIG. 9B).

Example 12

SCT1-h16.13, SCT1-h16.15 and SCT1-h16.25

20 Primary Lymphocytes Eliminate DLL3 Expressing Cells Upon Exposure

To demonstrate the ability of DLL3 sensitized primary lymphocytes to kill cells in a target-specific manner, CAR transduced cells of the instant invention (prepared substantially as set forth in Example 10) were exposed to engineered 293 cells expressing DLL3 (along with appropriate controls). Following exposure the number of living target cells remaining were
25 calculated with the results being set forth in FIG. 10.

More specifically primary T lymphocytes expressing anti-DLL3 CARs (SCT1-h16.13, SCT1-h16.15 and SCT1-h16.25) were co-cultured with 293T-DLL3 cells at an lymphocyte-to-target (L:T) ratio of 3:1. Co-cultures were incubated at 37°C (5%CO₂) for 48hrs prior to determination percentage of remaining viable DLL3-bearing cells.

30 The percentage of live cells was calculated as follows: co-cultures were harvested and washed as set forth herein prior to incubation for 30 minutes at 4°C in the dark with 1 microgram of anti-DLL3 antibody or isotype control followed by thrice washing in PBS/2% FCS. Cells were

then incubated for 30 minutes with 50 microliters per sample of AlexaFluor-647 labeled goat-anti-mouse IgG, Fc fragment-specific secondary antibody (Life Technologies) diluted 1:200 in PBS/2%FCS. Cells were washed three times with PBS/2% FCS, followed by resuspension in 200 microliters of PBS/2% FCS containing DAPI (Life Technologies) for cell viability discrimination, and 10000 absolute counting beads (Life Technologies) for normalizing cell counts. Analysis and enumeration of remaining viable DLL3-bearing target cells was performed on a BD FACS Canto II flow cytometer by quantifying the respective number of viable DLL3-bearing cells per 7500 absolute counting beads collected. Viable target cells remaining in presence of non-CAR-bearing T lymphocytes was used as the benchmark to compare target-specific killing of DLL3-bearing cells by DLL3 sensitized lymphocytes.

As shown in FIG. 10, SCT1-16.15 exhibited significant target-specific killing while SCT1-h16.13 and SCT1-h16.25 showed more moderate target-specific killing. The immunospecificity of killing mediated by the sensitized lymphocytes is evidenced by the lack of activity shown by the non-transduced primary T lymphocytes co-cultured with DLL3+ target cells (FIG. 10). These data demonstrate the target-specific activity among sensitized lymphocytes expressing various anti-DLL3 CARs.

Example 13

SCT1-h16.15 Primary T Lymphocytes

Induce Cytokine Production upon Contacting DLL3-Expressing Cells

In order to demonstrate that the disclosed CARs may be used to provide sensitized lymphocytes from various donors, primary human CD3+ T lymphocytes were isolated from commercially available peripheral blood mononuclear cell preparations (PBMCs: AllCells) using a human CD3 positive selection kit (Stemcell Technologies) and transduced. The resulting sensitized lymphocyte compositions comprising SCT1-h16.15 and PBMCs obtained from two different donors (donor 1 and donor 2) were assessed for CAR expression (FIG. 11) and target-specific activation by measuring TNF α and IFN γ induction upon contact with DLL3-expressing target cells. It will be appreciated that cytokine production (e.g., TNF α and IFN γ induction) is indicative of active chimeric antigen receptors that are capable of inducing an anti-tumor immune response.

More particularly, PMBC preparations from two different donors (donor 1 and donor 2) were used to provide CD3+ T lymphocyte preparations substantially as set forth in Example 10. The respective lymphocyte preparations were then transduced with SCT1-h16.15 (again as set

forth in Example 10) to provide donor 1 and donor 2 DLL3 sensitized lymphocyte preparations (along with non-transduced lymphocytes as controls). FIG. 11 shows that each of the lymphocyte preparations effectively express the DLL3 CAR as determined by flow cytometry performed as set forth above.

5 The resulting sensitized lymphocytes comprising host cells from the two different donors were then exposed to DLL3+ 293T cells and small cell lung cancer cells expressing DLL3 (both from Example 11). In this regard each of the sensitized lymphocyte preparations (with controls) were then co-cultured with either 293T-DLL3 or LU64 PDX target cells at a lymphocyte to target (L:T) ratio of 3:1. Co-cultures were incubated at 37°C (5%CO₂) for 48hrs, at which time media
10 was harvested and clarified of cell debris by centrifugation at 1200 rpm for 5 minutes. Clarified supernatant was then assessed for TNFα production by ELISA (Thermo Fisher) and IFNγ by ELISA (Invitrogen) per manufacturer's instructions. The resulting measurements for levels of TNFα and IFNγ are shown, respectively, in FIGS. 12A and 12B (TNFα) and FIGS. 13A and 13B (IFNγ) where higher cytokine production is indicative of more robust signaling from the CAR.

15 As evidenced by the data set forth in FIGS. 12A (293 cells) and 12B (tumor cells) and FIGS. 13A (293 cells) and 13B (tumor cells) both preparations of the SCT1-h16.15-bearing T lymphocytes were prompted to produce TNFα and IFNγ upon exposure to cells (engineered and tumor) expressing human DLL3, whereas the non-CAR-bearing T lymphocytes exhibited minimal TNFα and IFNγ induction when co-cultured with the same target cells. This confirms
20 that DLL3 sensitized lymphocytes from different donors are active and capable of generating immunostimulatory signals upon exposure to DLL3+ tumor cells.

Example 14

Targeted Killing of DLL3-expressing Cells *In Vitro* by SCT1-h16.15-T Lymphocytes

To demonstrate the ability of DLL3 sensitized lymphocytes to kill cells in a target-specific
25 manner, CAR transduced cells of the instant invention were exposed to engineered 293 cells and tumor cells expressing DLL3 (again from Example 11). Following exposure the number of living target cells remaining were calculated with the results being set forth in FIGS. 14A (293 cells) and 14B (tumor cells).

More particularly SCT1-h16.15 sensitized lymphocytes (prepared as per Example 13 with
30 host cells from two donors) were co-cultured with either 293T-DLL3 or LU64 PDX cells at an lymphocyte to target (L:T) ratio of 3:1. Co-cultures were incubated at 37°C (5%CO₂) for 48hrs prior to determination of remaining viable DLL3-bearing cells.

The percentage of live cells was calculated as follows: co-cultures were harvested and washed as set forth herein prior to incubation for 30 minutes at 4°C in the dark with 1 microgram of anti-DLL3 antibody or isotype control followed by thrice washing in PBS/2% FCS. Cells were then incubated for 30 minutes with 50 microliters per sample of AlexaFluor-647 labeled goat-
5 anti-mouse IgG, Fc fragment-specific secondary antibody (Life Technologies) diluted 1:200 in PBS/2%FCS. Cells were washed three times with PBS/2% FCS, followed by resuspension in 200 microliters of PBS/2% FCS containing DAPI (Life Technologies) for cell viability discrimination, and 10000 absolute counting beads (Life Technologies) for normalizing cell counts. Analysis and enumeration of remaining viable DLL3-bearing target cells was performed
10 on a BD FACS Canto II flow cytometer by quantifying the respective number of viable DLL3-bearing cells per 7500 absolute counting beads collected. Viable target cells remaining in presence of non-CAR-bearing T lymphocytes was used as the benchmark to compare target-specific killing of DLL3-bearing cells by SCT1-h16.15 sensitized lymphocytes.

As shown in FIGS. 14A (293 cells) and 14B (tumor cells) the DLL3+ cells exhibited
15 significant susceptibility to cytolysis by the sensitized lymphocytes derived from both donors with approximately 99% of target cells being eliminated. The DLL3 sensitized lymphocytes were also able to eliminate a substantial majority (approximately 70% to 80%) of LU64 PDX small cell lung cancer cells. Overall, these data demonstrate that the disclosed DLL3 sensitized lymphocytes are able to effectively eliminate DLL3+ cells, including DLL3+ tumor cells in a
20 target-specific manner.

Those skilled in the art will further appreciate that the present invention may be embodied in other specific forms without departing from the spirit or central attributes thereof. In that the foregoing description of the present invention discloses only exemplary embodiments thereof, it
25 is to be understood that other variations are contemplated as being within the scope of the present invention. Accordingly, the present invention is not limited to the particular embodiments that have been described in detail herein. Rather, reference should be made to the appended claims as indicative of the scope and content of the invention.

CLAIMS

1. A chimeric antigen receptor comprising an anti-DLL3 binding domain.
2. The chimeric antigen receptor of claim 1 wherein the anti-DLL3 binding domain comprises a scFv anti-DLL3 binding domain.
3. The chimeric antigen receptor of claim 1 or 2 wherein the scFv anti-DLL3 binding domain is derived from, comprises or competes for binding with an antibody comprising: a light chain variable region (VL) of SEQ ID NO: 21 and a heavy chain variable region (VH) of SEQ ID NO: 23; or a VL of SEQ ID NO: 25 and a VH of SEQ ID NO: 27; or a VL of SEQ ID NO: 29 and a VH of SEQ ID NO: 31; or a VL of SEQ ID NO: 33 and a VH of SEQ ID NO: 35; or a VL of SEQ ID NO: 37 and a VH of SEQ ID NO: 39; or a VL of SEQ ID NO: 41 and a VH of SEQ ID NO: 43; or a VL of SEQ ID NO: 45 and a VH of SEQ ID NO: 47; or a VL of SEQ ID NO: 49 and a VH of SEQ ID NO: 51; or a VL of SEQ ID NO: 53 and a VH of SEQ ID NO: 55; or a VL of SEQ ID NO: 57 and a VH of SEQ ID NO: 59; or a VL of SEQ ID NO: 61 and a VH of SEQ ID NO: 63; or a VL of SEQ ID NO: 65 and a VH of SEQ ID NO: 67; or a VL of SEQ ID NO: 69 and a VH of SEQ ID NO: 71; or a VL of SEQ ID NO: 73 and a VH of SEQ ID NO: 75; or a VL of SEQ ID NO: 77 and a VH of SEQ ID NO: 79; or a VL of SEQ ID NO: 81 and a VH of SEQ ID NO: 83; or a VL of SEQ ID NO: 85 and a VH of SEQ ID NO: 87; or a VL of SEQ ID NO: 89 and a VH of SEQ ID NO: 91; or a VL of SEQ ID NO: 93 and a VH of SEQ ID NO: 95; or a VL of SEQ ID NO: 97 and a VH of SEQ ID NO: 99; or a VL of SEQ ID NO: 101 and a VH of SEQ ID NO: 103; or a VL of SEQ ID NO: 105 and a VH of SEQ ID NO: 107; or a VL of SEQ ID NO: 109 and a VH of SEQ ID NO: 111; or a VL of SEQ ID NO: 113 and a VH of SEQ ID NO: 115; or a VL of SEQ ID NO: 117 and a VH of SEQ ID NO: 119; or a VL of SEQ ID NO: 121 and a VH of SEQ ID NO: 123; or a VL of SEQ ID NO: 125 and a VH of SEQ ID NO: 127; or a VL of SEQ ID NO: 129 and a VH of SEQ ID NO: 131; or a VL of SEQ ID NO: 133 and a VH of SEQ ID NO: 135; or a VL of SEQ ID NO: 137 and a VH of SEQ ID NO: 139; or a VL of SEQ ID NO: 141 and a VH of SEQ ID NO: 143; or a VL of SEQ ID NO: 145 and a VH of SEQ ID NO: 147; or a VL of SEQ ID NO: 149 and a VH of SEQ ID NO: 151; or a VL of SEQ ID NO: 153 and a VH of SEQ ID NO: 155; or a VL of SEQ ID NO: 157 and a VH of SEQ ID NO: 159; or a VL of SEQ ID NO: 161 and a VH of SEQ ID NO: 163; or a VL of SEQ ID NO: 165 and a VH of SEQ ID NO: 167; or a VL of SEQ ID NO:

169 and a VH of SEQ ID NO: 171; or a VL of SEQ ID NO: 173 and a VH of SEQ ID NO: 175; or a VL of SEQ ID NO: 177 and a VH of SEQ ID NO: 179; or a VL of SEQ ID NO: 181 and a VH of SEQ ID NO: 183; or a VL of SEQ ID NO: 185 and a VH of SEQ ID NO: 187; or a VL of SEQ ID NO: 189 and a VH of SEQ ID NO: 191; or a VL of SEQ ID NO: 193 and a VH of SEQ ID NO: 195; or a VL of SEQ ID NO: 197 and a VH of SEQ ID NO: 199; or a VL of SEQ ID NO: 201 and a VH of SEQ ID NO: 203; or a VL of SEQ ID NO: 205 and a VH of SEQ ID NO: 207; or a VL of SEQ ID NO: 209 and a VH of SEQ ID NO: 211; or a VL of SEQ ID NO: 213 and a VH of SEQ ID NO: 215; or a VL of SEQ ID NO: 217 and a VH of SEQ ID NO: 219; or a VL of SEQ ID NO: 221 and a VH of SEQ ID NO: 223; or a VL of SEQ ID NO: 225 and a VH of SEQ ID NO: 227; or a VL of SEQ ID NO: 229 and a VH of SEQ ID NO: 231; or a VL of SEQ ID NO: 233 and a VH of SEQ ID NO: 235; or a VL of SEQ ID NO: 237 and a VH of SEQ ID NO: 239; or a VL of SEQ ID NO: 241 and a VH of SEQ ID NO: 243; or a VL of SEQ ID NO: 245 and a VH of SEQ ID NO: 247; or a VL of SEQ ID NO: 249 and a VH of SEQ ID NO: 251; or a VL of SEQ ID NO: 253 and a VH of SEQ ID NO: 255; or a VL of SEQ ID NO: 257 and a VH of SEQ ID NO: 259; or a VL of SEQ ID NO: 261 and a VH of SEQ ID NO: 263; or a VL of SEQ ID NO: 265 and a VH of SEQ ID NO: 267; or a VL of SEQ ID NO: 269 and a VH of SEQ ID NO: 271; or a VL of SEQ ID NO: 273 and a VH of SEQ ID NO: 275; or a VL of SEQ ID NO: 277 and a VH of SEQ ID NO: 279; or a VL of SEQ ID NO: 281 and a VH of SEQ ID NO: 283; or a VL of SEQ ID NO: 285 and a VH of SEQ ID NO: 287; or a VL of SEQ ID NO: 289 and a VH of SEQ ID NO: 291; or a VL of SEQ ID NO: 293 and a VH of SEQ ID NO: 295; or a VL of SEQ ID NO: 297 and a VH of SEQ ID NO: 299; or a VL of SEQ ID NO: 301 and a VH of SEQ ID NO: 303; or a VL of SEQ ID NO: 305 and a VH of SEQ ID NO: 307; or a VL of SEQ ID NO: 309 and a VH of SEQ ID NO: 311; or a VL of SEQ ID NO: 313 and a VH of SEQ ID NO: 315; or a VL of SEQ ID NO: 317 and a VH of SEQ ID NO: 319; or a VL of SEQ ID NO: 321 and a VH of SEQ ID NO: 323; or a VL of SEQ ID NO: 325 and a VH of SEQ ID NO: 327; or a VL of SEQ ID NO: 329 and a VH of SEQ ID NO: 331; or a VL of SEQ ID NO: 333 and a VH of SEQ ID NO: 335; or a VL of SEQ ID NO: 337 and a VH of SEQ ID NO: 339; or a VL of SEQ ID NO: 341 and a VH of SEQ ID NO: 343; or a VL of SEQ ID NO: 345 and a VH of SEQ ID NO: 347; or a VL of SEQ ID NO: 349 and a VH of SEQ ID NO: 351; or a VL of SEQ ID NO: 353 and a VH of SEQ ID NO: 355; or a VL of SEQ ID NO: 357 and a VH of SEQ ID NO: 359; or a VL of SEQ ID NO: 361 and a VH of SEQ ID NO: 363; or a VL of SEQ ID NO: 365 and a VH of SEQ ID NO: 367; or a VL of SEQ ID NO: 369 and a VH of SEQ ID NO: 371; or a VL of SEQ ID NO: 373 and a VH of SEQ ID NO: 375; or a VL of SEQ ID NO: 377 and a VH of SEQ ID NO: 379; or a VL of SEQ ID NO: 381 and a VH of SEQ ID NO:

383; or a VL of SEQ ID NO: 385 and a VH of SEQ ID NO: 387; or a VL of SEQ ID NO: 389 and a VH of SEQ ID NO: 391; or a VL of SEQ ID NO: 393 and a VH of SEQ ID NO: 395; or a VL of SEQ ID NO: 397 and a VH of SEQ ID NO: 399; or a VL of SEQ ID NO: 401 and a VH of SEQ ID NO: 403; or a VL of SEQ ID NO: 405 and a VH of SEQ ID NO: 407.

4. The chimeric antigen receptor of any one of claims 1-3 comprising an intracellular domain comprising a 4-1BB signaling domain and/or a CD3 ζ signaling domain.
5. The chimeric antigen receptor of any one of claims 1- 4 comprising a transmembrane domain comprising a human CD8a hinge.
6. A pharmaceutical composition comprising a chimeric antigen receptor of any one of claims 1-5 and a pharmaceutically acceptable carrier
7. A polynucleotide encoding a chimeric antigen receptor of any one of claims 1 to 5.
8. A vector comprising a polynucleotide of claim 7.
9. The vector of claim 8 wherein the vector comprises a viral vector.
10. The vector of claim 9 wherein the viral vector comprises a lentiviral vector or a retroviral vector.
11. A pharmaceutical composition comprising a polynucleotide of claim 7 or a vector of any one of claims 8 to 10.
12. An isolated host cell comprising a chimeric antigen receptor of any one of claims 1 to 5.
13. The isolated host cell of claim 12 wherein the host cell comprises a DLL3 sensitized lymphocyte.
14. The isolated host cell of claim 13 wherein the DLL3 sensitized lymphocyte comprises an autologous cell obtained from a patient.

15. The isolated host cell of claim 13 wherein the DLL3 sensitized lymphocyte comprises an allogeneic cell.
16. The isolated host cell of claim 13 wherein the DLL3 sensitized lymphocyte comprises a T cell or a NK cell.
17. The isolated host cell of claim 16 wherein the T cell comprises a CD8⁺ T cell.
18. The isolated host cell of claim 16 wherein the DLL3 sensitized lymphocyte comprises a NK cell.
19. A pharmaceutical composition comprising a host cell of any one of claims 12 to 18.
20. A method of treating a patient suffering from cancer comprising the step of administering a pharmaceutical composition of claim 19.
21. The method of claim 20 wherein the patient is suffering from a cancer selected from the group consisting of lung cancer, melanoma, breast cancer, prostate cancer, colon cancer, renal cell carcinoma, ovarian cancer, neuroblastoma, rhabdomyosarcoma, leukemia and lymphoma.
22. The method of claim 21 wherein the cancer is lung cancer and the lung cancer is small cell lung cancer.
23. A method of producing a DLL3 sensitized lymphocyte comprising the step of transforming a lymphocyte with a DLL3 CAR.
24. A method of producing a DLL3 sensitized lymphocyte comprising the step of transducing a lymphocyte with a DLL3 CAR.
25. A method of producing a DLL3 sensitized lymphocyte comprising the step of transfecting a lymphocyte with a DLL3 CAR.

26. An article of manufacture comprising a receptacle containing a DLL3 sensitized lymphocyte and a pharmaceutically acceptable carrier.
27. An article of manufacture comprising a receptacle containing a pharmaceutical composition of claim 11.
28. The article of manufacture of claim 27 wherein the pharmaceutical composition comprises a viral vector.
29. An article of manufacture comprising a receptacle containing a pharmaceutical composition of claim 19.
30. The article of manufacture of any one of claims 26 to 29 wherein the receptacle comprises a syringe, an infusion bag or a vial.

Amino acid sequences of exemplary murine anti-DLL3 antibody light chain variable regions

mAb	FR1	CDRL1	FR2	CDRL2	FR3	CDRL3	FR4	SEQ ID NO.
SC16.3	QIVLTQSPAIMSVSLGERVTMTTC	TASSVSSSYLH	WYQQKPGSPKLLWIY	STSNLAS	GVPARFSGSGSGTSYFFTISSMEAEADAATYYC	HQYHRSPT	FGAGTKLIR	21
SC16.4	DIQMTQTITSSLSASLGDRVTISC	RASQDISNYLN	WYQQKPDGTVKLLIY	YTSRLHS	GVPFRFSGSGSGTDYSLTISNLEIEDIATYFC	QQGDMLPWT	FGGGTKLEIK	25
SC16.5	QIVLTQSPAIMSASPGKVTMTTC	SASSSVSYMH	WYQQKSGTSPKRWIY	DTSKLAS	GVPARFSGSGSGTYSYSLTISSMEAEADAATYYC	QQWTRNPLT	FGAGTKLELK	29
SC16.7	NIMLTQSPSSLAVSAGEKVTMSC	KSSQSLVLYSNQKNYLA	WYQQKPGQSPKLLIY	WASTRES	GVPDRFTGSGGTDFTLTISTVQVEDLAVYYC	HQYLSSWT	FGGGTKLEIK	33
SC16.8	EQIMLTQSPSSMSASLGDRITTC	QATQDIVKNLN	WYQQKPGKPPSELIY	YAIELAE	GVPFRFSGSGSGDYSLTISNLESEDFADYYC	LQFYEPFT	FGAGTKLELK	37
SC16.10	QIVLTQSPAIMSASLGERTMTTC	TASSVSSSYLH	WYQQKPGSPKLLWIY	STSNLAS	GVPTRFSGSGSGTYSYSLTISSMEAEADAATYYC	HQYHRSPT	FGSGTKLEIK	41
SC16.11	DVEMTQTPLTSLVTIGQPASISC	KSSQSLSDSDGKTYLN	WMFQRPGRSPKRLIY	LVSKLDS	GVPDRFTGSGGTDFTLKISRVEAEDLGVYYC	WQGHFPWT	FGGGTKLEIK	45
SC16.13	QIVLTQSPALVSASPGKVTMTTC	SASSSVSYMY	WYQQKPRSPKPMWIY	LTSNLAS	GVPARFSGSGSGTYSYSLTISSMEAEADAATYYC	QQWRSNPFT	FGSGTKLEIK	49
SC16.15	DIQMTQSPASLAASVGETVAITC	RASENIYNYLA	WYQQKPGKSPQLLIY	TANSLD	GVPFRFSGSGSGTGQYSLKINSIQPEDSATYFC	KQAYDVPPT	FGGGTKLEIK	53
SC16.18	DIQMTQTITSSLSASLGDRVTISC	RASQNIINYLN	WYQQKPDGTVKLLIY	YTSRLHS	GVPFRFSGSGSGTDYSLTISNLEPEDIAATYYC	QQYSERPYT	FGGGTKLEIK	57
SC16.19	DIQMTQSPSSLSASLGKVTFTTC	KASQDIHKYVA	WYQHKPGKGRLLIY	YTSTLQP	GISSRFSGSGSGRDYSFISNLEPEDIAATYYC	LQYNNLYT	FGGGTKLEIK	61
SC16.20	EQIMLTQSPSSMSASLGDRITTC	QATQDIVKNLN	WYQQKPGKPPSELIY	YATELAE	GVPFRFSGSGSGDYSLTIRNLESEDFADHYC	LQFYEPFT	FGAGTKLELK	65
SC16.21	DIVMTQSPSSLAASVGVKVTMSC	KSSQSLINSNQKNYLA	WYQQEPGQSPKLLVS	FASTRES	GVPDRFTGSGGTDFTLTISGVQAEADLAVYYC	QQHYSIPLT	FGAGTKLELK	69
SC16.22	DIQMTQTITSSLSASLGDRVTISC	RASQDIKNYLN	WYQQKPDGTVKPLIY	YTSRVHS	GVPFRFSGSGSGTDYSLTISNLEQEDIATYFC	QQGYTLPT	FGSGTKLEIK	73
SC16.23	QIVLTQSPAIMSASPGKVTLTTC	SASSSVSSRYLY	WYQQKPGSPKLLWIY	STSNLAS	GVPARFSGSGSGTYSYSLTISSMEAEADAATYYC	HQWSNYPLT	FGAGTKLELK	77
SC16.25	QIVLTQSPAIMSASPGKVTMTTC	SASSSVSYMH	WYQQKSGTSPKRWIY	DSSKLAS	GVPARFSGSGSGTYSYSLTISSMEAEADAATYYC	QQWSSNPFT	FGAGTKLELK	81
SC16.26	DVEMTQTPLTSLVTIGQPASISC	KSSQSLSDSDGKTYLN	WMFQRPGRSPKRLIY	LVSKLDS	GVPDRFTGSGGTDFTLKISRVEAEDLGVYYC	WQGHFPWT	FGGGTKLEIK	85
SC16.29	QIVLTQSPAIMSASPGKVTITTC	SASSSVSYMH	WFQKPGTSPKLLWIY	TTSNLAS	GVPARFSGSGSGTYSYSLTVSRMEAEADAATYYC	QQRSLYPYT	FGGGTKVEIK	89
SC16.30	QIVLTQSPITMSASLGERTMTTC	TASSVTSYSLH	WYQQKPGSPKLLWIY	STSNLAS	GVPARFSGSGSGTYSYSLTISSMEAEADAATYYC	HQHRSPT	FGSGTKLEIK	93
SC16.31	DIVLTQSPSLIPVNIQDQASISC	KSTKSLNSDGETYLD	WYLQRPQSPQLIY	LVSNRFS	GVPDRFSGSGGTDFTLKISRVEAEDLGVYYC	FQSNYPLT	FGAGTKLELR	97

FIG. 1A

Amino acid sequences of exemplary murine anti-DLL3 antibody light chain variable regions

mAb	FR1	CDRL1	FR2	CDRL2	FR3	CDRL3	FR4	SEQ ID NO.
SC16.34	SIVMTQTPKELLVSAGDRVITTC	KASQSVNDVA	WYQQKPGQSPKLLIY	YASNRYS	GVPDRFTGSGYGTDFTFTISTVQAEDLAVYFC	QQDYSSPWT	FGGGTKLEIK	101
SC16.35	DIQMTQITSSLSASLGDRVITSC	RASQDISNYLN	WYQQKPDGTVKLLIY	YTSRLHS	GVPDRFSGSGSGTDYSLTISNLEQEDIAITYFC	QQGNLPLYT	FGGGTKLEIK	105
SC16.36	ETTVTQSPASLSVTTGEKVTIRC	ITPDIDDDMN	WYQQKPGEPNLLIS	EGNSLRP	GVPDRFSSSGYGTMFVFTIENTLSLSEDVADYYC	LQSDNMPFT	FGSGTKLEIK	109
SC16.38	QIVLTQSPAIMSASPGEKVTMTTC	SASSSNYMH	WYQQKPGTSPKRWIY	DTSKLAS	GVPARFSGSGSGTSYSLTISNLEQEDIAITYFC	HQRSTWT	FGGGTKLEIK	113
SC16.41	DIQMTQITSSLSASLGDRVITSC	RASQDVINYLN	WYQQKPDGTVKLLIY	YTSRLHS	GVPDRFSGSGSGTDYSLTISNLEQEDIAITYFC	QQYSERPVT	FGGGTKLEIK	117
SC16.42	DVLTMTQSPSLSLVSLGDAQSISC	RSSQNIHSDRYTYLE	WYLLQKPGQSPKLLIY	GVSNRFS	GVPDRFSGSGSGTDFTLKISRVEAEDMGMVYYC	FQGTHVPYT	FGGGTKLEIK	121
SC16.45	EQMTQSPSSMSASLGDRITITC	QATQDVKNLN	WYQQKPGKPPSELIY	YATELAE	GVPARFSGSGSGSDYSLTISNLESEDFADYHC	LQYEFPT	FGAGTKLEIK	125
SC16.47	DVVLTSQPSLPLVNIQDQASISC	KSTKSLNSDGETYLD	WYLLQKPGQSPKLLIY	LVSNRFS	GVPDRFSGSGSGTDFTLKISRVEAEDLGMVYYC	FQSNYLPYT	FGAGTKLEIR	129
SC16.49	DIKMTQSPSSMYASISGERVTITC	KASQDINSYLS	WFQQKPGKSPKTIY	RANRLVD	GVPDRFSGSGSGQDYSLTISLEYEDMGYYC	LQYDEFPLT	FGAGTKLEIK	133
SC16.50	DIQMTQITSSLSASLGDRVITSC	RASQDISNYLN	WYQQKPDGTVKLLIY	YTSRLHS	GVPDRFSGSGSGTDYSLTISNLEQEDIAITYFC	QQGNLRT	FGGGTKLEIK	137
SC16.52	DIQMQSPSSMFASLGDRVSLSC	RASQIRGTLTD	WYQQKPNGTIKLIY	STSNLNS	GVPDRFSGSGSGSDYSLTISNLESEDFADYHC	LQRNAVPLT	FGAGTKLEIK	141
SC16.55	DIKMTQSPSSMYASISGERVTITC	KASQDINSYLN	WFQQKPGKSPKTIY	RANRLVD	GVPDRFSGSGSGQDYSLTISLEYEDMGYYC	LQYDEFPT	FGGGTKLEIK	145
SC16.56	SIVMTQTPKELLVSAGDRVITTC	KASQSVNDVW	WYQQKPGQSPKLLIY	YASNRYT	GVPDRFAGSGYGTDFTFTISTVQAEDLAVYFC	QQDYTSPWT	FGGGTKLEIR	149
SC16.57	DIVMTQSHKFMISISVGDVRSITC	KASQDVIFVA	WYQQKPGQSPKLLIY	SASYRYT	GVPDRFTGSGSGTDFTFTISTVQAEDLAVYHC	QQHYGTPFT	FGSGTKLIR	153
SC16.58	DIQMTQSPASLSVSSVGETVTITC	RASENIVSYLA	WYQQKQKSPQLLVY	NAKTAE	GVPDRFSGSGSGTQFSLKINSIQPEDFGTYFC	QHHYDSPLT	FGAGTKLEIR	157
SC16.61	DIVMTQSTSSLAHSVGGKVTMSC	KSSQSLNLSNQNKYLA	WYQQEPGQSPKLLVS	FASTRES	GVPDRFTGSGSGTDFTLTISGVQAEDLAVYHC	QQHYSIPLT	FGAGTKLEIK	161
SC16.62	DIKMTQSPSSMYASISGERVTITC	KASQDINSFLS	WFQRKPGKSPKTIY	RANRLVD	GVPDRFTGSGSGQEFSLTISLEYEDLGYYC	LQYDEFPT	FGGGTKLEIK	165
SC16.63	QIVLTQSPAIMSASPGEKVTMTTC	SASSSVSYMY	WYQQKSGTSPKRWIY	DTSKLAS	GVPARFSGSGSGTSYSLTISNLEQEDIAITYFC	QQWSSNPYT	FGGGTKLEIK	169
SC16.65	QIVLTQSPALMSASPGEKVTMTTC	SVTSSVSVMY	WYQQKPRSPKRWIY	LTSNLAS	GVPARFSGSGSGTSYSLTISNLEQEDIAITYFC	QQWRNPFT	FGSGTKVEIK	173
SC16.67	QAVVTQESALITSPGETVTLTC	RSSTGAVTTSNYAN	WIEKPDHLFTGLIG	GTNNRAP	GVPARFSGSLIGDKAALITGAQTEDEAIVFC	GLWYSNHLV	FGGGTKLTVL	177
SC16.68	ETTVTQSPAFSLVATGEKVTIRC	ITSTDIDDDMN	WYQQKPGEPNVLIS	EGNTRLP	GVPDRFSSSGYGTDFTFTIENTLSLSEDVADYYC	LQSDNMPFT	FGAGTKLEIK	181
SC16.72	ENVLTQSPAIMSASLGKVTMSC	RASSSVNYMS	WYQQKSDASPKLWIY	YTSNLAP	GVPARFSGSGSGNSYSLTISNLEQEDIAITYFC	QQFTSSPYT	FGGGTKLEIK	185

FIG. 1A cont.

Amino acid sequences of exemplary murine anti-DLL3 antibody light chain variable regions

mAb	FR1	CDRL1	FR2	CDRL2	FR3	CDRL3	FR4	SEQ ID NO.
SC16.73	DIQMTQSPSSLSASLGERVSLTC	RASQDIGSYLN	WLQEPDGTIKRLIY	ATSSDS	GVPKRFSGSRGSDYSYLSLTSSLESEDFVDYYC	LQYASSPWT	FGGGTKLEIK	189
SC16.78	DIKMTQSPSSMYASLGERVTITC	KASQDINSYLS	WFQOKPGRSPKTLIY	RANRLVD	GVPSRFSGSGGQDYSLTSSLDYEDMGYYC	LQYDEFPFT	FGSGTKLEIK	193
SC16.79	DIVMSQSPSSLAVSAGEKVTMSC	KSSQSLLNSRTRKNYLA	WYQOKPGQSPKLLIY	WASTRES	GVPRDFTGSGSGTDFTLTSSVQAEDLAVYYC	KQSYNLYT	FGGGTKLEIK	197
SC16.80	ETTVTQSPASLSMAIGKVTIRC	ITSTDIDDDMI	WYQOKPGEPKLLIS	EGNTLRP	GVPSRFSGGYGTDFVFTIENMLSEDVADYYC	LKRDDLPLYT	FGGGTQVEIK	201
SC16.81	QIVLTQSPAIMSASLGERVLTTC	TASSSVSSSYLH	WYQOKPGSSPKLWIY	STSNLAS	GVPTFRFSGSGGTYSYLSRISSMEADAATYYC	HQYNRSPLT	FGAGTKLELK	205
SC16.84	DIQMTQSPSSLSASLGGKVTITC	KASQDIKKIYA	WYQHKPGKGPRLLIH	YTSTLEP	GIPSRFSGSGGRDYSFISINLEPEDIATYYC	LQYDILWT	FGGGTKLEIK	209
SC16.88	ENVLTQSPAIMAASLGGKVTMTTC	SASSSVSSSYLH	WYQOKSGASPKPLIH	RTSNLAS	GVPARFSGSGGTSYSLTSSVVEAEDDATYYC	RQWSGYPWT	FGGGTKLEIK	213
SC16.101	QIVLTQSPAIMSASLGERVTMTTC	TASSSVSSSYLH	WYQOKPGSSPKLWIY	STSNLAS	GVPARFSGSGGTYSYLSLTSSVVEAADAATYYC	HQYHRSFFT	FGSGTKLEIK	217
SC16.103	DIVLTQSPASLAVSLGQRATISC	RASKSVSTSGYSYMH	WYQOKPGQPPKLLIY	LASNLES	GVPARFSGSGGTDFTLNIHPVEEEDAATYYC	QHSREPLT	FGAGTKLELK	221
SC16.104	QIVLSQSPAILSASPGEKVTMTTC	RASSSVSYIH	WYRQKPGSSPKPWY	ATSNLAS	GVPARFSGSGGTYSYLSLTISRVEAEDAATYYC	QQWSSNPPT	FGAGTKLELK	225
SC16.105	DIVMTQSHKFMSTSVGDRVSITC	KASQDVGTAVA	WYQOKPGQSPKLLIY	WASIRHT	GVPRDFTGSGSGTDFTLTISNVQSEDLAIFYC	QQYSSYPLT	FGAGTKLELK	229
SC16.106	DIKMTQSPSSMYASLGERVTITC	KASQDINSYLS	WFQOKPGKSPKTLIY	RANRLVD	GVPSRFSGSGGQDYSLTSSLEIEDMGYYC	LQYDEFPFT	FGSGTKLEIK	233
SC16.107	DIVMTQSHKFMSTSVGDRVSITC	KASQDVNTAVG	WYQOKPGQSPKLLIY	SASYRYT	GVPRDFTGSGSGTDFTLTSSVQAEDLAVYYC	QQHYSSPYT	FGGGTKVEIK	237
SC16.108	DIQMTQSPASLSASVGETVTITC	RASENIYSYLA	WYQOKQKGKSPQLLY	NAKTLAE	GVPSRFSGSRGSGQFSLKINSIQPEDFGSYYC	QHHYGTPT	FGGGTKLEIK	241
SC16.109	QIVLTQSPAIMSASPGEKVTMTTC	SASSSVSYMY	WYQOKPGSSPKLLIY	DTSNLAS	GVPRFRFSGSGGTDFTLTISRVEAEDAATYYC	QEWSGNPLT	FGDGTKLELK	245
SC16.110	NIVMTQTPKFLVLSAGDRVTITC	KASQSVNDVA	WYQOKPGQSPKLLIY	YASNRYT	GVPRDFTGSGYGTDFTLTISTVQAEDLAVFYC	QQDYSSPPT	FGGGTKLEIK	249
SC16.111	DIQMTQSPASLAASVGETVTITC	RASENIYSYLA	WYQOKQKGKSPQLLY	NANSLED	GVPSRFSGSGGTQYSMKINSMPEDATYFC	KQTYDVPLT	FGAGTKLELK	253
SC16.113	DVWMTQTPQLTSLVTIGQPASISC	KSSQSLLDSGDTTYLN	WILLQRPQSPKRLIY	LVSKLDS	GVPRDFTGSGGTDFTLTKISRVEAEDLGYYC	WQGTHTFPLT	FGAGTKLELK	257
SC16.114	QIVLSQSPAILSASPGEKVTMTTC	RASSSVSYMH	WYQOKPGSSPKPWY	ATSNLAS	GVPARFSGSGGTYSYLSLTISRVEAEDAATYYC	QQWSSNPYT	FGGGTKLEIK	261
SC16.115	DVWMTQTPQLTSLVTIGQPASISC	KSSQSLLDSGDTTYLN	WILLQRPQSPKRLIY	LVSKLDS	GVPRDFTGSGGTDFTLTKISRVEAEDLGYYC	WQGTHTFPLT	FGAGTKLELK	265

FIG. 1A cont.

Amino acid sequences of exemplary murine anti-DLL3 antibody light chain variable regions

mAb	FR1	CDRL1	FR2	CDRL2	FR3	CDRL3	FR4	SEQ ID NO.
SC16.116	DIVMTQSPSSLTVTAGEKVTMSC	TSSQSLLTSGNQKNYLT	WYQQKPGQPKLLIY	WASTRES	GVPDFRTGSGSGDTFTLTSSLOAEDAVYYC	QNDYSLT	FGAGTKLEIK	269
SC16.117	DIQMNQSPSSLASLGDITITTC	HVSQININWLS	WYQQKPGNIPKLLIQ	KASNLHT	GVPSRFSGSGSGTGFTLTSSLPEDIAITYYC	QQGQSYPT	FGSGTKLEIK	273
SC16.118	DIVLTQSPASLAVSLGQRATISC	KASQSVDYDGDSTLT	WYQQKPGQPKLLIY	AASNLES	GIPARFSGSGSGDTFTLNHPVEEEDAAITYYC	QQSNEDPYT	FGGGTKLEIK	277
SC16.120	DIVMSQSPSSLAVSVGEKVTMSC	KSSQGLLYSTQKNYLA	WYQQKPGQPKLLIY	WASTRES	GVPDFRTGSGSGDTFTLTSSVKAEDAVYYC	QQYYSYPYT	FGGGTKLEIK	281
SC16.121	QIVLTQSPAIMSASPGKVTITC	SASSSVSYMH	WFQOKPGTSPKLLIY	STSNLAS	GVPARFSGSGSGTSYSLTISRMEAEADAITYYC	QQRSSYPPT	FGGGTKLEIK	285
SC16.122	DIVMTQSQKFMTSVSGDRVSVTC	KASQNVGTNA	WYQQKPGQPKLLIY	SASYRYS	GVPDFRTGSGSGDTFTLTISNVSEDAIEFFC	QQYNSYPLT	FGGGTKLEIK	289
SC16.123	QIVLTQSPAIMSASLGERVTMTTC	TASSSVSSSYLH	WYQQKPGSSPKLLIY	STSNLAS	GVPARFSGSGSGTSYSLTSSMETEDAITYYC	HQYHRSPT	FGSGTKLEIK	293
SC16.124	DIQMTQSPASQSASLGSVTITC	LASQTIGTWLA	WYQQKPGKSPQLIS	AATSLAD	GVPSRFSGSGSGTKSFKISSLOAEDFVSYYC	QQLYSTPWT	FGGGTKLEIK	297
SC16.125	DIQMNQSPSSLASLGDITITTC	HASQININWLS	WYQQKPGNIPKLLIY	KASILHT	GVPSRFSGSGSGTGFTLTSSLPEDIAITYYC	QQGQSYPT	FGGGTKLEIK	301
SC16.126	DIQMNQSPSSLASLGDITITTC	HASQININWLS	WYQQKPGNIPKLLIY	KASNLHT	GVPSRFSGSGSGTGFTLTSSLPEDIAITYYC	QQGQSYPT	FGGGTKLEIK	305
SC16.129	DIQMTQSPASQSASLGSVTITC	LASQTIGTWLA	WYQQKPGKSPQLIY	AATSLAD	GVPSRFSGSGSGTKSFKISSLOAEDFVSYYC	QQLYSTPWT	FGGGTKLEIK	309
SC16.130	DIQLTQSPASLSASVGETVTITC	RASGSHNYLA	WYQQKQKSPQLIY	NAKTLVD	GVPSRFSGSGSGTGQYSLKINSLOPEDFGYYC	QHFWTTPWT	FGGGTKLEIK	313
SC16.131	DIQMNQSPSSLASLGDITITTC	HVSQININWLS	WYQQKPGNIPKLLIQ	KASNLHT	GVPSRFSGSGSGTGFTLTSSLPEDIAITYYC	QQGQSYPT	FGSGTKLEIK	317
SC16.132	DIQMTQSPASQSASLGSVTITC	LASQTIGTWLA	WYQQKPGKSPQLIY	AATSLAD	GVPSRFSGSGSGTKSFKISSLOAEDFVSYYC	QQLYSTPWT	FGGGTKLEIK	321
SC16.133	SIVMTQTPKFLVLSAGDRVITTC	KASQSVNDVA	WYQQKPGQPKLLIY	CASNRYT	GVPDFRTGSGYGTDFTFITSTVQAEDAVYFC	QQDYSSPLT	FGAGTKLEIK	325
SC16.134	DIVLTQSPASLAVSLGQRATISC	KASQSVDHAGDSYMN	WYQQKPGQPKLLIY	AASNLES	GIPARFSGSGSGDTFTLNHPVEEEDAAITYYC	QQSNEDPYT	FGGGTKLEIK	329
SC16.135	DIKMTQSPSSMYASLGERVTITC	KASQDINRYLS	WFQOKPGKSPKTLIY	RANRLVD	GVPSRFSGSGSGGDYSLTSSLEYEDMGYYC	LOYDEFPPT	FGSGTKLEIK	333
SC16.136	DIQMTQSPASLSASVGETVTITC	RASGNIHNYLA	WYQQKQKSPHLLIY	NAKTLAD	GVPSRFSGSGSGTGQYSLKINSLOPEDFGYYC	QHFWSPTWT	FGGGTKLEIK	337
SC16.137	QIVLTQSPAIMSASLGEETITTC	SASSSVSYMH	WYQQKSGTSPKLLIY	STSNLAS	GVPSRFSGSGSGTFYSLTSSVEAEADAITYYC	HQWSSYHT	FGGGTKLEIK	341

FIG. 1A cont.

Amino Acid Sequences of exemplary murine anti-DLL3 antibody light chain variable regions

mAb	FR1	CDRL1	FR2	CDRL2	FR3	CDRL3	FR4	SEQ ID NO.
SC16.138	DIQMTQSPASQASLGEVITTC	LASQTIGTWLA	WYQQKPGKSPQLLIY	SATSLAD	GVPSPRFGSGSGGTGKFSKISSLQAEDFVSYIC	QQLYSTPWT	FGGGTKLEIK	345
SC16.139	DIVMTQSHKFMSTSVGDRVITTC	KASQDVNTAVG	WYQQKPGQSPKLLIY	SASYRYT	GVPDRFTGSGSGGTDFTFTISSVQAEDLAVYYC	QQHYSSPYT	FGGGTKLEIK	349
SC16.140	DIVLTQSLASLAVSLGQRATISC	RASKSVSTSGYSYMH	WYQQKPGQPPKLLIY	LASNLES	GVPARFSGSGSGTDFTLNHPVEDEDAATYYC	QHSRELPEF	FGGGTKLEIK	353
SC16.141	DIKMTQSPSSMYASLGERTITTC	KASQDINSYLS	WFQQKPGKSPKTLIY	RANRLVD	GVPSPRFGSGSGGQDYSLTISSEYEDMGIIYYC	LQYDEFPPT	FGGGTKLEIK	357
SC16.142	DIKMTQSPSSMYASLGERTITTC	KASQDINNLYS	WFQQKPGKSPKTLIY	RANRLVD	GVPSPRFGSGSGGQDYSLTISSEYEDMGIIYYC	LQYDEFPPT	FGGGTKLEIK	361
SC16.143	DVLMTQTPLSLPVSIGDQASISC	RSSQSIHNSNGNTYLE	WYLQKPGQSPKLLIY	KVSNRFS	GVPDRFSGSGSGTDFTLNISRVEAEDLGVYYC	FGGSHVPLT	FGAGTKLEIK	365
SC16.144	SIVMTQTTPKFLVLSAGDRVITTC	KASQSVNDVG	WYQQKPGQSPKLLIY	YASNRYN	GVPDRFTGSGYGTDFTFITSTVQAEDLAVYFC	QQDYSSPWT	FGGGTKLEIK	369
SC16.147	DIQMTQTASSLSASLGDRVITTC	RASQDINNLYN	WYQQKPDGTVKLLIY	YTSRLHS	GVPSPRFGSGSGGTDYSLTISLEQEDATYFC	QQGDTLPWT	FGGGTKLEIK	373
SC16.148	QIVLTQSPAIMSASPGKEVITTC	SASSSVSYMY	WYQQKPGSSPRLIY	DTSNLAS	GVPVRFSGSGSGTSYSLTISRMEADTATYYC	QEWSNNPLT	FGDGTKLEIK	377
SC16.149	DIQMNQSPSSLSASLGDTITTC	HASQNNVWLS	WYQQKPGNIPKLLIY	KASHLHT	GVPRLSGSGSGTGFTLTISLQPEDATYYC	QQGQSYPT	FGSGTTLEIK	381
SC16.150	DIVMSQSPSSLTVSVGEKVTMSC	MSSQSLLYSSTQKNYLA	WYQQKPGQSPKLLIY	WASTRES	GVPDRFTGSGSGTDFTLTISSVKAEDLAVYYC	QQYYSYPYT	FGGGTKLEIK	385

FIG. 1A cont.

Amino acid sequences of exemplary humanized anti-DLL3 antibody light chain variable regions

mAb	FR1	CDRL1	FR2	CDRL2	FR3	CDRL3	FR4	SEQ ID NO.
hSC16.13	DIQMTQSPSSLASVGDRVTTTC	SASSSVSYMY	WYQQKPGKAPKLLIY	LTSNLAS	GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC	QQWRSNPFT	FGQGTKLEIK	389
hSC16.15	AIQLTQSPSSLASVGDRVTTTC	RASENIYYNLA	WYQQKPGKAPKLLIY	TANSLED	GVPSRFSGSGSGTDFTLTISSLQPEDFATYFC	KQAYDVPPT	FGGGTKLEIK	393
hSC16.25	EIVLTQSPDFQSVTPKEKVTTC	SASSSVSYMH	WYQQKPDQSPKLLIK	DSSKLAS	GVPSRFSGSGSGTDFTLTINSLEAEDAATYYC	QQWSSNPFT	FGQGTKLEIK	397
hSC16.34	DIQMTQSPSSLASVGDRVTTTC	KASQSVSNDVA	WYQQKPGKVPKLLIY	YASNRYT	GVPSRFSGSGSGTDFTLTISSLQPEDVATYFC	QQDYSSPWT	FGGGTKVEIK	401
hSC16.56	EIVMTQSPATLSVSPGERATLSC	KASQSVSNDVV	WYQQKPGQAPRLLIY	YASNRYT	GIPARFSGSGSGTEFTLTISSLQSEDFAVYYC	QQDYTSPWT	FGQGTKLEIK	405

FIG. 1A cont.

Amino acid sequences of exemplary murine anti-DLL3 antibody heavy chain variable regions

mAb	FR1	CDRH1	FR2	CDRH2	FR3	CDRH3	FR4	SEQ ID NO.
SC16.3	QVTLKESGPIQLPSQTLSTLCSFSGFSL	TSGMGVG	WIRQPSGKGLEWLA	HIWDDVKRYNPALKS	RLTISKDTSSSQVFLKIASVDTADTATYFCAR	IADYGGDYAMDY	WGQGTSTVTSS	23
SC16.4	QIQLVQSGPELKPGETVKISCKASGYTFT	DYSMH	WVKQAPGKGLKWMG	WINTETGEPGYADDFKG	RFAFSLSETSASTAYLQINNLIKNEEDTATYFCAR	YDGYAMDY	WGQGTSTVTSS	27
SC16.5	QVTLKESGPIQLPSQTLSTLCSFSGFSL	TSGMGVG	WIRQPSGKGLEWLA	DIWDDNKYYNPALKS	RLTISKDTSSNQVFLKITSVDTADTATYFCAR	RVNYYDPYYAMDY	WGQGTSTVTSS	31
SC16.7	EVQLQQSGPELVKPGASVKISCKASGYFT	GYKMH	WVKQSHVKSLWIG	RINPYNGATSYNQNFKD	KATLTVDKSSSTAYMDLHSLTSEDSAVYFCAR	GDYRYDWFAY	WGQGTSTVTSSA	35
SC16.8	QAQLQQSGAELVRPGTSVKVSKKASGYAFT	NYLIE	WVKQRPQGGLWIG	VINPGTGGTNYNENFKG	KATLTADKSSSTAYMQLSSLTSDSDSAVYFCAR	SPDYHEGAMDY	WGQGTSTVTSS	39
SC16.10	QVTLKESGPIQLPSQTLSTLCSFSGFSL	TSGMGVG	WIRQPSGKGLEWLA	HIWDDVKRYNPALKS	RLTISKDTSSSQVFLKIASVDTADTATYFCAR	LVDDLYYFDY	WGQGTSTVTSS	43
SC16.11	QIQLVQSGPELKPGETVKISCKASGYTFT	DYSMH	WVKQAPGKGLKWMG	WINTETVEPTYADDFWG	RFAFSLSETSASTAYLQINNLIKNEEDTATYFCAR	FGSYAMDY	WGQGTSTVTSS	47
SC16.13	QVTLKESGPIQLPSQTLSTLCSFSGFSL	TSGMGVG	WIRQPSGKGLEWLA	HIWDDVKRYNPALKS	RLTISKDTSSSQVFLKIASVDTADTATYFCAR	IVSFDNDVVSAMDY	WGQGTSTVTSS	51
SC16.15	QVQLQQSGAELAKPGASVKISCKASGYTFT	RYWH	WIKQRPQGGLWIG	YINPTTYTEFNQNFKD	KATLTADKSSSTAYMQLSSLTSEDSAVYFCAR	GGSNFFDY	WGQGTSTVTSS	55
SC16.18	EVKLEESGGGLVQPGESMKLSKAASGFTFS	DAWMD	WVRSPEKGLEWLA	EIRKANNHATYAESVKG	KFTISRDDSKSRVYLOMNNLRADTGTYCTA	YSNFAY	WGQGTSTVTST	59
SC16.19	EVQLQQSGAELVRPGASVYKLSCTASGFNIK	DSLH	WVKQRPKGLWIG	WIDPEDGETKYAPNFQD	KATITDSSSNTAYLQILSLTSDTATYFCAR	GNVYRHFY	WGQGTSTVTSS	63
SC16.20	QVQLQQSGTELVRPGTSVRVSKKASGYAFT	NHLIE	WVKQRPQGGLWIG	VINPGTGGTHYNEKFKD	KARLTADKSSNTAYMHLSLTSDSDSAVYFCAR	SPDYHEGAMDY	WGQGTSTVTSS	67
SC16.21	QVQLQQSGPELVKPGASVKISCKASGYAFT	SSWMN	WVKQRPKGLWIG	RIYPGDDTNYNGKFKG	KATLTADKSSSTAYMQLSSLTSEDSAVYFCAR	GIYNYDGSRYYSMDY	WGQGTSTVTSS	71
SC16.22	QVQLQQSGAELVKPGASVKLSCKASGYTFT	TYWMH	WVKQRPQGGLWIG	EIDPSDSTYTYNQKFKG	KATLTVDKSSSTAYMQLSSLTSEDSAVYFCAR	GDYGNPYAMDY	WGQGTSTVTSS	75
SC16.23	QVTLKESGPIQLPSQTLSTLCSFSGFSL	TSNTGIG	WIRQPSGKGLEWLA	HIWDDNKYYNPALKS	RLTISKETSNNQVFLKITNVDTADTATYFCAR	IGRDYSNYAWYFDV	WGAGTTVTSS	79
SC16.25	QVTLKESGPIQLPSQTLSTLCSFSGFSL	TSGMGVG	WIRQPSGKGLEWLT	DIWDDNKYYNPALKS	RLTISKDTSSNQVFLNITSVDTADTATYFCAR	RVNYYDPYYAMDY	WGQGTSTVTSS	83
SC16.26	QIQLVQSGPELKPGETVKISCKASGYFT	DYSMH	WVKQAPGKGLKWMG	WINTETVEPTYADDFWG	RFAFSLSETSASTAYLQINNLIKNEEDTATYFCAR	FGSYAMDY	WGQGTSTVTSS	87
SC16.29	QVQLQQSGAELARPGASVKLSCKASGYTFT	DQYIN	WVKQRTGGGLWIG	EIYPGRGNTYNEKFKG	KATLTADKSSSTAYMQLSSLTSEDSAVYFCAR	EDGGYDDAWFAY	WGQGTSTVTSSA	91
SC16.30	QVTLKESGPIQLPSQTLSTLCSFSGFSL	TSGMGVG	WIRQPSGKGLEWLA	HIWDDVKRYNPALKS	RLTISKDTSSNQVFLKIATVDAADTGTATYFCAR	IVDGHPPFAY	WGQGTSTVTSSA	95
SC16.31	EVQLQQSGPELVKPGASVKISCKASGYFTS	RFYMH	WVKQSPENSLEWIG	EINPSTGGTSYNQKFKG	KATLTVDKSSSTAYMQLKSLTSEESAVYCTR	GYGSNNWYFDV	WGAGTTVTST	99

FIG. 1B

Amino acid sequences of exemplary murine anti-DLL3 antibody heavy chain variable regions

mAb	FR1	CDRH1	FR2	CDRH2	FR3	CDRH3	FR4	SEQ ID NO.
SC16.34	QIQLVQSGPELKPGETVKISKASGYTFT	NYGMN	WVKQAPGKGLKWMG	WINTYTGDPITYADDFKG	RFAFSLETSASTAYLQINLNKIEDTATYFCAR	IGGNPSPDY	WGGGTSLVSS	103
SC16.35	DVQLQESGPGLVKPSQSLSLTCTVTGYSIT	SDYAWN	WIRQPGNKLEWMG	YISYSGSTSYNPSLKS	RISITRDTSKNQFELQLNSVTEDTATYYCAR	FYGGSSYAMDY	WGGGTSVTVSS	107
SC16.36	QVQLQQSGAELAKPGASVKMISCKASGYTFT	TYWMH	WVKQRPQGGLWIG	YINPSSGYTEYNQKFKD	KATLTADKSSSTAYMQLSSLTSEDSSVYYCAR	KGSNRGFAY	WGGGTLTVSS	111
SC16.38	EVQLQQSGAELVKPGASVKLSCTVSGFNIK	DTYIH	WVKQRPQGLWIG	RIDPANGNTKYDPKFG	KATTADTSSNTAYLQLSSLTSEDTAVYYCAR	PTGYFEY	WGGGTLTVSS	115
SC16.41	EVKLEESGGGLVQFGGSMKLSCAASGFTFS	DAWMD	WVRQSPKGLWVA	EIRKANNHATYYPESVKG	RFTISRDDSKSRVYLMNNLRAEDTGIYYCTG	YSSFAY	WGGGTLTVSA	119
SC16.42	QIQLVQSGPELKKPGETVKISKASGYTFT	TAGMQ	WVKQMPGKGFWMG	WINTHSGEPKYADDFKG	RFAFSLETSASTAYLQISLNKIEDTATFFCAP	LWSDSSFAY	WGGGTLTVSA	123
SC16.45	QVQLQQSGADLVRPGTSVKVSKKASGYST	NYLIE	WVKQRPQGGLWIG	VINPSSGGTHYNEKFKD	KAVLTADKSSSTTAHMQSSLTSDSDSAVYYCAR	SPDYNDGAMDY	WGGGTSVTVSS	127
SC16.47	EVQLQQSGPELVKPGASVKISCKASGYSFS	RFYMH	WVKQSPENSLEWIG	EINPSTGGTSYNQKFKG	KATLTVDKSSSTAYMQLKSLTSESAVYYCTR	GYGNCYFDV	WGAGTTVTVST	131
SC16.49	QVQLQQSGPELVKPGTLVKISKASGYTFT	SYDIN	WVKQRPQGGLWIG	WYVPGDNTKYSEKFKG	KATLTADKSSSTAYMQLTSLTSENDAVYYCAR	DYDYPFAY	WGGGTLTVSA	135
SC16.50	EVQLVEGGGCLVKPGGYLKLSCAASGFTFS	SYAMS	WVRQSPKRLWVA	EISIGGSYTYYPDVTGT	RFTISRDNKNTLYLEMSSLRSEDAMYYCAR	EGYDYDVRAMDY	WGGGTSVTVSS	139
SC16.52	QVQLKESGPGLVAPSQSLSLITCAVSGFSLT	SFAIH	WFRKPPGKGLWLG	VIVTGGTNNYSALMS	RLSISKDNSKSQVFLKMNSLQDDTAMYYCAR	DDYDNNYAMDY	WGGGTSVTVSS	143
SC16.55	EVQLVESGGGLVQPKGSLKLSCAVSAFTFT	TYAMN	WVRQAPGKGLWVA	RIRKSNNYATYYADSVKD	RFTISRDDSQSMLYLQMNLIKIEDTAMYYCVF	YYDYVY	WGGGTLTVSA	147
SC16.56	QIQLVQSGPELKKPGETVKISKASGYTFT	NYGMN	WVKQAPGKGLWMA	WINTYTGEPITYADDFKG	RFAFSLETSASTASLQINLNKIEDTATYFCAR	IGDSSPSDY	WGGGTLTVSS	151
SC16.57	EVKLVEGGDLVKPGGSLKLSCAASGFAFS	SYDMS	WVRQTPKRLWVA	TISSGGSYTYYPDSVKG	RFTISRDNVRLTLVLMSSLRSEDALYYCAR	QAIGTYFDY	WGGGTLTVSS	155
SC16.58	DVQLVESGGGLVQPGGSRKLSCAASGFTFS	SFGMH	WVRQAPKGLWVA	YISSGSSNIYYADTVKG	RFTISRDNPKNTLFLQMTSLRSEDAMYYCAR	GYGNYDAMDY	WGGGTSVTVSS	159
SC16.61	EVLLQRSQGLVKPGASVTIPCKASGYTFT	DYNMD	WVKQSHGKSLWIG	NINTYNGGTYNQKFKG	KATLTVDKPSSTAYMELRSLTSEDTAVYYCAR	RLRYGGHYFDY	WGGGTLTVSS	163
SC16.62	EVMLVESGGDLVKPGGSLKLSCAASGFTFS	SYAMS	WVRQTPKRLWVA	YISGGGDHYYPPDSVRG	RFTISRDNKNTLYLMSSLRSEDALYYCAR	VRDWMYFDV	WGAGTTVTVSS	167
SC16.63	QVQLQQSGTELLRPASVKISCKATGYTFS	SYWME	WVKQRPQGLWIG	EILPSSGTTQYNEKFKG	KATFTADTSSNTAYMHLSSLTSEDAMYYCAR	GTNSL	WGGGTLTVSA	171
SC16.65	QVTLKESGPGQLPSQTLSTCSFSGFSL	TSGMGVG	WIRQSPGKGLWLA	LIIWDDVKRYNPALKS	RLTISKDASSSQVFLKIASVDLTADTATYYCAR	IASYDYDVVYAMDY	WGGGTSVSVSS	175
SC16.67	EVQLVETGGGLVQPKGSLKLSCAVSAFTFT	TYAMN	WVRQAPGKGLWVA	RIRKSNNYATYYADSVKD	RFTISRDDSQSMLYLQMNLIKIEDTAMYYCVF	YYDYVY	WGGGTLTVSA	179

FIG. 1B cont.

Amino acid sequences of exemplary murine anti-DLL3 antibody heavy chain variable regions

mAb	FR1	CDRH1	FR2	CDRH2	FR3	CDRH3	FR4	SEQ ID NO.
SC16.68	QVQLQQPGAELVKPGASVKMSCKASGYTFT	NYNMH	WVKQTGGGLEWIG	AIFPGNGGTSYNQKFKG	KATLTADKSSSTAYMQLTSLTSGDSAVYYCAR	WGYGSLYAMDY	WGQGTSTVTVSS	183
SC16.72	EVQLQQSGPELVKPGASVKMSCKASGYTFT	SYVMH	WVKQKPGGGLEWIG	YINPYNDGTYNEKFKG	KATLTADKSSSTAYMELSSLTSEDASVYYCAR	LRSRAMDY	WGQGTSTVTVSS	187
SC16.73	QVQLQQSGAELMKPGASVKISCKANGYFTS	SYWIE	WLRQRPGHGLEWIG	EILPGSDNSNYNEKFKG	KATFTADTSSNTAYMQLSSLTSEESAVYYCTR	GLRRDGSYYYVMEH	WGQGTSTVTVSS	191
SC16.78	EVKLVEGGGLVKPGGSLKLSCAASGFTFG	RYVMS	WVRQTPEKLEWVA	SITSGGTTYYPDSVKG	RTISRDNARNILYLQMSLSRSEDAMYYCAR	VYYHYDDIFAY	WGQGLTVTVSA	195
SC16.79	EVQLQQSGPELVKPGASVKISCKTSGYTFT	EYTMH	WVKQSHGKSLWIG	GINPNNGGTSYNQKFKG	KATLTVDKSSSTAYMELRSLTSEDSAVYYCAR	GPAWFAY	WGQGLTVTVSA	199
SC16.80	EVQLQQSGPELVKPGGSKKISCKASGYST	GYSMN	WVKQSHGKNLEWIG	LINPYSGGTINQKFKG	KATLTVDKSSSTAYMELLSLTSEDASVYYCAR	RSDYPLVY	WGQGLTVTVSA	203
SC16.81	QVQLKESGPLVAPQSLSITCTVSGFSLT	SYGVH	WVRQPPGKLEWLG	VIWAGGSTNYNSALMS	RLSISKDNKSQVFLKMNSLQTDITAMYYCAK	QGNFYAMDY	WGQGTSTVTVSS	207
SC16.84	EVQLQQSGPELVKPGASMKISCKASGYST	GYTMN	WVKQSHGKNLEWIG	LINPYNGGTTYNQKFKG	KATLTVDKSSSTAYMELLSLTSEDASVYYCAL	GYGNYRRYFDV	WGAGTTVTVSS	211
SC16.88	QVQLQQSGAELARPGASVKLSCKASGYTCT	SYWMQ	WVKQRPGGGLEWIG	AIYPGDDTRYTQKFKG	KATLTADKSSSTAYMQLSSLASSEDASVYYCAR	GRRTEAWFAY	WGQGLTVTVSA	215
SC16.101	QVTLKESGPILQPSQTLSTLCSFSGFSL	TSGMGVG	WIRQPSGKLEWLA	HIWDDVVKRYNPALKS	RLTISKDASSSQVFLKIASVDTAETATYYCAH	ILDRAYYFDY	WGQGTTLTVTS	219
SC16.103	QVTLKESGPILKPSQTLSTLCSFSGFSL	TSGMGIG	WIRQPSGKLEWLA	HIWDDDKYYNPSLKS	QLTISKDSRRNQVFLKITSVDTADTATYYCAR	RGTAYYFDY	WGQGTTLTVSS	223
SC16.104	QVQLKESGPDLVQPSQTLSTLCTVSGFSLT	FYGVH	WVRQPPGKLEWVG	TMGWDDKYYNSALKS	RLSISRDTSKNQVFLKLSLQTEDTAMYYCTR	GGTGFDY	WGQGTTLTVSS	227
SC16.105	QVQLQQPGAELVKPGASVKLSCKASGYTFT	SYVMH	WVKQRPGGGLEWIG	VINPSNGRTNYNEKFKS	KATLTVDKSSSTAYMQLSSLTSEDASVYYCAR	RRELGLTYAMDY	WGQGTSTVTVSS	231
SC16.106	QVQLKQSGPLVAPQSFLITCTVSGFSLT	SYEIN	WVRQPPGKLEWLG	VIWGGSTNYNSALIS	RLSISKDNKSLVFLKMNSLQTDITAMYYCVR	GVYAMDY	WGQGTSTVTVSS	235
SC16.107	EVQLQQSGPELVKPGASVKMSCKASGYTFT	NYVMH	WVKQKPGGGLEWIG	YINPYNDGTYNEKFKG	KATLTADKSSSTAYMALSSLTSEDASVYYCAV	AYYSNWGFAY	WGQGLTVTVSA	239
SC16.108	QVQLQESGAELARPGASVKLSCKASGSYW	MQ	WIKQRPGGGLEWIG	AIYPGNGDTRYTQKFKG	KATLTADKSSSTAYMQLSSLASSEDASVYYCAR	SPAYRYGEGYFDY	WGQGTTLTVSS	243
SC16.109	QIQLVQSGPELVKPGGETVKISCKASGYTFT	NYGMN	WVKQAPGKGLKWMG	WINTYTGEPAVADDFKG	RFAFSLTASAAAYLQINNKNKEDTATFFCAN	MRPTRGFAY	WGQGLTVTVSA	247
SC16.110	EVQLQQSGPLVRTGASVKISCKASGYST	GYVMH	WVKQSHGKSLWIG	YISCYNGATTYNQKFKG	KATFIVDTSSSTAYMQFNLSLTSEDASVYYCAR	SDGGHAMDY	WGQGTSTVTVSS	251
SC16.111	EVQLQQSGPELVKPGASVKISCKASGYST	GYNMN	WVKQSGKSLWIG	NIDPYYGSSYKQKFEK	KATLTVDKSSSTAYMQLKSLTSEDASVYYCAR	GGSNFFDY	WGQGTTLTVSS	255

FIG. 1B cont.

Amino acid sequences of exemplary murine anti-DLL3 antibody heavy chain variable regions

mAb	FR1	CDRH1	FR2	CDRH2	FR3	CDRH3	FR4	SEQ ID NO.
SC16.113	DVKLVESGGGLVKPGGSLKLSAASGFTFS	SYTMS	WVRQTPEKRLWVA	TISGGGSPYPPDSVKG	RFTISRDNAKNTLYLQMSLSKSEDTAMYYCTR	DVYDGYSY	WGQGTTLTVSS	259
SC16.114	EVQLQQSGAEELVKPGASVKLSCTASGFNIK	DTYIH	WVKQRPEQGLEWIG	RIDPANGNTKYDPKFGQ	KATITPDTSSNTAYLQLSSLTSEDSTAVYYCAR	SWRNYSSEWFYFDV	WGAGTTVTSS	263
SC16.115	DVKLVESGGGLVKPGGSLKLSAASGFTFS	SYTMS	WVRQTPEKRLWVA	TISGGGSPYPPDSVKG	RFTISRDNAKNTLYLQMSLSKSEDTAMYYCTR	DVYDGYSY	WGQGTTLTVSS	267
SC16.116	QVQLKQSGPGRVQPSSQSLTCTVSGFSLT	SNQVH	WVRQSPGKGLEWLG	VLWSGGSTDYNAAFIS	RLSISKDNYSQVFFKMNLSLQANDTAIYYCAR	NNNRYGAMIDY	WGQGTSTVTSS	271
SC16.117	QVQLKESGPGLVAPSSQSLTCTVSGFSLT	NYGVH	WVRQPPGKGLEWLG	VIWAGGITNYSALMS	RLSISDNKSQVFLKMNLSLQTDGTAIYYCAR	NLGPYAMIDY	WGQGTSTVTSS	275
SC16.118	EVQLQQSGPDLVKPGASVKISCKASGYST	GYMH	WVKQSHGKSLWIG	RVNPNNGGTSYNQKFKG	KAILTADKSSSTAYMELRSLTSEDSAVYYCAR	GSYDYAEG	WGQGTTLTVSA	279
SC16.120	EIQLQQSGPELVKPGASVKVSKASGYAFT	SYNMY	WVMQSHGKSLWIG	YVDPYNGGTSYNQKFKG	KATLTVDKSSSTAYMHLNSLTSEDSAVYYCAR	ENRYFYDY	WGQGTTLTVSS	283
SC16.121	EVQLVESGGGLVQPKGSLKLSAASGFTFN	TYAMN	WVRQAPGKGLEWVA	RIKSNNTATYADSVKQ	RFTISRDSSQNMPLYLQMNLSLQTDGTAIYYCVR	QGYSDWGPWFAY	WGQGTTLTVSA	287
SC16.122	EVQLVESGGGLVKPGGSLKLSAASGFTFS	DYYMF	WVRQTPEKRLWVA	TISGGGTYTYPDSVKG	RFTISRDNAQNLYLQMSLSKSEDTAMYYCAR	AGTLYAMIDY	WGQGTSTVTSS	291
SC16.123	QVALKESGPGLVQPSQTLSTCTCSFGFSL	TSGMVG	WIRQPSGKGLEWLA	HIWDDVKRYNPALKS	RLTISKOTSSSQVFLKIASVDGTAIYYCAR	MEDYGSSSYFDF	WGHGTTTLTVSS	295
SC16.124	EVQLQQSGPELVKPGASVKMSCKASGYTFT	SYVMH	WVKQKPGQGLEWIG	YINPYNDGTYNEKFKG	KATLTSDKSSSTAYMELSSLTSEDSAVYYCAR	GALLYGNYLGYFDV	WGAGTTVTSS	299
SC16.125	DVQLQESGPDLVKPSQSLTCTVTGYSIT	SGYSWH	WIRQPGNKLWVG	YIYSGSTNYPNLSKS	RSITRDTSKNQFFLQKSVTTSEDSATYYCAL	EGNYDGFAY	WGQGTTLTVSS	303
SC16.126	QVQMKESGPGLVAPSSQSLTCTVSGFSLT	NYGVH	WVRQPPGKGLEWLG	VIWAGGSTNYSALMS	RLSISKDNKSQVFLKMNLSLQTDGTAIYYCAR	DWEGWFAY	WGQGTTLTVSA	307
SC16.129	QVQLKESGPGLVAPSSQSLTCTVSGFSLT	DYGVH	WIRQPPGKGLEWLG	VIWGGSTYNSALKS	RLSISKDNKSQVFLKMNLSLQTDGTAIYYCAR	HYGHYAAY	WGQGTTLTVSA	311
SC16.130	EVQLQQSGPELVKPGASVKMSCKASGYTFT	SYVMH	WVKQKPGQGLEWIG	YINPYNDGTYNEKFKG	KATLTSDKSSSTAYMELSSLTSEDSAVYYCAR	GVYDGYSYFYDY	WGQGTTLTVSS	315
SC16.131	QVQLKESGPGLVAPSSQSLTCTVSGFSLT	NYGVH	WVRQPPGKGLEWLG	VIWAGGITNYSALMS	RLSISDNKSQVFLKMNLSLQTDGTAIYYCAR	NLGPYAMIDY	WGQGTSTVTSS	319
SC16.132	QVQLKESGPGLVAPSSQSLTCTVSGFSLT	DYGVH	WIRQPPGKGLEWLG	VIWGGGSTYNSALKS	RLSITKDNKSQVFLKMNLSLQTDGTAIYYCAR	QRQYGYGAY	WGQGTTLTVSA	323
SC16.133	QVQLKESGPGLVAPSSQSLTCTVSGFSLT	NYAVH	WVRQSPGKGLEWLG	VIWSDGSTDYNAAFIS	RLSISKDNKSQVFFKMNLSLQANDTAIYYCAR	KKGWFWPWFAY	WGQGTTLTVSA	327
SC16.134	EVQLQQSGPDLVKPGASVKISCKASGYST	GYMH	WVKQSHGKRLWIG	RVNPNNGGTYNPKFKG	KAILTVDKSSSTAYMELRSLTSEDSAVYYCAR	GSYDVAEG	WGQGTTLTVSA	331
SC16.135	QVQLQQSGAEELVPRGTSVKVSKASGYAFT	NYLE	WVKQRPQGLEWIG	VINPNSGGTNSNEKFA	KATLTADKSSSTAYMQLSSLTSEDSAVYYCAR	SDYDYAFYAMIDY	WGQGTSTVTSS	335
SC16.136	EVQLQQSGPELVKPGASVKMSCKASGYTFT	SYVMH	WVKQKPGQGLEWIG	YINPYNDGTYNEKFKG	KATLTSDKSSSTAYMELSSLTSEDSAVYYCAR	DRSGYEDYYGMDY	WGQGTSTVTSS	339

FIG. 1B cont.

Amino acid sequences of exemplary murine anti-DLL3 antibody heavy chain variable regions

mAb	FR1	CDRH1	FR2	CDRH2	FR3	CDRH3	FR4	SEQ ID NO.
SC16.137	EVQLVESGGDLVKPGGSLKLSCAASGFTFS	SYGMS	WVRQTPDKRLEWVA	TISSGGSYTYYPDSVKG	RFTISRDNAKNTLYLQMISSLKSEDTAMYYCAR	RRADAMDY	WGQGTSTVTVSS	343
SC16.138	QVQLKESGPGLVAPSQSLSTCTVSGFSLT	DYGVS	WIRQPPGKGLEWLG	VWVGGSYYNNSALKS	RLSISKDNKSQVFLKMNSLQTDGDTAMYYCAK	QRQYGYAY	WGQGTSTVTVSA	347
SC16.139	EVQLQDSGPGLVKPGASVKMSCKASGYTFT	NYVMH	WVKQKPGQGLEWIG	YINPYNDGTYNEKFKG	KATLTSDKSSITAYMALSSLTSEDSAVYYCAV	AYYSNWGFAY	WGQGTSTVTVSA	351
SC16.140	QVQLQDSGPGLVRPGASVKMSCKASGYTFT	SYVMH	WVKQKPGQGLEWIG	MIDPSNSETRLNQKFKD	KATLNVDKSSNTAYMQLSSLTSEDSAVYYCAV	MDYYFDY	WGQGTSTVTVSS	355
SC16.141	QVQLKQSGPGLVAPSQSLFITCTVSGFSLT	SYEIN	WVRQPPGKGLEWLG	VIWTGGSTNYSALIS	RLSISKDNKSILVFLKMNSLQTDGTAIYYCVR	GVYAMDY	WGQGTSTVTVSS	359
SC16.142	EVQLQDSGPGLVKPGASVKISCKASGYTFT	DYNMH	WVKQSHGKSLWIG	FFYPYNGNTVYSQKFS	KATLTVDNSSSTAYMELRSLTSEDSAVYYCAR	LNWEGY	WGQGTSTVTVSS	363
SC16.143	QVQLQDSGPGLVKPGASVRIKCKASGYTFT	SYIYH	WVKQKPGQGLEWIG	WIYPGNGNTKYNEKFKG	KATLTADKSSSTAYMQISSLTSEDSAVYYCAR	ERWILLWFAY	WGQGTSTVTVSA	367
SC16.144	QIQLVQSGPELKKPGETVKISCKASGYTFT	NYGMN	WVKQAPGKGLKWWG	WINTYTGEPTYADDFKG	RFAFSLETSASTAYLQIDNLKNEEDTATYFCAR	VGYYVGFY	WGQGTSTVTVSS	371
SC16.147	QIQLVQSGPELTKPGETVKISCKASGYTFT	DYSLH	WVKQALGKGLKWWG	WINTETGEPAVADDFKG	RFAFSLETSASTAYLQINDLKNEDTTTTFYFCGI	YDGYAMDY	WGQGTSTVTVSS	375
SC16.148	QIQLVQSGPELKKPGETVKISCKASGYTLT	NYGMN	WVKQAPGKGLKWWG	WINTYTGEPTYADDFKG	RFAFSLETSASTAYLQINDLKNEDTATYFCAR	YEAHEGFY	WGQGTSTVTVSA	379
SC16.149	QVQLKESGPGLVAPSQSLSTCAVSGFSLT	SFGVH	WVRQPPGKGLEWLG	VIWAGGSTNYSALMS	RLSISIDNKSQVFLKMNSLQTDGDTAMYYCAR	DWEGWFAY	WGQGTSTVTVSA	383
SC16.150	EIQLQDSGPGLVKPGASVKVSKASGYAFT	SYNMY	WVSQSHGKSLWIG	YIDPYNGGTSYNQKFRG	KATLTVDKSSSTAYMHLNLSLTSEDSAVYYCAR	ENRYRFDY	WGQGTSTVTVSS	387

FIG. 1B cont.

Amino acid sequences of exemplary humanized anti-DLL3 antibody heavy chain variable regions

mAb	FR1	CDRH1	FR2	CDRH2	FR3	CDRH3	FR4	SEQ ID NO.
hSC16.13	QITLKESGPTLVKPTQTLTLTCTFSGFSL	TSGMGVG	WIRQPPGKALEWLA	HIWDDVKRYSPSLKS	RLTITKDTSKNQVLTMTNMDPVDATYYCAR	IVSFDNDVVSAMDY	WGQGLTVTVSS	391
hSC16.15	QVQLVQSGAEVKKPGASVKVSCKASGYTFT	RYWIH	WIRQAPGGQLEWMG	YINPTTVYTEFNQFKD	RVTMTTRDTSTSTVYMESSLRSRSEDVAVYYCAR	GGSNFFDY	WGQGTITVTVSS	395
hSC16.25	QITLKESGPTLVKPTQTLTLTCTFSGFSL	TSGMGVG	WIRQPPGKALEWLT	DIWDDNKYYNP SLKS	RLTITKDTSKNQVLTMTNMDPVDATYYCAR	RVNYYDPYYAMDY	WGQGLTVTVSS	399
hSC16.34	QVQLVQSGAEVKKPGASVKVSCKASGYTFT	NYGMN	WVRQAPGQRLEWMG	WINTYTGDPITYADDFKG	RVTITRDTASATAYMELSSRLSRSEDVAVYYCAR	IGGNSPSDY	WGQGTITVTVSS	403
hSC16.56	QVQLVQSGAEVKKPGASVKVSCKASGYTFT	NYGMN	WVRQAPGGQLEWMG	WINTYTGEPITYADDFKG	RVTMTTDTSTSTAYMELRSLRSRSDDTAVYYCAR	IGDSSPSDY	WGQGLTVTVSS	407

FIG. 1B cont.

Domain-level mapping of anti-DLL3 antibodies

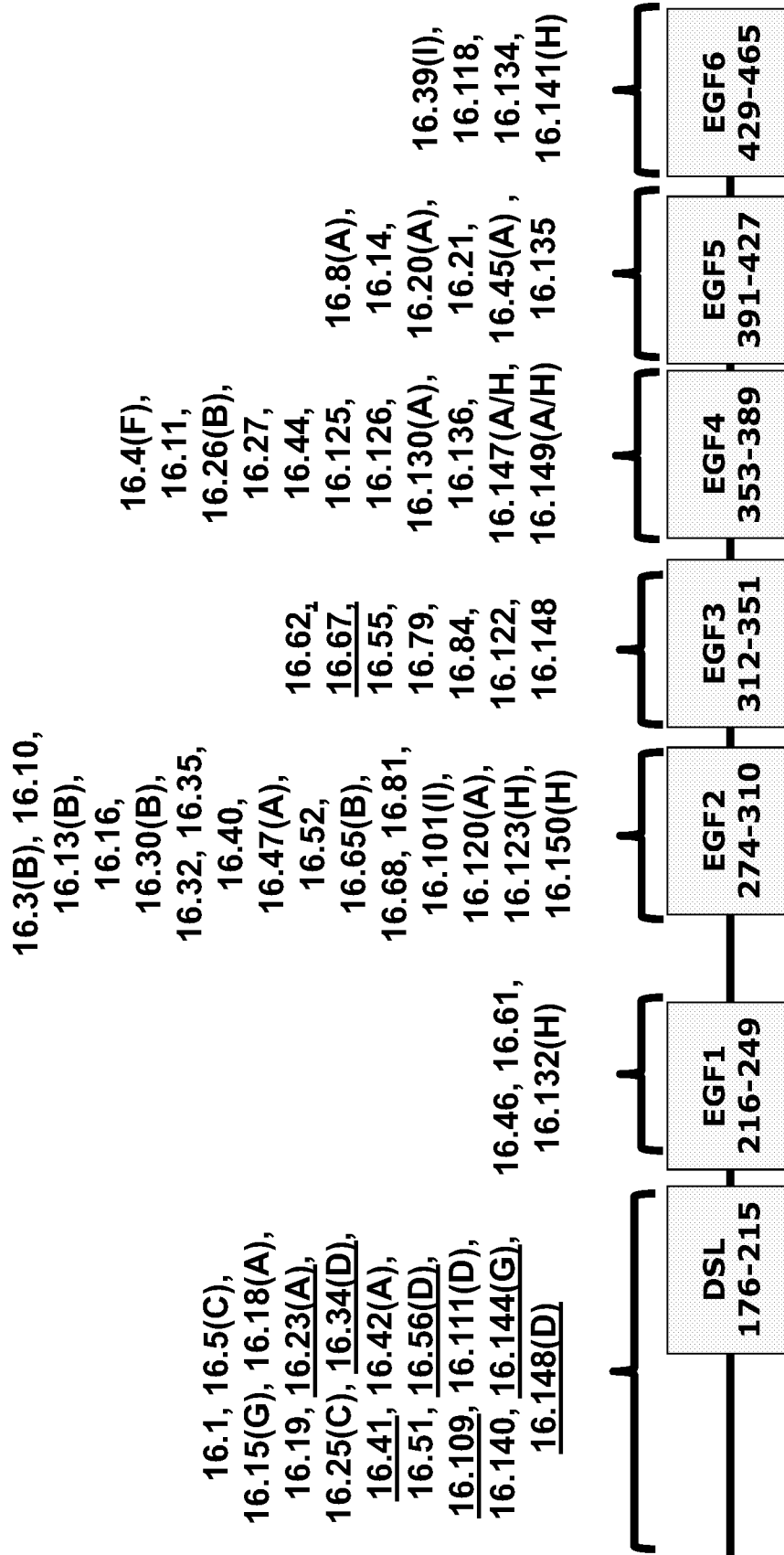


FIG. 2

Anti-DLL3 Chimeric Antigen Receptor Construct

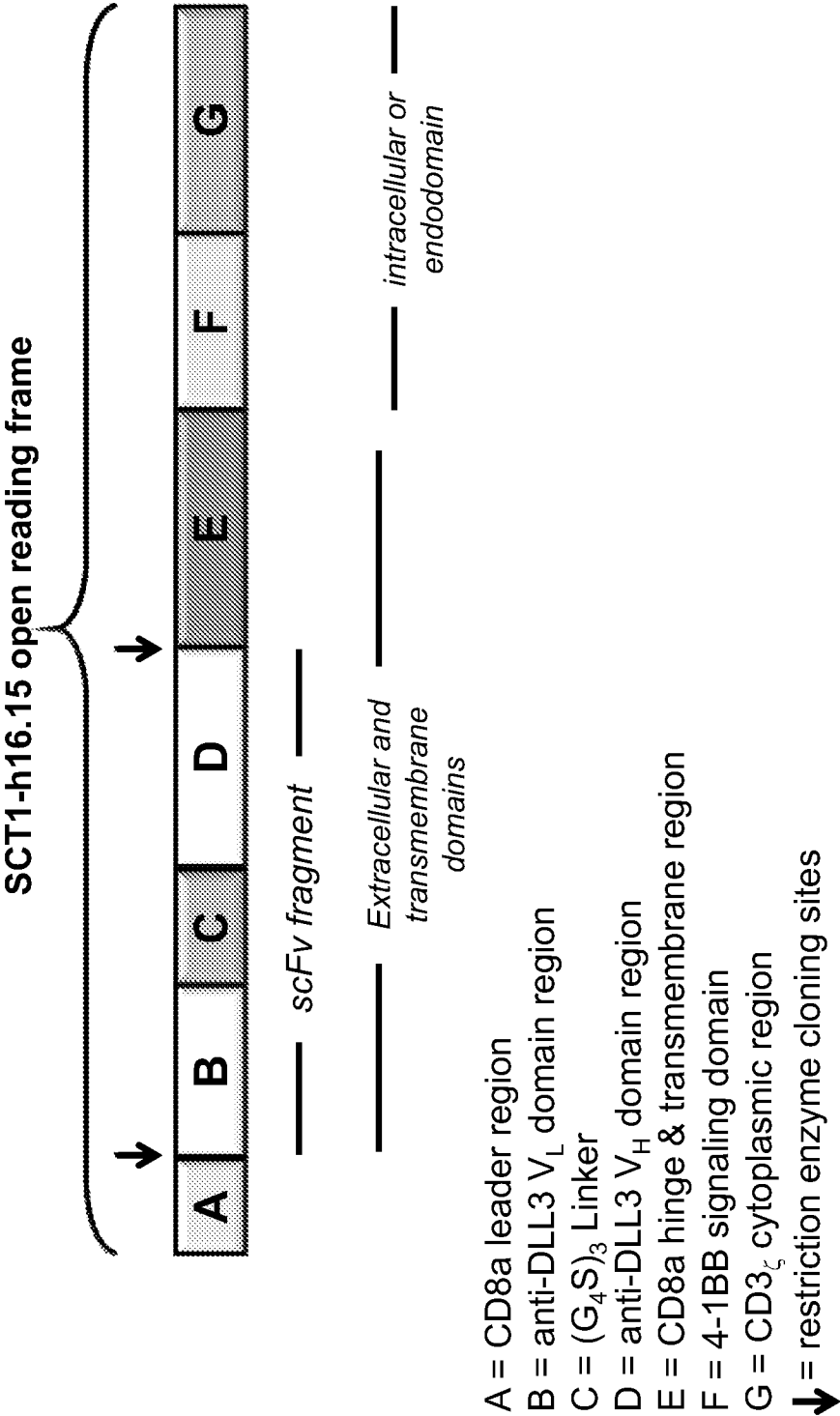


FIG. 3

Sequences of SCT1-h16.15

Anti-DLL3 Chimeric Antigen Receptor

1 ATGGCCCTGCCTGTG ACAGCCCTGCTGCTG CCTCTGGGTCTGCTG CTGCATGGCGCGGC CCCGCCATCCAGTTG
 1 M A L P V T A L L L P L A L L L H A R P A I Q L
 76 ACCAGTCTCCATCC TCCTGTCTGCATCT GTAGGAGACAGATC ACCATCACTTGCCGG GCAAGTGAGAACATT
 26 T Q S P S L S A S V G D R V T I T C R A S E N I
 151 TACTACAATTAGCC TGGTATCAGCAGAAA CCAGGAAAGCTCCT AAGTCCTGATCTAT ACTGCCAATAGTTTG
 51 Y Y N L A W Y Q Q K P G K A P K L L I Y T A N S L
 226 GAAGATGGGTCCCA TCAAGGTTTCAGCGC AGTGGATCTGGACA GATTTCACTCTCACC ATCAGCAGCCTGCAG
 76 E D G V P S R F S G S G S G T D F T L T I S S L Q
 301 CCTGAAGATTTTGA ACTTATTTTGTAAA CAGGCTTATGACGTT CCTCGACGTTCCGT GGAGGCACCAAGCTG
 101 P E D F A T Y F C K Q A Y D V P P T F G G T K L
 376 GAAATCAAAGCGC GGAGGATCTGGCGGA GCGGAAGTGGCGGA GGGGATCTCAGTG GGGGATCTCAGTG CAGTGGTGCAGTCT
 126 E I K G G G S G G G G S G G G G S Q V Q L V Q S
 451 GGGCTGAGGTGAAG AAGCTGGGGCTCA GTGAAGGTTTCCTGC AAGCATCTGGATAC ACCTTCACCAAGTAC
 151 G A E V K K P G A S V K V S C K A S G Y T F T R Y
 526 TGGATACACTGGATA CGACAGGCCCTTGA CAAGGGCTTGAGTG ATGGATACATCAAC CTTACAACTGTTTAT
 176 W I H W I R Q A P G Q G L E W M G Y I N P T T V Y
 601 ACTGAGTTCAATCAG AACTCAAGACAGA GTCAACATGACCAG GACAGTCCACGAGC ACAGTCTACATGGAG
 201 T E F N Q N F K D R V T M T R D T S T S T V Y M E
 676 CTGAGCAGCTGAGA TCTGAGGACAGGCGC GTGATTTACTGTGCG AGAGGGGTAGTAAC TTCTTTGACTACTGG
 226 L S S L R S E D T A V Y Y C A R G G S N F F D Y W
 751 GGCCAAAGGCACCACT GTACAGTCTCCTCG ACCACAGCCCTGCG CCCAGACCTCTACA CCGGCCCTTACAATT
 251 G Q G T T V T V S S T T T P A P R P P T P A P T I
 826 GCCAGCCAGCCTCTG TCTCTGAGGCCCGAG GCTTGTAGACCAGCT GCTGGCGGAGCCGTG CACACCAGAGGACTG
 276 A S Q P L S L R P E A C R P A A G G A V H T R G L
 901 GATTTCGCCTGGAC ATCTACATCTGGGCC CCTCTGGCGGCGACA TGTGGCGTGTCTG CTGAGCCCTGATGATC
 301 D F A C D I Y I W A P L A G T C G V L L L S L V I
 976 ACCCTGTACTGCAAG CGGGCAGAAAGAAA CTGCTGTACATCTTT AAGCAGCCCTTCATG CGGCCCGTGCAGACC
 326 T L Y C K R G R K K L L Y I F K Q P F M R P V Q T
 1051 ACCCAGGAAGAGGAC GGCTGCTCCTGCAGA TTCCCGGAGGAAGAA GAAGCGGTGGAG CTGAGAGTGAAGTTC
 1126 AGCAGATCCGCGAC GCCCTGCCTACAAG CAGGGCCAGAACCAG CTGTACAACGAGCTG AACCTGGGCGAGCGG
 376 S R S A D A P A Y K Q G Q N Q L Y N E L N L G R R
 1201 GAAGAGTACGACGTG CTGGACAAGCGGAGA GGCCGGATCCTGAA ATGGCGGCAAGCCC AGACGGAAGAACCCC
 401 E E Y D V L D K R R G R D P E M G G K P R R K N P
 1276 CAGGAAGGCCTGTAT AACGAATGCAGAAA GACAAGATGGCCGAG GCCTCAGCGAGATC GGAATGAAGGCGAG
 426 Q E G L Y N E L Q K D K M A E A Y S E I G M K G E
 1351 CGGAGAAGAGGCAAG GGCACGATGGCCTG TACCAGGCCTGAGC ACCGCACCAAGGAC ACCTATGACGCCCTG
 451 R R R G K G H D G L Y Q G L S T A T K D T Y D A L
 1426 CACATGAGGCCCTG CCACCTAGATGA **SEQ ID NO. 9**
 476 H M Q A L P P R **SEQ ID NO. 10**

FIG. 4A

Sequences of SCT1-h16.13
Anti-DLL3 Chimeric Antigen Receptor

1 ATGGCCCTGCGCTGTG ACAGCCCTGCTGCTG CCTCTGGCTCTGCTG CTGCATGGCGGGCGC CCCGACATCCAGATG
1 M A L P V T A L L L P L A L L L H A A R P D I Q M
76 ACCCAGTCTCCATCC TCCCTGTCTGCATCT GTAGAGACAGATC ACCATCACTTGCAGT GCAAGTAGCAGCGTT
26 T Q S S S L S A S V G D R V T I T C S A S S V
151 AGCTATATGTAITGG TATCAGCAGAAACCA GGGAAAGCCCTAAG CTCTGTACTTACCTC ACTAGTAACITGGCA
51 S Y M Y W Y Q Q K P G K A P K L L I Y L T S N L A
226 AGTGGGTGCCATCA AGGTTCACTGGCAGT GGAATGGACAGAT TTCACTGCACCATC AGCAGTCTGCACCT
76 S G V P S R F S G S G S G T D F T L T I S S L Q P
301 GAAGATTITGCACT TACTACTGTCAACAG TGGCTAGTAACCCA TTCACGTTGGCCAG GGGACAAAGTTGGAA
101 E D F A T Y Y C Q Q W R S N P F T F G Q G T K L E
376 ATAAAGCGGGGA GGATCTGGCGAGGC GGAAGTGGCGAGGG GGATCTCAGATCACC TTGAAGGAGTCTGGT
126 I K G G G S G S G G G S G G G G S Q I T L K E S G
451 CTTACGCTGGTGA A CCCACACAGACCTC ACGCTGACCTGCACC TTCTCTGGGTTCTCA CTCAGCACTAGTGA
151 P T L V K P T Q T L T L T C T F S G F S L S T S G
526 ATGGGTGGGCTGG ATCCGTACGCCCCCA GGAAGGCCCTGGAG TGGCTTGCACACATT TGGTGGATGATGTT
176 M G V G W I R Q P P G K A L E W L A H I W W D D V
601 AAGGCTACAGCCA TCTCTGAAGCAGG CTCACCATCACCAAG GACACCTCCAAAAC CAGTGGTCCCTACA
201 K R Y S P S L K S R L T I T K D T S K N Q V V L T
676 ATGACCAACATGGAC CTTGTGGACAGCC ACATATTACTGTGCA CGCATGTTTCCCTTT GATAACGACGTTGTC
226 M T N M D P V D T A T Y Y C A R I V S F D N D V V
751 TCTGCTATGGACTAC TGGGTCAAGGAACC CTAGTCACGCTCTCC TCGACCAACACCCCT GCGCCAGACCTCCT
251 S A M D Y W G Q G T L V T V S S T T P A P R P P
826 ACACCGCCCTACA ATTGCAAGCCAGCCT CTGTCTCTAGGCC GAGGCTGTAGACCA GCTGCTGGCGAGCC
276 T P A P T I A S Q P L S L R P E A C R P A A G G A
901 GTGCACACAGAGA CTGGATTTCGCTGC GACATCTACATCTGG GCGCCTCTGGCGGC ACATGTGGCGTGTG
301 V H T R G L D F A C D I Y I W A P L A G T C G V L
976 CTGCTAGCCTCGTG ATCACCTGTACTGC AAGCGGGCAGAA AACTGTGTATATC TTTAAGCAGCCCTTC
326 L S L V I T L Y C K R G R K L L Y I F K Q P F
1051 ATCGGGCCCGTGCAG ACCACCCAGGAAG GACGCTGCTCCTGC AGATCCCGAGGAA GAAGAAGCGGCTGC
351 M R P V Q T T Q E E D G C S C R F P E E E G G C
1126 GAGCTGAGAGTAAG TTCAGCAGATCCGCC GACGCCCTGCCTAC AAGCAGGCCCAAC CAGCTGTACACGAG
376 E L R V K F S R S A D A P A Y K Q G Q N Q L Y N E
1201 CTGAACCTGGGAGA CGGGAAGAGTACGAC GTGTGGACAAGCGG AGAGCGCGGATCCT GAAATGGCGGCAAG
401 L N L G R R E E Y D V L D K R R G R D P E M G G K
1276 CCAGACGGAAGAAC CCCAGGAAGCCTG TATACGAAGTGCAG AAAGCAGATGCCC GAGGCTACACGAG
426 P R R K N P Q E G L Y N E L Q K D K M A E A Y S E
1351 ATCGGAATGAAGGC GAGCGGAGAGAGG AAGGCCACGATGCC CTCTACAGGCGCTG AGCACCGCCACCAAG
451 I G M K G E R R R G K G H D G I Y Q G L S T A T K
1426 GACACCTATGAGGCC CTGCATGAGGCC CTGCACCTAGATGA
476 D T Y D A L H M Q A L P P R SEQ ID NO. 16
SEQ ID NO. 17

FIG. 4B

Sequences of SCT1-h16.25 Anti-DLL3 Chimeric Antigen Receptor

1 ATGGCCCTGCCTGTG ACAGCCCTGCTGTG CCTCTGGCTCTGTG CTGATGGCGGCGGC CCGAAATTGTGCTG
1 M A L P V T A L L L L P L A L L L H A A R P E I V L
76 ACTCAGTCTCCAGAC TTTCAGTCTGTGACT CCAAAGGAGAAAGTC ACCATCAGCTGCAGT GCCAGTAGCAGTGTG
26 T Q S P D F Q S V T P K E K V T I T C S A S S S V
151 AGCTACATGCACCTGG TACCAGCAGAAACCA GATCAGTCTCCAAAG CTCTCATCAAGGAT AGTTCAAAACCTCGC
51 S Y M H W Y Q Q K P D Q S P K L L I K D S S K L A
226 TCAGGGGTCCCCTCG AGGTCAGTGGCAGT GGATCTGGGACAGAT TTCACCCCTACCATC AATAGCCTGGAAGCT
76 S G V P S R F S G S G S G T D F T L T I N S L E A
301 GAAGATGCTGCAACG TATTACTGTGACGAG TGGAGTAGTAACCCG CTCACGTTGGTTCAG GGGACCAAGCTGGAG
101 E D A A T Y Y C Q Q W S S N P L T F G Q G T K L E
376 ATCAAAGCGGCGGA GGATCTGGCGGAGGC GGAAGTGGCGGAGGG GGATCTCAGATCACC TTGAAGGAGTCTGGT
126 I K G G G S G G G G S G G G G S Q I T L K E S G
451 CTTACGGCTGGTGAAA CCCACACAGACCCCTC ACGTGACCTGCACC TTCTCTGGTTCTCA CTCAGGACTAGTGA
151 P T L V K P T Q T L T L T C T F S G F S L S T S G
526 ATGGGTGTGGCTGG ATCCGTGAGCCCCA GGAAGGCCCTGGAG TGGCTTACAGACATT TGGTGGGATGATAAT
176 M G V G W I R Q P P G K A L E W L T D I W W D D N
601 AAGTACTACAACCA TCTCTGAAGAGCAGG CTCACCATACCAAC GACACCTCCAAAAC CAGTGGTCTCTTACA
201 K Y Y N P S L K S R L T I T K D T S K N Q V V L T
676 ATGACCAACATGGAC CCTGTGGACACAGCC ACATATTACTGTGCA CGAAGAGTTAACTAT TATTACGACCCGTAC
226 M T N M D P V D T A T Y Y C A R R V N Y Y Y D P Y
751 TATGCTATGGACTAC TGGGTCAAGGAACC CTAGTCACCGTCTCC TCGACCAACAACCCCT GCCCCAGAGACCTCCT
251 Y A M D Y W G Q G T L V T V S S T T P A P R P P
826 ACACCCGCCCTACA ATTGCCAGCCAGCCT CTGTCTCTGAGGCC GAGGCTTGTAGCCA GCTGCTGGCGGAGCC
276 T P A P T I A S Q P L S L R P E A C R P A A G G A
901 GTGCACACAGAGGA CTGGAATTCGCCTGC GACATCTACTCTGG GCCCTCTGGCCGGC ACATGTGGCGTGTG
301 V H T R G L D F A C D I Y I W A P L A G T C G V L
976 CTGCTGAGCCTCGTG ATCACCTGTACTGC AAGCGGGGAGAAAAG AAACCTGCTGTACATC TTTAAGCAGCCCTTC
326 L L S L V I T L Y C K R G R K K L L Y I F K Q P F
1051 ATGCGGGCCGTGCAG ACCACCCAGGAAGAG GACGGCTGCTCTGC AGATTCCCGAGGAA GAAGAAGCGGCTGC
351 M R P V Q T T Q E E D G C S C R F P E E E G G C
1126 GAGCTGAGAGTGAAG TTCAGCAGATCCGCC GAGCCCCCTGCCTAC AAGCAGGCGCAGAAC CAGCTGTACAACGAG
376 E L R V K F S R S A D A P A Y K Q G Q N Q L Y N E
1201 CTGAACCTGGGCGA CGGGAAGAGTACGAC GTGCTGGACAAGCGG AGAGCCCGGATCCT GAAATGGCGGCGAAG
401 L N L G R R E E Y D V L D K R R G R D P E M G G K
1276 CCCAGACGGAAGAAC CCCAGGAAGGCCCTG TATAACGAACCTGCAG AAAGACAAGATGGCC GAGGCGTACAGCGAG
426 P R R K N P Q E G L Y N E L Q K D K M A E A Y S E
1351 ATCGGAATGAAGGC GAGCGGAGAAGAGC AAGGCCACCATGGC CTGTACACAGGCCCTG AGCACCGCCACCAAG
451 I G M K G E R R R G K G H D G L Y Q G L S T A T K
1426 GACACCTATGACGCC CTGCACATGACGCC CTGCCACCTAGATGA SEQ ID NO. 18
476 D T Y D A L H M Q A L P P R SEQ ID NO. 19

FIG. 4C

Anti-hDLL3 CAR Transduction and Expression

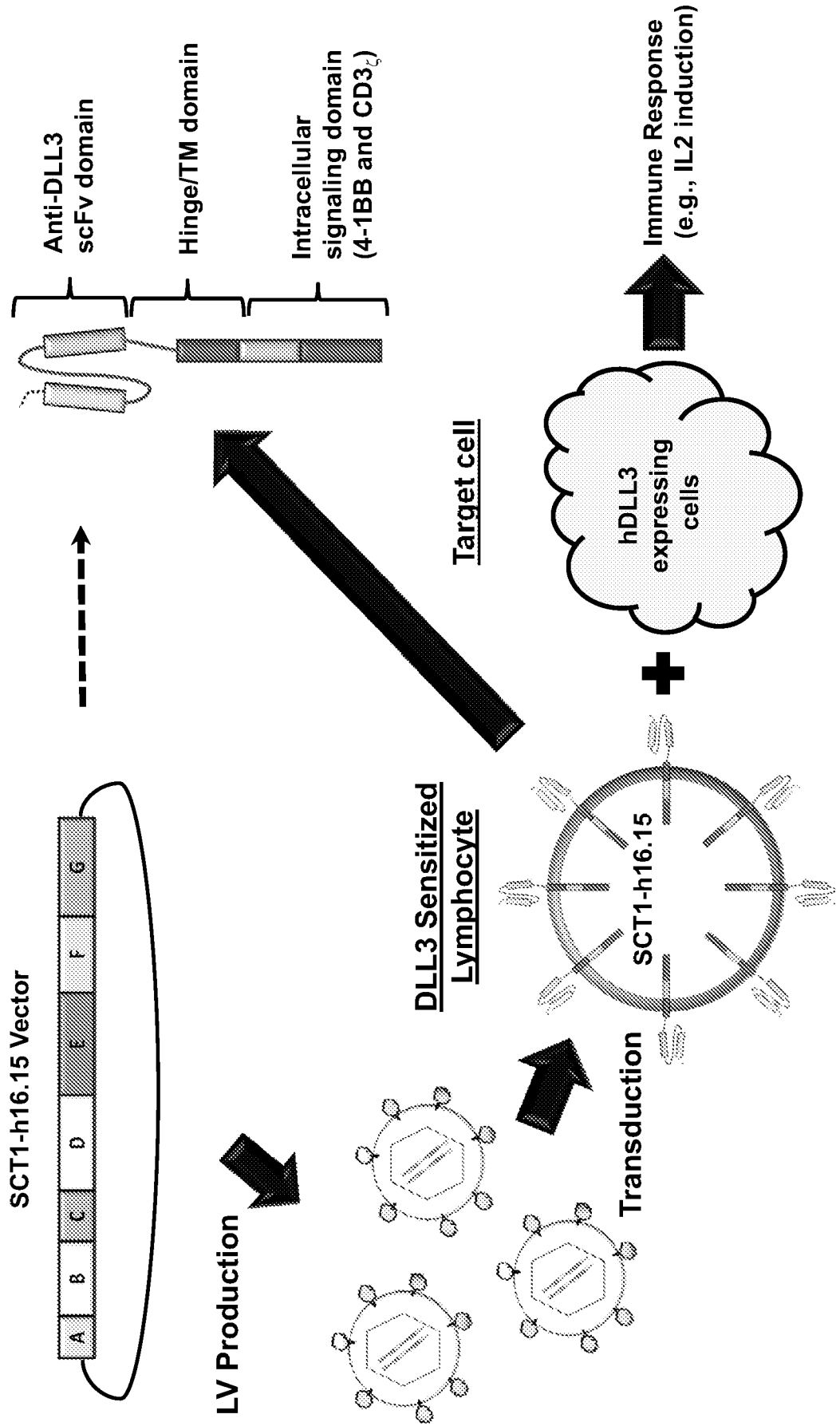


FIG. 5

Anti-DLL3 CAR is Expressed on Jurkat Cells Following Transduction

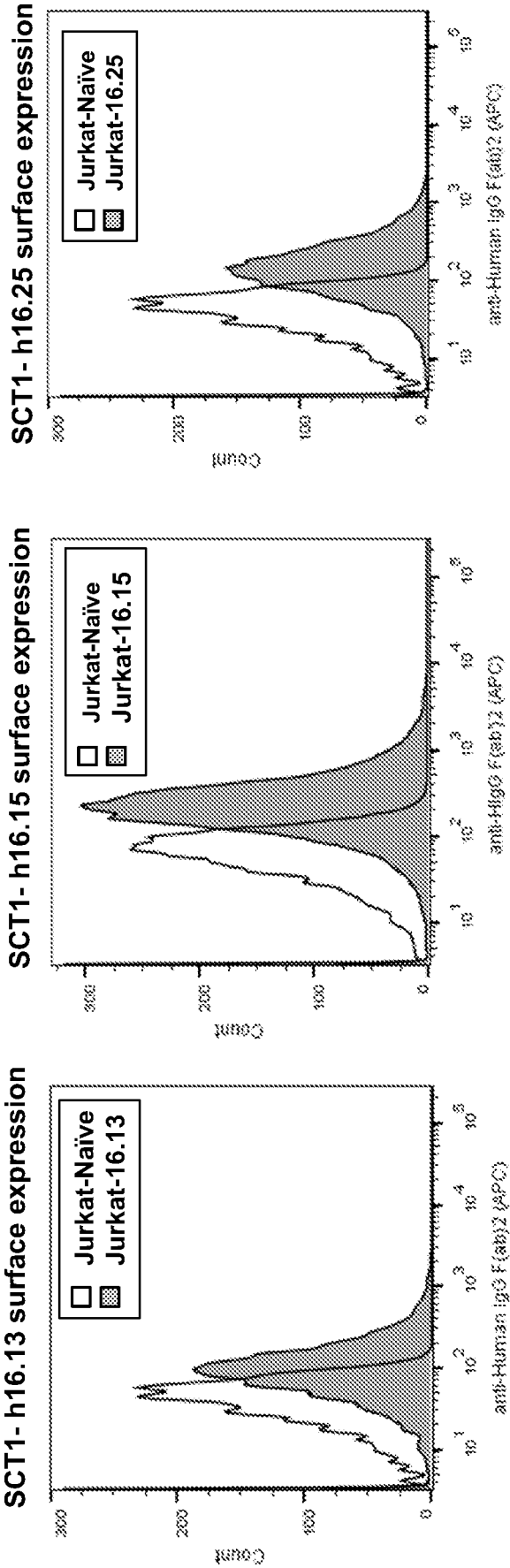


FIG. 6A

Engineered 293T Cells Express h DLL3

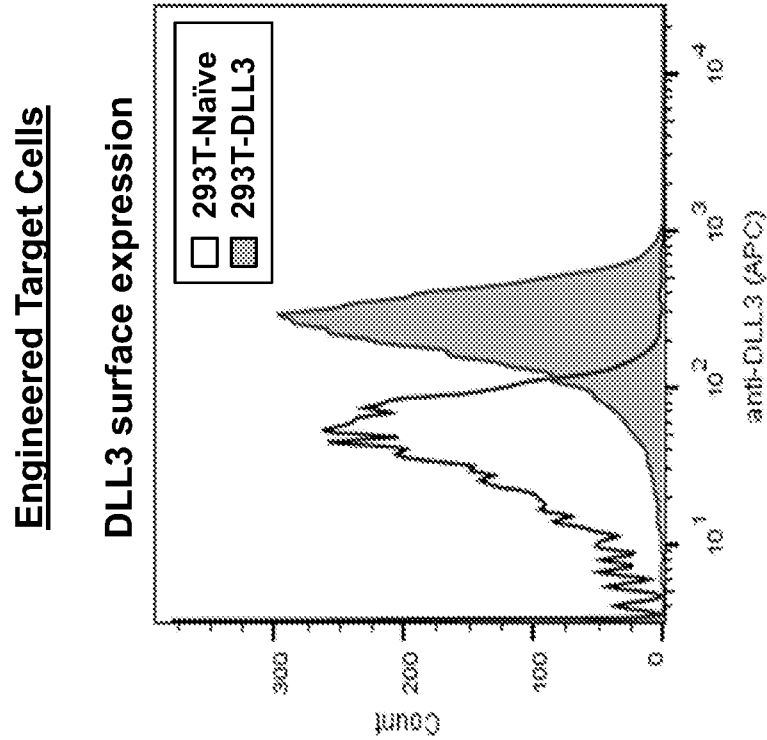


FIG. 6B

**SCT1-h16 Anti-DLL3 CAR Jurkat Cells
Produce IL-2 Upon Contact With hDLL3**

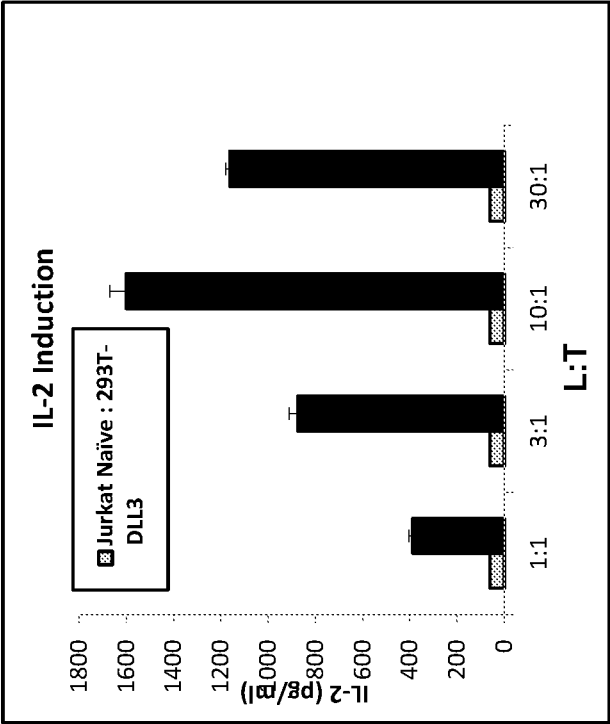


FIG. 7A

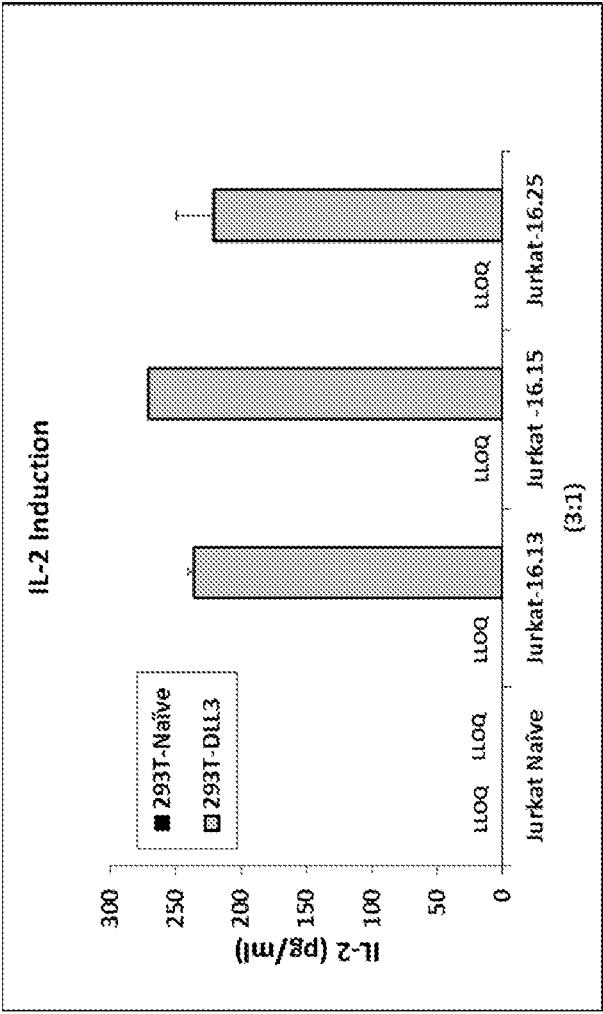


FIG. 7B

DLL3 Sensitized Human Lymphocytes Effectively Express Anti-hDLL3 CARs

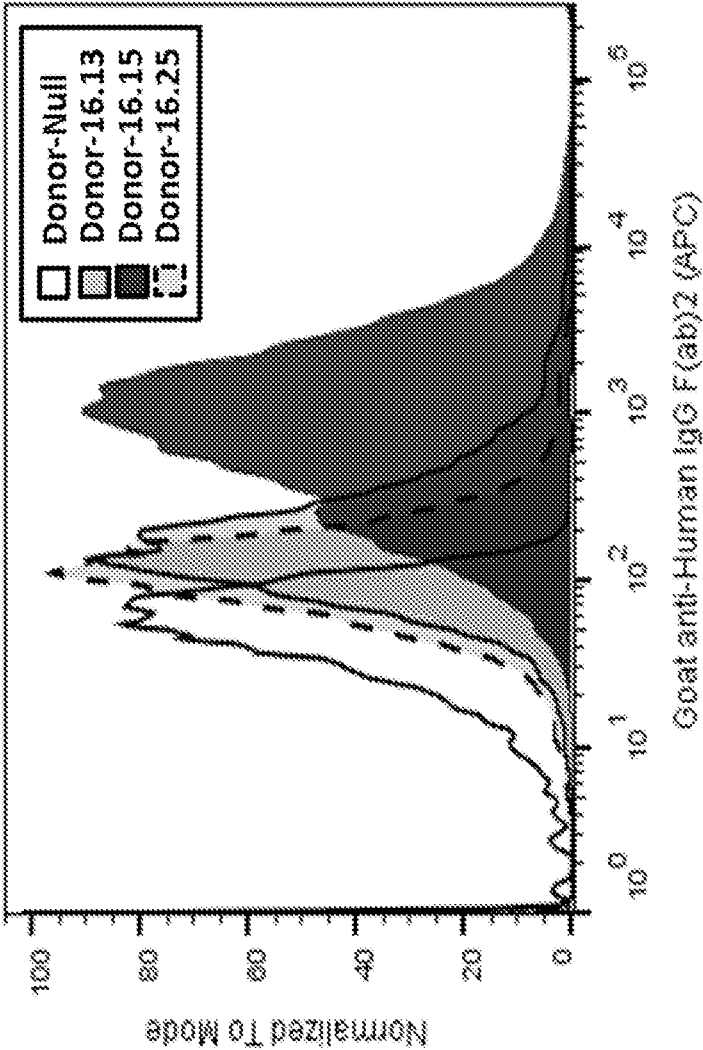


FIG. 8

Target Cell DLL3 Surface Expression Profiles

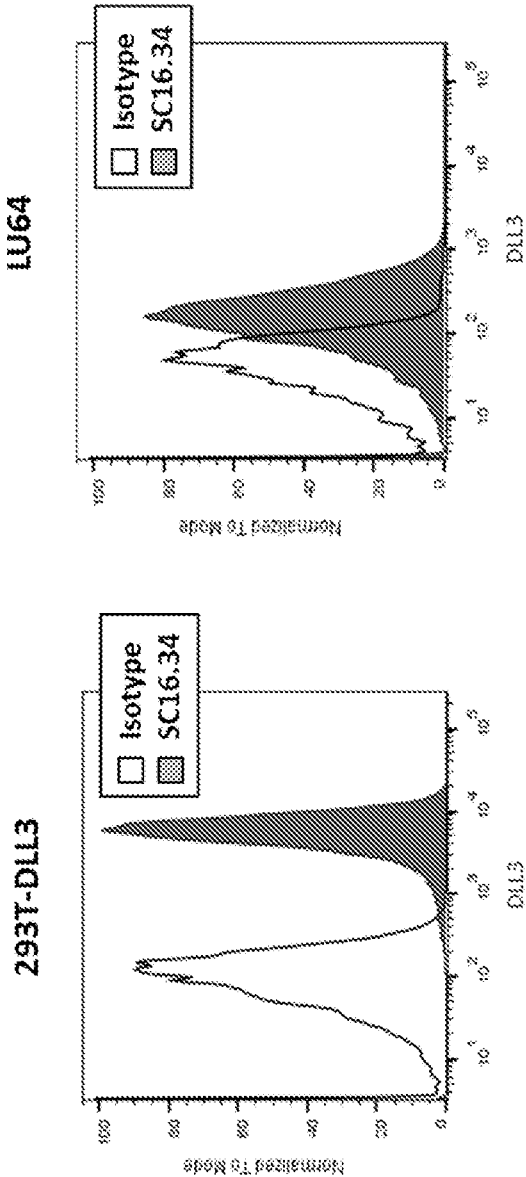


FIG. 9A

FIG. 9B

SCT1-h16.13, SCT1-h16.15 and SCT1-h16.25 Lymphocytes Eliminate DLL3 Expressing Cells

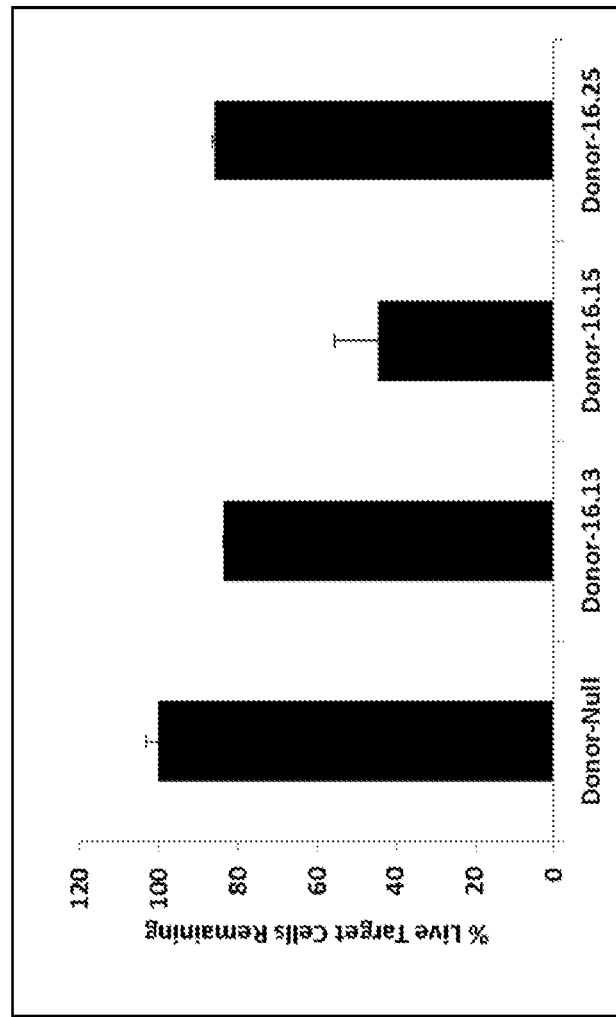


FIG. 10

DLL3 Sensitized Human Lymphocytes Effectively Express Anti-hDLL3 CARs

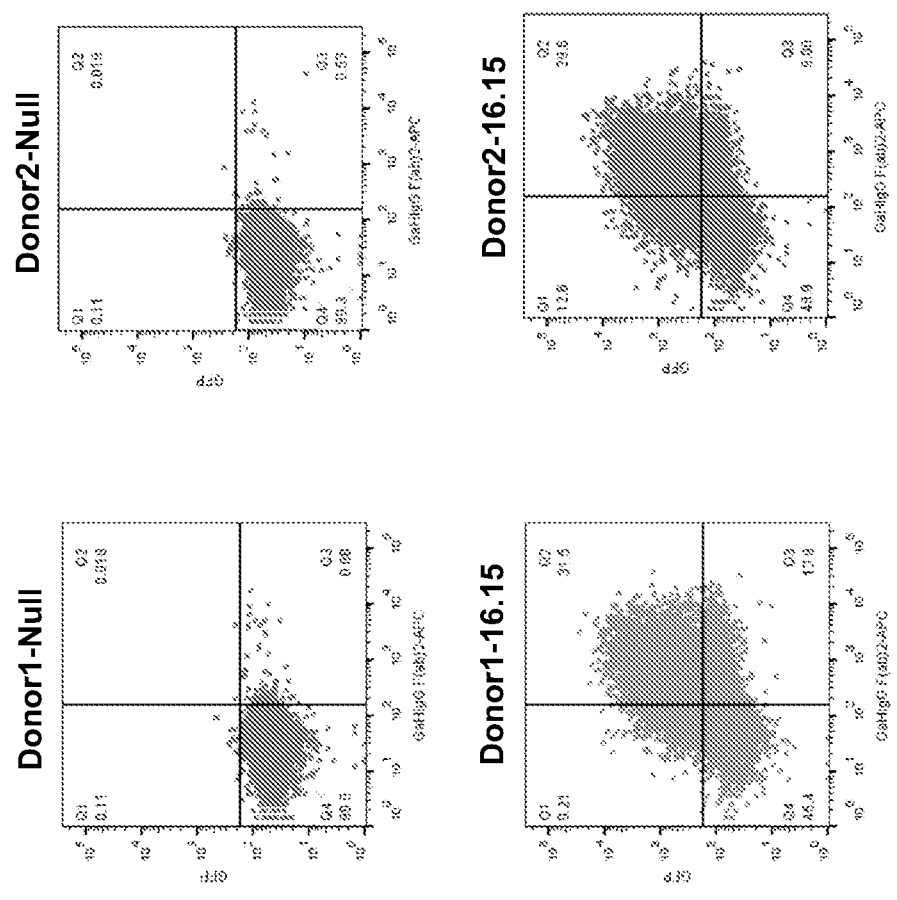
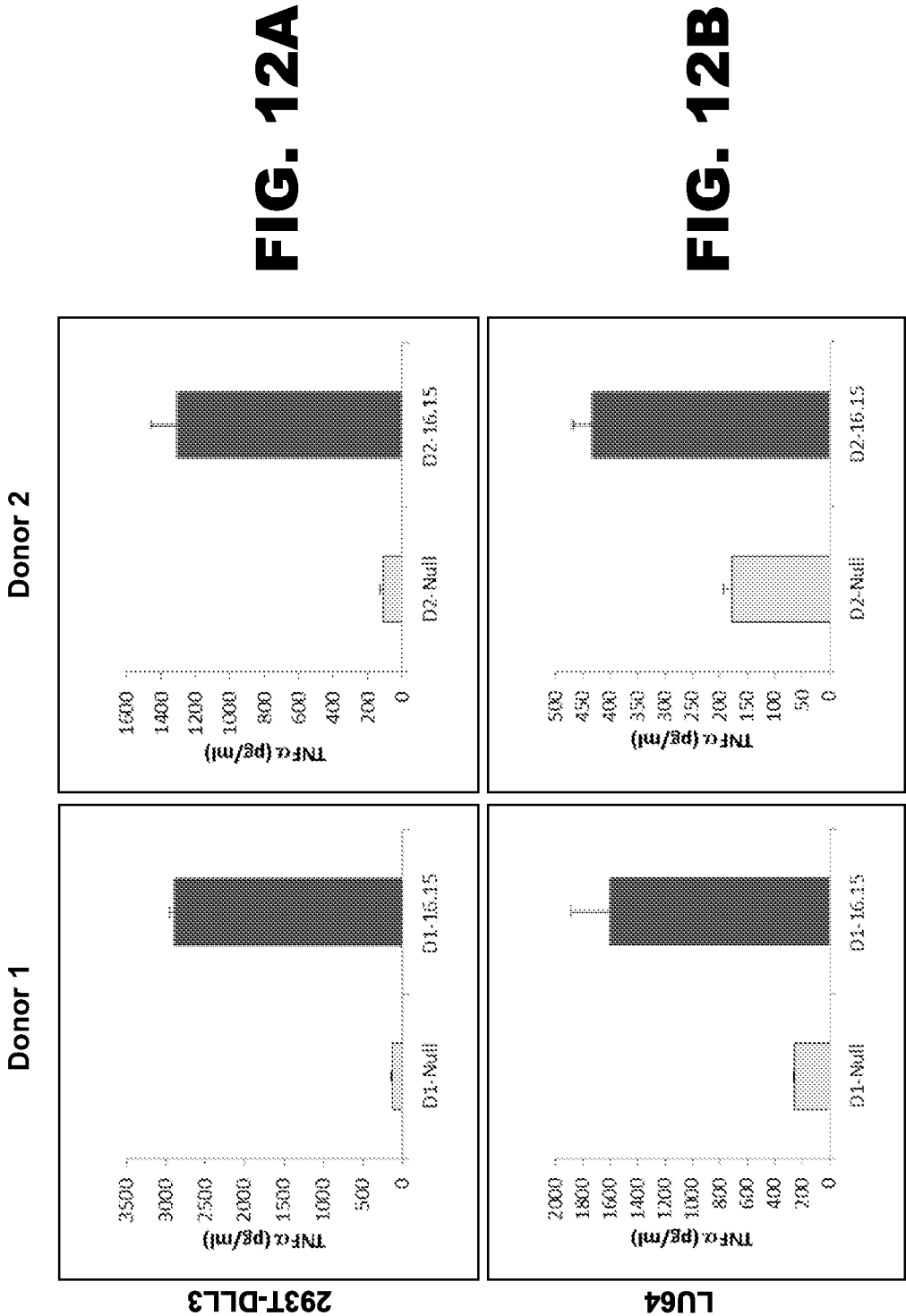
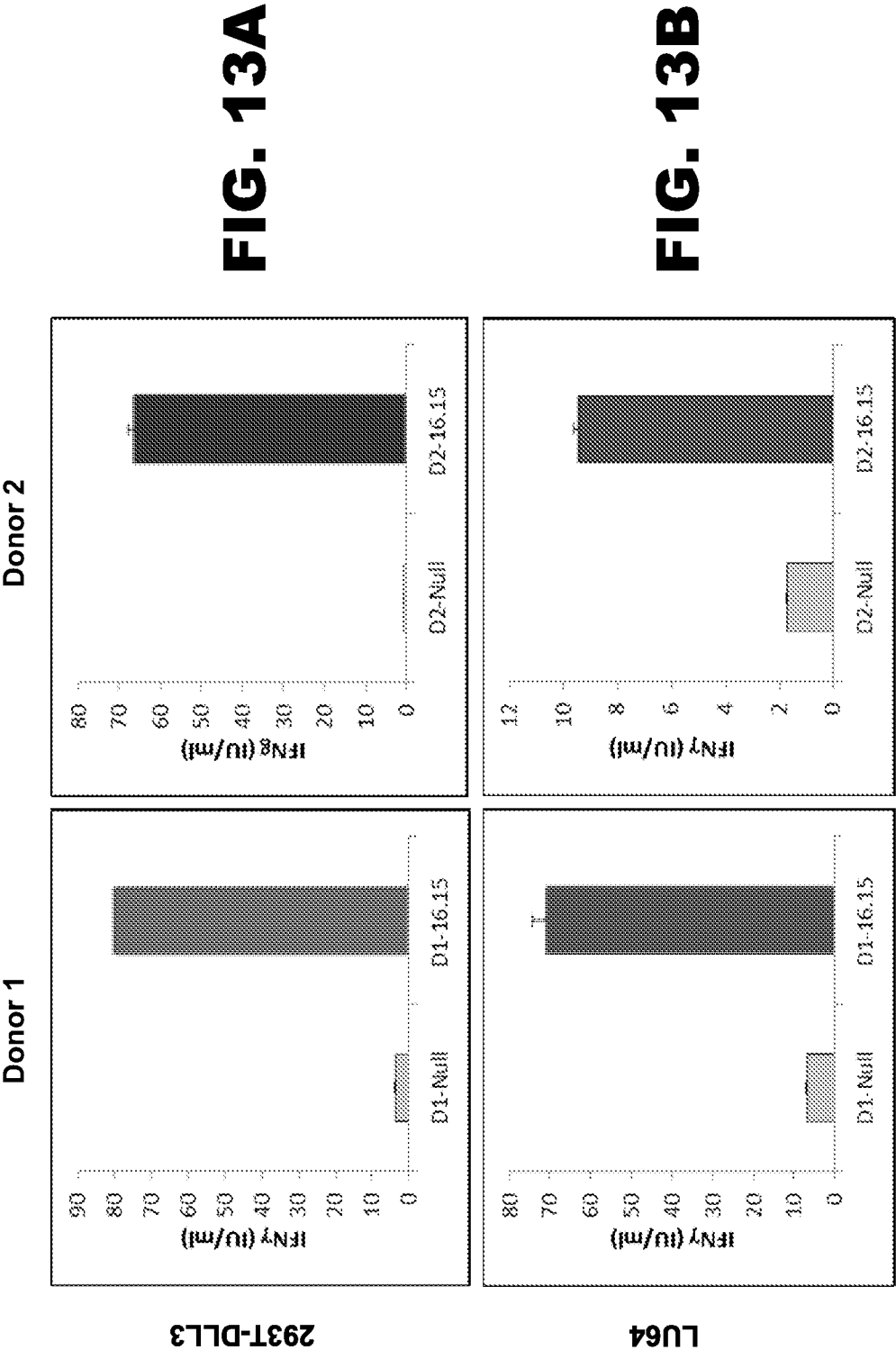


FIG. 11

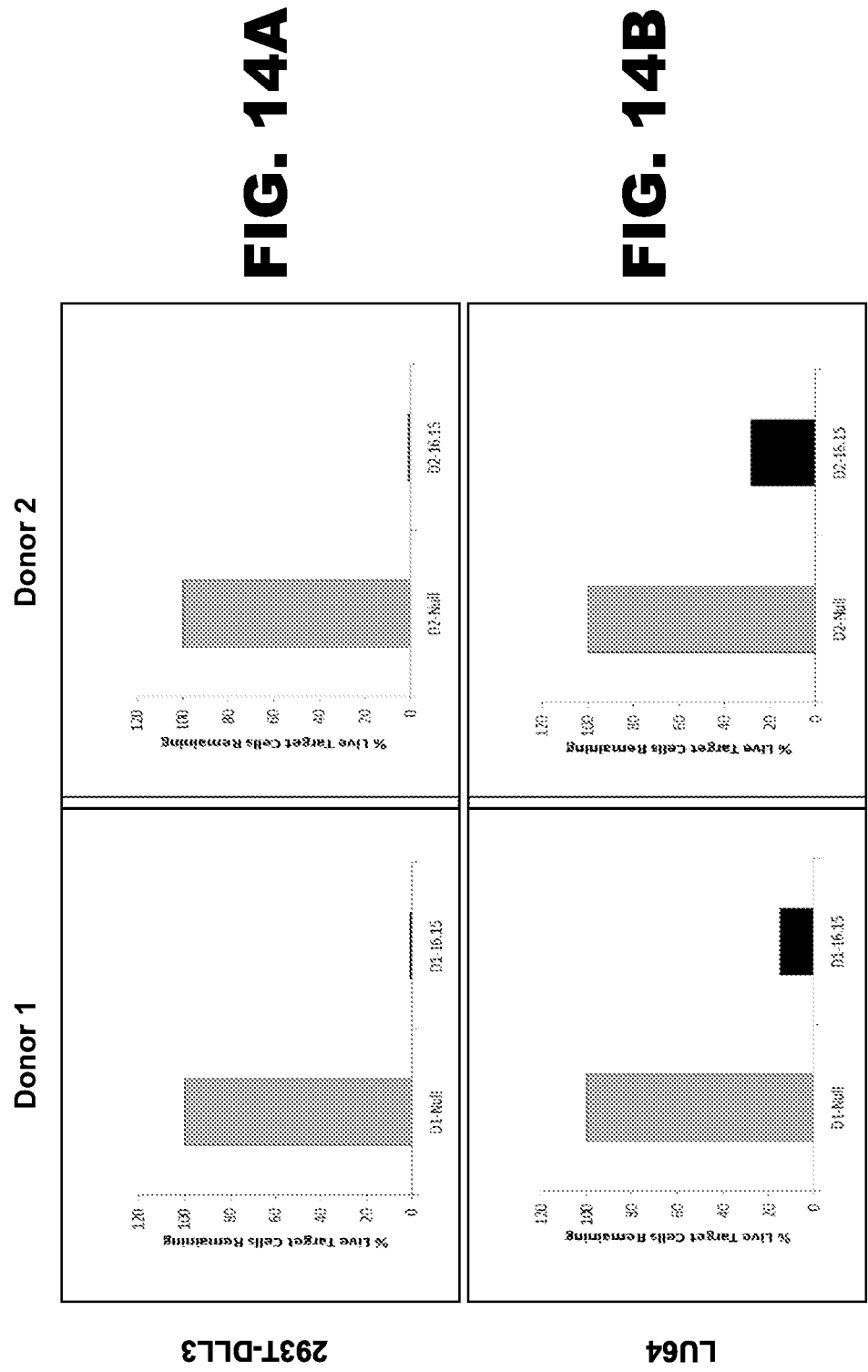
DLL3 Sensitized Lymphocytes Produce TNF- α Upon Exposure to DLL3 Expressing Cells



DLL3 Sensitized Lymphocytes Produce IFN γ Upon Exposure to DLL3 Expressing Cells



DLL3 Sensitized Lymphocytes Eliminate DLL3 Expressing Cells Upon Exposure



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 16/19192

A. CLASSIFICATION OF SUBJECT MATTER IPC(8) - A61K 35/12, A61K 35/14, A61K 38/00 (2016.01) CPC - A61K 2300/00, A61K 39/0011, A61K 39/39558 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) IPC(8) - A61K 35/12, A61K 35/14, A61K 38/00 (2016.01) CPC - A61K 2300/00, A61K 39/0011, A61K 39/39558 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched USPC - 424/135.1, 424/184.1, 424/93.21, 435/320.1 Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) pubWEST; PatBase; Google Scholar search terms - DLL3, DLL-3, CAR, chimeric antigen receptor, antigen receptor, antigen receptors, car, DLL 3, Delta-Like 3, delta3, Drosophila Delta Homolog 3, SCDO1		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2014/0363455 A1 (STEM CENTRX, INC.) 11 December 2014 (11.12.2014) para [0006]-[0009]; [0017]; [0018]; [0028]; [0177]; SEQ ID NOs: 20, 21, claim 21	1-3, 23-26
Y	US 2014/0106449 A1 (THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA) 17 April 2014 (17.04.2014) para [0008]; [0009]; [0038]; [0056]; [0090]; [0117]; [0221].	1-3, 23-26
☐ Further documents are listed in the continuation of Box C. ☐		
* 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 application or patent 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 05 May 2016		Date of mailing of the international search report 12 MAY 2016
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300		Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 16/19192

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.:
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:
3. ☒ Claims Nos.: 4-22, 27-30
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 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.

SEQUENCE LISTING

<110> Stemcentrx, Inc.

<120> ANTI-DLL3 CHIMERIC ANTIGEN RECEPTORS AND METHODS OF USE

<130> S69697 1250W0 / sc1605.pct

<150> US 62/119793

<151> 2015-02-23

<150> US 62/241662

<151> 2015-10-14

<150> US 62/296560

<151> 2016-02-17

<160> 437

<170> PatentIn version 3.5

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Pro Gly Leu Arg Pro Gly Asp Pro Gln Arg Tyr Leu Leu Pro Pro Ala
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Val Asp Trp Asn Arg Pro Glu Asp Val Asp Pro Gln Gly Ile Tyr Val
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				160
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Pro Gly Leu Arg Pro Gly Asp Pro Gln Arg Tyr Leu Leu Pro Pro Ala
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Leu Gly Leu Leu Val Ala Ala Gly Val Ala Gly Ala Ala Leu Leu Leu
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Val His Val Arg Arg Arg Gly His Ser Gln Asp Ala Gly Ser Arg Leu
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Leu Ala Gly Thr Pro Glu Pro Ser Val His Ala Leu Pro Asp Ala Leu
530 535 540

Asn Asn Leu Arg Thr Gln Glu Gly Ser Gly Asp Gly Pro Ser Ser Ser
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35 40 45

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
50 55 60

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
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Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
115 120 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
130 135 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145 150 155 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
165 170 175

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
180 185 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
195 200 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
210 215 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
225 230 235 240

Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
245 250 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
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Tyr Thr Ala Asn Ser Leu Glu Asp Val Pro Ser Arg Phe Ser Gly Ser
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Asp Phe Ala Thr Tyr Phe Cys Lys Gln Ala Tyr Asp Val Pro Pro Thr
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Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly
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Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser
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Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
130 135 140

Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Trp Ile His Trp Ile Arg Gln
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Ala Pro Gly Gln Gly Leu Glu Trp Met Gly Tyr Ile Asn Pro Thr Val
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Tyr Thr Glu Phe Asn Gln Asn Phe Lys Asp Arg Val Thr Met Thr Arg
180 185 190

Asp Thr Ser Thr Ser Thr Val Tyr Met Glu Leu Ser Ser Leu Arg Ser
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 actgagttca atcagaactt caaggacaga gtcacatga ccaggacac gtccacgagc 660
 acagtctaca tggagctgag cagcctgaga tctgaggaca cggccgtgta ttactgtgcg 720
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Ser	Ala	Ser	Val	Gly	Asp	Arg	Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Glu
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55

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Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Phe Cys Lys Gln Ala
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Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Trp
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180 185 190

Tyr Ile Asn Pro Thr Thr Val Tyr Thr Glu Phe Asn Gln Asn Phe Lys
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Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu
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410

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aaagccccta agctcctgat ctacctcact agtaacttgg caagtggggc cccatcaagg 180

ttcagtggca gtggatctgg gacagatttc actctcacca tcagcagtct gcaacctgaa 240

gattttgcaa ctactactg tcaacagtgg cgtagtaacc cattcacgtt cggccagggg 300

acaaagttag aaataaaagg cggcggagga tctggcggag gcggaagtgg cggaggggga 360

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Arg Ser Asn Pro Phe Thr
85 90 95

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Ile Thr Leu Lys Glu Ser
115 120 125

Gly Pro Thr Leu Val Lys Pro Thr Gln Thr Leu Thr Leu Thr Cys Thr
130 135 140

Phe Ser Gly Phe Ser Leu Ser Thr Ser Gly Met Gly Val Gly Trp Ile
145 150 155 160

Arg Gln Pro Pro Gly Lys Ala Leu Glu Trp Leu Ala His Ile Trp Trp
165 170 175

Asp Asp Val Lys Arg Tyr Ser Pro Ser Leu Lys Ser Arg Leu Thr Ile
180 185 190

Thr Lys Asp Thr Ser Lys Asn Gln Val Val Leu Thr Met Thr Asn Met
195 200 205

Asp Pro Val Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Ile Val Ser Phe
210 215 220

Asp Asn Asp Val Val Ser Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu
225 230 235 240

Val Thr Val Ser Ser
245

<210> 13
 <211> 735
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> h16.25 scFv DNA

<400> 13
 gaaattgtgc tgactcagtc tccagacttt cagtctgtga ctccaaagga gaaagtcacc 60
 atcacctgca gtgccagtag cagtgtgagc tacatgcact ggtaccagca gaaaccagat 120
 cagtctccaa agctcctcat caaggatagt tccaaactcg cctcaggggt cccctcgagg 180
 ttcagtggca gtggatctgg gacagatttc accctcacca tcaatagcct ggaagctgaa 240
 gatgctgcaa cgtattactg tcagcagtg agtagtaacc cgctcacgtt cggtcagggg 300
 accaagctgg agatcaaagg cggcggagga tctggcggag gcggaagtgg cggaggggga 360
 tctcagatca ccttgaagga gtctggctct acgctggtga aaccacaca gaccctcacg 420
 ctgacctgca ctttctctgg gttctcactc agcactagtg gaatgggtgt gggctggatc 480
 cgtcagcccc caggaaaggc cctggagtgg cttacagaca ttggtggga tgataataag 540
 tactacaacc catctctgaa gagcaggtc accatcacca aggacacctc caaaaaccag 600
 gtggtcctta caatgaccaa catggacct gtggacacag ccacatatta ctgtgcacga 660
 agagttaact attattacga cccgtactat gctatggact actggggtca aggaacccta 720
 gtcaccgtct cctcg 735

<210> 14
 <211> 245
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> sc16.25 scFv protein

<400> 14

Glu Ile Val Leu Thr Gln Ser Pro Asp Phe Gln Ser Val Thr Pro Lys
1 5 10 15

Glu Lys Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

His Trp Tyr Gln Gln Lys Pro Asp Gln Ser Pro Lys Leu Leu Ile Lys
35 40 45

Asp Ser Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly
100 105 110

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Ile Thr Leu Lys Glu Ser
115 120 125

Gly Pro Thr Leu Val Lys Pro Thr Gln Thr Leu Thr Leu Thr Cys Thr
130 135 140

Phe Ser Gly Phe Ser Leu Ser Thr Ser Gly Met Gly Val Gly Trp Ile
145 150 155 160

Arg Gln Pro Pro Gly Lys Ala Leu Glu Trp Leu Thr Asp Ile Trp Trp

	165	170	175
Asp Asp Asn Lys Tyr Tyr Asn Pro Ser Leu Lys Ser Arg Leu Thr Ile			
	180	185	190
Thr Lys Asp Thr Ser Lys Asn Gln Val Val Leu Thr Met Thr Asn Met			
	195	200	205
Asp Pro Val Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Arg Val Asn Tyr			
	210	215	220
Tyr Tyr Asp Pro Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu			
225	230	235	240
Val Thr Val Ser Ser			
	245		

<210> 15
 <211> 717
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> h16.15 scFv DNA

<400> 15	
gccatccagt tgaccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc	60
atcacttgcc gggcaagtga gaacatttac tacaatttag cctggtatca gcagaaacca	120
gggaaagctc ctaagctcct gatctatact gccaatagtt tggaagatgg ggtcccatca	180
aggttcagcg gcagtggatc tgggacagat ttcactctca ccatcagcag cctgcagcct	240
gaagattttg caacttattt ttgtaaacag gcttatgacg ttcttccgac gttcgggtgga	300
ggcaccaagc tggaaatcaa aggcggcgga ggatctggcg gaggcggaag tggcggaggg	360

ggatctcagg tgcagctggt gcagtctggg gctgaggtga agaagcctgg ggcctcagt	420
aaggtttcct gcaaggcatc tggatacacc ttcaccaggt actggataca ctggatacga	480
caggcccctg gacaagggtc tgagtggatg ggatacatca accctacaac tgtttatact	540
gagttcaatc agaacttcaa ggacagagtc accatgacca gggacacgtc cacgagcaca	600
gtctacatgg agctgagcag cctgagatct gaggacacgg ccgtgtatta ctgtgcgaga	660
ggcggtagta acttctttga ctactggggc caaggcacca ctgtcacagt ctctctcg	717

<210> 16

<211> 1470

<212> DNA

<213> Artificial Sequence

<220>

<223> SCT1-h16.13 CAR DNA

<400> 16

atggccctgc ctgtgacagc cctgtctctg cctctggctc tgctgctgca tgcggcgcgc	60
cccgacatcc agatgaccca gtctccatcc tccctgtctg catctgtagg agacagagtc	120
accatcactt gcagtgcaag tagcagcgtt agctatatgt attggtatca gcagaaacca	180
gggaaagccc ctaagctcct gatctacctc actagtaact tggcaagtgg ggtcccatca	240
aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct	300
gaagattttg caacttacta ctgtcaacag tggcgtagta acccattcac gttcggccag	360
gggacaaagt tggaaataaa aggcggcgga ggatctggcg gaggcggaag tggcggaggg	420
ggatctcaga tcaccttgaa ggagtctggt cctacgctgg tgaaaccac acagaccctc	480
acgtgacct gcaccttctc tgggttctca ctcagcacta gtggaatggg tgtgggctgg	540
atccgtcagc ccccaggaaa ggccctggag tggcttgcac acatttggtg ggatgatgtt	600
aagcgctaca gccatctct gaagagcagg ctcaccatca ccaaggacac ctccaaaaac	660

caggtggtcc ttacaatgac caacatggac cctgtggaca cagccacata ttactgtgca	720
cgcatagttt cctttgataa cgacgttgtc tctgctatgg actactgggg tcaaggaacc	780
ctagtcaccg tctcctcgac cacaaccctt gccccagac ctcctacacc cgcccctaca	840
attgccagcc agcctctgtc tctgaggccc gaggtttgta gaccagctgc tggcggagcc	900
gtgcacacca gaggactgga tttcgctgc gacatctaca tctgggcccc tctggccggc	960
acatgtggcg tgctgctgct gagcctctgt atcaccctgt actgcaagcg gggcagaaag	1020
aaactgctgt acatctttaa gcagcccttc atgcggcccc tgcagaccac ccaggaagag	1080
gacggctgct cctgcagatt ccccaggaa gaagaaggcg gctgcgagct gagagtgaag	1140
ttcagcagat ccgccgacgc ccctgcctac aagcagggcc agaaccagct gtacaacgag	1200
ctgaacctgg gcagacggga agagtacgac gtgctggaca agcggagagg ccgggaccc	1260
gaaatgggcg gcaagcccag acggaagaac ccccaggaag gcctgtataa cgaactgcag	1320
aaagacaaga tggccgaggc ctacagcgag atcggaatga agggcgagcg gagaagaggc	1380
aagggccacg atggcctgta ccaggcctg agcaccgcca ccaaggacac ctatgacgcc	1440
ctgcacatgc aggcctgcc acctagatga	1470

<210> 17

<211> 489

<212> PRT

<213> Artificial Sequence

<220>

<223> SCT1-h16.13 CAR protein

<400> 17

Met	Ala	Leu	Pro	Val	Thr	Ala	Leu	Leu	Leu	Pro	Leu	Ala	Leu	Leu	Leu
1				5					10					15	

His Ala Ala Arg Pro Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu

20

25

30

Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Ser
35 40 45

Ser Val Ser Tyr Met Tyr Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
50 55 60

Lys Leu Leu Ile Tyr Leu Thr Ser Asn Leu Ala Ser Gly Val Pro Ser
65 70 75 80

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
85 90 95

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Arg
100 105 110

Ser Asn Pro Phe Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Ile
130 135 140

Thr Leu Lys Glu Ser Gly Pro Thr Leu Val Lys Pro Thr Gln Thr Leu
145 150 155 160

Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser Gly Met
165 170 175

Gly Val Gly Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu Trp Leu
180 185 190

Ala His Ile Trp Trp Asp Asp Val Lys Arg Tyr Ser Pro Ser Leu Lys

195

200

205

Ser Arg Leu Thr Ile Thr Lys Asp Thr Ser Lys Asn Gln Val Val Leu
210 215 220

Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr Cys Ala
225 230 235 240

Arg Ile Val Ser Phe Asp Asn Asp Val Val Ser Ala Met Asp Tyr Trp
245 250 255

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro
260 265 270

Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu
275 280 285

Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg
290 295 300

Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly
305 310 315 320

Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys
325 330 335

Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg
340 345 350

Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro
355 360 365

Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser

370

375

380

Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu
 385 390 395 400

Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg
 405 410 415

Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln
 420 425 430

Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr
 435 440 445

Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp
 450 455 460

Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala
 465 470 475 480

Leu His Met Gln Ala Leu Pro Pro Arg
 485

<210> 18

<211> 1470

<212> DNA

<213> Artificial Sequence

<220>

<223> SCT1-h16.25 CAR DNA

<400> 18

atggccctgc ctgtgacagc cctgtgtctg cctctggctc tgctgctgca tgcggcgcgc 60

cccgaattg tgctgactca gtctccagac tttcagtctg tgactccaaa ggagaaagtc 120

accatcacct gcagtgccag tagcagtgtg agctacatgc actggtacca gcagaaacca	180
gatcagtctc caaagctcct catcaaggat agttccaaac tcgcctcagg ggtcccctcg	240
aggttcagtg gcagtggatc tgggacagat ttcacctca ccatcaatag cctggaagct	300
gaagatgctg caacgtatta ctgtcagcag tggagtagta acccgctcac gttcggtcag	360
gggaccaagc tggagatcaa aggcggcgga ggatctggcg gagcggaag tggcggaggg	420
ggatctcaga tcaccttgaa ggagtctggt cctacgctgg tgaaaccac acagacctc	480
acgctgacct gcaccttctc tgggttctca ctcagcacta gtggaatggg tgtgggctgg	540
atccgtcagc ccccgagaaa ggccctggag tggttacag acatttggtg ggatgataat	600
aagtactaca acccatctct gaagagcagg ctcaccatca ccaaggacac ctcaaaaac	660
caggtggtcc ttacaatgac caacatggac cctgtggaca cagccacata ttactgtgca	720
cgaagagtta actattatta cgacctgtac tatgctatgg actactgggg tcaaggaacc	780
ctagtcaccg tctcctcgac cacaacctt gccccagac ctcctacacc cgccccata	840
attgccagcc agcctctgtc tctgaggccc gaggttgta gaccagctgc tggcggagcc	900
gtgcacacca gaggactgga tttcgctgc gacatctaca tctgggcccc tctggccggc	960
acatgtggcg tgctgtgct gagcctcgtg atcacctgt actgcaagcg gggcagaaag	1020
aaactgctgt acatcttta gcagccctt atcgggccc tgcagaccac ccaggaagag	1080
gacggctgct cctgcagatt ccccgaggaa gaagaaggcg gctgcgagct gagagtgaag	1140
ttcagcagat ccgccgacgc ccctgcctac aagcagggcc agaaccagct gtacaacgag	1200
ctgaacctgg gcagacggga agagtacgac gtcttgaca agcggagagg ccgggatcct	1260
gaaatgggcg gcaagcccag acggaagaac ccccgaggaa gcctgtataa cgaactgcag	1320
aaagacaaga tgccgaggc ctacagcgag atcggaatga agggcgagcg gagaagaggc	1380
aagggccacg atggcctgta ccaggccctg agcaccgcca ccaaggacac ctatgacgcc	1440

ctgcacatgc aggcctgcc acctagatga

1470

<210> 19

<211> 489

<212> PRT

<213> Artificial Sequence

<220>

<223> SCT1-h16.25 CAR protein

<400> 19

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Val Leu Thr Gln Ser Pro Asp Phe Gln
20 25 30

Ser Val Thr Pro Lys Glu Lys Val Thr Ile Thr Cys Ser Ala Ser Ser
35 40 45

Ser Val Ser Tyr Met His Trp Tyr Gln Gln Lys Pro Asp Gln Ser Pro
50 55 60

Lys Leu Leu Ile Lys Asp Ser Ser Lys Leu Ala Ser Gly Val Pro Ser
65 70 75 80

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn
85 90 95

Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser
100 105 110

Ser Asn Pro Leu Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Ile
130 135 140

Thr Leu Lys Glu Ser Gly Pro Thr Leu Val Lys Pro Thr Gln Thr Leu
145 150 155 160

Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser Gly Met
165 170 175

Gly Val Gly Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu Trp Leu
180 185 190

Thr Asp Ile Trp Trp Asp Asp Asn Lys Tyr Tyr Asn Pro Ser Leu Lys
195 200 205

Ser Arg Leu Thr Ile Thr Lys Asp Thr Ser Lys Asn Gln Val Val Leu
210 215 220

Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr Cys Ala
225 230 235 240

Arg Arg Val Asn Tyr Tyr Tyr Asp Pro Tyr Tyr Ala Met Asp Tyr Trp
245 250 255

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro
260 265 270

Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu
275 280 285

Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg
290 295 300

Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly
305 310 315 320

Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys
325 330 335

Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg
340 345 350

Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro
355 360 365

Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser
370 375 380

Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu
385 390 395 400

Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg
405 410 415

Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln
420 425 430

Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr
435 440 445

Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp
450 455 460

Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala
465 470 475 480

Leu His Met Gln Ala Leu Pro Pro Arg
485

<210> 20
<211> 324
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(324)
<223> SC16.3 VL

<220>
<221> CDS
<222> (1)..(324)

<400> 20
caa att gtt ctc acc cag tct cca gca atc atg tct gta tct cta ggg 48
Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Val Ser Leu Gly
1 5 10 15

gaa cgg gtc acc atg acc tgc act gcc agc tca agt gta agt tcc agt 96
Glu Arg Val Thr Met Thr Cys Thr Ala Ser Ser Ser Val Ser Ser Ser
20 25 30

tac ttg cac tgg tac caa caa aag cca gga tcc tcc ccc aaa ctc tgg 144
Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Leu Trp
35 40 45

att tat agc aca tcc aac ctg gct tct gga gtc cca gct cgc ttc agt 192
Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser
50 55 60

ggc agt ggg tct ggg acc tct tat ttt ttc aca atc agc agc atg gag 240
Gly Ser Gly Ser Gly Thr Ser Tyr Phe Phe Thr Ile Ser Ser Met Glu
65 70 75 80

gct gaa gat gct gcc act tat tac tgc cac cag tat cat cgt tcc cca 288
Ala Glu Asp Ala Ala Thr Tyr Tyr Cys His Gln Tyr His Arg Ser Pro
85 90 95

ttc acg ttc ggc gcg ggg aca aag ttg aaa ata aga
 Phe Thr Phe Gly Ala Gly Thr Lys Leu Lys Ile Arg
 100 105

324

<210> 21
 <211> 108
 <212> PRT
 <213> Mus musculus

<400> 21

Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Val Ser Leu Gly
 1 5 10 15

Glu Arg Val Thr Met Thr Cys Thr Ala Ser Ser Ser Val Ser Ser Ser
 20 25 30

Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Leu Trp
 35 40 45

Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser
 50 55 60

Gly Ser Gly Ser Gly Thr Ser Tyr Phe Phe Thr Ile Ser Ser Met Glu
 65 70 75 80

Ala Glu Asp Ala Ala Thr Tyr Tyr Cys His Gln Tyr His Arg Ser Pro
 85 90 95

Phe Thr Phe Gly Ala Gly Thr Lys Leu Lys Ile Arg
 100 105

<210> 22
 <211> 369
 <212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1)..(369)

<223> SC16.3 VH

<220>

<221> CDS

<222> (1)..(369)

<400> 22

cag gtt act ctg aaa gag tct ggc cct ggg ata ttg cag ccc tcc cag	48
Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Gln Pro Ser Gln	
1 5 10 15	

acc ctc agt ctg act tgt tct ttc tct ggg ttt tca ctg agc act tct	96
Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser Thr Ser	
20 25 30	

ggt atg ggt gta ggc tgg att cgt cag cca tca ggg aag ggt ctg gag	144
Gly Met Gly Val Gly Trp Ile Arg Gln Pro Ser Gly Lys Gly Leu Glu	
35 40 45	

tgg ctg gca cac att tgg tgg gat gat gtc aag cgc tat aac cca gcc	192
Trp Leu Ala His Ile Trp Trp Asp Asp Val Lys Arg Tyr Asn Pro Ala	
50 55 60	

ctg aag agc cga cta act atc tcc aag gat acc tcc agc agc cag gta	240
Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Ser Ser Gln Val	
65 70 75 80	

ttc ctc aag atc gcc agt gtg gac act gca gat act gcc aca tac tac	288
Phe Leu Lys Ile Ala Ser Val Asp Thr Ala Asp Thr Ala Thr Tyr Tyr	
85 90 95	

tgt gct cga ata gct gac tat ggc gga gat tac tat gct atg gac tac	336
Cys Ala Arg Ile Ala Asp Tyr Gly Gly Asp Tyr Tyr Ala Met Asp Tyr	
100 105 110	

tgg ggt caa gga acc tca gtc acc gtc tcc tca	369
Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser	
115 120	

<210> 23
<211> 123
<212> PRT
<213> Mus musculus

<400> 23

Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Gln Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser Thr Ser
20 25 30

Gly Met Gly Val Gly Trp Ile Arg Gln Pro Ser Gly Lys Gly Leu Glu
35 40 45

Trp Leu Ala His Ile Trp Trp Asp Asp Val Lys Arg Tyr Asn Pro Ala
50 55 60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Ser Ser Gln Val
65 70 75 80

Phe Leu Lys Ile Ala Ser Val Asp Thr Ala Asp Thr Ala Thr Tyr Tyr
85 90 95

Cys Ala Arg Ile Ala Asp Tyr Gly Gly Asp Tyr Tyr Ala Met Asp Tyr
100 105 110

Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser
115 120

<210> 24
<211> 321
<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1).. (321)

<223> SC16.4 VL

<220>

<221> CDS

<222> (1).. (321)

<400> 24

gat atc cag atg aca cag act aca tct tcc ctg tct gcc tct ctg gga	48
Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly	
1 5 10 15	

gac aga gtc acc atc agt tgc agg gca agt cag gac att agc aat tat	96
Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Asn Tyr	
20 25 30	

tta aac tgg tat cag cag aaa cca gat gga act gtt aaa ctc ctg atc	144
Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile	
35 40 45	

tac tac aca tca aga tta cac tca ggc gtc cca tca agg ttc agt ggc	192
Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly	
50 55 60	

agt ggg tct gga aca gat tat tct ctc acc att agc aac ctg gag cta	240
Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Leu	
65 70 75 80	

gaa gat att gcc act tac ttt tgc caa cag ggt gat atg ctt ccg tgg	288
Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asp Met Leu Pro Trp	
85 90 95	

acg ttc ggt gga ggc acc aag ctg gaa atc aaa	321
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys	
100 105	

<210> 25

<211> 107

<212> PRT

<213> Mus musculus

<400> 25

Asp	Ile	Gln	Met	Thr	Gln	Thr	Thr	Ser	Ser	Leu	Ser	Ala	Ser	Leu	Gly
1				5				10						15	

Asp	Arg	Val	Thr	Ile	Ser	Cys	Arg	Ala	Ser	Gln	Asp	Ile	Ser	Asn	Tyr
		20						25					30		

Leu	Asn	Trp	Tyr	Gln	Gln	Lys	Pro	Asp	Gly	Thr	Val	Lys	Leu	Leu	Ile
	35						40					45			

Tyr	Tyr	Thr	Ser	Arg	Leu	His	Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly
	50					55					60				

Ser	Gly	Ser	Gly	Thr	Asp	Tyr	Ser	Leu	Thr	Ile	Ser	Asn	Leu	Glu	Leu
65					70					75				80	

Glu	Asp	Ile	Ala	Thr	Tyr	Phe	Cys	Gln	Gln	Gly	Asp	Met	Leu	Pro	Trp
				85					90					95	

Thr	Phe	Gly	Gly	Gly	Thr	Lys	Leu	Glu	Ile	Lys
			100					105		

<210> 26

<211> 351

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1)..(351)

<223> SC16.4 VH

<220>

<221> CDS

<222> (1).. (351)

<400> 26

cag atc cag ttg gtg cag tct gga cct gag ctg aag aag cct gga gag	48
Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu	
1 5 10 15	

aca gtc aag atc tcc tgc aag gct tct ggt tat acc ttc aca gac tat	96
Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr	
20 25 30	

tca atg cac tgg gtg aag cag gct cca gga aag ggt tta aag tgg atg	144
Ser Met His Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met	
35 40 45	

ggc tgg ata aac act gag act ggt gag cca gga tat gca gat gac ttc	192
Gly Trp Ile Asn Thr Glu Thr Gly Glu Pro Gly Tyr Ala Asp Asp Phe	
50 55 60	

aag gga cgg ttt gcc ttc tct ttg gaa acc tct gcc agc act gcc tat	240
Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr	
65 70 75 80	

ttg cag atc aac aac ctc aaa aat gag gac acg gct aca tat ttc tgt	288
Leu Gln Ile Asn Asn Leu Lys Asn Glu Asp Thr Ala Thr Tyr Phe Cys	
85 90 95	

gct cgg tac gac ggg tat gct atg gac tat tgg ggt caa gga acc tca	336
Ala Arg Tyr Asp Gly Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser	
100 105 110	

gtc acc gtc tcc tca	351
Val Thr Val Ser Ser	
115	

<210> 27

<211> 117

<212> PRT

<213> Mus musculus

<400> 27

Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1 5 10 15

Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Ser Met His Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met
35 40 45

Gly Trp Ile Asn Thr Glu Thr Gly Glu Pro Gly Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Leu Gln Ile Asn Asn Leu Lys Asn Glu Asp Thr Ala Thr Tyr Phe Cys
85 90 95

Ala Arg Tyr Asp Gly Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser
100 105 110

Val Thr Val Ser Ser
115

<210> 28
<211> 318
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (318)
<223> SC16.5 VL

<220>

<221> CDS

<222> (1).. (318)

<400> 28

caa att gtt ctc acc cag tct cca gca atc atg tct gca tct cca ggg	48
Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly	
1 5 10 15	

gag aag gtc acc atg acc tgc agt gcc agc tca agt gta agt tac atg	96
Glu Lys Val Thr Met Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met	
20 25 30	

cac tgg tac cag cag aag tca ggc acc tcc ccc aaa aga tgg att tat	144
His Trp Tyr Gln Gln Lys Ser Gly Thr Ser Pro Lys Arg Trp Ile Tyr	
35 40 45	

gac aca tcc aaa ctg gct tct gga gtc cct gct cgc ttc agt ggc agt	192
Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser	
50 55 60	

ggg tct ggg acc tct tac tct ctc aca atc agc agc atg gag gct gaa	240
Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu	
65 70 75 80	

gat gct gcc act tat tac tgc cag cag tgg act aga aac ccg ctc acg	288
Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Arg Asn Pro Leu Thr	
85 90 95	

ttc ggg gct gga acc aag ctg gag ctg aaa	318
Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys	
100 105	

<210> 29

<211> 106

<212> PRT

<213> Mus musculus

<400> 29

Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly	
1 5 10 15	

Glu Lys Val Thr Met Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

His Trp Tyr Gln Gln Lys Ser Gly Thr Ser Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Arg Asn Pro Leu Thr
85 90 95

Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105

<210> 30
<211> 372
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (372)
<223> SC16.5 VH

<220>
<221> CDS
<222> (1).. (372)

<400> 30
cag gtt act ctg aaa gag tct ggc cct ggg ata ttg cag ccc tcc cag
Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Gln Pro Ser Gln
1 5 10 15

acc ctc agt ctg act tgt tct ttc tct ggg ttt tca ctg agc act tct	96
Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser Thr Ser	
20 25 30	

ggt atg ggt gta ggc tgg att cgt cag cct tca gga gag ggt cta gag	144
Gly Met Gly Val Gly Trp Ile Arg Gln Pro Ser Gly Glu Gly Leu Glu	
35 40 45	

tgg ctg gca gac att tgg tgg gat gac aat aag tac tat aac cca tcc	192
Trp Leu Ala Asp Ile Trp Trp Asp Asp Asn Lys Tyr Tyr Asn Pro Ser	
50 55 60	

ctg aag agc cgg ctc aca atc tcc aag gat acc tcc agc aac cag gta	240
Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Ser Asn Gln Val	
65 70 75 80	

ttc ctc aag atc acc agt gtg gac act gca gat act gcc act tac tac	288
Phe Leu Lys Ile Thr Ser Val Asp Thr Ala Asp Thr Ala Thr Tyr Tyr	
85 90 95	

tgt gct cga aga gtt aac tat gtt tac gac ccg tac tat gct atg gac	336
Cys Ala Arg Arg Val Asn Tyr Val Tyr Asp Pro Tyr Tyr Ala Met Asp	
100 105 110	

tac tgg ggt caa gga acc tca gtc acc gtc tcc tca	372
Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser	
115 120	

<210> 31
 <211> 124
 <212> PRT
 <213> Mus musculus

<400> 31

Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Gln Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser Thr Ser
20 25 30

Gly Met Gly Val Gly Trp Ile Arg Gln Pro Ser Gly Glu Gly Leu Glu
35 40 45

Trp Leu Ala Asp Ile Trp Trp Asp Asp Asn Lys Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Ser Asn Gln Val
65 70 75 80

Phe Leu Lys Ile Thr Ser Val Asp Thr Ala Asp Thr Ala Thr Tyr Tyr
85 90 95

Cys Ala Arg Arg Val Asn Tyr Val Tyr Asp Pro Tyr Tyr Ala Met Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser
115 120

<210> 32
<211> 336
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (336)
<223> SC16.7 VL

<220>
<221> CDS
<222> (1).. (336)

<400> 32
aac att atg atg aca cag tcg cca tca tct ctg gct gtg tct gca gga
Asn Ile Met Met Thr Gln Ser Pro Ser Ser Leu Ala Val Ser Ala Gly
1 5 10 15

gaa aag gtc act atg agc tgt aag tcc agt caa agt gtt tta tac agt	96
Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Val Leu Tyr Ser	
20 25 30	

tca aat cag aag aac tac ttg gcc tgg tac caa cag aaa cca ggg cag	144
Ser Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln	
35 40 45	

tct cct aaa ctg ctg atc tac tgg gca tcc act agg gaa tct ggt gtc	192
Ser Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val	
50 55 60	

cct gat cgc ttc aca ggc agt gga tct ggg aca gat ttt act ctt acc	240
Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr	
65 70 75 80	

atc agc act gta caa gtt gaa gac ctg gca gtt tat tac tgt cat caa	288
Ile Ser Thr Val Gln Val Glu Asp Leu Ala Val Tyr Tyr Cys His Gln	
85 90 95	

tac ctc tcc tcg tgg acg ttc ggt gga ggc acc aag ctg gaa atc aaa	336
Tyr Leu Ser Ser Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys	
100 105 110	

<210> 33
 <211> 112
 <212> PRT
 <213> Mus musculus

<400> 33

Asn Ile Met Met Thr Gln Ser Pro Ser Ser Leu Ala Val Ser Ala Gly
1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Val Leu Tyr Ser
20 25 30

Ser Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Ser Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Thr Val Gln Val Glu Asp Leu Ala Val Tyr Tyr Cys His Gln
85 90 95

Tyr Leu Ser Ser Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 34
<211> 357
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (357)
<223> SC16.7 VH

<220>
<221> CDS
<222> (1).. (357)

<400> 34
gag gtc cag ctg caa cag tct gga cct gag ctg gtg aag cct ggg gct 48
Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1 5 10 15
tca gtg aag att tcc tgc aag gct tct ggt tac tca ttc act ggc tat 96
Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr
20 25 30
aaa atg cac tgg gtg aag caa agc cat gta aag agc ctt gag tgg att 144
Lys Met His Trp Val Lys Gln Ser His Val Lys Ser Leu Glu Trp Ile
35 40 45

gga cgt att aat cct tac aat ggt gct act agc tac aac cag aat ttc	192
Gly Arg Ile Asn Pro Tyr Asn Gly Ala Thr Ser Tyr Asn Gln Asn Phe	
50 55 60	

aag gac aag gcc acc ttg act gta gat aag tcc tcc agc aca gcc tac	240
Lys Asp Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr	
65 70 75 80	

atg gac ctc cac agc ctg aca tct gag gac tct gca gtc tat ttc tgt	288
Met Asp Leu His Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys	
85 90 95	

gca aga ggg gac tat agg tac gac tgg ttt gct tac tgg ggc caa ggg	336
Ala Arg Gly Asp Tyr Arg Tyr Asp Trp Phe Ala Tyr Trp Gly Gln Gly	
100 105 110	

act ctg gtc act gtc tct gca	357
Thr Leu Val Thr Val Ser Ala	
115	

<210> 35
 <211> 119
 <212> PRT
 <213> Mus musculus

<400> 35

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr
20 25 30

Lys Met His Trp Val Lys Gln Ser His Val Lys Ser Leu Glu Trp Ile
35 40 45

Gly Arg Ile Asn Pro Tyr Asn Gly Ala Thr Ser Tyr Asn Gln Asn Phe
50 55 60

Lys Asp Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Asp Leu His Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Gly Asp Tyr Arg Tyr Asp Trp Phe Ala Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ala
115

<210> 36
<211> 321
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (321)
<223> SC16.8 VL

<220>
<221> CDS
<222> (1).. (321)

<400> 36
gaa atc cag atg acc cag tct cca tcc tct atg tct gca tct ctg gga 48
Glu Ile Gln Met Thr Gln Ser Pro Ser Ser Met Ser Ala Ser Leu Gly
1 5 10 15

gac aga ata acc atc act tgc cag gca act caa gac att gtt aag aat 96
Asp Arg Ile Thr Ile Thr Cys Gln Ala Thr Gln Asp Ile Val Lys Asn
20 25 30

tta aac tgg tat cag cag aaa cca ggg aaa ccc cct tca ttc ctg atc 144
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Pro Pro Ser Phe Leu Ile
35 40 45

tat	tat	gca	att	gaa	ctg	gca	gaa	ggg	gtc	cca	tca	agg	ttc	agt	ggc	192
Tyr	Tyr	Ala	Ile	Glu	Leu	Ala	Glu	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	
50						55									60	

agt	ggg	tct	ggg	tca	gac	tat	tct	ctg	aca	atc	agc	aac	ctg	gag	tct	240
Ser	Gly	Ser	Gly	Ser	Asp	Tyr	Ser	Leu	Thr	Ile	Ser	Asn	Leu	Glu	Ser	
65						70									80	

gaa	gat	ttt	gca	gac	tat	tac	tgt	cta	cag	ttt	tat	gag	ttt	ccg	ttc	288
Glu	Asp	Phe	Ala	Asp	Tyr	Tyr	Cys	Leu	Gln	Phe	Tyr	Glu	Phe	Pro	Phe	
						85									95	

acg	ttc	ggt	gct	ggg	acc	aag	ctg	gag	ctg	aaa	321
Thr	Phe	Gly	Ala	Gly	Thr	Lys	Leu	Glu	Leu	Lys	
						100				105	

<210> 37
 <211> 107
 <212> PRT
 <213> Mus musculus

<400> 37

Glu	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Ser	Met	Ser	Ala	Ser	Leu	Gly
1				5						10					15

Asp	Arg	Ile	Thr	Ile	Thr	Cys	Gln	Ala	Thr	Gln	Asp	Ile	Val	Lys	Asn
				20						25					30

Leu	Asn	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Pro	Pro	Ser	Phe	Leu	Ile
				35						40					45

Tyr	Tyr	Ala	Ile	Glu	Leu	Ala	Glu	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly
				50						55					60

Ser	Gly	Ser	Gly	Ser	Asp	Tyr	Ser	Leu	Thr	Ile	Ser	Asn	Leu	Glu	Ser
65										70					80

Glu	Asp	Phe	Ala	Asp	Tyr	Tyr	Cys	Leu	Gln	Phe	Tyr	Glu	Phe	Pro	Phe
				85					90					95	

Thr	Phe	Gly	Ala	Gly	Thr	Lys	Leu	Glu	Leu	Lys
			100				105			

<210> 38
 <211> 363
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1).. (363)
 <223> SC16.8 VH

<220>
 <221> CDS
 <222> (1).. (363)

<400> 38	
cag gcc cag ctg cag cag tct gga gct gag ctg gta agg cct ggg act	48
Gln Ala Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Thr	
1 5 10 15	
tca gtg aag gtg tcc tgc aag gct tct gga tac gcc ttc act aat tac	96
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr	
20 25 30	
ttg ata gag tgg gta aag cag agg cct gga cag ggc ctt gag tgg att	144
Leu Ile Glu Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile	
35 40 45	
gga gtg att aat cct gga act ggt ggt act aac tac aat gag aac ttc	192
Gly Val Ile Asn Pro Gly Thr Gly Gly Thr Asn Tyr Asn Glu Asn Phe	
50 55 60	
aag ggc aag gca act ctg act gca gac aaa tcc tcc agt act gcc tac	240
Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr	
65 70 75 80	

atg cag ctc agc agc ctg aca tct gat gac tct gcg gtc tat ttc tgt	288
Met Gln Leu Ser Ser Leu Thr Ser Asp Asp Ser Ala Val Tyr Phe Cys	
85 90 95	

gca aga tcc ccc tat gat tac cac gag ggt gct atg gac tac tgg ggt	336
Ala Arg Ser Pro Tyr Asp Tyr His Glu Gly Ala Met Asp Tyr Trp Gly	
100 105 110	

caa gga acc tca gtc acc gtc tcc tca	363
Gln Gly Thr Ser Val Thr Val Ser Ser	
115 120	

<210> 39
 <211> 121
 <212> PRT
 <213> Mus musculus

<400> 39

Gln Ala Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Thr
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr
20 25 30

Leu Ile Glu Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Val Ile Asn Pro Gly Thr Gly Gly Thr Asn Tyr Asn Glu Asn Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Asp Asp Ser Ala Val Tyr Phe Cys
85 90 95

gct gaa gat gct gcc act tat tac tgc cac cag tat cat cgt tcc cca	288
Ala Glu Asp Ala Ala Thr Tyr Tyr Cys His Gln Tyr His Arg Ser Pro	
85 90 95	

ttc acg ttc ggc tcg ggg aca aag ttg gaa ata aaa	324
Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys	
100 105	

<210> 41
 <211> 108
 <212> PRT
 <213> Mus musculus

<400> 41

Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Leu Gly
1 5 10 15

Glu Arg Val Thr Met Thr Cys Thr Ala Ser Ser Ser Val Ser Ser Ser
20 25 30

Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Leu Trp
35 40 45

Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Thr Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu
65 70 75 80

Ala Glu Asp Ala Ala Thr Tyr Tyr Cys His Gln Tyr His Arg Ser Pro
85 90 95

Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 42
 <211> 360
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1)..(360)
 <223> SC16.10 VH

<220>
 <221> CDS
 <222> (1)..(360)

<400> 42
 cag gtt act ctg aaa gag tct ggc cct ggg ata ttg cag tcc tcc cag 48
 Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Gln Ser Ser Gln
 1 5 10 15
 acc ctc agt ctg act tgt tct ttc tct ggg ttt tca ctg agc act tct 96
 Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser Thr Ser
 20 25 30
 ggt atg ggt gta ggc tgg att cgt cag cca tca ggg aag ggt ctg gag 144
 Gly Met Gly Val Gly Trp Ile Arg Gln Pro Ser Gly Lys Gly Leu Glu
 35 40 45
 tgg ctg gca cac att tgg tgg gat gat gtc aag cgc tat aac cca gtc 192
 Trp Leu Ala His Ile Trp Trp Asp Asp Val Lys Arg Tyr Asn Pro Val
 50 55 60
 ctg aag agc cga ctg act atc tcc aag gat acc tcc agc agc cag gta 240
 Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Ser Ser Gln Val
 65 70 75 80
 ttc ctc aag atc gcc agt gtg gac act gca gat act gcc aca tac tat 288
 Phe Leu Lys Ile Ala Ser Val Asp Thr Ala Asp Thr Ala Thr Tyr Tyr
 85 90 95
 tgt gct cga tta gtt gat gat ctg tac tac ttt gac tac tgg ggc caa 336
 Cys Ala Arg Leu Val Asp Asp Leu Tyr Tyr Phe Asp Tyr Trp Gly Gln
 100 105 110

ggc acc act ctc aca gtc tcc tca
 Gly Thr Thr Leu Thr Val Ser Ser
 115 120

360

<210> 43
 <211> 120
 <212> PRT
 <213> Mus musculus

<400> 43

Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Gln Ser Ser Gln
 1 5 10 15

Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser Thr Ser
 20 25 30

Gly Met Gly Val Gly Trp Ile Arg Gln Pro Ser Gly Lys Gly Leu Glu
 35 40 45

Trp Leu Ala His Ile Trp Trp Asp Asp Val Lys Arg Tyr Asn Pro Val
 50 55 60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Ser Ser Gln Val
 65 70 75 80

Phe Leu Lys Ile Ala Ser Val Asp Thr Ala Asp Thr Ala Thr Tyr Tyr
 85 90 95

Cys Ala Arg Leu Val Asp Asp Leu Tyr Tyr Phe Asp Tyr Trp Gly Gln
 100 105 110

Gly Thr Thr Leu Thr Val Ser Ser
 115 120

<210> 44
 <211> 336
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1).. (336)
 <223> SC16.11 VL

<220>
 <221> CDS
 <222> (1).. (336)

<400> 44
 gat gtt gag atg acc cag act cca ctc act ttg tcg gtt acc att gga 48
 Asp Val Glu Met Thr Gln Thr Pro Leu Thr Leu Ser Val Thr Ile Gly
 1 5 10 15

 caa cca gcc tcc atc tct tgc aag tca agt cag agc ctc tca gac agt 96
 Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Ser Asp Ser
 20 25 30

 gat gga aag aca tat ttg aat tgg atg ttt cag agg cca ggc cgg tct 144
 Asp Gly Lys Thr Tyr Leu Asn Trp Met Phe Gln Arg Pro Gly Arg Ser
 35 40 45

 cca aag cgc cta atc tat ctg gtg tct aaa ctg gac tct gga gtc cct 192
 Pro Lys Arg Leu Ile Tyr Leu Val Ser Lys Leu Asp Ser Gly Val Pro
 50 55 60

 gac agg ttc act ggc agt gga tca ggg aca gat ttc aca ctg aaa atc 240
 Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80

 agc aga gtg gag gct gag gat ttg gga gtt tac tat tgc tgg caa ggt 288
 Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Trp Gln Gly
 85 90 95

 aaa cat ttt ccg tgg acg ttc ggt gga ggc acc aag ctg gaa atc aaa 336
 Lys His Phe Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 100 105 110

<210> 45
<211> 112
<212> PRT
<213> Mus musculus

<400> 45

Asp Val Glu Met Thr Gln Thr Pro Leu Thr Leu Ser Val Thr Ile Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Ser Asp Ser
20 25 30

Asp Gly Lys Thr Tyr Leu Asn Trp Met Phe Gln Arg Pro Gly Arg Ser
35 40 45

Pro Lys Arg Leu Ile Tyr Leu Val Ser Lys Leu Asp Ser Gly Val Pro
50 55 60

Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Trp Gln Gly
85 90 95

Lys His Phe Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 46
<211> 351
<212> DNA
<213> Mus musculus

<220>

<221> misc_feature

<222> (1).. (351)

<223> SC16.11 VH

<220>

<221> CDS

<222> (1).. (351)

<400> 46

cag atc cag ttg gtg cag tct gga cct gag ctg aag aag cct gga gag 48
Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1 5 10 15

aca gtc aag atc tcc tgc aag gct tct ggt tat acc ttc aca gac tat 96
Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

tca atg cac tgg gtg aag cag gct cca gga aag ggt tta aag tgg atg 144
Ser Met His Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met
35 40 45

ggc tgg ata aac act gag act gtt gag cca aca tat gca gat gac ttc 192
Gly Trp Ile Asn Thr Glu Thr Val Glu Pro Thr Tyr Ala Asp Asp Phe
50 55 60

atg gga cgg ttt gcc ttc tct ttg gaa acc tct gcc agc act gcc ttt 240
Met Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Phe
65 70 75 80

ttg cag atc aac aac ctc gaa aat gag gac acg gct aca tat ttc tgt 288
Leu Gln Ile Asn Asn Leu Glu Asn Glu Asp Thr Ala Thr Tyr Phe Cys
85 90 95

gct aga ttt ggt tcc tat gct atg gac tac tgg ggt caa gga acc tca 336
Ala Arg Phe Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser
100 105 110

gtc acc gtc tcc tca 351
Val Thr Val Ser Ser
115

<210> 47

<211> 117

<212> PRT

<213> Mus musculus

<400> 47

Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1 5 10 15

Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Ser Met His Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met
35 40 45

Gly Trp Ile Asn Thr Glu Thr Val Glu Pro Thr Tyr Ala Asp Asp Phe
50 55 60

Met Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Phe
65 70 75 80

Leu Gln Ile Asn Asn Leu Glu Asn Glu Asp Thr Ala Thr Tyr Phe Cys
85 90 95

Ala Arg Phe Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser
100 105 110

Val Thr Val Ser Ser
115

<210> 48

<211> 318

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1).. (318)

<223> SC16.13 VL

<220>

<221> CDS

<222> (1).. (318)

<400> 48

caa att gtt ctc acc cag tct cca gca ctc gtg tct gca tct cca ggg 48

Gln Ile Val Leu Thr Gln Ser Pro Ala Leu Val Ser Ala Ser Pro Gly

1 5 10 15

gag aag gtc acc atg acc tgc agt gcc agc tca agt gta agt tac atg 96

Glu Lys Val Thr Met Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met

20 25 30

tac tgg tac cag cag aaa cca aga tcc tcc ccc aaa ccc tgg att tat 144

Tyr Trp Tyr Gln Gln Lys Pro Arg Ser Ser Pro Lys Pro Trp Ile Tyr

35 40 45

ctc aca tcc aac ctg gct tct gga gtc cct gct cgc ttc agt ggc agt 192

Leu Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser

50 55 60

ggg tct ggg acc tct tac tct ctc aca atc agc agc atg gag gct gaa 240

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu

65 70 75 80

gat gct gcc act tat tac tgc cag cag tgg cgt agt aac cca ttc acg 288

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Arg Ser Asn Pro Phe Thr

85 90 95

ttc ggc tcg ggg aca aag ttg gaa ata aaa 318

Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys

100 105

<210> 49

<211> 106

<212> PRT

<213> Mus musculus

<400> 49

Gln Ile Val Leu Thr Gln Ser Pro Ala Leu Val Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Met Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

Tyr Trp Tyr Gln Gln Lys Pro Arg Ser Ser Pro Lys Pro Trp Ile Tyr
35 40 45

Leu Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Arg Ser Asn Pro Phe Thr
85 90 95

Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 50
<211> 372
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (372)
<223> SC16.13 VH

<220>
<221> CDS
<222> (1).. (372)

<400> 50

cag gtt act ctg aaa gag tct ggc cct ggg ata ttg cag ccc tcc cag	48
Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Gln Pro Ser Gln	
1 5 10 15	

acc ctc agt ctg act tgt tct ttc tct ggg ttt tca ctg agc act tct	96
Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser Thr Ser	
20 25 30	

ggt atg ggt gta ggc tgg att cgg cag cca tca ggg aag ggt ctg gag	144
Gly Met Gly Val Gly Trp Ile Arg Gln Pro Ser Gly Lys Gly Leu Glu	
35 40 45	

tgg ctg gca cac att tgg tgg gat gat gtc aag cgc tat aac cca gcc	192
Trp Leu Ala His Ile Trp Trp Asp Asp Val Lys Arg Tyr Asn Pro Ala	
50 55 60	

ctg aag agc cga ctg act atc tcc aag gat acc tcc agc agc cag gta	240
Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Ser Ser Gln Val	
65 70 75 80	

ttc ctc aag atc gcc agt gtg gac act gca gat act gcc aca tac tac	288
Phe Leu Lys Ile Ala Ser Val Asp Thr Ala Asp Thr Ala Thr Tyr Tyr	
85 90 95	

tgt gct cgc ata gtt tcc ttt gat aac gac gtt gtc tct gct atg gac	336
Cys Ala Arg Ile Val Ser Phe Asp Asn Asp Val Val Ser Ala Met Asp	
100 105 110	

tac tgg ggt caa gga acc tca gtc acc gtc tcc tcn	372
Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Xaa	
115 120	

<210> 51

<211> 124

<212> PRT

<213> Mus musculus

<220>

<221> misc_feature

<222> (124)..(124)

<223> The 'Xaa' at location 124 stands for Ser.

<400> 51

Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Gln Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser Thr Ser
20 25 30

Gly Met Gly Val Gly Trp Ile Arg Gln Pro Ser Gly Lys Gly Leu Glu
35 40 45

Trp Leu Ala His Ile Trp Trp Asp Asp Val Lys Arg Tyr Asn Pro Ala
50 55 60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Ser Ser Gln Val
65 70 75 80

Phe Leu Lys Ile Ala Ser Val Asp Thr Ala Asp Thr Ala Thr Tyr Tyr
85 90 95

Cys Ala Arg Ile Val Ser Phe Asp Asn Asp Val Val Ser Ala Met Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Xaa
115 120

<210> 52

<211> 321

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1)..(321)

<223> SC16.15 VL

$\langle 222 \rangle \quad (1) \dots (321)$

<400> 52

gac atc cag atg act cag tct cca gcc tcc ctg gct gca tct gtg gga 48
Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ala Ala Ser Val Gly
1 5 10 15

gaa act gtc gcc atc aca tgt cga gca agt gag aac att tac tac aat 96
Glu Thr Val Ala Ile Thr Cys Arg Ala Ser Glu Asn Ile Tyr Tyr Asn
20 25 30

tta gca tgg tat cag cag aaa caa ggg aaa tct cct cag ctc ctg atc 144
Leu Ala Trp Tyr Gln Gln Lys Gln Gly Lys Ser Pro Gln Leu Leu Ile
35 40 45

tat act gca aac agt ttg gaa gat ggt gtc cca tcg agg ttc agt ggc 192
Tyr Thr Ala Asn Ser Leu Glu Asp Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

agt gga tct ggg aca cag tat tct ttg aag atc aac agc atg cag cct 240
 Ser Gly Ser Gly Thr Gln Tyr Ser Leu Lys Ile Asn Ser Met Gln Pro
 65 70 75 80

gaa gat tcc gca act tat ttc tgt aaa cag gct tat gac gtt cct ccg 288
Glu Asp Ser Ala Thr Tyr Phe Cys Lys Gln Ala Tyr Asp Val Pro Pro
85 90 95

acg ttc ggt gga ggc acc aag ctg gaa atc aaa 321
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 53

<211> 107

<212> PRT

⟨213⟩ Mus musculus

<400> 53

Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ala Ala Ser Val Gly
1 5 10 15

Glu Thr Val Ala Ile Thr Cys Arg Ala Ser Glu Asn Ile Tyr Tyr Asn
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Gln Gly Lys Ser Pro Gln Leu Leu Ile
35 40 45

Tyr Thr Ala Asn Ser Leu Glu Asp Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Gln Tyr Ser Leu Lys Ile Asn Ser Met Gln Pro
65 70 75 80

Glu Asp Ser Ala Thr Tyr Phe Cys Lys Gln Ala Tyr Asp Val Pro Pro
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 54
<211> 351
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(351)
<223> SC16.15 VH

<220>
<221> CDS
<222> (1)..(351)

<400> 54
cag gtc cag ctt cag cag tct ggg gct gaa ctg gca aaa cct ggg gcc
Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Ala Lys Pro Gly Ala

1	5	10	15	
tca gtg aag atg tcc tgt aag gct tct ggc tac acc ttt act cgc tac				96
Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr				
20	25	30		
tgg ata cac tgg ata aaa cag agg cct gga cag ggt ctg gaa tgg att				144
Trp Ile His Trp Ile Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile				
35	40	45		
gga tac att aat cct aca act gtt tat act gag ttc aat cag aac ttc				192
Gly Tyr Ile Asn Pro Thr Thr Val Tyr Thr Glu Phe Asn Gln Asn Phe				
50	55	60		
aag gac aag gcc act ttg act gca gac aaa tcc tcc acc aca gcc tcc				240
Lys Asp Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Thr Thr Ala Ser				
65	70	75	80	
atg caa ctg agc agc ctg aca tct gag gac tct gca gtc tat tac tgt				288
Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys				
85	90	95		
gca aga ggc ggt agt aac ttc ttt gac tac tgg ggc caa ggc acc act				336
Ala Arg Gly Gly Ser Asn Phe Phe Asp Tyr Trp Gly Gln Gly Thr Thr				
100	105	110		
ctc aca gtc tcc tca				351
Leu Thr Val Ser Ser				
115				

<210> 55
 <211> 117
 <212> PRT
 <213> Mus musculus

 <400> 55

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Ala Lys Pro Gly Ala			
1	5	10	15
Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr			
20	25	30	

Trp Ile His Trp Ile Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Thr Thr Val Tyr Thr Glu Phe Asn Gln Asn Phe
50 55 60

Lys Asp Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Thr Thr Ala Ser
65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Ser Asn Phe Phe Asp Tyr Trp Gly Gln Gly Thr Thr
100 105 110

Leu Thr Val Ser Ser
115

<210> 56
<211> 321
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(321)
<223> SC16.18 VL

<220>
<221> CDS
<222> (1)..(321)

<400> 56
gat atc cag atg aca cag act aca tcc tcc ctg tct gcc tct ttg gga
Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly

1	5	10	15	
gac aga gtc acc atc agt tgc agg gca agt cag aat att atc aat tat				96
Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asn Ile Ile Asn Tyr				
	20	25	30	
tta aac tgg tat cag cag aag cca gat gga act gtt aaa ctc ctg atc				144
Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile				
	35	40	45	
tac tac aca tca aga tta cac tca gga gtc cca tca agg ttc agt ggc				192
Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly				
	50	55	60	
agt ggg tct ggg aca gat tat tct ctc acc atc agc aac ctg gaa cct				240
Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Pro				
65	70	75	80	
gaa gat att gcc act tac tat tgt caa cag tat agt gag cgt ccg tac				288
Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Glu Arg Pro Tyr				
	85	90	95	
acg ttc ggg ggg ggg acc aag ctg gaa ata aaa				321
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys				
	100	105		

<210> 57
 <211> 107
 <212> PRT
 <213> Mus musculus

<400> 57

Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly	
1	15
Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asn Ile Ile Asn Tyr	
20	30
Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile	
35	45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Glu Arg Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 58
<211> 351
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (351)
<223> SC16.18 VH

<220>
<221> CDS
<222> (1).. (351)

<400> 58
gaa gtg aag ctg gag gag tca gga gga ggc ttg gta caa cct gga gaa 48
Glu Val Lys Leu Glu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Glu
1 5 10 15

tcc atg aaa ctc tct tgt gct gct tct gga ttc act ttt agt gat gcc 96
Ser Met Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Ala
20 25 30

tgg atg gac tgg gtc cgc cag tct cca gag aag gga ctt gag tgg gtt 144
Trp Met Asp Trp Val Arg Gln Ser Pro Glu Lys Gly Leu Glu Trp Val

35	40	45	
gct gaa att aga aac aaa	gct aat aat cat	gca aca tat tat	gct gag
Ala Glu Ile Arg Asn Lys	Ala Asn Asn His	Ala Thr Tyr Tyr	Ala Glu
50	55	60	192
tct gtg aaa ggg aaa ttc	acc atc tca aga	gat gat tcc aaa	agt aga
Ser Val Lys Gly Lys Phe	Thr Ile Ser Arg	Asp Asp Ser Lys	Ser Arg
65	70	75	80
gtg tac ctg caa atg aac	aac tta aga gct	gca gac act ggc	att tat
Val Tyr Leu Gln Met Asn	Asn Leu Arg Ala	Ala Asp Thr Gly	Ile Tyr
85	90	95	288
tac tgt acg gcc tat agt	aac ttt gct tac	tgg ggc caa ggg	act ctg
Tyr Cys Thr Ala Tyr Ser	Asn Phe Ala Tyr	Trp Gly Gln Gly	Thr Leu
100	105	110	336
gtc act gtc tct aca			351
Val Thr Val Ser Thr			
115			

Glu Val Lys Leu Glu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Glu
1 5 10 15

Trp Met Asp Trp Val Arg Gln Ser Pro Glu Lys Gly Leu Glu Trp Val
35 40 45

Ser Val Lys Gly Lys Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Arg
65 70 75 80

Val Tyr Leu Gln Met Asn Asn Leu Arg Ala Ala Asp Thr Gly Ile Tyr
85 90 95

Tyr Cys Thr Ala Tyr Ser Asn Phe Ala Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Thr
115

<210> 60
<211> 318
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (318)
<223> SC16.19 VL

<220>
<221> CDS
<222> (1).. (318)

<400> 60
gac atc cag atg aca cag tct cca tcc tca ctg tct gca tct ctg gga 48
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

ggc aaa gtc acc ttc act tgc aag gca agc caa gac att cac aag tat 96
Gly Lys Val Thr Phe Thr Cys Lys Ala Ser Gln Asp Ile His Lys Tyr
20 25 30

gta gct tgg tac caa cac aag cct gga aaa ggt cct agg ctg ctc ata 144
Val Ala Trp Tyr Gln His Lys Pro Gly Lys Gly Pro Arg Leu Leu Ile

35	40	45	
cat tac aca tct aca tta cag cca ggc atc tca tca agg ttc agt gga			192
His Tyr Thr Ser Thr Leu Gln Pro Gly Ile Ser Ser Arg Phe Ser Gly			
50	55	60	
agt ggg tct ggg aga gat tat tcc ttc agc atc agc aac ctg gag cct			240
Ser Gly Ser Gly Arg Asp Tyr Ser Phe Ser Ile Ser Asn Leu Glu Pro			
65	70	75	80
gaa gat att gca act tat tat tgt cta cag tat aat aat ctg tac acg			288
Glu Asp Ile Ala Thr Tyr Tyr Cys Leu Gln Tyr Asn Asn Leu Tyr Thr			
85	90	95	
ttc gga ggg ggg acc aag ctg gaa ata aaa			318
Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys			
100	105		
<210>	61		
<211>	106		
<212>	PRT		
<213>	Mus musculus		
<400>	61		
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Leu Gly			
1	5	10	15
Gly Lys Val Thr Phe Thr Cys Lys Ala Ser Gln Asp Ile His Lys Tyr			
20	25	30	
Val Ala Trp Tyr Gln His Lys Pro Gly Lys Gly Pro Arg Leu Leu Ile			
35	40	45	
His Tyr Thr Ser Thr Leu Gln Pro Gly Ile Ser Ser Arg Phe Ser Gly			
50	55	60	
Ser Gly Ser Gly Arg Asp Tyr Ser Phe Ser Ile Ser Asn Leu Glu Pro			
65	70	75	80

Glu Asp Ile Ala Thr Tyr Tyr Cys Leu Gln Tyr Asn Asn Leu Tyr Thr
85 90 95

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 62
<211> 354
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (354)
<223> SC16.19 VH

<220>
<221> CDS
<222> (1).. (354)

<400> 62
gag gtt cag ctg cag cag tct ggg gct gag ctt gtg agg cca ggg gcc 48
Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ala
1 5 10 15

tca gtc aag ttg tcc tgc aca gct tct ggc ttc aac att aaa gac agc 96
Ser Val Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Ser
20 25 30

ctt ttg cac tgg gtg aag cag agg cct gaa aag ggc ctg gag tgg att 144
Leu Leu His Trp Val Lys Gln Arg Pro Glu Lys Gly Leu Glu Trp Ile
35 40 45

ggg tgg att gat cct gag gat ggt gaa act aaa tat gcc ccg aac ttc 192
Gly Trp Ile Asp Pro Glu Asp Gly Glu Thr Lys Tyr Ala Pro Asn Phe
50 55 60

cag gac aag gcc act ata act aca gac tca tcc tcc aac aca gcc tac 240
Gln Asp Lys Ala Thr Ile Thr Thr Asp Ser Ser Ser Asn Thr Ala Tyr

65	70	75	80	
ctg caa ctc atc agc ctg aca tct gtt gac act gcc atc tat tac tgt				288
Leu Gln Leu Ile Ser Leu Thr Ser Val Asp Thr Ala Ile Tyr Tyr Cys				
85	90	95		
gcc tat ggt aac tac gtg cgg cac ttt gac tac tgg ggc caa ggc acc				336
Ala Tyr Gly Asn Tyr Val Arg His Phe Asp Tyr Trp Gly Gln Gly Thr				
100	105	110		
act ctc aca gtc tcc tca				354
Thr Leu Thr Val Ser Ser				
115				
<210>	63			
<211>	118			
<212>	PRT			
<213>	Mus musculus			
<400>	63			
Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ala				
1	5	10	15	
Ser Val Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Ser				
20	25	30		
Leu Leu His Trp Val Lys Gln Arg Pro Glu Lys Gly Leu Glu Trp Ile				
35	40	45		
Gly Trp Ile Asp Pro Glu Asp Gly Glu Thr Lys Tyr Ala Pro Asn Phe				
50	55	60		
Gln Asp Lys Ala Thr Ile Thr Thr Asp Ser Ser Ser Asn Thr Ala Tyr				
65	70	75	80	
Leu Gln Leu Ile Ser Leu Thr Ser Val Asp Thr Ala Ile Tyr Tyr Cys				
85	90	95		

Ala Tyr Gly Asn Tyr Val Arg His Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Thr Leu Thr Val Ser Ser
115

<210> 64
<211> 321
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(321)
<223> SC16.20 VL

<220>
<221> CDS
<222> (1)..(321)

<400> 64
gaa atc cag atg acc cag tct cca tcc tct atg tct gca tct ctg gga 48
Glu Ile Gln Met Thr Gln Ser Pro Ser Ser Met Ser Ala Ser Leu Gly
1 5 10 15
gac aga ata acc atc act tgc cag gca act caa gac att gtt aag aat 96
Asp Arg Ile Thr Ile Thr Cys Gln Ala Thr Gln Asp Ile Val Lys Asn
20 25 30
tta aac tgg tat cag cag aaa cca ggg aaa ccc cct tca ttc ctg atc 144
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Pro Pro Ser Phe Leu Ile
35 40 45
tat tat gca act gaa ctg gca gaa ggg gtc cca tca agg ttc agt ggc 192
Tyr Tyr Ala Thr Glu Leu Ala Glu Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
agt ggg tct ggg tca gac tat tct ctg aca atc agg aac ctg gag tct 240
Ser Gly Ser Gly Ser Asp Tyr Ser Leu Thr Ile Arg Asn Leu Glu Ser

65	70	75	80	
gaa gac ttt gca gac cat tac tgt cta cag ttt tat gag ttt ccg ttc 288				
Glu Asp Phe Ala Asp His Tyr Cys Leu Gln Phe Tyr Glu Phe Pro Phe				

	85	90	95	
acg ttc ggt gct ggg acc aag ctg gag ctg aaa				321
Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys				
	100	105		

$\langle 210 \rangle$	65
$\langle 211 \rangle$	107
$\langle 212 \rangle$	PRT
$\langle 213 \rangle$	Mus musculus

<400> 65

Glu Ile Gln Met Thr Gln Ser Pro Ser Ser Met Ser Ala Ser Leu Gly
1 5 10 15

Asp Arg Ile Thr Ile Thr Cys Gln Ala Thr Gln Asp Ile Val Lys Asn
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Pro Pro Ser Phe Leu Ile
35 40 45

Tyr Tyr Ala Thr Glu Leu Ala Glu Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Ser Asp Tyr Ser Leu Thr Ile Arg Asn Leu Glu Ser
65 70 75 80

Glu Asp Phe Ala Asp His Tyr Cys Leu Gln Phe Tyr Glu Phe Pro Phe
85 90 95

Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105

<210> 66
 <211> 363
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1)..(363)
 <223> SC16.20 VH

<220>
 <221> CDS
 <222> (1)..(363)

<400> 66
 cag gtc cag ttg cag cag tct gga act gag ctg gta agg cct ggg act 48
 Gln Val Gln Leu Gln Gln Ser Gly Thr Glu Leu Val Arg Pro Gly Thr
 1 5 10 15

tca gtg agg gtg tcc tgc aag gct tct gga tac gcc ttc ggt aat cac 96
 Ser Val Arg Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Gly Asn His
 20 25 30

ttg att gag tgg gtg aag cag agg cct gga cag ggc ctt gag tgg att 144
 Leu Ile Glu Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

gga gtg att aat cct gga act ggt ggt act cac tac aat gag aag ttc 192
 Gly Val Ile Asn Pro Gly Thr Gly Gly Thr His Tyr Asn Glu Lys Phe
 50 55 60

aag gac aag gca aga ctg acc gca gac aaa tcc tcc aac act gcc tac 240
 Lys Asp Lys Ala Arg Leu Thr Ala Asp Lys Ser Ser Asn Thr Ala Tyr
 65 70 75 80

atg cac ctc aac agc ctg aca tct gat gac tct gcg gtc tat ttc tgt 288
 Met His Leu Asn Ser Leu Thr Ser Asp Asp Ser Ala Val Tyr Phe Cys
 85 90 95

gca aga tcc ccc tat gat tac cac gag ggt gct atg gac tac tgg ggt 336
 Ala Arg Ser Pro Tyr Asp Tyr His Glu Gly Ala Met Asp Tyr Trp Gly

	100	105	110	
	caa gga acc tca gtc acc gtc tcc tca			363
	Gln Gly Thr Ser Val Thr Val Ser Ser			
	115	120		
<210>	67			
<211>	121			
<212>	PRT			
<213>	Mus musculus			
<400>	67			
Gln Val Gln Leu Gln Gln Ser Gly Thr Glu Leu Val Arg Pro Gly Thr				
1	5	10	15	
Ser Val Arg Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Gly Asn His				
	20	25	30	
Leu Ile Glu Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile				
	35	40	45	
Gly Val Ile Asn Pro Gly Thr Gly Gly Thr His Tyr Asn Glu Lys Phe				
	50	55	60	
Lys Asp Lys Ala Arg Leu Thr Ala Asp Lys Ser Ser Asn Thr Ala Tyr				
65	70	75	80	
Met His Leu Asn Ser Leu Thr Ser Asp Asp Ser Ala Val Tyr Phe Cys				
	85	90	95	
Ala Arg Ser Pro Tyr Asp Tyr His Glu Gly Ala Met Asp Tyr Trp Gly				
	100	105	110	
Gln Gly Thr Ser Val Thr Val Ser Ser				
	115	120		

<210> 68
 <211> 339
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1).. (339)
 <223> SC16.21 VL

<220>
 <221> CDS
 <222> (1).. (339)

<400> 68
 gac att gtg atg aca cag tct cca tcc tcc ctg gct atg tca gta gga 48
 Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ala Met Ser Val Gly
 1 5 10 15

 cag aag gtc act atg agc tgc aag tcc agt cag agc ctt tta aat agt 96
 Gln Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
 20 25 30

 agc aat caa aag aat tat ttg gcc tgg tat cag cag gaa cca gga cag 144
 Ser Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Glu Pro Gly Gln
 35 40 45

 tct cct aaa ctt ctg gta tcc ttt gca tcc act agg gaa tct ggg gtc 192
 Ser Pro Lys Leu Leu Val Ser Phe Ala Ser Thr Arg Glu Ser Gly Val
 50 55 60

 cct gat cgc ttc aca ggc agt gga tct ggg aca gat ttc act ctt acc 240
 Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
 65 70 75 80

 atc agc ggt gtg cag gct gaa gac ctg gca gtt tat tac tgt cag caa 288
 Ile Ser Gly Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln
 85 90 95

 cat tat agc att ccg ctc acg ttc ggt gct ggg acc aag ctg gag ctg 336
 His Tyr Ser Ile Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu

	100	105	110	
aaa				339
Lys				
<210>	69			
<211>	113			
<212>	PRT			
<213>	Mus musculus			
<400>	69			
Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ala Met Ser Val Gly				
1	5	10	15	
Gln Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser				
	20	25	30	
Ser Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Glu Pro Gly Gln				
	35	40	45	
Ser Pro Lys Leu Leu Val Ser Phe Ala Ser Thr Arg Glu Ser Gly Val				
	50	55	60	
Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr				
65	70	75	80	
Ile Ser Gly Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln				
	85	90	95	
His Tyr Ser Ile Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu				
	100	105	110	
Lys				

<210> 70
 <211> 372
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1).. (372)
 <223> SC16.21 VH

<220>
 <221> CDS
 <222> (1).. (372)

<400> 70
 cag gtt cag cta caa cag tct gga cct gag ctg gtg aag cct ggg gcc 48
 Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
 1 5 10 15

 tca gtg aag att tcc tgc aag gct tct ggc tat gca ttc agt agc tcc 96
 Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Ser
 20 25 30

 tgg atg aac tgg gtg aag cag agg cct gga aag ggt ctt gag tgg att 144
 Trp Met Asn Trp Val Lys Gln Arg Pro Gly Lys Gly Leu Glu Trp Ile
 35 40 45

 gga cgg att tat cct gga gat gga gat act aac tac aat ggg aag ttc 192
 Gly Arg Ile Tyr Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
 50 55 60

 aag ggc aag gcc aca ctg act gca gac aaa tcc tcc agc aca gcc tac 240
 Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
 65 70 75 80

 atg caa ctc agc agc ctg aca tct gag gac tct gcg gtc tac ttc tgt 288
 Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
 85 90 95

 gca atg ggt att tat aac tac gat ggt agc cgt tac tat tct atg gac 336
 Ala Met Gly Ile Tyr Asn Tyr Asp Gly Ser Arg Tyr Tyr Ser Met Asp

	100	105	110	
	tac tgg ggt caa gga acc tca gtc acc gtc tcc tca			372
	Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser			
	115	120		
<210>	71			
<211>	124			
<212>	PRT			
<213>	Mus musculus			
<400>	71			
Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala				
1	5	10	15	
Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Ser				
	20	25	30	
Trp Met Asn Trp Val Lys Gln Arg Pro Gly Lys Gly Leu Glu Trp Ile				
	35	40	45	
Gly Arg Ile Tyr Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe				
	50	55	60	
Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr				
65	70	75	80	
Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys				
	85	90	95	
Ala Met Gly Ile Tyr Asn Tyr Asp Gly Ser Arg Tyr Tyr Ser Met Asp				
	100	105	110	
Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser				
	115	120		

<210> 72
 <211> 321
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1).. (321)
 <223> SC16.22 VL

<220>
 <221> CDS
 <222> (1).. (321)

<400> 72
 gat atc cag atg aca cag act aca tcc tcc ctg tct gcc tct ctg gga 48
 Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
 1 5 10 15

 gac aga gtc acc atc agt tgc agg gca agt cag gac att aag aat tat 96
 Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Lys Asn Tyr
 20 25 30

 tta aac tgg tat cag cag aaa cca gat gga act gtt aaa ccc ctg atc 144
 Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Pro Leu Ile
 35 40 45

 tac tac aca tca aga gta cac tca gga gtc cca tca agg ttc agt ggc 192
 Tyr Tyr Thr Ser Arg Val His Ser Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

 agt ggg tct gga aca gat tat tct ctc acc att agc aac ctg gag caa 240
 Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
 65 70 75 80

 gaa gat att gcc act tac ttt tgc cag cag ggt tat acg ctt cca ttc 288
 Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Tyr Thr Leu Pro Phe
 85 90 95

 acg ttc ggc tcg ggg aca aag ttg gaa ath aar 321
 Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys

100

105

<210> 73

<211> 107

<212> PRT

<213> Mus musculus

<400> 73

Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
 1 5 10 15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Lys Asn Tyr
 20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Pro Leu Ile
 35 40 45

Tyr Tyr Thr Ser Arg Val His Ser Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
 65 70 75 80

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Tyr Thr Leu Pro Phe
 85 90 95

Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
 100 105

<210> 74

<211> 360

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1).. (360)

<223> SC16.22 VH

<220>

<221> CDS

<222> (1).. (360)

<400> 74

cag gtc cag ctg cag cag cct ggg gct gaa ctg gtg aag cct ggg gct	48
Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Ala	
1 5 10 15	

tca gtg aag ctg tcc tgt aag gct tct gga tac acc ttc act acc tac	96
Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Thr Tyr	
20 25 30	

tgg atg cac tgg gtg aag cag agg cct gga caa ggc ctt gag tgg atc	144
Trp Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile	
35 40 45	

gga gag att gat cct tct gat agt tat act tac tac aat caa aag ttc	192
Gly Glu Ile Asp Pro Ser Asp Ser Tyr Thr Tyr Tyr Asn Gln Lys Phe	
50 55 60	

aag ggc aag gcc aca ttg act gta gac aaa tcc tcc agc aca gcc tac	240
Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr	
65 70 75 80	

atg caa ctc agc agc ctg aca tct gag gac tct gcg gtc tat tat tgt	288
Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys	
85 90 95	

gca aga ggg gac tat ggt aac ccc tat gct atg gac tac tgg ggt caa	336
Ala Arg Gly Asp Tyr Gly Asn Pro Tyr Ala Met Asp Tyr Trp Gly Gln	
100 105 110	

gga tcc tca gtc acc gtc tcc tca	360
Gly Ser Ser Val Thr Val Ser Ser	
115 120	

<210> 75

<211> 120
<212> PRT
<213> Mus musculus

<400> 75

Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Thr Tyr
20 25 30

Trp Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asp Pro Ser Asp Ser Tyr Thr Tyr Tyr Asn Gln Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Asp Tyr Gly Asn Pro Tyr Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Ser Ser Val Thr Val Ser Ser
115 120

<210> 76
<211> 324
<212> DNA
<213> Mus musculus

<220>

<221> misc_feature

<222> (1).. (324)

<223> SC16.23 VL

<220>

<221> CDS

<222> (1).. (324)

<400> 76

caa att gtt ctc acc cag tct cca gca atc atg tct gca tct cct ggg	48
Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly	
1 5 10 15	

gag aag gtc acc ttg acc tgc agt gcc agc tca agt gta agt tcc agg	96
Glu Lys Val Thr Leu Thr Cys Ser Ala Ser Ser Ser Val Ser Ser Arg	
20 25 30	

tac ttg tac tgg tac cag cag aag cca gga tcc tcc ccc aaa ctc tgg	144
Tyr Leu Tyr Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Leu Trp	
35 40 45	

att tat agc aca tcc aac ctg gct tct gga gtc cct gct cgc ttc agt	192
Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser	
50 55 60	

ggc agt ggg tct ggg acc tct tac tct ctc ata atc agc agc atg gag	240
Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Ile Ile Ser Ser Met Glu	
65 70 75 80	

gct gaa gat gct gcc tct tat ttc tgc cat cag tgg agt aat tac cca	288
Ala Glu Asp Ala Ala Ser Tyr Phe Cys His Gln Trp Ser Asn Tyr Pro	
85 90 95	

ctc acg ttc ggt gct ggg acc aag ctg gag ctg aaa	324
Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys	
100 105	

<210> 77

<211> 108

<212> PRT

<213> Mus musculus

<400> 77

Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Leu Thr Cys Ser Ala Ser Ser Ser Val Ser Ser Arg
20 25 30

Tyr Leu Tyr Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Leu Trp
35 40 45

Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Ile Ile Ser Ser Met Glu
65 70 75 80

Ala Glu Asp Ala Ala Ser Tyr Phe Cys His Gln Trp Ser Asn Tyr Pro
85 90 95

Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105

<210> 78

<211> 372

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1)..(372)

<223> SC16.23 VH

<220>

<221> CDS

<222> (1)..(372)

<400> 78

cag gtt act ctg aaa gag tct ggc cct ggg ata ttg cag ccc tcc cag	48
Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Gln Pro Ser Gln	
1 5 10 15	

acc ctc agt ctg act tgt tct ttc tct ggg ttt tca ctg agc act tct	96
Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser Thr Ser	
20 25 30	

aat acg ggc ata ggc tgg att cgt cag cct tca ggg acg ggt ctg gag	144
Asn Thr Gly Ile Gly Trp Ile Arg Gln Pro Ser Gly Thr Gly Leu Glu	
35 40 45	

tgg ctg gca cac att tgg tgg aat gat gat aag tac tat aat cca tcc	192
Trp Leu Ala His Ile Trp Trp Asn Asp Asp Lys Tyr Tyr Asn Pro Ser	
50 55 60	

ctg aag agc cgg ctc aca atc tcc aag gaa acc tcc aac aac cag gta	240
Leu Lys Ser Arg Leu Thr Ile Ser Lys Glu Thr Ser Asn Asn Gln Val	
65 70 75 80	

ttc ctc aag atc acc aat gtg gac act gca gat act gcc tca tac ttc	288
Phe Leu Lys Ile Thr Asn Val Asp Thr Ala Asp Thr Ala Ser Tyr Phe	
85 90 95	

tgt gtt caa atc ggg cgc gac tac agt aac tac gcc tgg tat ttc gat	336
Cys Val Gln Ile Gly Arg Asp Tyr Ser Asn Tyr Ala Trp Tyr Phe Asp	
100 105 110	

gtc tgg ggc gca ggg acc acg gtc acc gtc tcc tca	372
Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser	
115 120	

<210> 79

<211> 124

<212> PRT

<213> Mus musculus

<400> 79

Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Gln Pro Ser Gln	
1 5 10 15	

Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser Thr Ser
20 25 30

Asn Thr Gly Ile Gly Trp Ile Arg Gln Pro Ser Gly Thr Gly Leu Glu
35 40 45

Trp Leu Ala His Ile Trp Trp Asn Asp Asp Lys Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Glu Thr Ser Asn Asn Gln Val
65 70 75 80

Phe Leu Lys Ile Thr Asn Val Asp Thr Ala Asp Thr Ala Ser Tyr Phe
85 90 95

Cys Val Gln Ile Gly Arg Asp Tyr Ser Asn Tyr Ala Trp Tyr Phe Asp
100 105 110

Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 80
<211> 318
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (318)
<223> SC16.25 VL

<220>
<221> CDS
<222> (1).. (318)

<400> 80

caa att gtt ctc acc cag tct cca gca atc atg tct gca tct cca ggg 48
Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1 5 10 15

gag aag gtc acc atg acc tgc agt gcc agc tca agt gta agt tac atg 96
Glu Lys Val Thr Met Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

cac tgg tac cag cag aag tca ggc acc tcc ccc aaa aga tgg att tat 144
His Trp Tyr Gln Gln Lys Ser Gly Thr Ser Pro Lys Arg Trp Ile Tyr
35 40 45

gac tca tcc aaa ctg gct tct gga gtc cct gct cgc ttc agt ggc agt 192
Asp Ser Ser Lys Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

ggg tct ggg acc tct tac tct ctc aca atc agc agc atg gag gct gaa 240
Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu
65 70 75 80

gat gct gcc act tat tac tgc cag cag tgg agt agt aac ccg ctc acg 288
Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

ttc ggt gct ggg acc aag ctg gag ctg aaa 318
Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105

<210> 81

<211> 106

<212> PRT

<213> Mus musculus

<400> 81

Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Met Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

His Trp Tyr Gln Gln Lys Ser Gly Thr Ser Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Ser Ser Lys Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105

<210> 82
<211> 372
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (372)
<223> SC16.25 VH

<220>
<221> CDS
<222> (1).. (372)

<400> 82
cag gtt act ctg aaa gag tct ggc cct ggg ata ttg cag ccc tcc cag 48
Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Gln Pro Ser Gln
1 5 10 15

acc ctc agt ctg act tgt tct ttc tct ggg ttt tca ctg agc act tct 96
Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser Thr Ser

Trp Leu Thr Asp Ile Trp Trp Asp Asp Asn Lys Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Ser Asn Gln Val
65 70 75 80

Phe Leu Asn Ile Thr Ser Val Asp Thr Ala Asp Thr Ala Thr Tyr Tyr
85 90 95

Cys Ala Arg Arg Val Asn Tyr Tyr Tyr Asp Pro Tyr Tyr Ala Met Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser
115 120

<210> 84
<211> 336
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(336)
<223> SC16.26 VL

<220>
<221> CDS
<222> (1)..(336)

<400> 84
gat gtt gag atg acc cag act cca ctc act ttg tcg gtt acc att gga 48
Asp Val Glu Met Thr Gln Thr Pro Leu Thr Leu Ser Val Thr Ile Gly
1 5 10 15

caa cca gcc tcc atc tct tgc aag tca agt cag agc ctc tca gac agt 96
Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Ser Asp Ser

Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Trp Gln Gly
85 90 95

Lys His Phe Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 86
<211> 351
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (351)
<223> SC16.26 VH

<220>
<221> CDS
<222> (1).. (351)

<400> 86
cag atc cag ttg gtg cag tct gga cct gag ctg aag aag cct gga gag 48
Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1 5 10 15

aca gtc aag atc tcc tgc aag gct tct ggt tat tcc ttc aca gac tat 96
Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Asp Tyr
20 25 30

tca atg cac tgg gtg aag cag gct cca gga aag ggt tta aag tgg atg 144
Ser Met His Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met
35 40 45

ggc tgg ata aac act gag act gtt gag cca aca tat gca gat gac ttc 192
Gly Trp Ile Asn Thr Glu Thr Val Glu Pro Thr Tyr Ala Asp Asp Phe

50	55	60	
atg gga cgg ttt gcc ttc tct ttg gaa acc tct gcc agc act gcc ttt			240
Met Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Phe			
65	70	75	80
ttg cag atc aac aac ctc gaa aat gag gac acg gct aca tat ttc tgt			288
Leu Gln Ile Asn Asn Leu Glu Asn Glu Asp Thr Ala Thr Tyr Phe Cys			
	85	90	95
gct aga ttt ggt tcc tat gct atg gac tac tgg ggt caa gga acc tca			336
Ala Arg Phe Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser			
	100	105	110
gtn acv gtn tcn tcn			351
Val Xaa Val Xaa Xaa			
	115		

<210> 87
 <211> 117
 <212> PRT
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (114)..(114)
 <223> The 'Xaa' at location 114 stands for Thr.

<220>
 <221> misc_feature
 <222> (116)..(116)
 <223> The 'Xaa' at location 116 stands for Ser.

<220>
 <221> misc_feature
 <222> (117)..(117)
 <223> The 'Xaa' at location 117 stands for Ser.

<400> 87

Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1 5 10 15

Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Asp Tyr
20 25 30

Ser Met His Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met
35 40 45

Gly Trp Ile Asn Thr Glu Thr Val Glu Pro Thr Tyr Ala Asp Asp Phe
50 55 60

Met Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Phe
65 70 75 80

Leu Gln Ile Asn Asn Leu Glu Asn Glu Asp Thr Ala Thr Tyr Phe Cys
85 90 95

Ala Arg Phe Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser
100 105 110

Val Xaa Val Xaa Xaa
115

<210> 88
<211> 318
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (318)
<223> SC16.29 VL

<220>
<221> CDS
<222> (1).. (318)

<400> 88

caa att gtt ctc acc cag tct cca gca atc atg tct gca tct cca ggg	48
Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly	
1 5 10 15	

gag aag gtc acc ata acc tgc agt gcc agc tca agt gta agt tac atg	96
Glu Lys Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met	
20 25 30	

cac tgg ttc cag cag aag cca ggc act tct ccc aaa ctc tgg att tat	144
His Trp Phe Gln Gln Lys Pro Gly Thr Ser Pro Lys Leu Trp Ile Tyr	
35 40 45	

acc aca tcc aac ctg gct tct gga gtc cct gct cgc ttc agt ggc agt	192
Thr Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser	
50 55 60	

gga tct ggg acc tct tac tct ctc aca gtc agc cga atg gag gct gaa	240
Gly Ser Gly Thr Ser Tyr Ser Leu Thr Val Ser Arg Met Glu Ala Glu	
65 70 75 80	

gat gct gcc act tat tac tgc cag caa agg agt ctt tat ccg tac acg	288
Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Arg Ser Leu Tyr Pro Tyr Thr	
85 90 95	

ttc gga ggg ggg acc aag gtg gaa ata aaa	318
Phe Gly Gly Gly Thr Lys Val Glu Ile Lys	
100 105	

<210> 89

<211> 106

<212> PRT

<213> Mus musculus

<400> 89

Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly	
1 5 10 15	

Glu Lys Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met	
20 25 30	

His Trp Phe Gln Gln Lys Pro Gly Thr Ser Pro Lys Leu Trp Ile Tyr
35 40 45

Thr Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Val Ser Arg Met Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Arg Ser Leu Tyr Pro Tyr Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 90
<211> 363
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(363)
<223> SC16.29 VH

<220>
<221> CDS
<222> (1)..(363)

<400> 90
cag gtt cag cta cag cag tct gga gct gag ctg gcg agg ccc ggg gct 48
Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
1 5 10 15

tca gtg aag ctg tcc tgc aag gct tca ggc tac acc ttc act gac cag 96
Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Gln
20 25 30

tat ata aac tgg gtg aag cag agg act gga cag ggc ctt gag tgg att	144
Tyr Ile Asn Trp Val Lys Gln Arg Thr Gly Gln Gly Leu Glu Trp Ile	
35 40 45	

gga gag att tat ccc gga agg ggt aat act tac tac aat gag aag ttc	192
Gly Glu Ile Tyr Pro Gly Arg Gly Asn Thr Tyr Tyr Asn Glu Lys Phe	
50 55 60	

aag ggc aag gcc aca ctg act gca gac aaa tcc tcc agc aca gcc tac	240
Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr	
65 70 75 80	

atg caa ctc agc agc ctg aca tct gag gac tct gca gtc tat ttc tgt	288
Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys	
85 90 95	

gca aga gag gat ggt ggt tac gac gat gcc tgg ttt gct tac tgg ggc	336
Ala Arg Glu Asp Gly Gly Tyr Asp Asp Ala Trp Phe Ala Tyr Trp Gly	
100 105 110	

caa ggg act ctg gtc act gtc tct gca	363
Gln Gly Thr Leu Val Thr Val Ser Ala	
115 120	

<210> 91
 <211> 121
 <212> PRT
 <213> Mus musculus

<400> 91

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Gln
20 25 30

Tyr Ile Asn Trp Val Lys Gln Arg Thr Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Tyr Pro Gly Arg Gly Asn Thr Tyr Tyr Asn Glu Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Glu Asp Gly Gly Tyr Asp Asp Ala Trp Phe Ala Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ala
115 120

<210> 92
<211> 324
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(324)
<223> SC16.30 VL

<220>
<221> CDS
<222> (1)..(324)

<400> 92
caa att gtt ctg acc cag tct cca aca atc atg tct gca tct cta ggg 48
Gln Ile Val Leu Thr Gln Ser Pro Thr Ile Met Ser Ala Ser Leu Gly
1 5 10 15

gaa cgg gtc acc atg acc tgc act gcc agc tca agt gta act tcc agt 96
Glu Arg Val Thr Met Thr Cys Thr Ala Ser Ser Ser Val Thr Ser Ser
20 25 30

tac ttg cac tgg tac cag cag aag cca gga tcc tcc ccc aaa ctc tgg	144
Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Leu Trp	
35 40 45	

att tat agc aca tcc aac ctg gct tct gga gtc cca gct cgc ttc agt	192
Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser	
50 55 60	

ggc agt ggg tct ggg acc tct tac tct ctc aca atc agc agc atg gag	240
Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu	
65 70 75 80	

gct gaa gat gct gcc act tat tac tgc cac cag ttt cat cgt tcc cca	288
Ala Glu Asp Ala Ala Thr Tyr Tyr Cys His Gln Phe His Arg Ser Pro	
85 90 95	

ttc acg ttc ggc tcg ggg aca aag ttg gaa ata aaa	324
Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys	
100 105	

<210> 93
 <211> 108
 <212> PRT
 <213> Mus musculus

<400> 93

Gln Ile Val Leu Thr Gln Ser Pro Thr Ile Met Ser Ala Ser Leu Gly
1 5 10 15

Glu Arg Val Thr Met Thr Cys Thr Ala Ser Ser Ser Val Thr Ser Ser
20 25 30

Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Leu Trp
35 40 45

Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu
65 70 75 80

Ala Glu Asp Ala Ala Thr Tyr Tyr Cys His Gln Phe His Arg Ser Pro
85 90 95

Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
100 105

$\langle 210 \rangle$	94
$\langle 211 \rangle$	360
$\langle 212 \rangle$	DNA
$\langle 213 \rangle$	Mus musculus

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<220>
<221>  misc_feature
<222>  (1).. (360)
<223>  SC16.30 VH

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$\langle 220 \rangle$	
$\langle 221 \rangle$	CDS
$\langle 222 \rangle$	(1) .. (360)

<400> 94
cag gtt act ctg aaa gag tct ggc cct ggg ata ttg cag ccc tcc cag 48
Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Gln Pro Ser Gln
1 5 10 15

acc ctc agt ctg act tgt tct ttc tct ggg ttt tca ctg agc act tct 96
Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser Thr Ser
20 25 30

ggt atg ggt gta ggc tgg att cgt cag cca tca ggg aag ggt ctg gag 144
Gly Met Gly Val Gly Trp Ile Arg Gln Pro Ser Gly Lys Gly Leu Glu
35 40 45

tgg ctg gca cac att tgg tgg gat gat gtc aag cgc tat aaa cca gcc 192
Trp Leu Ala His Ile Trp Trp Asp Asp Val Lys Arg Tyr Lys Pro Ala
50 55 60

ctg aag agc cga ctg act gtc tcc aag gat acc tcc agc aac cag gtt 240
Leu Lys Ser Arg Leu Thr Val Ser Lys Asp Thr Ser Ser Asn Gln Val
65 70 75 80

ttc ctc aag atc gcc act gtg gac gct gca gat act ggc aca tac tac 288
Phe Leu Lys Ile Ala Thr Val Asp Ala Ala Asp Thr Gly Thr Tyr Tyr
85 90 95

tgt gct cga atc gtt gat ggt cac ccc ccg ttt gct tac tgg ggc caa 336
Cys Ala Arg Ile Val Asp Gly His Pro Pro Phe Ala Tyr Trp Gly Gln
100 105 110

ggg act ctg gtc act gtc tct gca 360
Gly Thr Leu Val Thr Val Ser Ala
115 120

<210> 95

 $\langle 211 \rangle$ 120

⟨212⟩ PRT

⟨213⟩ Mus musculus

<400> 95

Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Gln Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser Thr Ser
20 25 30

Gly Met Gly Val Gly Trp Ile Arg Gln Pro Ser Gly Lys Gly Leu Glu
35 40 45

Trp Leu Ala His Ile Trp Trp Asp Asp Val Lys Arg Tyr Lys Pro Ala
50 55 60

Leu Lys Ser Arg Leu Thr Val Ser Lys Asp Thr Ser Ser Asn Gln Val
65 70 75 80

gac agg ttc agt ggc agt ggg tca gga aca gat ttc aca ctc aag atc 240
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

aac tat ctt ccg ctc acg ttc ggt gct ggg acc aag ctg gag ctg aga 336
Asn Tyr Leu Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Arg
100 105 110

<400> 97

Asp Gln Ala Ser Ile Ser Cys Lys Ser Thr Lys Ser Leu Leu Asn Ser
20 25 30

Asp Gly Phe Thr Tyr Leu Asp Trp Tyr Leu Gln Arg Pro Gly Gln Ser
35 40 45

Pro Gln Phe Leu Ile Tyr Leu Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Phe Gln Ser
85 90 95

Asn Tyr Leu Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Arg
100 105 110

$\langle 210 \rangle$	98
$\langle 211 \rangle$	357
$\langle 212 \rangle$	DNA
$\langle 213 \rangle$	Mus musculus

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<220>
<221>  misc_feature
<222>  (1)..(357)
<223>  SC16.31 VH
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$\langle 220 \rangle$	
$\langle 221 \rangle$	CDS
$\langle 222 \rangle$	(1) .. (357)

<400> 98
gag gtc caa ctg cag cag tct gga cct gag ctg gtg aag cct ggg gct 48
Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1 5 10 15

tca gtg aag ata tcc tgc aag gct tct ggt tac tca ttc agt cgt ttc 96
Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Ser Arg Phe
20 25 30

tat atg cac tgg gtg aag caa agt cct gaa aat agt ctt gag tgg att 144
Tyr Met His Trp Val Lys Gln Ser Pro Glu Asn Ser Leu Glu Trp Ile
35 40 45

gga gag att aat cct agc act ggg ggt aca agc tac aac cag aag ttc 192
Gly Glu Ile Asn Pro Ser Thr Gly Gly Thr Ser Tyr Asn Gln Lys Phe
50 55 60

aag ggc aag gcc aca tta act gta gat aaa tcc tcc agc aca gcc tac 240
Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

atg cag ctc aag agc ctg aca tct gaa gag tct gca gtc tat tac tgt 288
Met Gln Leu Lys Ser Leu Thr Ser Glu Glu Ser Ala Val Tyr Tyr Cys
85 90 95

act	agg	ggt	tac	ggg	agc	aac	tgg	tac	ttc	gat	gtc	tgg	ggc	gca	ggg	336
Thr	Arg	Gly	Tyr	Gly	Ser	Asn	Trp	Tyr	Phe	Asp	Val	Trp	Gly	Ala	Gly	
			100					105					110			

acc	acg	gtc	acc	gtc	tcc	aca	357
Thr	Thr	Val	Thr	Val	Ser	Thr	
			115				

<210> 99
 <211> 119
 <212> PRT
 <213> Mus musculus

<400> 99

Glu	Val	Gln	Leu	Gln	Gln	Ser	Gly	Pro	Glu	Leu	Val	Lys	Pro	Gly	Ala
1				5					10					15	

Ser	Val	Lys	Ile	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Ser	Phe	Ser	Arg	Phe
			20					25					30		

Tyr	Met	His	Trp	Val	Lys	Gln	Ser	Pro	Glu	Asn	Ser	Leu	Glu	Trp	Ile
		35				40						45			

Gly	Glu	Ile	Asn	Pro	Ser	Thr	Gly	Gly	Thr	Ser	Tyr	Asn	Gln	Lys	Phe
	50					55					60				

Lys	Gly	Lys	Ala	Thr	Leu	Thr	Val	Asp	Lys	Ser	Ser	Ser	Thr	Ala	Tyr
65					70					75					80

Met	Gln	Leu	Lys	Ser	Leu	Thr	Ser	Glu	Glu	Ser	Ala	Val	Tyr	Tyr	Cys
				85					90					95	

Thr	Arg	Gly	Tyr	Gly	Ser	Asn	Trp	Tyr	Phe	Asp	Val	Trp	Gly	Ala	Gly
			100					105					110		

Thr Thr Val Thr Val Ser Thr
115

<210> 100
<211> 321
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(321)
<223> SC16.34 VL

<220>
<221> CDS
<222> (1)..(321)

<400> 100
agt att gtg atg acc cag act ccc aaa ttc ctg ctt gta tca gca gga 48
Ser Ile Val Met Thr Gln Thr Pro Lys Phe Leu Leu Val Ser Ala Gly
1 5 10 15

gac agg gtt acc ata acc tgc aag gcc agt cag agt gtg agt aat gat 96
Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Ser Val Ser Asn Asp
20 25 30

gta gct tgg tac caa cag aag cca ggg cag tct cct aaa ctg ctg ata 144
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile
35 40 45

tac tat gca tcc aat cgc tac agt gga gtc cct gat cgc ttc act ggc 192
Tyr Tyr Ala Ser Asn Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr Gly
50 55 60

agt gga tat ggg acg gat ttc act ttc acc atc agc act gtg cag gct 240
Ser Gly Tyr Gly Thr Asp Phe Thr Phe Thr Ile Ser Thr Val Gln Ala
65 70 75 80

gaa gac ctg gca gtt tat ttc tgt cag cag gat tat agc tct ccg tgg 288
Glu Asp Leu Ala Val Tyr Phe Cys Gln Gln Asp Tyr Ser Ser Pro Trp
85 90 95

acg ttc ggt gga ggc acc aag ctg gaa atc aaa
 Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 100 105

321

<210> 101
 <211> 107
 <212> PRT
 <213> Mus musculus

<400> 101

Ser Ile Val Met Thr Gln Thr Pro Lys Phe Leu Leu Val Ser Ala Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Ser Val Ser Asn Asp
 20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile
 35 40 45

Tyr Tyr Ala Ser Asn Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr Gly
 50 55 60

Ser Gly Tyr Gly Thr Asp Phe Thr Phe Thr Ile Ser Thr Val Gln Ala
 65 70 75 80

Glu Asp Leu Ala Val Tyr Phe Cys Gln Gln Asp Tyr Ser Ser Pro Trp
 85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 100 105

<210> 102
 <211> 354
 <212> DNA

tct ctc aca gtc tcc tca 354
Ser Leu Thr Val Ser Ser
115

<210> 103
<211> 118
<212> PRT
<213> Mus musculus

<400> 103

Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Arg Pro Gly Glu
1 5 10 15

Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Asp Pro Thr Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Leu Gln Ile Asn Asn Leu Lys Asn Glu Asp Thr Ala Thr Tyr Phe Cys
85 90 95

Ala Arg Ile Gly Gly Asn Ser Pro Ser Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Ser Leu Thr Val Ser Ser
115

<210> 104
<211> 321
<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1).. (321)

<223> SC16.35 VL

<220>

<221> CDS

<222> (1).. (321)

<400> 104

gat atc cag atg aca cag act aca tcc tcc ctg tct gcc tct ctg gga 48

Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly

1 5 10 15

gac aga gtc acc atc agt tgc agg gca agt cag gac att agc aat tat 96

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Asn Tyr

20 25 30

tta aac tgg tat cag cag aaa cca gat gga act gtt aaa ctc ctg atc 144

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile

35 40 45

tac tac aca tca aga tta cac tca gga gtc cca tca agg ttc agt ggc 192

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly

50 55 60

agt ggg tct gga aca gat tat tct ctc acc att agc aac ctg gag caa 240

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln

65 70 75 80

gaa gat att gcc act tac ttt tgc caa cag ggt aat acg ctt ccg tac 288

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr

85 90 95

acg ttc gga ggg ggg acc aag ctg gaa ata aaa 321

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys

100 105

<210> 105

<211> 107

<212> PRT

<213> Mus musculus

<400> 105

Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Asn Tyr
 20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
 35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65 70 75 80

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
 85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 100 105

<210> 106

<211> 360

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1)..(360)

<223> SC16.35 VH

<220>

<221> CDS

<222> (1).. (360)

<400> 106

gat	gtg	cag	ctt	cag	gag	tcg	gga	cct	ggc	ctg	gtg	aaa	cct	tct	cag	48
Asp	Val	Gln	Leu	Gln	Glu	Ser	Gly	Pro	Gly	Leu	Val	Lys	Pro	Ser	Gln	
1			5				10					15				

tct	ctg	tcc	ctc	acc	tgc	act	gtc	act	ggc	tac	tca	atc	acc	agt	gat	96
Ser	Leu	Ser	Leu	Thr	Cys	Thr	Val	Thr	Gly	Tyr	Ser	Ile	Thr	Ser	Asp	
			20				25					30				

tat	gcc	tgg	aac	tgg	atc	cgg	cag	ttt	cca	gga	aac	aaa	ctg	gag	tgg	144
Tyr	Ala	Trp	Asn	Trp	Ile	Arg	Gln	Phe	Pro	Gly	Asn	Lys	Leu	Glu	Trp	
		35				40					45					

atg	ggc	tac	ata	agc	tac	agt	ggt	agc	act	agc	tac	aac	cca	tct	ctc	192
Met	Gly	Tyr	Ile	Ser	Tyr	Ser	Gly	Ser	Thr	Ser	Tyr	Asn	Pro	Ser	Leu	
	50					55					60					

aaa	agt	cga	atc	tct	atc	act	cga	gac	aca	tcc	aag	aac	cag	ttc	ttc	240
Lys	Ser	Arg	Ile	Ser	Ile	Thr	Arg	Asp	Thr	Ser	Lys	Asn	Gln	Phe	Phe	
65				70				75					80			

ctg	cag	ttg	aat	tct	gtg	act	act	gag	gac	aca	gcc	aca	tat	tac	tgt	288
Leu	Gln	Leu	Asn	Ser	Val	Thr	Thr	Glu	Asp	Thr	Ala	Thr	Tyr	Tyr	Cys	
			85					90					95			

gca	aga	ttt	tac	tac	ggt	agt	agc	tat	gct	atg	gac	tac	tgg	ggt	caa	336
Ala	Arg	Phe	Tyr	Tyr	Gly	Ser	Ser	Tyr	Ala	Met	Asp	Tyr	Trp	Gly	Gln	
			100					105					110			

gga	acc	tca	gtc	acc	gtc	tcc	tca									360
Gly	Thr	Ser	Val	Thr	Val	Ser	Ser									
			115				120									

<210> 107

<211> 120

<212> PRT

<213> Mus musculus

<400> 107

Asp Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Ser Leu Ser Leu Thr Cys Thr Val Thr Gly Tyr Ser Ile Thr Ser Asp
20 25 30

Tyr Ala Trp Asn Trp Ile Arg Gln Phe Pro Gly Asn Lys Leu Glu Trp
35 40 45

Met Gly Tyr Ile Ser Tyr Ser Gly Ser Thr Ser Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe
65 70 75 80

Leu Gln Leu Asn Ser Val Thr Thr Glu Asp Thr Ala Thr Tyr Tyr Cys
85 90 95

Ala Arg Phe Tyr Tyr Gly Ser Ser Tyr Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Ser Val Thr Val Ser Ser
115 120

<210> 108

<211> 321

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1)..(321)

<223> SC16.36 VL

<220>

<221> CDS

<222> (1).. (321)

<400> 108

gaa	aca	act	gtg	acc	cag	tct	cca	gca	tcc	ctg	tcc	gtg	act	aca	gga	48
Glu	Thr	Thr	Val	Thr	Gln	Ser	Pro	Ala	Ser	Leu	Ser	Val	Thr	Thr	Gly	
1			5					10					15			

gaa	aaa	gtc	act	atc	aga	tgc	ata	acc	acc	cct	gat	att	gat	gat	gat	96
Glu	Lys	Val	Thr	Ile	Arg	Cys	Ile	Thr	Thr	Pro	Asp	Ile	Asp	Asp	Asp	
		20					25					30				

atg	aac	tgg	tac	cag	cag	aag	cca	ggg	gaa	cct	cct	aac	ctc	ctt	att	144
Met	Asn	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Glu	Pro	Pro	Asn	Leu	Leu	Ile	
	35					40						45				

tca	gaa	ggc	aat	agt	ctt	cgt	cct	gga	gtc	cca	tcc	cga	ttc	tcc	agc	192
Ser	Glu	Gly	Asn	Ser	Leu	Arg	Pro	Gly	Val	Pro	Ser	Arg	Phe	Ser	Ser	
	50					55						60				

agt	ggc	tat	ggc	aca	aat	ttt	gtt	ttt	aca	att	gaa	aac	acg	ctc	tca	240
Ser	Gly	Tyr	Gly	Thr	Asn	Phe	Val	Phe	Thr	Ile	Glu	Asn	Thr	Leu	Ser	
65				70				75				80				

gaa	gat	gtt	gca	gat	tac	tac	tgt	ttg	caa	agt	gat	aac	atg	cca	ttc	288
Glu	Asp	Val	Ala	Asp	Tyr	Tyr	Cys	Leu	Gln	Ser	Asp	Asn	Met	Pro	Phe	
			85					90					95			

acg	ttc	ggc	tcg	ggg	aca	aag	ttg	gaa	ata	aar						321
Thr	Phe	Gly	Ser	Gly	Thr	Lys	Leu	Glu	Ile	Lys						
		100					105									

<210> 109

<211> 107

<212> PRT

<213> Mus musculus

<400> 109

Glu	Thr	Thr	Val	Thr	Gln	Ser	Pro	Ala	Ser	Leu	Ser	Val	Thr	Thr	Gly
1			5					10					15		

Glu Lys Val Thr Ile Arg Cys Ile Thr Thr Pro Asp Ile Asp Asp Asp
20 25 30

Met Asn Trp Tyr Gln Gln Lys Pro Gly Glu Pro Pro Asn Leu Leu Ile
35 40 45

Ser Glu Gly Asn Ser Leu Arg Pro Gly Val Pro Ser Arg Phe Ser Ser
50 55 60

Ser Gly Tyr Gly Thr Asn Phe Val Phe Thr Ile Glu Asn Thr Leu Ser
65 70 75 80

Glu Asp Val Ala Asp Tyr Tyr Cys Leu Gln Ser Asp Asn Met Pro Phe
85 90 95

Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 110
<211> 354
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (354)
<223> SC16.35 VH

<220>
<221> CDS
<222> (1).. (354)

<400> 110
cag gtc cag ctg cag cag tct ggg gct gaa ctg gca aaa cct ggg gcc
Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Ala Lys Pro Gly Ala
1 5 10 15

tca	gtg	aag	atg	tcc	tgc	aag	gct	tct	ggc	tac	acc	ttt	act	acc	tac	96
Ser	Val	Lys	Met	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Thr	Phe	Thr	Thr	Tyr	
		20						25					30			

tgg	atg	cac	tgg	gta	aaa	cag	agg	cct	gga	cag	ggg	ctg	gaa	tgg	att	144
Trp	Met	His	Trp	Val	Lys	Gln	Arg	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Ile	
		35					40					45				

gga	tac	att	aat	cct	agc	agt	ggg	tat	act	gag	tac	aat	cag	aag	ttc	192
Gly	Tyr	Ile	Asn	Pro	Ser	Ser	Gly	Tyr	Thr	Glu	Tyr	Asn	Gln	Lys	Phe	
	50					55					60					

aag	gac	aag	gcc	aca	ttg	act	gca	gac	aaa	tcc	tcc	agc	aca	gcc	tac	240
Lys	Asp	Lys	Ala	Thr	Leu	Thr	Ala	Asp	Lys	Ser	Ser	Ser	Thr	Ala	Tyr	
65					70					75				80		

atg	caa	cta	agc	agc	ctg	aca	tct	gag	gac	tct	tca	gtc	tat	tac	tgt	288
Met	Gln	Leu	Ser	Ser	Leu	Thr	Ser	Glu	Asp	Ser	Ser	Val	Tyr	Tyr	Cys	
			85					90					95			

gca	aga	aag	ggg	agt	aac	agg	ggg	ttt	gct	tac	tgg	ggc	caa	ggg	act	336
Ala	Arg	Lys	Gly	Ser	Asn	Arg	Gly	Phe	Ala	Tyr	Trp	Gly	Gln	Gly	Thr	
		100					105					110				

ctg	gtc	act	gtc	tct	tcn	354
Leu	Val	Thr	Val	Ser	Xaa	
		115				

<210> 111
 <211> 118
 <212> PRT
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (118)..(118)
 <223> The 'Xaa' at location 118 stands for Ser.

<400> 111

Gln	Val	Gln	Leu	Gln	Gln	Ser	Gly	Ala	Glu	Leu	Ala	Lys	Pro	Gly	Ala
1				5				10				15			

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Thr Tyr
20 25 30

Trp Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Ser Gly Tyr Thr Glu Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ser Val Tyr Tyr Cys
85 90 95

Ala Arg Lys Gly Ser Asn Arg Gly Phe Ala Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Xaa
115

<210> 112
<211> 312
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (312)
<223> SC16.38 VL

<220>
<221> CDS
<222> (1).. (312)

<400> 112

caa att gtt ctc acc cag tct cca gca atc atg tct gca tct cca ggg 48
Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1 5 10 15

gag aag gtc acc atg acc tgc agt gcc agc tca agt ata aat tac atg 96
Glu Lys Val Thr Met Thr Cys Ser Ala Ser Ser Ser Ile Asn Tyr Met
20 25 30

cac tgg tac cag cag aag cca ggc acc tcc ccc aaa aga tgg att tat 144
His Trp Tyr Gln Gln Lys Pro Gly Thr Ser Pro Lys Arg Trp Ile Tyr
35 40 45

gac aca tcc aaa ctg gct tct gga gtc cct gct cgc ttc agt ggc agt 192
Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

ggg tct ggg acc tct tat tct ctc aca atc agc agc atg gag gct gaa 240
Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu
65 70 75 80

gat gct gcc act tat tac tgc cat cag cgg agt acg tgg acg ttc ggt 288
Asp Ala Ala Thr Tyr Tyr Cys His Gln Arg Ser Thr Trp Thr Phe Gly
85 90 95

gga ggc acc aag ctg gaa atc aaa 312
Gly Gly Thr Lys Leu Glu Ile Lys
100

<210> 113

<211> 104

<212> PRT

<213> Mus musculus

<400> 113

Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Met Thr Cys Ser Ala Ser Ser Ser Ile Asn Tyr Met
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Thr Ser Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys His Gln Arg Ser Thr Trp Thr Phe Gly
85 90 95

Gly Gly Thr Lys Leu Glu Ile Lys
100

<210> 114
<211> 348
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(348)
<223> SC16.38 VH

<220>
<221> CDS
<222> (1)..(348)

<400> 114
gag gtt cag ctg cag cag tct ggg gca gag ctt gtg aag cca ggg gcc 48
Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Lys Pro Gly Ala
1 5 10 15

tca gtc aag ttg tcc tgc aca gtt tct ggc ttc aac att aaa gac acc 96
Ser Val Lys Leu Ser Cys Thr Val Ser Gly Phe Asn Ile Lys Asp Thr

Gly Arg Ile Asp Pro Ala Asn Gly Asn Thr Lys Tyr Asp Pro Lys Phe
50 55 60

Gln Gly Lys Ala Thr Ile Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr
65 70 75 80

Leu Gln Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Pro Thr Gly Tyr Phe Glu Tyr Trp Gly Gln Gly Thr Thr Leu
100 105 110

Thr Val Ser Ser
115

<210> 116
<211> 321
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(321)
<223> SC16.41 VL

<220>
<221> CDS
<222> (1)..(321)

<400> 116
gat atc cag atg aca cag act aca tcc tcc ctg tct gcc tct ttg gga 48
Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

gac aga gtc acc atc agt tgc agg gca agt cag gat gtt atc aat tat 96
Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Val Ile Asn Tyr

Ser Gly Ser Arg Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Glu Arg Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 118
<211> 351
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (351)
<223> SC16.41 VH

<220>
<221> CDS
<222> (1).. (351)

<400> 118
gaa gtg aag ctt gag gag tct gga gga ggc ttg gtg caa ttt gga gga 48
Glu Val Lys Leu Glu Glu Ser Gly Gly Gly Leu Val Gln Phe Gly Gly
1 5 10 15

tcc atg aaa ctc tct tgt gct gct tct gga ttc act ttt agt gat gcc 96
Ser Met Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Ala
20 25 30

tgg atg gac tgg gtc cgc cag tct cca gag aag ggg ctt gag tgg gtt 144
Trp Met Asp Trp Val Arg Gln Ser Pro Glu Lys Gly Leu Glu Trp Val
35 40 45

gct gaa att aga aac aaa gct aat aat cat gca aca tat tat cct gag 192
Ala Glu Ile Arg Asn Lys Ala Asn Asn His Ala Thr Tyr Tyr Pro Glu

50	55	60	
tct gtg aaa ggg agg ttc acc atc tca aga gat gat tcc aaa agt aga			240
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Arg			
65	70	75	80
gtg tac ctg caa atg aac aac tta aga gct gaa gac act ggc att tat			288
Val Tyr Leu Gln Met Asn Asn Leu Arg Ala Glu Asp Thr Gly Ile Tyr			
	85	90	95
tac tgt acg ggt tac tcc tcg ttt gct tac tgg ggc caa ggg act ctg			336
Tyr Cys Thr Gly Tyr Ser Ser Phe Ala Tyr Trp Gly Gln Gly Thr Leu			
	100	105	110
gtc act gtc tct gca			351
Val Thr Val Ser Ala			
	115		
<210>	119		
<211>	117		
<212>	PRT		
<213>	Mus musculus		
<400>	119		
Glu Val Lys Leu Glu Glu Ser Gly Gly Gly Leu Val Gln Phe Gly Gly			
1	5	10	15
Ser Met Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Ala			
	20	25	30
Trp Met Asp Trp Val Arg Gln Ser Pro Glu Lys Gly Leu Glu Trp Val			
	35	40	45
Ala Glu Ile Arg Asn Lys Ala Asn Asn His Ala Thr Tyr Tyr Pro Glu			
	50	55	60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Arg			
65	70	75	80

Val Tyr Leu Gln Met Asn Asn Leu Arg Ala Glu Asp Thr Gly Ile Tyr
85 90 95

Tyr Cys Thr Gly Tyr Ser Ser Phe Ala Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ala
115

<210> 120
<211> 336
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (336)
<223> SC16.42 VL

<220>
<221> CDS
<222> (1).. (336)

<400> 120
gat gtt ttg atg aca cag tct cca ctc tcc ctg tct gtc agt ctt gga 48
Asp Val Leu Met Thr Gln Ser Pro Leu Ser Leu Ser Val Ser Leu Gly
1 5 10 15

gat caa gcc tcc atc tct tgt aga tct agt cag aac att gta cac agt 96
Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Asn Ile Val His Ser
20 25 30

gat aga tac acc tat tta gaa tgg tac ctg cag aaa cca ggc cag tcg 144
Asp Arg Tyr Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

cca aaa ctc ctg ata tat ggg gtt tcc aac cga ttt tct ggg gtc cca 192
Pro Lys Leu Leu Ile Tyr Gly Val Ser Asn Arg Phe Ser Gly Val Pro

	85	90	95	
gcg ccc cta tgg tcc gat agt agt ttt gct tac tgg ggc caa gga act				336
Ala Pro Leu Trp Ser Asp Ser Ser Phe Ala Tyr Trp Gly Gln Gly Thr				
	100	105	110	
ctg gtc act gtc tct gca				354
Leu Val Thr Val Ser Ala				
	115			
<210> 123				
<211> 118				
<212> PRT				
<213> Mus musculus				
<400> 123				
Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu				
1 5 10 15				
Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Thr Ala				
20 25 30				
Gly Met Gln Trp Val Gln Lys Met Pro Gly Lys Gly Phe Lys Trp Ile				
35 40 45				
Gly Trp Ile Asn Thr His Ser Gly Glu Pro Lys Tyr Ala Asp Asp Phe				
50 55 60				
Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr				
65 70 75 80				
Leu Gln Ile Ser Asn Leu Lys Asp Glu Asp Thr Ala Thr Phe Phe Cys				
85 90 95				
Ala Pro Leu Trp Ser Asp Ser Ser Phe Ala Tyr Trp Gly Gln Gly Thr				
100 105 110				

Leu Val Thr Val Ser Ala
115

<210> 124
<211> 321
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(321)
<223> SC16.45 VL

<220>
<221> CDS
<222> (1)..(321)

<400> 124
gaa atc cag atg acc cag tct cca tcc tct atg tct gca tct ctg gga 48
Glu Ile Gln Met Thr Gln Ser Pro Ser Ser Met Ser Ala Ser Leu Gly
1 5 10 15

gac aga ata acc atc act tgc cag gca act caa gac att gtt aag aat 96
Asp Arg Ile Thr Ile Thr Cys Gln Ala Thr Gln Asp Ile Val Lys Asn
20 25 30

tta aac tgg tat cag cag aaa cca ggg aaa ccc cct tca ttc ctg atc 144
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Pro Pro Ser Phe Leu Ile
35 40 45

tat tat gca act gaa ctg gca gaa ggg gtc cca gca agg ttc agt ggc 192
Tyr Tyr Ala Thr Glu Leu Ala Glu Gly Val Pro Ala Arg Phe Ser Gly
50 55 60

agt ggg tct ggg tca gac tat tct ctg aca atc agc aac ctg gag tct 240
Ser Gly Ser Gly Ser Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Ser
65 70 75 80

gaa gat ttt gca gac tat cac tgt cta cag ttt tat gag ttt ccg ttc 288
Glu Asp Phe Ala Asp Tyr His Cys Leu Gln Phe Tyr Glu Phe Pro Phe

	85	90	95	
acg ttc ggt gct ggg acc aag ctg gag ctg aaa				321
Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys				
	100	105		

$\langle 210 \rangle$	125
$\langle 211 \rangle$	107
$\langle 212 \rangle$	PRT
$\langle 213 \rangle$	Mus musculus

$\langle 400 \rangle$ 125

Glu Ile Gln Met Thr Gln Ser Pro Ser Ser Met Ser Ala Ser Leu Gly
1 5 10 15

Asp Arg Ile Thr Ile Thr Cys Gln Ala Thr Gln Asp Ile Val Lys Asn
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Pro Pro Ser Phe Leu Ile
35 40 45

Tyr Tyr Ala Thr Glu Leu Ala Glu Gly Val Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Ser Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Ser
65 70 75 80

Glu Asp Phe Ala Asp Tyr His Cys Leu Gln Phe Tyr Glu Phe Pro Phe
85 90 95

Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105

$\langle 210 \rangle$	126
$\langle 211 \rangle$	363

<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(363)
<223> SC16.45 VH

<220>
<221> CDS
<222> (1)..(363)

<400> 126
cag gtc cag ctg cag cag tct gga gct gac ctg gta agg cct ggg act 48
Gln Val Gln Leu Gln Gln Ser Gly Ala Asp Leu Val Arg Pro Gly Thr
1 5 10 15

tca gtg aag gtg tcc tgc aag gct tct gga tac tcc ttc act aat tac 96
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Asn Tyr
20 25 30

ctg ata gag tgg gta aag cag agg cca gga cag ggc ctt gag tgg att 144
Leu Ile Glu Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

gga gtg att aat cct gga agt ggt gga act cac tac aat gag aaa ttc 192
Gly Val Ile Asn Pro Gly Ser Gly Gly Thr His Tyr Asn Glu Lys Phe
50 55 60

aag gac aag gca gtt ctg act gca gac aaa tcc tcc act act gcc cac 240
Lys Asp Lys Ala Val Leu Thr Ala Asp Lys Ser Ser Thr Thr Ala His
65 70 75 80

atg cag ctc agc agc ctg aca tct gat gac tct gcg gtc tat ttc tgt 288
Met Gln Leu Ser Ser Leu Thr Ser Asp Asp Ser Ala Val Tyr Phe Cys
85 90 95

gca aga tcc ccc tat gat tat aac gat ggt gct atg gac tac tgg ggt 336
Ala Arg Ser Pro Tyr Asp Tyr Asn Asp Gly Ala Met Asp Tyr Trp Gly
100 105 110

caa gga acc tca gtc acc gtc tct tca 363
Gln Gly Thr Ser Val Thr Val Ser Ser

115

120

<210> 127

<211> 121

<212> PRT

<213> Mus musculus

<400> 127

Gln Val Gln Leu Gln Gln Ser Gly Ala Asp Leu Val Arg Pro Gly Thr
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Asn Tyr
 20 25 30

Leu Ile Glu Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Val Ile Asn Pro Gly Ser Gly Gly Thr His Tyr Asn Glu Lys Phe
 50 55 60

Lys Asp Lys Ala Val Leu Thr Ala Asp Lys Ser Ser Thr Thr Ala His
 65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Asp Asp Ser Ala Val Tyr Phe Cys
 85 90 95

Ala Arg Ser Pro Tyr Asp Tyr Asn Asp Gly Ala Met Asp Tyr Trp Gly
 100 105 110

Gln Gly Thr Ser Val Thr Val Ser Ser
 115 120

<210> 128

<211> 336

<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(336)
<223> SC16.47 VL

<220>
<221> CDS
<222> (1)..(336)

<400> 128
gat gtt gtt ctg acc cag tct cca ctc tct ctg cct gtc aat att gga 48
Asp Val Val Leu Thr Gln Ser Pro Leu Ser Leu Pro Val Asn Ile Gly
1 5 10 15

gat caa gcc tct atc tct tgc aag tct act aag agt ctt ctg aat agt 96
Asp Gln Ala Ser Ile Ser Cys Lys Ser Thr Lys Ser Leu Leu Asn Ser
20 25 30

gat gga ttc act tat ttg gac tgg tat ttg cag agg cca ggc cag tct 144
Asp Gly Phe Thr Tyr Leu Asp Trp Tyr Leu Gln Arg Pro Gly Gln Ser
35 40 45

cca caa ttc cta ata tat ttg gtt tct aat cga ttt tct gga gtt cca 192
Pro Gln Phe Leu Ile Tyr Leu Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

gac agg ttc agt ggc agt ggg tca gga aca gat ttc aca ctc aag atc 240
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

agc aga gtg gag gct gag gat ttg gga gta tat tat tgc ttc cag agt 288
Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Phe Gln Ser
85 90 95

aac tat ctt ccg ctc acg ttc ggt gct ggg acc aag ctg gag ctg aga 336
Asn Tyr Leu Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Arg
100 105 110

<210> 129

<211> 112
<212> PRT
<213> Mus musculus

<400> 129

Asp Val Val Leu Thr Gln Ser Pro Leu Ser Leu Pro Val Asn Ile Gly
1 5 10 15

Asp Gln Ala Ser Ile Ser Cys Lys Ser Thr Lys Ser Leu Leu Asn Ser
20 25 30

Asp Gly Phe Thr Tyr Leu Asp Trp Tyr Leu Gln Arg Pro Gly Gln Ser
35 40 45

Pro Gln Phe Leu Ile Tyr Leu Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Phe Gln Ser
85 90 95

Asn Tyr Leu Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Arg
100 105 110

<210> 130
<211> 357
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(357)
<223> SC16.47 VH

$\langle 222 \rangle$ (1) .. (357)

 $\langle 400 \rangle$ 130

gag gtc caa ctg cag cag tct gga cct gag ctg gtg aag cct ggg gct 48
Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1 5 10 15

tca gtg aag ata tcc tgc aag gct tct ggt tac tca ttc agt cgt ttc 96
Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Ser Arg Phe
20 25 30

tat atg cac tgg gtg aag caa agt cct gaa aat agt ctt gag tgg att 144
Tyr Met His Trp Val Lys Gln Ser Pro Glu Asn Ser Leu Glu Trp Ile
35 40 45

gga gag att aat cct agc act ggg ggt aca agc tac aac cag aag ttc 192
Gly Glu Ile Asn Pro Ser Thr Gly Gly Thr Ser Tyr Asn Gln Lys Phe
50 55 60

aag ggc aag gcc aca tta act gta gat aaa tcc tcc agc aca gcc tac 240
Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

atg cag ctc aag agc ctg aca tct gaa gag tct gca gtc tat tac tgt 288
Met Gln Leu Lys Ser Leu Thr Ser Glu Glu Ser Ala Val Tyr Tyr Cys
85 90 95

act agg ggt tac ggg agc aac tgt tac ttc gat gtc tgg ggc gca ggg 336
Thr Arg Gly Tyr Gly Ser Asn Cys Tyr Phe Asp Val Trp Gly Ala Gly
100 105 110

acc acg gtc acc gtc tcc aca 357
Thr Thr Val Thr Val Ser Thr
115

⟨210⟩ 131

<211> 119

⟨212⟩ PRT

<213> Mus musculus

<400> 131

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Ser Arg Phe
20 25 30

Tyr Met His Trp Val Lys Gln Ser Pro Glu Asn Ser Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asn Pro Ser Thr Gly Gly Thr Ser Tyr Asn Gln Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Lys Ser Leu Thr Ser Glu Glu Ser Ala Val Tyr Tyr Cys
85 90 95

Thr Arg Gly Tyr Gly Ser Asn Cys Tyr Phe Asp Val Trp Gly Ala Gly
100 105 110

Thr Thr Val Thr Val Ser Thr
115

<210> 132

<211> 321

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1)..(321)

<223> SC16.49 VL

$\langle 222 \rangle \quad (1) \dots (321)$

<400> 132

gac atc aag atg acc cag tct cca tct tcc atg tat gca tct cta gga 48
Asp Ile Lys Met Thr Gln Ser Pro Ser Ser Met Tyr Ala Ser Leu Gly
1 5 10 15

gag aga gtc act atc act tgc aag gcg agt cag gac att aat agt tat 96
Glu Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Ile Asn Ser Tyr
20 25 30

tta agc tgg ttc cag cag aaa cca ggg aaa tct cct aag acc ctg atc 144
Leu Ser Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Thr Leu Ile
35 40 45

tat cga gca aac aga ttg gta gat ggg gtc cca tca agg ttc agt ggc 192
Tyr Arg Ala Asn Arg Leu Val Asp Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

agt gga tct ggg caa gat tat tct ctc acc atc acc agc ctg gag tat 240
 Ser Gly Ser Gly Gln Asp Tyr Ser Leu Thr Ile Thr Ser Leu Glu Tyr
 65 70 75 80

gaa gat atg gga att tat tat tgt cta cag tat gat gaa ttt ccg ctc 288
Glu Asp Met Gly Ile Tyr Tyr Cys Leu Gln Tyr Asp Glu Phe Pro Leu
85 90 95

acg ttc ggt gct ggg acc aag ctg gag ctg aaa 321
Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105

<210> 133

<211> 107

⟨212⟩ PRT

⟨213⟩ Mus musculus

<400> 133

Asp Ile Lys Met Thr Gln Ser Pro Ser Ser Met Tyr Ala Ser Leu Gly
1 5 10 15

Glu Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Ile Asn Ser Tyr
20 25 30

Leu Ser Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Thr Leu Ile
35 40 45

Tyr Arg Ala Asn Arg Leu Val Asp Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Gln Asp Tyr Ser Leu Thr Ile Thr Ser Leu Glu Tyr
65 70 75 80

Glu Asp Met Gly Ile Tyr Tyr Cys Leu Gln Tyr Asp Glu Phe Pro Leu
85 90 95

Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105

<210> 134
<211> 351
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (351)
<223> SC16.49 VH

<220>
<221> CDS
<222> (1).. (351)

<400> 134
cag gtt caa ctg cag cag tct gga cct gag ctg gtg aag cct ggg act
Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Thr

1	5	10	15	
tta gtg aag ata tcc tgc aag gct tct ggt tac acc ttc aca agc tac				96
Leu Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr				
20	25	30		
gat ata aac tgg gtg aag cag agg cct gga cag gga ctt gaa tgg att				144
Asp Ile Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile				
35	40	45		
gga tgg att tat cct gga gat ggt aat act aag tac agt gag aaa ttc				192
Gly Trp Ile Tyr Pro Gly Asp Gly Asn Thr Lys Tyr Ser Glu Lys Phe				
50	55	60		
aag ggc aag gcc aca ctg act gca gac aaa tcc tcc agc aca gcc tac				240
Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr				
65	70	75	80	
atg cag ctc acc agc ctg act tct gag aac tct gca gtc tat ttc tgt				288
Met Gln Leu Thr Ser Leu Thr Ser Glu Asn Ser Ala Val Tyr Phe Cys				
85	90	95		
gca aga gac tat gat tac cct ttt gct tac tgg ggc caa ggg act ctg				336
Ala Arg Asp Tyr Asp Tyr Pro Phe Ala Tyr Trp Gly Gln Gly Thr Leu				
100	105	110		
gtc act gtc tct gca				351
Val Thr Val Ser Ala				
115				

<210> 135
 <211> 117
 <212> PRT
 <213> Mus musculus

<400> 135

Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Thr
1 5 10 15

Leu Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asp Ile Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Trp Ile Tyr Pro Gly Asp Gly Asn Thr Lys Tyr Ser Glu Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Thr Ser Leu Thr Ser Glu Asn Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Asp Tyr Asp Tyr Pro Phe Ala Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ala
115

<210> 136
<211> 318
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (318)
<223> SC16.50 VL

<220>
<221> CDS
<222> (1).. (318)

<400> 136
gat atc cag atg aca cag act aca tcc tcc ctg tct gcc tct ctg gga
Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly

1	5	10	15	
gac aga gtc acc atc agt tgc agg gca agt cag gac att agc aat tat				96
Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Asn Tyr				
	20	25	30	
tta aac tgg tat cag cag aaa cca gat gga act gtt aaa ctc ctg atc				144
Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile				
	35	40	45	
tac tac aca tca aga tta cac tca gga gtc cca tca agg ttc agt ggc				192
Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly				
	50	55	60	
agt ggg tct ggt aca gat tat tct ctc acc att agc aac ctg gag caa				240
Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln				
65	70	75	80	
gaa gat att gcc act tac ttt tgc caa cag ggt aat acg ctt cgg acg				288
Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Arg Thr				
	85	90	95	
ttc ggt gga ggc acc aag ctg gaa atc aaa				318
Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys				
	100	105		

<210> 137
 <211> 106
 <212> PRT
 <213> Mus musculus

<400> 137

Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly	
1	5 10 15
Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Asn Tyr	
20 25 30	
Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile	
35 40 45	

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65 70 75 80

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Arg Thr
85 90 95

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 138
<211> 363
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (363)
<223> SC16.50 VH

<220>
<221> CDS
<222> (1).. (363)

<400> 138
gaa gtg cag ctg gtg gag tgt ggg gga tgc tta gtg aag cct gga ggg 48
Glu Val Gln Leu Val Glu Cys Gly Gly Cys Leu Val Lys Pro Gly Gly
1 5 10 15

tac ctg aaa ctc tcc tgt gca gcc tct gga ttc act ttc agt agc tat 96
Tyr Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

gcc atg tct tgg gtt cgc cag tct cca gag aag agg ctg gag tgg gtc 144
Ala Met Ser Trp Val Arg Gln Ser Pro Glu Lys Arg Leu Glu Trp Val

35	40	45	
gca gaa atc agt att ggt ggt agc tac acc tac tat cca gac act gtg			192
Ala Glu Ile Ser Ile Gly Gly Ser Tyr Thr Tyr Tyr Pro Asp Thr Val			
50	55	60	
acg ggc cga ttc acc atc tcc aga gac aat gcc aag aac acc ctg tac			240
Thr Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr			
65	70	75	80
ctg gaa atg agc agt ctg agg tct gag gac acg gcc atg tat tac tgt			288
Leu Glu Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Met Tyr Tyr Cys			
	85	90	95
gca agg gag ggc tat gat tac gac gtg aga gct atg gac tac tgg ggt			336
Ala Arg Glu Gly Tyr Asp Tyr Asp Val Arg Ala Met Asp Tyr Trp Gly			
	100	105	110
caa gga acc tca gtc acc gtc tcc tca			363
Gln Gly Thr Ser Val Thr Val Ser Ser			
	115	120	
<210> 139			
<211> 121			
<212> PRT			
<213> Mus musculus			
<400> 139			
Glu Val Gln Leu Val Glu Cys Gly Gly Cys Leu Val Lys Pro Gly Gly			
1	5	10	15
Tyr Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr			
	20	25	30
Ala Met Ser Trp Val Arg Gln Ser Pro Glu Lys Arg Leu Glu Trp Val			
	35	40	45
Ala Glu Ile Ser Ile Gly Gly Ser Tyr Thr Tyr Tyr Pro Asp Thr Val			
50	55	60	

Thr Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
65 70 75 80

Leu Glu Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Glu Gly Tyr Asp Tyr Asp Val Arg Ala Met Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Ser Val Thr Val Ser Ser
115 120

$\langle 210 \rangle$	140
$\langle 211 \rangle$	321
$\langle 212 \rangle$	DNA
$\langle 213 \rangle$	Mus musculus

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<222>  (1)..(321)
<223>  SC16.52 VL
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$\langle 220 \rangle$	
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$\langle 222 \rangle$	(1).. (321)

<400> 140
gac atc cag atg att cag tct cca tcg tcc atg ttt gcc tct ctg gga 48
Asp Ile Gln Met Ile Gln Ser Pro Ser Ser Met Phe Ala Ser Leu Gly
1 5 10 15

gac aga gtc agt ctc tct tgt cgg gct agt cag ggc att aga ggg act 96
Asp Arg Val Ser Leu Ser Cys Arg Ala Ser Gln Gly Ile Arg Gly Thr
20 25 30

tta gac tgg tat caa cag aaa cca aat gga act att aaa ctc ctg atc 144
Leu Asp Trp Tyr Gln Gln Lys Pro Asn Gly Thr Ile Lys Leu Leu Ile

Glu Asp Phe Ala Asp Tyr Tyr Cys Leu Gln Arg Asn Ala Tyr Pro Leu
85 90 95

Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105

<210> 142
<211> 357
<212> DNA
<213> Mus musculus

<220>
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<222> (1).. (357)
<223> SC16.52 VH

<220>
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<222> (1).. (357)

<400> 142
cag gtg cag ctg aag gag tca gga cct ggc ctg gtg gcg ccc tca cag 48
Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln
1 5 10 15

agc ctg tcc atc acg tgc gct gtc tct gga ttt tca tta acc agc ttt 96
Ser Leu Ser Ile Thr Cys Ala Val Ser Gly Phe Ser Leu Thr Ser Phe
20 25 30

gca ata cac tgg ttt cgc aag cct cca gga aag ggt ctg gag tgg ctg 144
Ala Ile His Trp Phe Arg Lys Pro Pro Gly Lys Gly Leu Glu Trp Leu
35 40 45

gga gta ata tgg act ggt gga acc aca aat tat aat tcg gct ctc atg 192
Gly Val Ile Trp Thr Gly Gly Thr Thr Asn Tyr Asn Ser Ala Leu Met
50 55 60

tcc aga ctg agc atc agc aaa gac aac tcc aag agc caa gtt ttc tta 240
Ser Arg Leu Ser Ile Ser Lys Asp Asn Ser Lys Ser Gln Val Phe Leu

65	70	75	80	
aaa atg aac agt ctg caa act gat gac aca gcc atg tac tac tgt gcc Lys Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Met Tyr Tyr Cys Ala				288
	85	90	95	
aga gac gat tac gac aat aat tat gct atg gac tac tgg ggt caa gga Arg Asp Asp Tyr Asp Asn Asn Tyr Ala Met Asp Tyr Trp Gly Gln Gly				336
	100	105	110	
acc tca gtc acc gtc tcc tca Thr Ser Val Thr Val Ser Ser				357
	115			
<210> 143 <211> 119 <212> PRT <213> Mus musculus				
<400> 143				
Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln 1 5 10 15				
Ser Leu Ser Ile Thr Cys Ala Val Ser Gly Phe Ser Leu Thr Ser Phe 20 25 30				
Ala Ile His Trp Phe Arg Lys Pro Pro Gly Lys Gly Leu Glu Trp Leu 35 40 45				
Gly Val Ile Trp Thr Gly Gly Thr Thr Asn Tyr Asn Ser Ala Leu Met 50 55 60				
Ser Arg Leu Ser Ile Ser Lys Asp Asn Ser Lys Ser Gln Val Phe Leu 65 70 75 80				
Lys Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Met Tyr Tyr Cys Ala 85 90 95				

Arg Asp Asp Tyr Asp Asn Asn Tyr Ala Met Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Ser Val Thr Val Ser Ser
115

<210> 144
<211> 321
<212> DNA
<213> Mus musculus

<220>
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<222> (1)..(321)
<223> SC16.55 VL

<220>
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<222> (1)..(321)

<400> 144
gac atc aag atg acc cag tct cca tct tcc atg tat gca tct cta gga 48
Asp Ile Lys Met Thr Gln Ser Pro Ser Ser Met Tyr Ala Ser Leu Gly
1 5 10 15

gag aga gtc act atc act tgc aag gcg agt cag gac att aat agc tat 96
Glu Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Ile Asn Ser Tyr
20 25 30

tta aac tgg ttc cag cag aaa cca ggg aaa tct cct aag acc ctg atc 144
Leu Asn Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Thr Leu Ile
35 40 45

tat cgt gca aac aga ttg gta gat ggg gtc cca tca agg ttc agt ggc 192
Tyr Arg Ala Asn Arg Leu Val Asp Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

agt gga tct ggg caa gat tat tct ctc acc atc agc agc ctg gag tat 240
Ser Gly Ser Gly Gln Asp Tyr Ser Leu Thr Ile Ser Ser Leu Glu Tyr

65	70	75	80	
gaa gat atg gga att tat tat tgt cta cag tat gat gag ttt ccg tac				288
Glu Asp Met Gly Ile Tyr Tyr Cys Leu Gln Tyr Asp Glu Phe Pro Tyr				
	85	90	95	
acg ttc gga ggg ggg acc aag ctg gaa ata aaa				321
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys				
	100	105		
<210> 145				
<211> 107				
<212> PRT				
<213> Mus musculus				
<400> 145				
Asp Ile Lys Met Thr Gln Ser Pro Ser Ser Met Tyr Ala Ser Leu Gly				
1	5	10	15	
Glu Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Ile Asn Ser Tyr				
	20	25	30	
Leu Asn Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Thr Leu Ile				
	35	40	45	
Tyr Arg Ala Asn Arg Leu Val Asp Gly Val Pro Ser Arg Phe Ser Gly				
	50	55	60	
Ser Gly Ser Gly Gln Asp Tyr Ser Leu Thr Ile Ser Ser Leu Glu Tyr				
65	70	75	80	
Glu Asp Met Gly Ile Tyr Tyr Cys Leu Gln Tyr Asp Glu Phe Pro Tyr				
	85	90	95	
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys				
	100	105		

<210> 146
 <211> 351
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1)..(351)
 <223> SC16.55 VH

<220>
 <221> CDS
 <222> (1)..(351)

<400> 146
 gag gtg cag ctt gtt gag tct ggt gga gga ttg gtg cag cct aaa ggg 48
 Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Lys Gly
 1 5 10 15

tca ttg aaa ctc tca tgt gca gtc tct gca ttc acc ttc act acc tac 96
 Ser Leu Lys Leu Ser Cys Ala Val Ser Ala Phe Thr Phe Thr Thr Tyr
 20 25 30

gcc atg aac tgg gtc cgc cag gct cca gga aag ggt ttg gag tgg gtt 144
 Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

gct cgc ata aga aat aaa agt aat aat tat gca aca tat tat gcc gat 192
 Ala Arg Ile Arg Asn Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
 50 55 60

tca gtg aaa gac agg ttc acc atc tcc aga gat gat tca caa agc atg 240
 Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Gln Ser Met
 65 70 75 80

ctc tat ctg caa atg aac aac ttg aaa att gag gac aca gcc atg tat 288
 Leu Tyr Leu Gln Met Asn Asn Leu Lys Ile Glu Asp Thr Ala Met Tyr
 85 90 95

tac tgt gtg ttc tac tat gat tac gtc tac tgg ggc caa ggg act ctg 336
 Tyr Cys Val Phe Tyr Tyr Asp Tyr Val Tyr Trp Gly Gln Gly Thr Leu

	100	105	110	
	gtc act gtc tct gca			351
	Val Thr Val Ser Ala			
	115			
<210>	147			
<211>	117			
<212>	PRT			
<213>	Mus musculus			
<400>	147			
	Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Lys Gly			
	1 5 10 15			
	Ser Leu Lys Leu Ser Cys Ala Val Ser Ala Phe Thr Phe Thr Thr Tyr			
	20 25 30			
	Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val			
	35 40 45			
	Ala Arg Ile Arg Asn Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp			
	50 55 60			
	Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Gln Ser Met			
	65 70 75 80			
	Leu Tyr Leu Gln Met Asn Asn Leu Lys Ile Glu Asp Thr Ala Met Tyr			
	85 90 95			
	Tyr Cys Val Phe Tyr Tyr Asp Tyr Val Tyr Trp Gly Gln Gly Thr Leu			
	100 105 110			
	Val Thr Val Ser Ala			
	115			

<210> 148
 <211> 321
 <212> DNA
 <213> Mus musculus

<220>
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 <222> (1)..(321)
 <223> SC16.56 VL

<220>
 <221> CDS
 <222> (1)..(321)

<400> 148
 agt att gtg atg acc cag act ccc aaa ttc ctg ctt gta tca gca gga 48
 Ser Ile Val Met Thr Gln Thr Pro Lys Phe Leu Leu Val Ser Ala Gly
 1 5 10 15

 gac agg gtt acc ata acc tgc aag gcc agt cag agt gtg agt aat gat 96
 Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Ser Val Ser Asn Asp
 20 25 30

 gta gta tgg tac caa cag aag cca ggg cag tct cct aaa ctg ctg ata 144
 Val Val Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile
 35 40 45

 tac tat gca tcc aat cgc tac act gga gtc cct gat cgc ttc gct ggc 192
 Tyr Tyr Ala Ser Asn Arg Tyr Thr Gly Val Pro Asp Arg Phe Ala Gly
 50 55 60

 agt gga tat ggg acg gat ttc tct ttc acc atc agc act gtg cag gct 240
 Ser Gly Tyr Gly Thr Asp Phe Ser Phe Thr Ile Ser Thr Val Gln Ala
 65 70 75 80

 gaa gac ctg gca gtt tat ttc tgt cag cag gat tat acc tct ccg tgg 288
 Glu Asp Leu Ala Val Tyr Phe Cys Gln Gln Asp Tyr Thr Ser Pro Trp
 85 90 95

 acg ttc ggt gga ggc acc aag ctg gaa atc aga 321
 Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Arg

100

105

<210> 149

<211> 107

<212> PRT

<213> Mus musculus

<400> 149

Ser Ile Val Met Thr Gln Thr Pro Lys Phe Leu Leu Val Ser Ala Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Ser Val Ser Asn Asp
20 25 30

Val Val Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Ala Ser Asn Arg Tyr Thr Gly Val Pro Asp Arg Phe Ala Gly
50 55 60

Ser Gly Tyr Gly Thr Asp Phe Ser Phe Thr Ile Ser Thr Val Gln Ala
65 70 75 80

Glu Asp Leu Ala Val Tyr Phe Cys Gln Gln Asp Tyr Thr Ser Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Arg
100 105

<210> 150

<211> 354

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1).. (354)

<223> SC16.56 VH

<220>

<221> CDS

<222> (1).. (354)

<400> 150

cag atc cag ttg gtg cag tct gga cct gaa ctg aag aag cct gga gag	48
Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu	
1 5 10 15	

aca gtc aag atc tcc tgc aag gct tct ggg tat acc ttc aca aac tat	96
Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr	
20 25 30	

gga atg aac tgg gtg aag cag gct cca gga aag ggt tta aag tgg atg	144
Gly Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met	
35 40 45	

gcc tgg ata aac acc tac act gga gag cca aca tat gct gat gac ttc	192
Ala Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe	
50 55 60	

aag gga cgg ttt gcc ttc tct ttg gaa acc tct gcc agc act gcc tct	240
Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Ser	
65 70 75 80	

ttg cag atc atc aac ctc aaa aat gag gac acg gct aca tat ttc tgt	288
Leu Gln Ile Ile Asn Leu Lys Asn Glu Asp Thr Ala Thr Tyr Phe Cys	
85 90 95	

gca agg atc ggc gat agt agt ccc tct gac tac tgg ggg cag ggc acc	336
Ala Arg Ile Gly Asp Ser Ser Pro Ser Asp Tyr Trp Gly Gln Gly Thr	
100 105 110	

act ctc aca gtc tcc tca	354
Thr Leu Thr Val Ser Ser	
115	

<210> 151

<211> 118
<212> PRT
<213> Mus musculus

<400> 151

Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1 5 10 15

Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met
35 40 45

Ala Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Ser
65 70 75 80

Leu Gln Ile Ile Asn Leu Lys Asn Glu Asp Thr Ala Thr Tyr Phe Cys
85 90 95

Ala Arg Ile Gly Asp Ser Ser Pro Ser Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Thr Leu Thr Val Ser Ser
115

<210> 152
<211> 321
<212> DNA
<213> Mus musculus

<220>

<221> misc_feature

<222> (1).. (321)

<223> SC16.57 VL

<220>

<221> CDS

<222> (1).. (321)

<400> 152

gac att gtg atg acc cag tct cac aaa ttc atg tcc ata tca gta gga	48
Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Ile Ser Val Gly	
1 5 10 15	

gac agg gtc agc atc acc tgc aag gcc agt cag gat gtg agt att ttt	96
Asp Arg Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Ile Phe	
20 25 30	

gta gcc tgg tat caa cag aaa cca gga caa tct cct aaa cta ctg att	144
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile	
35 40 45	

tac tcg gca tcc tac cgg tac act gga gtc cct gat cgc ttc act ggc	192
Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Thr Gly	
50 55 60	

agt gga tct ggg acg gat ttc att ttc acc atc agc agt gtg cag gct	240
Ser Gly Ser Gly Thr Asp Phe Ile Phe Thr Ile Ser Ser Val Gln Ala	
65 70 75 80	

gaa gac ctg gca gtt tac tac tgt cag caa cat tat ggt act cca ttc	288
Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Gly Thr Pro Phe	
85 90 95	

acg ttc ggc tcg ggg aca aag ttg aaa ata aga	321
Thr Phe Gly Ser Gly Thr Lys Leu Lys Ile Arg	
100 105	

<210> 153

<211> 107

<212> PRT

<213> Mus musculus

<400> 153

Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Ile Ser Val Gly
1 5 10 15

Asp Arg Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Ser Ile Phe
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Thr Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Ile Phe Thr Ile Ser Ser Val Gln Ala
65 70 75 80

Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Gly Thr Pro Phe
85 90 95

Thr Phe Gly Ser Gly Thr Lys Leu Lys Ile Arg
100 105

<210> 154

<211> 354

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1)..(354)

<223> SC16.57 VH

<220>

<221> CDS

<222> (1)..(354)

<400> 154

gaa	gtg	aaa	ctg	gtg	gag	tct	ggg	gga	gac	tta	gtg	aag	cct	gga	ggg	48
Glu	Val	Lys	Leu	Val	Glu	Ser	Gly	Gly	Asp	Leu	Val	Lys	Pro	Gly	Gly	
1			5					10					15			

tcc	cta	aaa	ctc	tcc	tgt	gca	gcc	tct	gga	ttc	gct	ttc	agt	agt	tat	96
Ser	Leu	Lys	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Ala	Phe	Ser	Ser	Tyr	
		20					25				30					

gac	atg	tct	tgg	gtt	cgc	cag	act	ccg	gag	aag	aga	ctg	gag	tgg	gtc	144
Asp	Met	Ser	Trp	Val	Arg	Gln	Thr	Pro	Glu	Lys	Arg	Leu	Glu	Trp	Val	
	35				40						45					

gca	acc	att	agc	agt	ggg	ggg	agt	tac	acc	tat	tat	cca	gac	agt	gtg	192
Ala	Thr	Ile	Ser	Ser	Gly	Gly	Ser	Tyr	Thr	Tyr	Tyr	Pro	Asp	Ser	Val	
	50				55					60						

aag	ggc	cga	ttc	acc	atc	tcc	aga	gac	aat	gtc	agg	gac	acc	ctg	tac	240
Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Val	Arg	Asp	Thr	Leu	Tyr	
65			70					75					80			

ctg	caa	atg	agc	agt	ttg	agg	tct	gag	gac	acg	gcc	ttg	tat	tac	tgt	288
Leu	Gln	Met	Ser	Ser	Leu	Arg	Ser	Glu	Asp	Thr	Ala	Leu	Tyr	Tyr	Cys	
			85					90				95				

gca	aga	cag	gca	att	ggg	acg	tac	ttt	gac	tac	tgg	ggc	caa	ggc	acc	336
Ala	Arg	Gln	Ala	Ile	Gly	Thr	Tyr	Phe	Asp	Tyr	Trp	Gly	Gln	Gly	Thr	
		100					105					110				

act	ctc	aca	gtc	tcc	tca											354
Thr	Leu	Thr	Val	Ser	Ser											
		115														

<210> 155

<211> 118

<212> PRT

<213> Mus musculus

<400> 155

Glu	Val	Lys	Leu	Val	Glu	Ser	Gly	Gly	Asp	Leu	Val	Lys	Pro	Gly	Gly
1			5					10					15		

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Ala Phe Ser Ser Tyr
20 25 30

Asp Met Ser Trp Val Arg Gln Thr Pro Glu Lys Arg Leu Glu Trp Val
35 40 45

Ala Thr Ile Ser Ser Gly Gly Ser Tyr Thr Tyr Tyr Pro Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Val Arg Asp Thr Leu Tyr
65 70 75 80

Leu Gln Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95

Ala Arg Gln Ala Ile Gly Thr Tyr Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Thr Leu Thr Val Ser Ser
115

<210> 156
<211> 321
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (321)
<223> SC16.58 VL

<220>
<221> CDS
<222> (1).. (321)

<400> 156

gac atc cag atg act cag tct cca gcc tcc cta tct tca tct gtg gga	48
Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ser Ser Val Gly	
1 5 10 15	

gaa act gtc acc atc aca tgt cga gca agt gag aat att tac agt tat	96
Glu Thr Val Thr Ile Thr Cys Arg Ala Ser Glu Asn Ile Tyr Ser Tyr	
20 25 30	

tta gca tgg tat cag cag aaa cag gga aaa tct cct cag ctc ctg gtc	144
Leu Ala Trp Tyr Gln Gln Lys Gln Gly Lys Ser Pro Gln Leu Leu Val	
35 40 45	

tat aat gca aaa act tta gca gaa ggt gtg cca tca agg ttc agt ggc	192
Tyr Asn Ala Lys Thr Leu Ala Glu Gly Val Pro Ser Arg Phe Ser Gly	
50 55 60	

agt gga tca ggc aca cag ttt tct ctg aag atc aac agc ctg cag cct	240
Ser Gly Ser Gly Thr Gln Phe Ser Leu Lys Ile Asn Ser Leu Gln Pro	
65 70 75 80	

gaa gat ttt ggg act tat tac tgt caa cat cat tat gat tct ccg ctc	288
Glu Asp Phe Gly Thr Tyr Tyr Cys Gln His His Tyr Asp Ser Pro Leu	
85 90 95	

acg ttc ggt gct ggg acc aag ctg gag ctg aga	321
Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Arg	
100 105	

<210> 157

<211> 107

<212> PRT

<213> Mus musculus

<400> 157

Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ser Ser Val Gly	
1 5 10 15	

Glu Thr Val Thr Ile Thr Cys Arg Ala Ser Glu Asn Ile Tyr Ser Tyr	
20 25 30	

Leu Ala Trp Tyr Gln Gln Lys Gln Gly Lys Ser Pro Gln Leu Leu Val
35 40 45

Tyr Asn Ala Lys Thr Leu Ala Glu Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Gln Phe Ser Leu Lys Ile Asn Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Gly Thr Tyr Tyr Cys Gln His His Tyr Asp Ser Pro Leu
85 90 95

Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Arg
100 105

<210> 158
<211> 360
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(360)
<223> SC16.58 VH

<220>
<221> CDS
<222> (1)..(360)

<400> 158
gat gtg cag ctg gtg gag tct ggg gga ggc tta gtg cag cct gga ggg 48
Asp Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

tcc cgg aaa ctc tcc tgt gca gcc tct gga ttc act ttc agt agc ttt 96
Ser Arg Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Phe

Ala Tyr Ile Ser Ser Gly Ser Ser Asn Ile Tyr Tyr Ala Asp Thr Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Pro Lys Asn Thr Leu Phe
65 70 75 80

Leu Gln Met Thr Ser Leu Arg Ser Glu Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Gly Tyr Tyr Gly Asn Tyr Asp Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Ser Val Thr Val Ser Ser
115 120

<210> 160
<211> 339
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (339)
<223> SC16.61 VL

<220>
<221> CDS
<222> (1).. (339)

<400> 160
gat att gtg atg aca cag tct aca tcc tcc ctg gct atg tca gta gga 48
Asp Ile Val Met Thr Gln Ser Thr Ser Ser Leu Ala Met Ser Val Gly
1 5 10 15

cag aag gtc act atg agc tgc aag tcc agt cag agc ctt tta aat agt 96
Gln Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser

Ser Pro Lys Leu Leu Val Ser Phe Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Gly Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln
85 90 95

His Tyr Ser Ile Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu
100 105 110

Lys

<210> 162
<211> 360
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(360)
<223> SC16.61 VH

<220>
<221> CDS
<222> (1)..(360)

<400> 162
gag gtc ctg ctc caa cgg tct gga cct gac ctg gtg aag cct ggg gct 48
Glu Val Leu Leu Gln Arg Ser Gly Pro Asp Leu Val Lys Pro Gly Ala
1 5 10 15

tca gtg acg ata ccc tgc aag gct tct gga tac aca ttc act gac tac 96
Ser Val Thr Ile Pro Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr

Gly Asn Ile Asn Thr Tyr Asn Gly Gly Thr Ile Tyr Asn Gln Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Pro Ser Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Leu Arg Tyr Gly Gly His Tyr Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Ala Leu Thr Val Ser Ser
115 120

<210> 164
<211> 321
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(321)
<223> SC16.62 VL

<220>
<221> CDS
<222> (1)..(321)

<400> 164
gac atc aag atg acc cag tct cca tct tcc atg tat gca tct cta gga 48
Asp Ile Lys Met Thr Gln Ser Pro Ser Ser Met Tyr Ala Ser Leu Gly
1 5 10 15

gag aga gtc act atc act tgc aag gcg agt cag gac att aat agc ttt 96
Glu Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Ile Asn Ser Phe

Ser Gly Ser Gly Gln Glu Phe Ser Leu Thr Ile Ser Ser Leu Glu Tyr
65 70 75 80

Glu Asp Leu Gly Ile Tyr Tyr Cys Leu Gln Tyr Asp Glu Phe Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 166
<211> 351
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (351)
<223> SC16.62 VH

<220>
<221> CDS
<222> (1).. (351)

<400> 166
gaa gtg atg ctg gta gag tct ggg gga gac tta gtg aag cct gga ggg 48
Glu Val Met Leu Val Glu Ser Gly Gly Asp Leu Val Lys Pro Gly Gly
1 5 10 15

tcc ctg aaa ctc tcc tgt gca gcc tct gga ttc act ttc agt agc tat 96
Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

gcc atg tct tgg gtt cgc cag act ccg gag aag agg ctg gag tgg gtc 144
Ala Met Ser Trp Val Arg Gln Thr Pro Glu Lys Arg Leu Glu Trp Val
35 40 45

gca tac att agc ggt ggt ggt gat cac atc tat tat cca gac agt gtg 192
Ala Tyr Ile Ser Gly Gly Gly Asp His Ile Tyr Tyr Pro Asp Ser Val

50	55	60	
agg ggc cga ttc acc atc tcc aga gac aat gcc aag gac acc ctg tac			240
Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asp Thr Leu Tyr			
65	70	75	80
ctg caa atg agc agt ctg agg tct gag gac acg gcc ttg tat gac tgt			288
Leu Gln Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Leu Tyr Asp Cys			
	85	90	95
gca aga gtg aga gac tgg tac ttc gat gtc tgg ggc gca ggg acc acg			336
Ala Arg Val Arg Asp Trp Tyr Phe Asp Val Trp Gly Ala Gly Thr Thr			
	100	105	110
gtc acc gtc tcc tca			351
Val Thr Val Ser Ser			
	115		
<210>	167		
<211>	117		
<212>	PRT		
<213>	Mus musculus		
<400>	167		
Glu Val Met Leu Val Glu Ser Gly Gly Asp Leu Val Lys Pro Gly Gly			
1	5	10	15
Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr			
	20	25	30
Ala Met Ser Trp Val Arg Gln Thr Pro Glu Lys Arg Leu Glu Trp Val			
	35	40	45
Ala Tyr Ile Ser Gly Gly Gly Asp His Ile Tyr Tyr Pro Asp Ser Val			
	50	55	60
Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asp Thr Leu Tyr			
65	70	75	80

Leu Gln Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Leu Tyr Asp Cys
85 90 95

Ala Arg Val Arg Asp Trp Tyr Phe Asp Val Trp Gly Ala Gly Thr Thr
100 105 110

Val Thr Val Ser Ser
115

<210> 168
<211> 318
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (318)
<223> SC16.63 VL

<220>
<221> CDS
<222> (1).. (318)

<400> 168
caa att gtt ctc acc cag tct cca gca atc atg tct gca tct cca ggg 48
Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1 5 10 15

gag aag gtc acc atg acc tgc agt gcc agc tca agt gtc agt tac atg 96
Glu Lys Val Thr Met Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

tac tgg tac cag cag aag tca ggc acc tcc ccc aaa aga tgg att tat 144
Tyr Trp Tyr Gln Gln Lys Ser Gly Thr Ser Pro Lys Arg Trp Ile Tyr
35 40 45

gac aca tcc aaa ctg gct tct gga gtc cct gct cgc ttc agt ggc agt 192
Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser

50	55	60	
ggg tct ggg acc tct tac tct ctc aca atc agc agc atg gag gct gaa	240		
Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu			
65	70	75	80
gat gct gcc act tat tac tgc cag cag tgg agt agt aac ccg tac acg	288		
Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Tyr Thr			
85	90	95	
ttc gga ggg ggg acc aag ctg gaa ata aar	318		
Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys			
100	105		

Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1 5 10 15

Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 170
<211> 342
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(342)
<223> SC16.63 VH

<220>
<221> CDS
<222> (1)..(342)

<400> 170
cag gtt cag ctg cag cag tct gga act gag ctg ctg agg cct ggg gcc 48
Gln Val Gln Leu Gln Gln Ser Gly Thr Glu Leu Leu Arg Pro Gly Ala
1 5 10 15

tca gtg aag ata tcc tgc aag gct act ggc tac aca ttc agt agc tac 96
Ser Val Lys Ile Ser Cys Lys Ala Thr Gly Tyr Thr Phe Ser Ser Tyr
20 25 30

tgg atg gag tgg gta aag cag agg cct gga cat ggc ctt gag tgg att 144
Trp Met Glu Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp Ile
35 40 45

gga gag att tta cct gga agt ggt act act cag tac aat gag aag ttc 192
Gly Glu Ile Leu Pro Gly Ser Gly Thr Thr Gln Tyr Asn Glu Lys Phe
50 55 60

aag ggc aag gcc acc ttc act gca gat aca tcc tcc aac aca gcc tac 240
Lys Gly Lys Ala Thr Phe Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr
65 70 75 80

atg cat ctc agc agc ctg aca tct gag gac tct gcc gtc tat tac tgt 288
Met His Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys

	85	90	95	
gca aga ggg act aac tct ctc tgg ggc caa ggg act ctg gtc act gtc				336
Ala Arg Gly Thr Asn Ser Leu Trp Gly Gln Gly Thr Leu Val Thr Val				
	100	105	110	

tct gca		342
Ser Ala		

<210> 171
 <211> 114
 <212> PRT
 <213> Mus musculus

 <400> 171

Gln Val Gln Leu Gln Gln Ser Gly Thr Glu Leu Leu Arg Pro Gly Ala
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Thr Gly Tyr Thr Phe Ser Ser Tyr
20 25 30

Trp Met Glu Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Leu Pro Gly Ser Gly Thr Thr Gln Tyr Asn Glu Lys Phe
50 55 60

Lys Gly Lys Ala Thr Phe Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr
65 70 75 80

Met His Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Thr Asn Ser Leu Trp Gly Gln Gly Thr Leu Val Thr Val
100 105 110

Ser Ala

<210> 172
<211> 318
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(318)
<223> SC16.65 VL

<220>
<221> CDS
<222> (1)..(318)

<400> 172
caa att gtt ctc acc cag tct cca gca ctc atg tct gca tct cca ggg 48
Gln Ile Val Leu Thr Gln Ser Pro Ala Leu Met Ser Ala Ser Pro Gly
1 5 10 15

gag aag gtc acc atg acc tgc agt gtc acc tca agt gta agt tac atg 96
Glu Lys Val Thr Met Thr Cys Ser Val Thr Ser Ser Val Ser Tyr Met
20 25 30

tac tgg tac cag cag aag cct aga tcc tcc ccc aaa ccc tgg att tat 144
Tyr Trp Tyr Gln Gln Lys Pro Arg Ser Ser Pro Lys Pro Trp Ile Tyr
35 40 45

ctc aca tcc aac ctg gct tct gga gtc cct gct cgc ttc agt ggc agt 192
Leu Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

ggg tct ggg acc tct tac tct ctc aca atc agc agc gtg gag gct gaa 240
Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Val Glu Ala Glu
65 70 75 80

gat gct gcc act tat tac tgc cag cag tgg agg aat aac cca ttc acg 288
Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Arg Asn Asn Pro Phe Thr

85	90	95	
ttc ggc tcg ggg aca aag gtg gaa ata aaa			318
Phe Gly Ser Gly Thr Lys Val Glu Ile Lys			
100	105		

$\langle 210 \rangle$	173
$\langle 211 \rangle$	106
$\langle 212 \rangle$	PRT
$\langle 213 \rangle$	Mus musculus

<400> 173

Gln Ile Val Leu Thr Gln Ser Pro Ala Leu Met Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Met Thr Cys Ser Val Thr Ser Ser Val Ser Tyr Met
20 25 30

Tyr Trp Tyr Gln Gln Lys Pro Arg Ser Ser Pro Lys Pro Trp Ile Tyr
35 40 45

Leu Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Val Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Arg Asn Asn Pro Phe Thr
85 90 95

Phe Gly Ser Gly Thr Lys Val Glu Ile Lys
100 105

$\langle 210 \rangle$	174
$\langle 211 \rangle$	372

<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (372)
<223> SC16.65 VH

<220>
<221> CDS
<222> (1).. (372)

<400> 174

cag gtt act ctg aaa gag tct ggc cct ggg ata ttg cag ccc tcc cag	48
Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Gln Pro Ser Gln	
1 5 10 15	

acc ctc agt ctg act tgt tct ttc tct ggg ttt tca ctg agc act tct	96
Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser Thr Ser	
20 25 30	

ggg atg ggt gta ggc tgg att cgt cag cca tca ggg aag ggt ctg gag	144
Gly Met Gly Val Gly Trp Ile Arg Gln Pro Ser Gly Lys Gly Leu Glu	
35 40 45	

tgg ctg gca ctc att tgg tgg gat gat gtc aag cgc tat aat cca gcc	192
Trp Leu Ala Leu Ile Trp Trp Asp Asp Val Lys Arg Tyr Asn Pro Ala	
50 55 60	

ctg aag agt cga ctg act atc tcc aag gat gcc tcc agc agc cag gtc	240
Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Ala Ser Ser Ser Gln Val	
65 70 75 80	

ttc ctc aag atc gcc agt gtg gac act gca gat act gcc aca tac tac	288
Phe Leu Lys Ile Ala Ser Val Asp Thr Ala Asp Thr Ala Thr Tyr Tyr	
85 90 95	

tgt gct cga ata gct tcc tat gat tac gac gta gtc tat gct atg gac	336
Cys Ala Arg Ile Ala Ser Tyr Asp Tyr Asp Val Val Tyr Ala Met Asp	
100 105 110	

tac tgg ggt caa gga acc tca gtc agc gtc tcc tca	372
Tyr Trp Gly Gln Gly Thr Ser Val Ser Val Ser Ser	

115

120

<210> 175

<211> 124

<212> PRT

<213> Mus musculus

<400> 175

Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Gln Pro Ser Gln
 1 5 10 15

Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser Thr Ser
 20 25 30

Gly Met Gly Val Gly Trp Ile Arg Gln Pro Ser Gly Lys Gly Leu Glu
 35 40 45

Trp Leu Ala Leu Ile Trp Trp Asp Asp Val Lys Arg Tyr Asn Pro Ala
 50 55 60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Ala Ser Ser Ser Gln Val
 65 70 75 80

Phe Leu Lys Ile Ala Ser Val Asp Thr Ala Asp Thr Ala Thr Tyr Tyr
 85 90 95

Cys Ala Arg Ile Ala Ser Tyr Asp Tyr Asp Val Val Tyr Ala Met Asp
 100 105 110

Tyr Trp Gly Gln Gly Thr Ser Val Ser Val Ser Ser
 115 120

<210> 176

<211> 327

<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (327)
<223> SC16.67 VL

<220>
<221> CDS
<222> (1).. (327)

<400> 176
cag gct gtt gtg act cag gaa tct gca ctc acc aca tca cct ggt gaa 48
Gln Ala Val Val Thr Gln Glu Ser Ala Leu Thr Thr Ser Pro Gly Glu
1 5 10 15

aca gtc aca ctc act tgt cgc tca agt act ggg gct gtt aca act agt 96
Thr Val Thr Leu Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Thr Ser
20 25 30

aac tat gcc aac tgg atc caa gaa aaa cca gat cat tta ttc act ggt 144
Asn Tyr Ala Asn Trp Ile Gln Glu Lys Pro Asp His Leu Phe Thr Gly
35 40 45

cta ata ggt ggt acc aac aac cga gct cca ggt gtt cct gcc aga ttc 192
Leu Ile Gly Gly Thr Asn Asn Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

tca ggc tcc ctg att gga gac aag gct gcc ctc acc atc aca ggg gca 240
Ser Gly Ser Leu Ile Gly Asp Lys Ala Ala Leu Thr Ile Thr Gly Ala
65 70 75 80

cag act gag gat gag gca ata tat ttc tgt ggt cta tgg tac agc aac 288
Gln Thr Glu Asp Glu Ala Ile Tyr Phe Cys Gly Leu Trp Tyr Ser Asn
85 90 95

cat ttg gtg ttc ggt gga gga acc aaa ctg act gtc cta 327
His Leu Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 177

<211> 109
<212> PRT
<213> Mus musculus

<400> 177

Gln Ala Val Val Thr Gln Glu Ser Ala Leu Thr Thr Ser Pro Gly Glu
1 5 10 15

Thr Val Thr Leu Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Ile Gln Glu Lys Pro Asp His Leu Phe Thr Gly
35 40 45

Leu Ile Gly Gly Thr Asn Asn Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Ile Gly Asp Lys Ala Ala Leu Thr Ile Thr Gly Ala
65 70 75 80

Gln Thr Glu Asp Glu Ala Ile Tyr Phe Cys Gly Leu Trp Tyr Ser Asn
85 90 95

His Leu Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 178
<211> 351
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(351)
<223> SC16.67 VH

<220>

<221> CDS

<222> (1)..(351)

<400> 178

gag	gtg	cag	ctt	gtt	gag	act	ggt	gga	gga	ttg	gtg	cag	cct	aaa	ggg	48
Glu	Val	Gln	Leu	Val	Glu	Thr	Gly	Gly	Gly	Leu	Val	Gln	Pro	Lys	Gly	
1				5					10					15		

tca	ttg	aaa	ctc	tca	tgt	gca	gtc	tct	gca	ttc	acc	ttc	act	acc	tac	96
Ser	Leu	Lys	Leu	Ser	Cys	Ala	Val	Ser	Ala	Phe	Thr	Phe	Thr	Thr	Tyr	
		20					25					30				

gcc	atg	aac	tgg	gtc	cgc	cag	gct	cca	gga	aag	ggt	ttg	gag	tgg	gtt	144
Ala	Met	Asn	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val	
		35				40					45					

gct	cgc	ata	aga	aat	aaa	agt	aat	aat	tat	gca	aca	tat	tat	gcc	gat	192
Ala	Arg	Ile	Arg	Asn	Lys	Ser	Asn	Asn	Tyr	Ala	Thr	Tyr	Tyr	Ala	Asp	
	50				55				60							

tca	gtg	aaa	gac	agg	ttc	acc	atc	tcc	aga	gat	gat	tca	caa	agc	atg	240
Ser	Val	Lys	Asp	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asp	Ser	Gln	Ser	Met	
65				70					75					80		

ctc	tat	ctg	caa	atg	aac	aac	ttg	aaa	att	gag	gac	aca	gcc	atg	tat	288
Leu	Tyr	Leu	Gln	Met	Asn	Asn	Leu	Lys	Ile	Glu	Asp	Thr	Ala	Met	Tyr	
			85					90					95			

tac	tgt	gtg	ttc	tac	tat	gat	tac	gtc	tac	tgg	ggc	caa	ggg	act	ctg	336
Tyr	Cys	Val	Phe	Tyr	Tyr	Asp	Tyr	Val	Tyr	Trp	Gly	Gln	Gly	Thr	Leu	
		100					105					110				

gtc	act	gtc	tct	gca												351
Val	Thr	Val	Ser	Ala												
		115														

<210> 179

<211> 117

<212> PRT

<213> Mus musculus

<400> 179

Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Lys Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Val Ser Ala Phe Thr Phe Thr Thr Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Asn Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Gln Ser Met
65 70 75 80

Leu Tyr Leu Gln Met Asn Asn Leu Lys Ile Glu Asp Thr Ala Met Tyr
85 90 95

Tyr Cys Val Phe Tyr Tyr Asp Tyr Val Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ala
115

<210> 180

<211> 321

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1)..(321)

<223> SC16.68 VL

<220>

<221> CDS

<222> (1)..(321)

<400> 180

gaa	aca	act	gtg	acc	cag	tct	cca	gca	ttc	ctg	tcc	gtg	gct	aca	gga	48
Glu	Thr	Thr	Val	Thr	Gln	Ser	Pro	Ala	Phe	Leu	Ser	Val	Ala	Thr	Gly	
1				5					10					15		

gaa	aaa	gtc	act	atc	aga	tgc	ata	acc	agc	act	gat	att	gat	gat	gat	96
Glu	Lys	Val	Thr	Ile	Arg	Cys	Ile	Thr	Ser	Thr	Asp	Ile	Asp	Asp	Asp	
		20					25					30				

atg	aac	tgg	tac	cag	cag	aag	cca	ggg	gaa	cct	cct	aat	gtc	ctt	att	144
Met	Asn	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Glu	Pro	Pro	Asn	Val	Leu	Ile	
		35					40					45				

tca	gaa	ggc	aat	act	ctt	cgt	cct	gga	gtc	cca	tcc	cga	ttc	tcc	agc	192
Ser	Glu	Gly	Asn	Thr	Leu	Arg	Pro	Gly	Val	Pro	Ser	Arg	Phe	Ser	Ser	
	50					55				60						

agt	ggc	tat	ggc	aca	gat	ttt	gtt	ttt	aca	att	gaa	aac	acg	ctc	tca	240
Ser	Gly	Tyr	Gly	Thr	Asp	Phe	Val	Phe	Thr	Ile	Glu	Asn	Thr	Leu	Ser	
65				70					75					80		

gaa	gat	gtt	gca	gat	tac	tac	tgt	ttg	caa	agt	gat	aac	atg	cct	ctc	288
Glu	Asp	Val	Ala	Asp	Tyr	Tyr	Cys	Leu	Gln	Ser	Asp	Asn	Met	Pro	Leu	
				85					90					95		

acg	ttc	ggt	gct	ggg	acc	aag	ctg	gag	ctg	aaa						321
Thr	Phe	Gly	Ala	Gly	Thr	Lys	Leu	Glu	Leu	Lys						
			100					105								

<210> 181

<211> 107

<212> PRT

<213> Mus musculus

<400> 181

Glu	Thr	Thr	Val	Thr	Gln	Ser	Pro	Ala	Phe	Leu	Ser	Val	Ala	Thr	Gly
1				5					10					15	

Glu Lys Val Thr Ile Arg Cys Ile Thr Ser Thr Asp Ile Asp Asp Asp
20 25 30

Met Asn Trp Tyr Gln Gln Lys Pro Gly Glu Pro Pro Asn Val Leu Ile
35 40 45

Ser Glu Gly Asn Thr Leu Arg Pro Gly Val Pro Ser Arg Phe Ser Ser
50 55 60

Ser Gly Tyr Gly Thr Asp Phe Val Phe Thr Ile Glu Asn Thr Leu Ser
65 70 75 80

Glu Asp Val Ala Asp Tyr Tyr Cys Leu Gln Ser Asp Asn Met Pro Leu
85 90 95

Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105

<210> 182
<211> 363
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (363)
<223> SC16.68 VH

<220>
<221> CDS
<222> (1).. (363)

<400> 182
cag gtg caa ctg cag cag cct ggg gct gag ctg gtg aag cct ggg gcc
Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Ala

1	5	10	15	
tca gtg aag atg tcc tgc aag gct tct ggc tac aca ttt acc aat tac				96
Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr				
20	25	30		
aat atg cac tgg gta aag cag aca cct gga cag ggc ctg gaa tgg att				144
Asn Met His Trp Val Lys Gln Thr Pro Gly Gln Gly Leu Glu Trp Ile				
35	40	45		
ggg gct att ttt cca gga aat ggt ggt act tcc tac aat cag aag ttc				192
Gly Ala Ile Phe Pro Gly Asn Gly Gly Thr Ser Tyr Asn Gln Lys Phe				
50	55	60		
aaa ggc aag gcc aca ttg act gca gac aaa tcc tcc agc aca gcc tac				240
Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr				
65	70	75	80	
atg cag ctc acc agt ttg aca tct ggg gac tct gca gtc tat tac tgt				288
Met Gln Leu Thr Ser Leu Thr Ser Gly Asp Ser Ala Val Tyr Tyr Cys				
85	90	95		
gca aga tgg ggc tac ggt agt ggc ctt tat gct atg gac tac tgg ggt				336
Ala Arg Trp Gly Tyr Gly Ser Gly Leu Tyr Ala Met Asp Tyr Trp Gly				
100	105	110		
caa gga acc tca gtc acc gtc tcc tca				363
Gln Gly Thr Ser Val Thr Val Ser Ser				
115	120			

<210> 183
 <211> 121
 <212> PRT
 <213> Mus musculus

 <400> 183

Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Ala			
1	5	10	15
Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr			
20	25	30	

Asn Met His Trp Val Lys Gln Thr Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Ala Ile Phe Pro Gly Asn Gly Gly Thr Ser Tyr Asn Gln Lys Phe
 50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
 65 70 75 80

Met Gln Leu Thr Ser Leu Thr Ser Gly Asp Ser Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Trp Gly Tyr Gly Ser Gly Leu Tyr Ala Met Asp Tyr Trp Gly
 100 105 110

Gln Gly Thr Ser Val Thr Val Ser Ser
 115 120

<210> 184
 <211> 318
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1).. (318)
 <223> SC16.72 VL

<220>
 <221> CDS
 <222> (1).. (318)

<400> 184
 gaa aat gta ctc acc cag tct cca gca atc atg tct gca tct cta ggg
 Glu Asn Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Leu Gly

1	5	10	15	
gag aag gtc acc atg agc tgc agg gcc agc tca agt gta aat tac atg				96
Glu Lys Val Thr Met Ser Cys Arg Ala Ser Ser Ser Val Asn Tyr Met				
	20	25	30	
tcc tgg tac cag cag aag tca gat gcc tcc ccc aaa cta tgg att tat				144
Ser Trp Tyr Gln Gln Lys Ser Asp Ala Ser Pro Lys Leu Trp Ile Tyr				
	35	40	45	
tac aca tcc aac ctg gct cct gga gtc cca gct cgc ttc agt ggc agt				192
Tyr Thr Ser Asn Leu Ala Pro Gly Val Pro Ala Arg Phe Ser Gly Ser				
	50	55	60	
ggg tct ggg aac tct tat tct ctc aca atc agc agc atg gag ggt gaa				240
Gly Ser Gly Asn Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Gly Glu				
65		70	75	80
gat gct gcc act tat tac tgc cag cag ttt act agt tcc ccg tac acg				288
Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Phe Thr Ser Ser Pro Tyr Thr				
	85	90	95	
ttc gga ggg ggg acc aag ctg gaa ata aaa				318
Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys				
	100	105		

<210> 185
 <211> 106
 <212> PRT
 <213> Mus musculus

<400> 185

Glu Asn Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Leu Gly	
1	5 10 15
Glu Lys Val Thr Met Ser Cys Arg Ala Ser Ser Ser Val Asn Tyr Met	
20	25 30
Ser Trp Tyr Gln Gln Lys Ser Asp Ala Ser Pro Lys Leu Trp Ile Tyr	
35	40 45

Tyr Thr Ser Asn Leu Ala Pro Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Asn Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Gly Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Phe Thr Ser Ser Pro Tyr Thr
85 90 95

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 186
<211> 351
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (351)
<223> SC16.72 VH

<220>
<221> CDS
<222> (1).. (351)

<400> 186
gag gtc cag ctg cag cag tct gga cct gag ctg gta aag cct ggg gct 48
Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1 5 10 15

tca gtg aag atg tcc tgc aag gct tct gga tac aca ttc act agc tat 96
Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

gtt atg cac tgg gtg aag cag aag cct ggg cag ggc ctt gag tgg att 144
Val Met His Trp Val Lys Gln Lys Pro Gly Gln Gly Leu Glu Trp Ile

35	40	45	
gga tat att aat cct tac aat gat ggt act aag tac aat gag aag ttc	192		
Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Thr Lys Tyr Asn Glu Lys Phe			
50	55	60	
aaa ggc aag gcc aca ctg act tca gac aaa tcc tcc agc aca gcc tac	240		
Lys Gly Lys Ala Thr Leu Thr Ser Asp Lys Ser Ser Ser Thr Ala Tyr			
65	70	75	80
atg gag ctc agc agc ctg acc tct gag gac tct gcg gtc tat tac tgt	288		
Met Glu Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys			
85	90	95	
gca aga ttg agg tcg agg gct atg gac tac tgg ggt caa gga acc tca	336		
Ala Arg Leu Arg Ser Arg Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser			
100	105	110	
gtc acc gtc tcc tca	351		
Val Thr Val Ser Ser			
115			

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1 5 10 15

Val Met His Trp Val Lys Gln Lys Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Lys Gly Lys Ala Thr Leu Thr Ser Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Leu Arg Ser Arg Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser
100 105 110

Val Thr Val Ser Ser
115

<210> 188
<211> 321
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(321)
<223> SC16.73 VL

<220>
<221> CDS
<222> (1)..(321)

<400> 188
gac atc cag atg acc cag tct cca tcc tcc tta tct gcc tct ctg gga 48
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

gag aga gtc agt ctc act tgt cgg gca agt cag gac att ggt tat agc 96
Glu Arg Val Ser Leu Thr Cys Arg Ala Ser Gln Asp Ile Gly Tyr Ser
20 25 30

tta aac tgg ctt cag cag gaa cca gat gga act att aaa cgc ctg atc 144
Leu Asn Trp Leu Gln Gln Glu Pro Asp Gly Thr Ile Lys Arg Leu Ile

35	40	45	
tac gcc aca tcc agt tta gat tct ggt gtc ccc aaa agg ttc agt ggc			192
Tyr Ala Thr Ser Ser Leu Asp Ser Gly Val Pro Lys Arg Phe Ser Gly			
50	55	60	
agt agg tct ggg tca gat tat tct ctc acc atc agc agc ctt gag tct			240
Ser Arg Ser Gly Ser Asp Tyr Ser Leu Thr Ile Ser Ser Leu Glu Ser			
65	70	75	80
gaa gat ttt gta gac tat tac tgt cta caa tat gct agt tct ccg tgg			288
Glu Asp Phe Val Asp Tyr Tyr Cys Leu Gln Tyr Ala Ser Ser Pro Trp			
85	90	95	
acg ttc ggt gga ggc acc aag ctg gaa atc aaa			321
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys			
100	105		
<210>	189		
<211>	107		
<212>	PRT		
<213>	Mus musculus		
<400>	189		
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Leu Gly			
1	5	10	15
Glu Arg Val Ser Leu Thr Cys Arg Ala Ser Gln Asp Ile Gly Tyr Ser			
20	25	30	
Leu Asn Trp Leu Gln Gln Glu Pro Asp Gly Thr Ile Lys Arg Leu Ile			
35	40	45	
Tyr Ala Thr Ser Ser Leu Asp Ser Gly Val Pro Lys Arg Phe Ser Gly			
50	55	60	
Ser Arg Ser Gly Ser Asp Tyr Ser Leu Thr Ile Ser Ser Leu Glu Ser			
65	70	75	80

Glu Asp Phe Val Asp Tyr Tyr Cys Leu Gln Tyr Ala Ser Ser Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 190
<211> 369
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(369)
<223> SC16.73 VH

<220>
<221> CDS
<222> (1)..(369)

<400> 190
cag gtg cag ctg cag cag tct gga gct gag ctg atg aag cct ggg gcc 48
Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Met Lys Pro Gly Ala
1 5 10 15

tca gtg aag ata tcc tgc aag gct aat ggc tac aca ttc agt agc tac 96
Ser Val Lys Ile Ser Cys Lys Ala Asn Gly Tyr Thr Phe Ser Ser Tyr
20 25 30

tgg ata gag tgg tta agg cag agg cct gga cat ggc ctt gag tgg att 144
Trp Ile Glu Trp Leu Arg Gln Arg Pro Gly His Gly Leu Glu Trp Ile
35 40 45

gga gag att tta cct gga agt gat aat agt aat tat aat gag aag ttc 192
Gly Glu Ile Leu Pro Gly Ser Asp Asn Ser Asn Tyr Asn Glu Lys Phe
50 55 60

aag ggc aag gcc aca ttc act gca gat aca tcc tcc aac aca gcc tac 240
Lys Gly Lys Ala Thr Phe Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr

65	70	75	80	
atg caa ctc agc agc ctg aca tct gag gaa tct gcc gtc tat tac tgt				288
Met Gln Leu Ser Ser Leu Thr Ser Glu Glu Ser Ala Val Tyr Tyr Cys				
	85	90	95	
aca agg gga tta cga cga gac ggc tca tat tac tat gtt atg gaa cat				336
Thr Arg Gly Leu Arg Arg Asp Gly Ser Tyr Tyr Tyr Val Met Glu His				
	100	105	110	
tgg ggt caa gga acc tca gtc acc gtc tcc tca				369
Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser				
	115	120		
<210> 191				
<211> 123				
<212> PRT				
<213> Mus musculus				
<400> 191				
Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Met Lys Pro Gly Ala				
1	5	10	15	
Ser Val Lys Ile Ser Cys Lys Ala Asn Gly Tyr Thr Phe Ser Ser Tyr				
	20	25	30	
Trp Ile Glu Trp Leu Arg Gln Arg Pro Gly His Gly Leu Glu Trp Ile				
	35	40	45	
Gly Glu Ile Leu Pro Gly Ser Asp Asn Ser Asn Tyr Asn Glu Lys Phe				
50	55	60		
Lys Gly Lys Ala Thr Phe Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr				
65	70	75	80	
Met Gln Leu Ser Ser Leu Thr Ser Glu Glu Ser Ala Val Tyr Tyr Cys				
	85	90	95	

Thr Arg Gly Leu Arg Arg Asp Gly Ser Tyr Tyr Tyr Val Met Glu His
100 105 110

Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser
115 120

<210> 192
<211> 321
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(321)
<223> SC16.78 VL

<220>
<221> CDS
<222> (1)..(321)

<400> 192
gac atc aag atg acc cag tct cca tct tcc atg tat gca tct cta gga 48
Asp Ile Lys Met Thr Gln Ser Pro Ser Ser Met Tyr Ala Ser Leu Gly
1 5 10 15

gag aga gtc act atc act tgc aag gcg agt cag gac att aat agc tat 96
Glu Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Ile Asn Ser Tyr
20 25 30

tta agc tgg ttc cag cag aag cca ggg aga tct cct aag acc ctg atc 144
Leu Ser Trp Phe Gln Gln Lys Pro Gly Arg Ser Pro Lys Thr Leu Ile
35 40 45

tat cgt gca aac aga ttg gta gat ggg gtc cca tca agg ttc agt ggc 192
Tyr Arg Ala Asn Arg Leu Val Asp Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

agt gga tct ggg caa gat tat tct ctc acc atc agc agc ctg gac tat 240
Ser Gly Ser Gly Gln Asp Tyr Ser Leu Thr Ile Ser Ser Leu Asp Tyr

65	70	75	80	
gaa gat atg gga att tat tat tgt cta cag tat gat gaa ttt cca ttc				288
Glu Asp Met Gly Ile Tyr Tyr Cys Leu Gln Tyr Asp Glu Phe Pro Phe				
	85	90	95	
acg ttc ggc tcg ggg aca aag ttg gar ath aar				321
Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys				
	100	105		
<210> 193				
<211> 107				
<212> PRT				
<213> Mus musculus				
<400> 193				
Asp Ile Lys Met Thr Gln Ser Pro Ser Ser Met Tyr Ala Ser Leu Gly				
1	5	10	15	
Glu Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Ile Asn Ser Tyr				
	20	25	30	
Leu Ser Trp Phe Gln Gln Lys Pro Gly Arg Ser Pro Lys Thr Leu Ile				
	35	40	45	
Tyr Arg Ala Asn Arg Leu Val Asp Gly Val Pro Ser Arg Phe Ser Gly				
	50	55	60	
Ser Gly Ser Gly Gln Asp Tyr Ser Leu Thr Ile Ser Ser Leu Asp Tyr				
65	70	75	80	
Glu Asp Met Gly Ile Tyr Tyr Cys Leu Gln Tyr Asp Glu Phe Pro Phe				
	85	90	95	
Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys				
	100	105		

<210> 194
 <211> 357
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1).. (357)
 <223> SC16.78 VH

<220>
 <221> CDS
 <222> (1).. (357)

<400> 194
 gaa gtg aag ctg gtg gag tct ggg gga ggc tta gtg aag cct gga ggg 48
 Glu Val Lys Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
 1 5 10 15
 tcc ctg aaa ctc tcc tgt gca gcc tct gga ttc act ttc ggt cgc tat 96
 Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Arg Tyr
 20 25 30
 gtc atg tct tgg gtt cgc cag act cca gaa aag aaa ctg gag tgg gtc 144
 Val Met Ser Trp Val Arg Gln Thr Pro Glu Lys Lys Leu Glu Trp Val
 35 40 45
 gca tcc att act agt ggt ggt act acc tac tat cca gac agt gtg aag 192
 Ala Ser Ile Thr Ser Gly Gly Thr Thr Tyr Tyr Pro Asp Ser Val Lys
 50 55 60
 ggc cga ttc acc atc tcc aga gat aat gcc agg aac atc ctg tac cta 240
 Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Arg Asn Ile Leu Tyr Leu
 65 70 75 80
 caa atg agc agt ctg agg tct gag gac acg gcc atg tat tac tgt gca 288
 Gln Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Met Tyr Tyr Cys Ala
 85 90 95
 aga gtc tac tat cat tac gac gac atc ttt gct tac tgg ggc caa ggg 336
 Arg Val Tyr Tyr His Tyr Asp Asp Ile Phe Ala Tyr Trp Gly Gln Gly

	100	105	110	
	act ctg gtc act gtc tct gca			357
	Thr Leu Val Thr Val Ser Ala			
	115			
<210>	195			
<211>	119			
<212>	PRT			
<213>	Mus musculus			
<400>	195			
	Glu Val Lys Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly			
	1 5 10 15			
	Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Gly Arg Tyr			
	20 25 30			
	Val Met Ser Trp Val Arg Gln Thr Pro Glu Lys Lys Leu Glu Trp Val			
	35 40 45			
	Ala Ser Ile Thr Ser Gly Gly Thr Thr Tyr Tyr Pro Asp Ser Val Lys			
	50 55 60			
	Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Arg Asn Ile Leu Tyr Leu			
	65 70 75 80			
	Gln Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Met Tyr Tyr Cys Ala			
	85 90 95			
	Arg Val Tyr Tyr His Tyr Asp Asp Ile Phe Ala Tyr Trp Gly Gln Gly			
	100 105 110			
	Thr Leu Val Thr Val Ser Ala			
	115			

<210> 196
 <211> 336
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1).. (336)
 <223> SC16.79 VL

<220>
 <221> CDS
 <222> (1).. (336)

<400> 196
 gac att gtg atg tca cag tct cca tcc tcc ctg gct gtg tca gca gga 48
 Asp Ile Val Met Ser Gln Ser Pro Ser Ser Leu Ala Val Ser Ala Gly
 1 5 10 15
 gag aag gtc act atg agc tgc aaa tcc agt cag agt ctg ctc aac agt 96
 Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
 20 25 30
 aga acc cga aag aac tac ttg gct tgg tac cag cag aaa cca ggg cag 144
 Arg Thr Arg Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
 35 40 45
 tct cct aaa ctg ctg atc tac tgg gca tcc act agg gaa tct ggg gtc 192
 Ser Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
 50 55 60
 cct gat cgc ttc aca ggc agt gga tct ggg aca gat ttc act ctc acc 240
 Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
 65 70 75 80
 atc agc agt gtg cag gct gaa gac ctg gca gtt tat tac tgc aag caa 288
 Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Lys Gln
 85 90 95
 tct tat aat ctt tac acg ttc gga ggg ggg acc aag ctg aaa ata aaa 336
 Ser Tyr Asn Leu Tyr Thr Phe Gly Gly Gly Thr Lys Leu Lys Ile Lys

100

105

110

<210> 197

<211> 112

<212> PRT

<213> Mus musculus

<400> 197

Asp Ile Val Met Ser Gln Ser Pro Ser Ser Leu Ala Val Ser Ala Gly
 1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
 20 25 30

Arg Thr Arg Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
 35 40 45

Ser Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
 50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
 65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Lys Gln
 85 90 95

Ser Tyr Asn Leu Tyr Thr Phe Gly Gly Gly Thr Lys Leu Lys Ile Lys
 100 105 110

<210> 198

<211> 348

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1).. (348)

<223> SC16.79 VH

<220>

<221> CDS

<222> (1).. (348)

<400> 198

gag gtc cag ctg caa cag tct gga cct gag ctg gtg aag cct ggg gct	48
Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala	
1 5 10 15	

tca gtg aag ata tcc tgc aag act tct gga tac aca ttc act gaa tac	96
Ser Val Lys Ile Ser Cys Lys Thr Ser Gly Tyr Thr Phe Thr Glu Tyr	
20 25 30	

acc atg cac tgg gtg aag cag agc cat gga aag agc ctt gag tgg att	144
Thr Met His Trp Val Lys Gln Ser His Gly Lys Ser Leu Glu Trp Ile	
35 40 45	

gga ggt att aat cct aac aat ggt ggt act agc tac aac cag aag ttc	192
Gly Gly Ile Asn Pro Asn Asn Gly Gly Thr Ser Tyr Asn Gln Lys Phe	
50 55 60	

aag ggc aag gcc aca ttg act gta gac aag tcc tcc agc aca gcc tac	240
Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr	
65 70 75 80	

atg gag ctc cgc agc ctg aca tct gag gat tct gca gtc tat tac tgt	288
Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys	
85 90 95	

gca agg ggt ccc gcc tgg ttt gct tac tgg ggc caa ggg act ctg gtc	336
Ala Arg Gly Pro Ala Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val	
100 105 110	

act gtc tct gca	348
Thr Val Ser Ala	
115	

<210> 199

<211> 116
<212> PRT
<213> Mus musculus

<400> 199

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Thr Ser Gly Tyr Thr Phe Thr Glu Tyr
20 25 30

Thr Met His Trp Val Lys Gln Ser His Gly Lys Ser Leu Glu Trp Ile
35 40 45

Gly Gly Ile Asn Pro Asn Asn Gly Gly Thr Ser Tyr Asn Gln Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Pro Ala Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ala
115

<210> 200
<211> 321
<212> DNA
<213> Mus musculus

<220>

<221> misc_feature

<222> (1).. (321)

<223> SC16.80 VL

<220>

<221> CDS

<222> (1).. (321)

<400> 200

gaa	aca	act	gtg	acc	cag	tct	cca	gca	tcc	ctg	tcc	atg	gct	ata	gga	48
Glu	Thr	Thr	Val	Thr	Gln	Ser	Pro	Ala	Ser	Leu	Ser	Met	Ala	Ile	Gly	
1			5					10					15			

gaa	aaa	gtc	acc	atc	aga	tgc	ata	acc	agc	act	gat	att	gat	gat	gat	96
Glu	Lys	Val	Thr	Ile	Arg	Cys	Ile	Thr	Ser	Thr	Asp	Ile	Asp	Asp	Asp	
		20					25					30				

atg	atc	tgg	tac	cag	cag	aag	cca	ggg	gaa	cct	cct	aag	ctc	ctt	att	144
Met	Ile	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Glu	Pro	Pro	Lys	Leu	Leu	Ile	
		35				40						45				

tca	gaa	ggc	aat	act	ctt	cgt	cct	gga	gtc	cca	tcc	cga	ttc	tcc	agc	192
Ser	Glu	Gly	Asn	Thr	Leu	Arg	Pro	Gly	Val	Pro	Ser	Arg	Phe	Ser	Ser	
	50					55				60						

agt	ggc	tat	ggt	aca	gat	ttt	gtt	ttt	aca	att	gaa	aac	atg	ctc	tca	240
Ser	Gly	Tyr	Gly	Thr	Asp	Phe	Val	Phe	Thr	Ile	Glu	Asn	Met	Leu	Ser	
65				70				75						80		

gaa	gat	gtt	gcc	gat	tac	tac	tgt	ttg	aaa	agg	gat	gac	ttg	cct	tac	288
Glu	Asp	Val	Ala	Asp	Tyr	Tyr	Cys	Leu	Lys	Arg	Asp	Asp	Leu	Pro	Tyr	
			85					90					95			

acg	ttc	ggc	ggg	ggg	aca	cag	gtg	gaa	att	aaa	321
Thr	Phe	Gly	Gly	Gly	Thr	Gln	Val	Glu	Ile	Lys	
		100					105				

<210> 201

<211> 107

<212> PRT

<213> Mus musculus

<400> 201

Glu Thr Thr Val Thr Gln Ser Pro Ala Ser Leu Ser Met Ala Ile Gly
1 5 10 15

Glu Lys Val Thr Ile Arg Cys Ile Thr Ser Thr Asp Ile Asp Asp Asp
20 25 30

Met Ile Trp Tyr Gln Gln Lys Pro Gly Glu Pro Pro Lys Leu Leu Ile
35 40 45

Ser Glu Gly Asn Thr Leu Arg Pro Gly Val Pro Ser Arg Phe Ser Ser
50 55 60

Ser Gly Tyr Gly Thr Asp Phe Val Phe Thr Ile Glu Asn Met Leu Ser
65 70 75 80

Glu Asp Val Ala Asp Tyr Tyr Cys Leu Lys Arg Asp Asp Leu Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Gln Val Glu Ile Lys
100 105

<210> 202

<211> 351

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1)..(351)

<223> SC16.80 VH

<220>

<221> CDS

<222> (1)..(351)

<400> 202

gag gtc cag ctg caa cag tct gga cct gag ctg gtg aag cct gga ggt 48
Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Gly
1 5 10 15

tca aag aag ata tcc tgc aag gct tct ggt tac tca ttc act ggc tac 96
Ser Lys Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr
20 25 30

agt atg aac tgg gtg aag cag agc cat gga aag aac ctt gag tgg att 144
Ser Met Asn Trp Val Lys Gln Ser His Gly Lys Asn Leu Glu Trp Ile
35 40 45

gga ctt att aat cct tac agt ggt ggt act atc tac aac cag aaa ttc 192
Gly Leu Ile Asn Pro Tyr Ser Gly Gly Thr Ile Tyr Asn Gln Lys Phe
50 55 60

aag ggc aag gcc aca tta act gta gac aag tca tcc agc aca gcc tac 240
Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

atg gag ctc ctc agt ctg aca tct gag gac tct gca gtc tat tac tgt 288
Met Glu Leu Leu Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

gca aga agg agt gat tac ccg tta gtt tac tgg ggc caa ggg act ctg 336
Ala Arg Arg Ser Asp Tyr Pro Leu Val Tyr Trp Gly Gln Gly Thr Leu
100 105 110

gtc act gtc tct gca 351
Val Thr Val Ser Ala
115

<210> 203

<211> 117

<212> PRT

<213> Mus musculus

<400> 203

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Lys Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr
20 25 30

Ser Met Asn Trp Val Lys Gln Ser His Gly Lys Asn Leu Glu Trp Ile
35 40 45

Gly Leu Ile Asn Pro Tyr Ser Gly Gly Thr Ile Tyr Asn Gln Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Leu Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Ser Asp Tyr Pro Leu Val Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ala
115

<210> 204
<211> 324
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (324)
<223> SC16.81 VL

<220>
<221> CDS
<222> (1).. (324)

<400> 204

caa att gtt ctc acc cag tct cca gca atc atg tct gca tct cta ggg 48
Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Leu Gly
1 5 10 15

gaa cgg gtc acc ctg acc tgc act gcc agc tca agt gta agt tcc agt 96
Glu Arg Val Thr Leu Thr Cys Thr Ala Ser Ser Ser Val Ser Ser Ser
20 25 30

tac ttg cac tgg tac cag cag aag cca gga tcc tcc ccc aaa ctc tgg 144
Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Leu Trp
35 40 45

att tat agc aca tcc aac ctg gct tct gga gtc cca act cgc ttc agt 192
Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Thr Arg Phe Ser
50 55 60

ggc agt ggg tct ggg acc tct tac tct ctc aga atc agc agc atg gag 240
Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Arg Ile Ser Ser Met Glu
65 70 75 80

gct gaa gat gct gcc act tat tac tgc cac cag tat aat cgt tcc ccg 288
Ala Glu Asp Ala Ala Thr Tyr Tyr Cys His Gln Tyr Asn Arg Ser Pro
85 90 95

ctc acg ttc ggt gct ggg acc aag ctg gag ctg aaa 324
Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105

<210> 205

<211> 108

<212> PRT

<213> Mus musculus

<400> 205

Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Leu Gly
1 5 10 15

Glu Arg Val Thr Leu Thr Cys Thr Ala Ser Ser Ser Val Ser Ser Ser
20 25 30

Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Leu Trp
35 40 45

Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Thr Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Arg Ile Ser Ser Met Glu
65 70 75 80

Ala Glu Asp Ala Ala Thr Tyr Tyr Cys His Gln Tyr Asn Arg Ser Pro
85 90 95

Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105

<210> 206
<211> 351
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(351)
<223> SC16.81 VH

<220>
<221> CDS
<222> (1)..(351)

<400> 206
cag gtg cag ctg aag gag tca gga cct gtc ctg gtg gcg ccc tca cag 48
Gln Val Gln Leu Lys Glu Ser Gly Pro Val Leu Val Ala Pro Ser Gln
1 5 10 15

agc ctg tcc atc act tgc act gtc tct ggg ttt tca tta acc agc tat 96
Ser Leu Ser Ile Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Ser Tyr

20					25					30						
ggt	gta	cac	tgg	gtt	cgc	cag	cct	cca	gga	aag	ggt	ctg	gag	tgg	ctg	144
Gly	Val	His	Trp	Val	Arg	Gln	Pro	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Leu	
35					40					45						
gga	gta	att	tgg	gct	ggt	gga	agt	aca	aat	tat	aat	tca	gct	ctc	atg	192
Gly	Val	Ile	Trp	Ala	Gly	Gly	Ser	Thr	Asn	Tyr	Asn	Ser	Ala	Leu	Met	
50					55					60						
tcc	aga	ctg	agc	atc	agc	aaa	gac	aac	tcc	aag	agc	caa	gtt	ttc	tta	240
Ser	Arg	Leu	Ser	Ile	Ser	Lys	Asp	Asn	Ser	Lys	Ser	Gln	Val	Phe	Leu	
65					70					75					80	
aaa	atg	aac	agt	ctg	caa	act	gat	gac	aca	gcc	atg	tac	tac	tgt	gcc	288
Lys	Met	Asn	Ser	Leu	Gln	Thr	Asp	Asp	Thr	Ala	Met	Tyr	Tyr	Cys	Ala	
85					90					95						
aaa	cag	ggc	aac	ttc	tat	gct	atg	gac	tac	tgg	ggt	caa	gga	acc	tca	336
Lys	Gln	Gly	Asn	Phe	Tyr	Ala	Met	Asp	Tyr	Trp	Gly	Gln	Gly	Thr	Ser	
100					105					110						
gtc	acc	gtc	tcc	tca											351	
Val	Thr	Val	Ser	Ser												
115																

Gln Val Gln Leu Lys Glu Ser Gly Pro Val Leu Val Ala Pro Ser Gln
1 5 10 15

Gly Val His Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Leu
35 40 45

Gly Val Ile Trp Ala Gly Gly Ser Thr Asn Tyr Asn Ser Ala Leu Met
50 55 60

Ser Arg Leu Ser Ile Ser Lys Asp Asn Ser Lys Ser Gln Val Phe Leu
65 70 75 80

Lys Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Met Tyr Tyr Cys Ala
85 90 95

Lys Gln Gly Asn Phe Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser
100 105 110

Val Thr Val Ser Ser
115

<210> 208
<211> 318
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (318)
<223> SC16.84 VL

<220>
<221> CDS
<222> (1).. (318)

<400> 208
gac atc cag atg aca cag tct cca tcc tca ctg tct gca tct ctg gga 48
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

ggc aaa gtc acc atc act tgc aag gca agc caa gac att aag aag tat 96
Gly Lys Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Ile Lys Lys Tyr

Ser Gly Ser Gly Arg Asp Tyr Ser Phe Ser Ile Ser Asn Leu Glu Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Leu Gln Tyr Asp Ile Leu Trp Thr
85 90 95

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 210
<211> 363
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (363)
<223> SC16.84 VH

<220>
<221> CDS
<222> (1).. (363)

<400> 210
gag gtc cag ctg caa cag tct gga cct gag ctg gtg aag cct gga gct 48
Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1 5 10 15

tca atg aag ata tcc tgc aag gct tct ggt tac tca ttc act ggc tac 96
Ser Met Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr
20 25 30

acc atg aac tgg gtg aag cag agc cat gga aag aac ctt gag tgg att 144
Thr Met Asn Trp Val Lys Gln Ser His Gly Lys Asn Leu Glu Trp Ile
35 40 45

gga ctt att aat cct tac aat ggt ggt act acc tac aac cag aag ttc 192
Gly Leu Ile Asn Pro Tyr Asn Gly Gly Thr Thr Tyr Asn Gln Lys Phe

50	55	60	
aag ggc aag gcc aca tta act gta gac aag tca tcc agc aca gcc tac			240
Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr			
65	70	75	80
atg gag ctc ctc agt ctg aca tct gag gac tct gca gtc tat tac tgt			288
Met Glu Leu Leu Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys			
	85	90	95
gca tta ggt tac tat ggt aac tac agg agg tac ttc gat gtc tgg gcc			336
Ala Leu Gly Tyr Tyr Gly Asn Tyr Arg Arg Tyr Phe Asp Val Trp Gly			
	100	105	110
gca ggg acc acg gtc acc gtc tcc tca			363
Ala Gly Thr Thr Val Thr Val Ser Ser			
	115	120	
<210> 211 <211> 121 <212> PRT <213> Mus musculus			
<400> 211			
Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala			
1	5	10	15
Ser Met Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr			
	20	25	30
Thr Met Asn Trp Val Lys Gln Ser His Gly Lys Asn Leu Glu Trp Ile			
	35	40	45
Gly Leu Ile Asn Pro Tyr Asn Gly Gly Thr Thr Tyr Asn Gln Lys Phe			
	50	55	60
Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr			
65	70	75	80

Met Glu Leu Leu Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Leu Gly Tyr Tyr Gly Asn Tyr Arg Arg Tyr Phe Asp Val Trp Gly
100 105 110

Ala Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 212
<211> 324
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (324)
<223> SC16.88 VL

<220>
<221> CDS
<222> (1).. (324)

<400> 212
gaa aat gtg ctc acc cag tct cca gca ata atg gct gcc tct ctg ggg 48
Glu Asn Val Leu Thr Gln Ser Pro Ala Ile Met Ala Ala Ser Leu Gly
1 5 10 15

cag aag gtc acc atg acc tgc agt gcc agc tca agt gta agt tcc agt 96
Gln Lys Val Thr Met Thr Cys Ser Ala Ser Ser Ser Val Ser Ser Ser
20 25 30

tac ttg cac tgg tac cag cag aag tca ggc gct tcc ccc aaa ccc ttg 144
Tyr Leu His Trp Tyr Gln Gln Lys Ser Gly Ala Ser Pro Lys Pro Leu
35 40 45

att cat agg aca tcc aac ctg gct tct gga gtc cca gct cgc ttc agt 192
Ile His Arg Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser

Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 214
<211> 357
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (357)
<223> SC16.88 VH

<220>
<221> CDS
<222> (1).. (357)

<400> 214
cag gtt cag ctg cag cag tct ggg gct gag ctg gca aga cct ggg gct 48
Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
1 5 10 15

tca gtg aag ttg tcc tgc aag gct tct ggc tac acc tgt act agc tac 96
Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Cys Thr Ser Tyr
20 25 30

tgg atg cag tgg gta aaa cag agg cct gga cag ggt ctg gaa tgg att 144
Trp Met Gln Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

ggg gct att tat cct gga gat ggt gat act agg tac act cag aag ttc 192
Gly Ala Ile Tyr Pro Gly Asp Gly Asp Thr Arg Tyr Thr Gln Lys Phe
50 55 60

aag ggc aag gcc aca ttg act gca gat aaa tcc tcc agc aca gcc tac 240
Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

atg caa ctc agc agc ttg gca tct gag gac tct gcg gtc tat tac tgt 288
Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Tyr Cys

	85	90	95	
gca agg ggg agg cgg acg gag gcc tgg ttt gct tac tgg ggc caa ggg				336
Ala Arg Gly Arg Arg Thr Glu Ala Trp Phe Ala Tyr Trp Gly Gln Gly				
	100	105	110	
act ctg gtc act gtc tct gca				357
Thr Leu Val Thr Val Ser Ala				
	115			
<210> 215				
<211> 119				
<212> PRT				
<213> Mus musculus				
<400> 215				
Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala				
1 5 10 15				
Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Cys Thr Ser Tyr				
20 25 30				
Trp Met Gln Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile				
35 40 45				
Gly Ala Ile Tyr Pro Gly Asp Gly Asp Thr Arg Tyr Thr Gln Lys Phe				
50 55 60				
Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr				
65 70 75 80				
Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Tyr Cys				
85 90 95				
Ala Arg Gly Arg Arg Thr Glu Ala Trp Phe Ala Tyr Trp Gly Gln Gly				
100 105 110				

Thr Leu Val Thr Val Ser Ala
115

<210> 216
<211> 324
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(324)
<223> SC16.101 VL

<220>
<221> CDS
<222> (1)..(324)

<400> 216
caa att gtt ctc acc cag tct cca gca atc atg tct gca tct cta ggg 48
Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Leu Gly
1 5 10 15

gaa cgg gtc acc atg acc tgc act gcc agc tca agt gta agt tcc agt 96
Glu Arg Val Thr Met Thr Cys Thr Ala Ser Ser Ser Val Ser Ser Ser
20 25 30

tac ttg cac tgg tac cag cag aag cca gga tcc tcc ccc aaa ctc tgg 144
Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Leu Trp
35 40 45

att tat agc aca tcc aac ctg gct tct gga gtc cca gct cgc ttc agt 192
Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser
50 55 60

ggc agt gag tct ggg acc tct tac tct ctc aca atc agc aac atg gag 240
Gly Ser Glu Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Asn Met Glu
65 70 75 80

gct gag gat gct gcc act tat tac tgc cac cag tat cat cgt tcc cca 288
Ala Glu Asp Ala Ala Thr Tyr Tyr Cys His Gln Tyr His Arg Ser Pro

85

90

95

ttc acg ttc ggc tcg ggg aca aag ttg gaa ata aaa

324

Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys

100

105

<210> 217

<211> 108

<212> PRT

<213> Mus musculus

<400> 217

Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Leu Gly

1

5

10

15

Glu Arg Val Thr Met Thr Cys Thr Ala Ser Ser Ser Val Ser Ser Ser

20

25

30

Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Leu Trp

35

40

45

Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser

50

55

60

Gly Ser Glu Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Asn Met Glu

65

70

75

80

Ala Glu Asp Ala Ala Thr Tyr Tyr Cys His Gln Tyr His Arg Ser Pro

85

90

95

Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys

100

105

<210> 218

<211> 360

<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(360)
<223> SC16.101 VH

<220>
<221> CDS
<222> (1)..(360)

<400> 218
cag gtt act ctg aaa gag tct ggc cct ggg ata ttg cag ccc tcc cag 48
Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Gln Pro Ser Gln
1 5 10 15

acc ctc agt ctg act tgt tct ttc tct gga ttt tca ctg agc act tct 96
Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser Thr Ser
20 25 30

ggg atg ggc gta ggc tgg att cgt cag cca tca ggg aag ggt ctg gag 144
Gly Met Gly Val Gly Trp Ile Arg Gln Pro Ser Gly Lys Gly Leu Glu
35 40 45

tgg ctg gca cac att tgg tgg gat gat gtc aag cgc tat aac cca gcc 192
Trp Leu Ala His Ile Trp Trp Asp Asp Val Lys Arg Tyr Asn Pro Ala
50 55 60

ctt aag agc cga ctg act atc tcc aag gat gcc tcc agc agc cag gta 240
Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Ala Ser Ser Ser Gln Val
65 70 75 80

ttc ctc aag atc gcc agt gtg gac act gca gaa act gcc aca tac tac 288
Phe Leu Lys Ile Ala Ser Val Asp Thr Ala Glu Thr Ala Thr Tyr Tyr
85 90 95

tgt gcc cac atc ctc gac cgg gct tac tac ttt gac tac tgg ggc caa 336
Cys Ala His Ile Leu Asp Arg Ala Tyr Tyr Phe Asp Tyr Trp Gly Gln
100 105 110

ggc acc act ctc aca gtc acc tca 360
Gly Thr Thr Leu Thr Val Thr Ser

115

120

<210> 219

<211> 120

<212> PRT

<213> Mus musculus

<400> 219

Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Gln Pro Ser Gln
 1 5 10 15

Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser Thr Ser
 20 25 30

Gly Met Gly Val Gly Trp Ile Arg Gln Pro Ser Gly Lys Gly Leu Glu
 35 40 45

Trp Leu Ala His Ile Trp Trp Asp Asp Val Lys Arg Tyr Asn Pro Ala
 50 55 60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Ala Ser Ser Ser Gln Val
 65 70 75 80

Phe Leu Lys Ile Ala Ser Val Asp Thr Ala Glu Thr Ala Thr Tyr Tyr
 85 90 95

Cys Ala His Ile Leu Asp Arg Ala Tyr Tyr Phe Asp Tyr Trp Gly Gln
 100 105 110

Gly Thr Thr Leu Thr Val Thr Ser
 115 120

<210> 220

<211> 333

<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(333)
<223> SC16.103 VL

<220>
<221> CDS
<222> (1)..(333)

<400> 220
gac att gtg ctg aca cag tct cct gct tcc tta gct gta tct ctg ggg 48
Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

cag agg gcc acc atc tca tgc agg gcc agc aaa agt gtc agt aca tct 96
Gln Arg Ala Thr Ile Ser Cys Arg Ala Ser Lys Ser Val Ser Thr Ser
20 25 30

ggc tat agt tat atg cac tgg tac caa cag aaa cca gga cag cca ccc 144
Gly Tyr Ser Tyr Met His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

aaa ctc ctc atc tat ctt gca tcc aac cta gaa tct ggg gtc cct gcc 192
Lys Leu Leu Ile Tyr Leu Ala Ser Asn Leu Glu Ser Gly Val Pro Ala
50 55 60

agg ttc agt ggc agt ggg tct ggg aca gac ttc acc ctc aac atc cat 240
Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

cct gtg gag gag gag gat gct gca acc tat tac tgt cag cac agt agg 288
Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His Ser Arg
85 90 95

gag ctt cct ctc acg ttc ggt gct ggg acc aag ctg gag ctg aaa 333
Glu Leu Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105 110

<210> 221

<211> 111
<212> PRT
<213> Mus musculus

<400> 221

Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Arg Ala Ser Lys Ser Val Ser Thr Ser
20 25 30

Gly Tyr Ser Tyr Met His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Leu Ala Ser Asn Leu Glu Ser Gly Val Pro Ala
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His Ser Arg
85 90 95

Glu Leu Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105 110

<210> 222
<211> 357
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(357)
<223> SC16.103 VH

⟨222⟩ (1).. (357)

 $\langle 400 \rangle$ 222

caa gtt act cta aaa gag tct ggc cct ggg ata ttg aag ccc tca cag 48
Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Lys Pro Ser Gln
1 5 10 15

acc ctc agt ctg act tgt tct ttc tct ggg ttt tca ctg agc act tct 96
Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser Thr Ser
20 25 30

ggt atg ggt ata ggc tgg att cgt cag cct tca ggg aag ggt ctg gag 144
Gly Met Gly Ile Gly Trp Ile Arg Gln Pro Ser Gly Lys Gly Leu Glu
35 40 45

tgg ctg gca cac att tgg tgg gat gat gat aag tac tat aac cca tcc 192
Trp Leu Ala His Ile Trp Trp Asp Asp Asp Lys Tyr Tyr Asn Pro Ser
50 55 60

ctg aag agc cag ctc aca atc tcc aag gat tcc tcc aga aac cag gtt 240
Leu Lys Ser Gln Leu Thr Ile Ser Lys Asp Ser Ser Arg Asn Gln Val
65 70 75 80

ttc ctc aag atc acc agt gtg gac act gca gat act gcc act tac tac 288
Phe Leu Lys Ile Thr Ser Val Asp Thr Ala Asp Thr Ala Thr Tyr Tyr
85 90 95

tgt gct cga aga ggg act gcg tac tac ttt gac tac tgg ggc caa ggc 336
Cys Ala Arg Arg Gly Thr Ala Tyr Tyr Phe Asp Tyr Trp Gly Gln Gly
100 105 110

acc act ctc aca gtc tcc tca 357
Thr Thr Leu Thr Val Ser Ser
115

210 223

<211> 119

⟨212⟩ PRT

⟨213⟩ Mus musculus

<400> 223

Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser Thr Ser
20 25 30

Gly Met Gly Ile Gly Trp Ile Arg Gln Pro Ser Gly Lys Gly Leu Glu
35 40 45

Trp Leu Ala His Ile Trp Trp Asp Asp Asp Lys Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Gln Leu Thr Ile Ser Lys Asp Ser Ser Arg Asn Gln Val
65 70 75 80

Phe Leu Lys Ile Thr Ser Val Asp Thr Ala Asp Thr Ala Thr Tyr Tyr
85 90 95

Cys Ala Arg Arg Gly Thr Ala Tyr Tyr Phe Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Leu Thr Val Ser Ser
115

<210> 224

<211> 318

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1)..(318)

<223> SC16.104 VL

<220>

<221> CDS

<222> (1)..(318)

<400> 224

caa att gtt ctc tcc cag tct cca gca atc ctg tct gca tct cca ggg	48
Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly	
1 5 10 15	

gag aag gtc aca atg act tgc agg gcc agt tca agt gta agt tac att	96
Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Ile	
20 25 30	

cac tgg tac cgg cag aag cca gga tcc tcc ccc aaa ccc tgg att tat	144
His Trp Tyr Arg Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr	
35 40 45	

gcc aca tcc aac ctg gct tct gga gtc cct gct cgc ttc agt ggc agt	192
Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser	
50 55 60	

ggg tct ggg acc tct tac tct ctc aca atc agc aga gtg gag gct gaa	240
Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu	
65 70 75 80	

gat gct gcc act tat tac tgc cag cag tgg agc agt aat cca ccc acg	288
Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Pro Thr	
85 90 95	

ttc ggt gct ggg acc aag ctg gag ctg aaa	318
Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys	
100 105	

<210> 225

<211> 106

<212> PRT

<213> Mus musculus

<400> 225

Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly	
1 5 10 15	

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Ile
 20 25 30

His Trp Tyr Arg Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
 35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Pro Thr
 85 90 95

Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
 100 105

<210> 226
 <211> 345
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1)..(345)
 <223> SC16.104 VH

<220>
 <221> CDS
 <222> (1)..(345)

<400> 226
 cag gtg cag ctg aag gag tca gga cct gac ctt gtg cag ccc tca cag
 Gln Val Gln Leu Lys Glu Ser Gly Pro Asp Leu Val Gln Pro Ser Gln

1	5	10	15	
acc ctg tct ctc acc tgc act gtc tct ggg ttc tca tta acc ttc tat				96
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Phe Tyr				
	20	25	30	
ggg gtt cac tgg gtt cgc cag cct cca gga aag gga ctg gag tgg gtg				144
Gly Val His Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Val				
	35	40	45	
gga aca atg ggc tgg gat gac aaa aaa tat tat aat tca gct cta aaa				192
Gly Thr Met Gly Trp Asp Asp Lys Lys Tyr Tyr Asn Ser Ala Leu Lys				
	50	55	60	
tct cga ctg agc atc agc agg gat acc tcc aag aac cag gtt ttc tta				240
Ser Arg Leu Ser Ile Ser Arg Asp Thr Ser Lys Asn Gln Val Phe Leu				
65		70	75	80
aaa ctg agc agt ctg caa act gaa gac aca gcc atg tac tac tgt act				288
Lys Leu Ser Ser Leu Gln Thr Glu Asp Thr Ala Met Tyr Tyr Cys Thr				
	85	90	95	
aga ggt ggg acg ggg ttt gac tac tgg ggc caa ggc acc act ctc aca				336
Arg Gly Gly Thr Gly Phe Asp Tyr Trp Gly Gln Gly Thr Thr Leu Thr				
	100	105	110	
gtc tcc tca				345
Val Ser Ser				
	115			

<210> 227
 <211> 115
 <212> PRT
 <213> Mus musculus

<400> 227

Gln Val Gln Leu Lys Glu Ser Gly Pro Asp Leu Val Gln Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Phe Tyr
20 25 30

Gly Val His Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly Thr Met Gly Trp Asp Asp Lys Lys Tyr Tyr Asn Ser Ala Leu Lys
50 55 60

Ser Arg Leu Ser Ile Ser Arg Asp Thr Ser Lys Asn Gln Val Phe Leu
65 70 75 80

Lys Leu Ser Ser Leu Gln Thr Glu Asp Thr Ala Met Tyr Tyr Cys Thr
85 90 95

Arg Gly Gly Thr Gly Phe Asp Tyr Trp Gly Gln Gly Thr Thr Leu Thr
100 105 110

Val Ser Ser
115

<210> 228
<211> 321
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(321)
<223> SC16.105 VL

<220>
<221> CDS
<222> (1)..(321)

<400> 228
gac att gtg atg acc cag tcg cac aaa ttc atg tcc aca tca gta gga
Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly

1	5	10	15	
gac agg gtc agc atc acc tgc aag gcc agt cag gat gtg ggt act gct				96
Asp Arg Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Gly Thr Ala				
	20	25	30	
gta gcc tgg tat caa cag aaa cca ggg caa tct cct aaa cta ctg att				144
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile				
	35	40	45	
tac tgg gca tcc atc cgg cac act gga gtc cct gat cgc ttc aca ggc				192
Tyr Trp Ala Ser Ile Arg His Thr Gly Val Pro Asp Arg Phe Thr Gly				
	50	55	60	
agt gga tct ggg aca gat ttc act ctc acc att agc aat gtg cag tct				240
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Asn Val Gln Ser				
65		70	75	80
gaa gac ttg gca gat tat ttc tgt cag caa tat agc agc tat ccg ctc				288
Glu Asp Leu Ala Asp Tyr Phe Cys Gln Gln Tyr Ser Ser Tyr Pro Leu				
	85	90	95	
acg ttc ggt gct ggg acc aag ctg gag ctg aaa				321
Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys				
	100	105		

<210> 229
 <211> 107
 <212> PRT
 <213> Mus musculus

<400> 229

Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly	
1	5 10 15
Asp Arg Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Gly Thr Ala	
20	25 30
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile	
35	40 45

Tyr Trp Ala Ser Ile Arg His Thr Gly Val Pro Asp Arg Phe Thr Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Asn Val Gln Ser
65 70 75 80

Glu Asp Leu Ala Asp Tyr Phe Cys Gln Gln Tyr Ser Ser Tyr Pro Leu
85 90 95

Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105

<210> 230
<211> 363
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(363)
<223> SC16.105 VH

<220>
<221> CDS
<222> (1)..(363)

<400> 230
cag gtc caa ctg cag cag cct ggg gct gag ctt gtg aag cct ggg gct 48
Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Ala
1 5 10 15

tca gtg aag ctg tcc tgc aag gct tct ggc tac acc ttc acc agc tac 96
Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

tgg atg cac tgg gtg aag cag agg cct gga caa ggc ctt gag tgg att 144
Trp Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile

35	40	45	
gga gtg att aat cct agc aac ggt cgt act aac tac aat gag aag ttc			192
Gly Val Ile Asn Pro Ser Asn Gly Arg Thr Asn Tyr Asn Glu Lys Phe			
50	55	60	
aag agc aag gcc aca ctg act gta gac aaa tcc tcc agc aca gcc tac			240
Lys Ser Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr			
65	70	75	80
atg caa ctc agc agc ctg aca tct gag gac tct gcg gtc tat tac tgt			288
Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys			
	85	90	95
gca aga aga agg gaa ctg gga acc ctc tat gct atg gac tac tgg ggt			336
Ala Arg Arg Arg Glu Leu Gly Thr Leu Tyr Ala Met Asp Tyr Trp Gly			
	100	105	110
caa gga acc tca gtc acc gtc tcc tca			363
Gln Gly Thr Ser Val Thr Val Ser Ser			
	115	120	
<210> 231			
<211> 121			
<212> PRT			
<213> Mus musculus			
<400> 231			
Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Ala			
1	5	10	15
Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr			
	20	25	30
Trp Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile			
	35	40	45
Gly Val Ile Asn Pro Ser Asn Gly Arg Thr Asn Tyr Asn Glu Lys Phe			
50	55	60	

Lys Ser Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Arg Glu Leu Gly Thr Leu Tyr Ala Met Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Ser Val Thr Val Ser Ser
115 120

<210> 232
<211> 321
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(321)
<223> SC16.106 VL

<220>
<221> CDS
<222> (1)..(321)

<400> 232
gac atc aag atg acc cag tct cca tct tcc atg tat gca tct cta gga 48
Asp Ile Lys Met Thr Gln Ser Pro Ser Ser Met Tyr Ala Ser Leu Gly
1 5 10 15

gag aga gtc act atc act tgc aag gcg agt cag gac att aat agc tat 96
Glu Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Ile Asn Ser Tyr
20 25 30

tta agc tgg ttc cag cag aaa cca ggg aaa tct cct aag acc ctg atc 144
Leu Ser Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Thr Leu Ile

35	40	45	
tat cgt gca aac aga ttg gta gat ggg gtc cca tca agg ttc agt ggc			192
Tyr Arg Ala Asn Arg Leu Val Asp Gly Val Pro Ser Arg Phe Ser Gly			
50	55	60	
agt gga tct ggg caa gat tat tct ctc acc atc agc agc ctg gag tat			240
Ser Gly Ser Gly Gln Asp Tyr Ser Leu Thr Ile Ser Ser Leu Glu Tyr			
65	70	75	80
gaa gat atg gga att tat tat tgt cta cag tat gat gag ttt cca ttc			288
Glu Asp Met Gly Ile Tyr Tyr Cys Leu Gln Tyr Asp Glu Phe Pro Phe			
85	90	95	
acg ttc ggc tcg ggg aca aag ttg gaa ata aaa			321
Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys			
100	105		
<210>	233		
<211>	107		
<212>	PRT		
<213>	Mus musculus		
<400>	233		
Asp Ile Lys Met Thr Gln Ser Pro Ser Ser Met Tyr Ala Ser Leu Gly			
1	5	10	15
Glu Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Ile Asn Ser Tyr			
20	25	30	
Leu Ser Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Thr Leu Ile			
35	40	45	
Tyr Arg Ala Asn Arg Leu Val Asp Gly Val Pro Ser Arg Phe Ser Gly			
50	55	60	
Ser Gly Ser Gly Gln Asp Tyr Ser Leu Thr Ile Ser Ser Leu Glu Tyr			
65	70	75	80

Glu	Asp	Met	Gly	Ile	Tyr	Tyr	Cys	Leu	Gln	Tyr	Asp	Glu	Phe	Pro	Phe
				85					90					95	

Thr	Phe	Gly	Ser	Gly	Thr	Lys	Leu	Glu	Ile	Lys
			100				105			

<210> 234
 <211> 345
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1)..(345)
 <223> SC16.106 VH

<220>
 <221> CDS
 <222> (1)..(345)

<400>	234															
cag	gtg	caa	ctg	aag	cag	tca	gga	cct	ggc	ctg	gtg	gcg	ccc	tca	cag	48
Gln	Val	Gln	Leu	Lys	Gln	Ser	Gly	Pro	Gly	Leu	Val	Ala	Pro	Ser	Gln	
1				5					10					15		

agc	ctg	ttc	atc	aca	tgc	acc	gtc	tca	ggg	ttc	tca	tta	acc	agc	tat	96
Ser	Leu	Phe	Ile	Thr	Cys	Thr	Val	Ser	Gly	Phe	Ser	Leu	Thr	Ser	Tyr	
			20					25					30			

gaa	ata	aac	tgg	gtt	cgc	cag	cct	cca	gga	aag	ggt	ctg	gag	tgg	ctg	144
Glu	Ile	Asn	Trp	Val	Arg	Gln	Pro	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Leu	
		35					40					45				

gga	gtg	ata	tgg	act	ggt	gga	agc	aca	aat	tat	aat	tca	gct	ctc	ata	192
Gly	Val	Ile	Trp	Thr	Gly	Gly	Ser	Thr	Asn	Tyr	Asn	Ser	Ala	Leu	Ile	
	50				55					60						

tcc	aga	ctg	agc	atc	agc	aaa	gac	aac	tcc	aag	agc	cta	gtt	ttc	tta	240
Ser	Arg	Leu	Ser	Ile	Ser	Lys	Asp	Asn	Ser	Lys	Ser	Leu	Val	Phe	Leu	

65	70	75	80	
aaa atg aac agt ctg caa act gat gac aca gcc ata tat tac tgt gta Lys Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Val				288
	85	90	95	
aga ggt gtt tat gct atg gac tac tgg ggt caa gga acc tca gtc acc Arg Gly Val Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr				336
	100	105	110	
gtc tcc tca Val Ser Ser				345
	115			
<210> 235 <211> 115 <212> PRT <213> Mus musculus				
<400> 235				
Gln Val Gln Leu Lys Gln Ser Gly Pro Gly Leu Val Ala Pro Ser Gln 1 5 10 15				
Ser Leu Phe Ile Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Ser Tyr 20 25 30				
Glu Ile Asn Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Leu 35 40 45				
Gly Val Ile Trp Thr Gly Gly Ser Thr Asn Tyr Asn Ser Ala Leu Ile 50 55 60				
Ser Arg Leu Ser Ile Ser Lys Asp Asn Ser Lys Ser Leu Val Phe Leu 65 70 75 80				
Lys Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Val 85 90 95				

Arg Gly Val Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr
100 105 110

Val Ser Ser
115

<210> 236
<211> 321
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(321)
<223> SC16.107 VL

<220>
<221> CDS
<222> (1)..(321)

<400> 236
gac att gtg atg acc cag tct cac aaa ttc atg tcc aca tca gta gga 48
Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly
1 5 10 15

gac agg gtc agc atc acc tgc aag gcc agt cag gat gtg aat act gct 96
Asp Arg Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Asn Thr Ala
20 25 30

gta ggc tgg tat caa cag aaa cca gga caa tct cct aaa cta ctg att 144
Val Gly Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile
35 40 45

tac tcg gca tcc tac cgg tac act gga gtc cct gat cgc ttc act ggc 192
Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Thr Gly
50 55 60

agt gga tct ggg acg gat ttc act ttc acc atc agc agt gtg cag gct 240
Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Val Gln Ala

65	70	75	80	
gaa gac ctg gca gtt tat tac tgt cag caa cat tat agt agt ccg tac				288
Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Ser Pro Tyr				
	85	90	95	
acg ttc gga ggg ggg acc aag gtg gaa ata aaa				321
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys				
	100	105		
<210> 237 <211> 107 <212> PRT <213> Mus musculus <400> 237				
Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly 1 5 10 15				
Asp Arg Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Asn Thr Ala 20 25 30				
Val Gly Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile 35 40 45				
Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Thr Gly 50 55 60				
Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Val Gln Ala 65 70 75 80				
Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Ser Pro Tyr 85 90 95				
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys 100 105				

<210> 238
 <211> 357
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1).. (357)
 <223> SC16.107 VH

<220>
 <221> CDS
 <222> (1).. (357)

<400> 238
 gag gtc cag ctg cag cag tct gga cct gag ctg gta aag cct ggg gct 48
 Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
 1 5 10 15

 tca gtg aag atg tcc tgc aag gct tct gga tac aca ttc act aac tat 96
 Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
 20 25 30

 gtt atg cac tgg gtg aag cag aag cct ggg cag ggc ctt gag tgg att 144
 Val Met His Trp Val Lys Gln Lys Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45

 gga tat att aat cct tac aat gat ggt act aaa tac aat gag aag ttc 192
 Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Thr Lys Tyr Asn Glu Lys Phe
 50 55 60

 aaa ggc aag gcc aca ctg act tca gac aaa tcc tcc acc aca gcc tac 240
 Lys Gly Lys Ala Thr Leu Thr Ser Asp Lys Ser Ser Thr Thr Ala Tyr
 65 70 75 80

 atg gcg ctc agc agc ctg acc tct gag gac tct gcg gtc tat tac tgt 288
 Met Ala Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
 85 90 95

 gca gta gcc tac tat agt aac tgg ggg ttt gct tac tgg ggc caa ggg 336
 Ala Val Ala Tyr Tyr Ser Asn Trp Gly Phe Ala Tyr Trp Gly Gln Gly

	100	105	110	
	act ctg gtc act gtc tct gca			357
	Thr Leu Val Thr Val Ser Ala			
	115			
<210>	239			
<211>	119			
<212>	PRT			
<213>	Mus musculus			
<400>	239			
	Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala			
	1 5 10 15			
	Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr			
	20 25 30			
	Val Met His Trp Val Lys Gln Lys Pro Gly Gln Gly Leu Glu Trp Ile			
	35 40 45			
	Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Thr Lys Tyr Asn Glu Lys Phe			
	50 55 60			
	Lys Gly Lys Ala Thr Leu Thr Ser Asp Lys Ser Ser Thr Thr Ala Tyr			
	65 70 75 80			
	Met Ala Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys			
	85 90 95			
	Ala Val Ala Tyr Tyr Ser Asn Trp Gly Phe Ala Tyr Trp Gly Gln Gly			
	100 105 110			
	Thr Leu Val Thr Val Ser Ala			
	115			

<210> 240
 <211> 321
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1).. (321)
 <223> SC16.108 VL

<220>
 <221> CDS
 <222> (1).. (321)

<400> 240
 gac atc cag atg act cag tct cca gcc tcc cta tct gca tct gtg gga 48
 Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Val Gly
 1 5 10 15

 gaa act gtc acc atc aca tgt cga gca agt gag aat att tac agt tat 96
 Glu Thr Val Thr Ile Thr Cys Arg Ala Ser Glu Asn Ile Tyr Ser Tyr
 20 25 30

 tta gca tgg tat cag cag aaa cag gga aaa tct cct cag ctc ctg gtc 144
 Leu Ala Trp Tyr Gln Gln Lys Gln Gly Lys Ser Pro Gln Leu Leu Val
 35 40 45

 tat aat gca aaa acc tta gca gaa ggt gtg cca tca agg ttc agt ggc 192
 Tyr Asn Ala Lys Thr Leu Ala Glu Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

 agt aga tca ggc tca cag ttt tct ctg aag atc aac agc ctg cag cct 240
 Ser Arg Ser Gly Ser Gln Phe Ser Leu Lys Ile Asn Ser Leu Gln Pro
 65 70 75 80

 gaa gat ttt ggg agt tat tac tgt caa cat cat tat ggt act ccg tac 288
 Glu Asp Phe Gly Ser Tyr Tyr Cys Gln His His Tyr Gly Thr Pro Tyr
 85 90 95

 acg ttc gga ggg ggg acc aag ctg gaa ata aaa 321
 Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys

100

105

<210> 241

<211> 107

<212> PRT

<213> Mus musculus

<400> 241

Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Val Gly
 1 5 10 15

Glu Thr Val Thr Ile Thr Cys Arg Ala Ser Glu Asn Ile Tyr Ser Tyr
 20 25 30

Leu Ala Trp Tyr Gln Gln Lys Gln Gly Lys Ser Pro Gln Leu Leu Val
 35 40 45

Tyr Asn Ala Lys Thr Leu Ala Glu Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

Ser Arg Ser Gly Ser Gln Phe Ser Leu Lys Ile Asn Ser Leu Gln Pro
 65 70 75 80

Glu Asp Phe Gly Ser Tyr Tyr Cys Gln His His Tyr Gly Thr Pro Tyr
 85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 100 105

<210> 242

<211> 360

<212> DNA

<213> Mus musculus

<220>
 <221> misc_feature
 <222> (1).. (360)
 <223> SC16.108 VH

<220>
 <221> CDS
 <222> (1).. (360)

<400> 242
 cag gtt cag ctg gag gag tca ggg gct gag ctg gca aga cct ggg gct 48
 Gln Val Gln Leu Glu Glu Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
 1 5 10 15
 tca gtg aag ttg tcc tgc aag gct tct ggc tat agc tac tgg atg cag 96
 Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ser Tyr Trp Met Gln
 20 25 30
 tgg ata aaa cag agg cct gga cag ggt ctg gaa tgg att ggg gct att 144
 Trp Ile Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile
 35 40 45
 tat cct gga aat ggt gat act agg tac act cag aag ttc aag ggc aag 192
 Tyr Pro Gly Asn Gly Asp Thr Arg Tyr Thr Gln Lys Phe Lys Gly Lys
 50 55 60
 gcc aca ttg act gca gat aaa tcc tcc agc aca gcc tac atg caa ctc 240
 Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu
 65 70 75 80
 agc agc ttg gca tct gag gac tct gcg gtc tat tac tgt gca aga tct 288
 Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Ser
 85 90 95
 ccg gcc tac tat agg tac ggc gag ggc tac ttt gac tac tgg ggc caa 336
 Pro Ala Tyr Tyr Arg Tyr Gly Glu Gly Tyr Phe Asp Tyr Trp Gly Gln
 100 105 110
 ggc acc act ctc aca gtc tcc tca 360
 Gly Thr Thr Leu Thr Val Ser Ser
 115 120

<210> 243

<211> 120
<212> PRT
<213> Mus musculus

<400> 243

Gln Val Gln Leu Glu Glu Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ser Tyr Trp Met Gln
20 25 30

Trp Ile Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile
35 40 45

Tyr Pro Gly Asn Gly Asp Thr Arg Tyr Thr Gln Lys Phe Lys Gly Lys
50 55 60

Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu
65 70 75 80

Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Tyr Cys Ala Arg Ser
85 90 95

Pro Ala Tyr Tyr Arg Tyr Gly Glu Gly Tyr Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Thr Leu Thr Val Ser Ser
115 120

<210> 244
<211> 318
<212> DNA
<213> Mus musculus

<220>
 <221> misc_feature
 <222> (1).. (318)
 <223> SC16.109 VL

<220>
 <221> CDS
 <222> (1).. (318)

<400> 244
 caa att gtt ctc acc cag tct cca gca atc atg tct gca tct cca ggg 48
 Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
 1 5 10 15
 gag aag gtc acc atg acc tgc agt gcc agc tca agt gta agt tac atg 96
 Glu Lys Val Thr Met Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
 20 25 30
 tac tgg tac cag cag aag cca gga tcc tcc ccc aga ctc ctg att tat 144
 Tyr Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Arg Leu Leu Ile Tyr
 35 40 45
 gac aca tcc aac ctg gct tct gga gtc cct gtt cgc ttc agt ggc agt 192
 Asp Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser
 50 55 60
 ggg tct ggg acc tct ttc tct ctc aca atc agc cga atg gag gct gaa 240
 Gly Ser Gly Thr Ser Phe Ser Leu Thr Ile Ser Arg Met Glu Ala Glu
 65 70 75 80
 gat act gcc act tat tac tgc cag gag tgg agt ggt aat ccg ctc acg 288
 Asp Thr Ala Thr Tyr Tyr Cys Gln Glu Trp Ser Gly Asn Pro Leu Thr
 85 90 95
 ttc ggt gat ggg acc aag ctg gag ctg aaa 318
 Phe Gly Asp Gly Thr Lys Leu Glu Leu Lys
 100 105

<210> 245
 <211> 106
 <212> PRT
 <213> Mus musculus

<400> 245

Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Met Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

Tyr Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Arg Leu Leu Ile Tyr
35 40 45

Asp Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Phe Ser Leu Thr Ile Ser Arg Met Glu Ala Glu
65 70 75 80

Asp Thr Ala Thr Tyr Tyr Cys Gln Glu Trp Ser Gly Asn Pro Leu Thr
85 90 95

Phe Gly Asp Gly Thr Lys Leu Glu Leu Lys
100 105

<210> 246

<211> 354

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1)..(354)

<223> SC16.109 VH

<220>

<221> CDS

<222> (1)..(354)

<400> 246

cag atc cag ttg gtg cag tct gga cct gag ctg aag aag cct gga gag
Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1 5 10 15

aca gtc aag atc tcc tgc aag gct tct ggg tat acc ttc aca aac tat
Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

gga atg aac tgg gtg aag cag gct cca gga aag ggt tta aag tgg atg
Gly Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met
35 40 45

ggc tgg ata aac acc tac act gga gag cca gca tat gct gat gac ttc
Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Ala Tyr Ala Asp Asp Phe
50 55 60

aag gga cgg ttt gcc ttc tct ttg gaa acc tct gcc agc gct gcc tat
Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Ala Ala Tyr
65 70 75 80

ttg cag atc aac aac ctc aaa aat gag gac acg gct act ttt ttc tgt
Leu Gln Ile Asn Asn Leu Lys Asn Glu Asp Thr Ala Thr Phe Phe Cys
85 90 95

gca aat atg agg ccc acg agg ggg ttt gct tac tgg ggg caa ggg act
Ala Asn Met Arg Pro Thr Arg Gly Phe Ala Tyr Trp Gly Gln Gly Thr
100 105 110

ctg ggc act gtc tct gca
Leu Gly Thr Val Ser Ala
115

<211> 118

⟨213⟩ Mus musculus

Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1 5 10 15

Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Ala Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Ala Ala Tyr
65 70 75 80

Leu Gln Ile Asn Asn Leu Lys Asn Glu Asp Thr Ala Thr Phe Phe Cys
85 90 95

Ala Asn Met Arg Pro Thr Arg Gly Phe Ala Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Gly Thr Val Ser Ala
115

<210> 248
<211> 321
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (321)
<223> SC16.110 VL

<220>
<221> CDS
<222> (1).. (321)

<400> 248

aat att gtg atg acc cag act ccc aaa ttc ctg ctt gta tca gca gga 48
Asn Ile Val Met Thr Gln Thr Pro Lys Phe Leu Leu Val Ser Ala Gly
1 5 10 15

gac agg gtt acc ata acc tgc aag gcc agt cag agt gtg agt aat gat 96
Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Ser Val Ser Asn Asp
20 25 30

gta gct tgg tac caa cag aag cca ggg cag tct cct aaa ctg ctg ata 144
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile
35 40 45

tac tat gca tcc aat cgc tac act gga gtc cct gat cgc ttc act ggc 192
Tyr Tyr Ala Ser Asn Arg Tyr Thr Gly Val Pro Asp Arg Phe Thr Gly
50 55 60

agt gga tat ggg acg gat ttc act ttc acc atc agc act gtg cag gct 240
Ser Gly Tyr Gly Thr Asp Phe Thr Phe Thr Ile Ser Thr Val Gln Ala
65 70 75 80

gaa gac ctg gca gtt tat ttc tgt cag cag gat tat agc tct cct ccg 288
Glu Asp Leu Ala Val Tyr Phe Cys Gln Gln Asp Tyr Ser Ser Pro Pro
85 90 95

acg ttc ggt gga ggc acc aag ctg gaa atc aaa 321
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 249

<211> 107

<212> PRT

<213> Mus musculus

<400> 249

Asn Ile Val Met Thr Gln Thr Pro Lys Phe Leu Leu Val Ser Ala Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Ser Val Ser Asn Asp
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Ala Ser Asn Arg Tyr Thr Gly Val Pro Asp Arg Phe Thr Gly
50 55 60

Ser Gly Tyr Gly Thr Asp Phe Thr Phe Thr Ile Ser Thr Val Gln Ala
65 70 75 80

Glu Asp Leu Ala Val Tyr Phe Cys Gln Gln Asp Tyr Ser Ser Pro Pro
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 250
<211> 354
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (354)
<223> SC16.110 VH

<220>
<221> CDS
<222> (1).. (354)

<400> 250
gag gtc cag ctg cag cag tct gga cct ggg cta gtg agg act ggg gct 48
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Arg Thr Gly Ala
1 5 10 15

tca gtg aag ata tcc tgc aag gct tct ggt tac tca ttc act ggt tac 96
Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr

Gly Tyr Ile Ser Cys Tyr Asn Gly Ala Thr Thr Tyr Asn Gln Asn Phe
50 55 60

Lys Gly Lys Ala Thr Phe Ile Val Asp Thr Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Phe Asn Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Asp Gly Gly His Ala Met Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Ser Val Thr Val Ser Ser
115

<210> 252
<211> 321
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(321)
<223> SC16.111 VL

<220>
<221> CDS
<222> (1)..(321)

<400> 252
gac atc cag atg act cag tct cca gcc tcc ctg gct gca tct gtg gga 48
Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ala Ala Ser Val Gly
1 5 10 15

gaa act gtc acc atc aca tgt cga gca agt gag aac att tac tac agt 96
Glu Thr Val Thr Ile Thr Cys Arg Ala Ser Glu Asn Ile Tyr Tyr Ser

Ser Gly Ser Gly Thr Gln Tyr Ser Met Lys Ile Asn Ser Met Gln Pro
65 70 75 80

Glu Asp Thr Ala Thr Tyr Phe Cys Lys Gln Thr Tyr Asp Val Pro Leu
85 90 95

Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105

<210> 254
<211> 351
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (351)
<223> SC16.111 VH

<220>
<221> CDS
<222> (1).. (351)

<400> 254
gag gtt cag ctg cag cag tct gga cct gag ctg gag aag cct ggc gct 48
Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Glu Lys Pro Gly Ala
1 5 10 15

tca gtg aag ata tcc tgc aag gct tct ggt tac tca ttc act ggc tac 96
Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr
20 25 30

aac atg aac tgg gtg aag cag agc aat gga aag agc ctt gag tgg att 144
Asn Met Asn Trp Val Lys Gln Ser Asn Gly Lys Ser Leu Glu Trp Ile
35 40 45

gga aat att gat cct tat tat ggt ggt tct agc tac aaa cag aag ttc 192
Gly Asn Ile Asp Pro Tyr Tyr Gly Gly Ser Ser Tyr Lys Gln Lys Phe

50	55	60	
gag ggc aag gcc aca ttg act gta gac aaa tcc tcc agc aca gcc tac			240
Glu Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr			
65	70	75	80
atg cag ctc aag agc ctg aca tct gag gac tct gca gtc tat tac tgt			288
Met Gln Leu Lys Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys			
	85	90	95
gca aga ggt ggt agt aac ttc ttt gac tac tgg ggc caa ggc acc act			336
Ala Arg Gly Gly Ser Asn Phe Phe Asp Tyr Trp Gly Gln Gly Thr Thr			
	100	105	110
ctc aca gtc tcc tca			351
Leu Thr Val Ser Ser			
	115		
<210> 255			
<211> 117			
<212> PRT			
<213> Mus musculus			
<400> 255			
Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Glu Lys Pro Gly Ala			
1	5	10	15
Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr			
	20	25	30
Asn Met Asn Trp Val Lys Gln Ser Asn Gly Lys Ser Leu Glu Trp Ile			
	35	40	45
Gly Asn Ile Asp Pro Tyr Tyr Gly Gly Ser Ser Tyr Lys Gln Lys Phe			
50	55	60	
Glu Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr			
65	70	75	80

Met Gln Leu Lys Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Ser Asn Phe Phe Asp Tyr Trp Gly Gln Gly Thr Thr
100 105 110

Leu Thr Val Ser Ser
115

<210> 256
<211> 336
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (336)
<223> SC16.113 VL

<220>
<221> CDS
<222> (1).. (336)

<400> 256
gat gtt gtg atg acc cag act cca ctc act ttg tcg gtt acc att gga 48
Asp Val Val Met Thr Gln Thr Pro Leu Thr Leu Ser Val Thr Ile Gly
1 5 10 15

caa cca gcc tcc atc tct tgc aag tca agt cag agc ctc tta gat agt 96
Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser
20 25 30

gat gga acg aca tat ttg aat tgg ttg tta cag agg cca ggc cag tct 144
Asp Gly Thr Thr Tyr Leu Asn Trp Leu Leu Gln Arg Pro Gly Gln Ser
35 40 45

cca aag cgc cta atc tat ctg gtg tct aaa ctg gac tct gga gtc cct 192
Pro Lys Arg Leu Ile Tyr Leu Val Ser Lys Leu Asp Ser Gly Val Pro

50	55	60														
gac agg ttc act ggc agt gga tca ggg aca gat ttc aca ctg aaa atc																240
Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile																
65	70	75	80													
agc aga gtg gag gct gag gat ttg gga gtt tat tat tgc tgg caa ggt																288
Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Trp Gln Gly																
	85	90	95													
aca cat ttt ccg ctc acg ttc ggt gct ggg acc aag ctg gag ctg aaa																336
Thr His Phe Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys																
	100	105	110													

$\langle 210 \rangle$	257
$\langle 211 \rangle$	112
$\langle 212 \rangle$	PRT
$\langle 213 \rangle$	Mus musculus

<400> 257

Asp Val Val Met Thr Gln Thr Pro Leu Thr Leu Ser Val Thr Ile Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser
20 25 30

Asp Gly Thr Thr Tyr Leu Asn Trp Leu Leu Gln Arg Pro Gly Gln Ser
35 40 45

Pro Lys Arg Leu Ile Tyr Leu Val Ser Lys Leu Asp Ser Gly Val Pro
50 55 60

Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Trp Gln Gly
85 90 95

Thr His Phe Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105 110

<210> 258
<211> 351
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(351)
<223> SC16.113 VH

<220>
<221> CDS
<222> (1)..(351)

<400> 258
gac gtg aag ctg gtg gag tct ggg gga ggc tta gtg aag cct gga ggg 48
Asp Val Lys Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

tcc ctg aaa ctc tcc tgt gca gcc tct gga ttc act ttc agt agc tat 96
Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

acc atg tct tgg gtt cgc cag act ccg gag aag agg ctg gag tgg gtc 144
Thr Met Ser Trp Val Arg Gln Thr Pro Glu Lys Arg Leu Glu Trp Val
35 40 45

gca acc att agt agt ggt ggt agt tac ccc tac tat cca gac agt gtg 192
Ala Thr Ile Ser Ser Gly Gly Ser Tyr Pro Tyr Tyr Pro Asp Ser Val
50 55 60

aag ggc cga ttc acc atc tcc aga gac aat gcc aag aac acc ctg tac 240
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
65 70 75 80

ctg caa atg agc agt ctg aag tct gag gac aca gcc atg tat tac tgt 288
Leu Gln Met Ser Ser Leu Lys Ser Glu Asp Thr Ala Met Tyr Tyr Cys

	85	90	95	
aca aga gat gtc tat gat ggt tac tcc tac tgg ggc caa ggc acc act				336
Thr Arg Asp Val Tyr Asp Gly Tyr Ser Tyr Trp Gly Gln Gly Thr Thr				
	100	105	110	
ctc aca gtc tcc tca				351
Leu Thr Val Ser Ser				
	115			
<210> 259				
<211> 117				
<212> PRT				
<213> Mus musculus				
<400> 259				
Asp Val Lys Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly				
1 5 10 15				
Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr				
20 25 30				
Thr Met Ser Trp Val Arg Gln Thr Pro Glu Lys Arg Leu Glu Trp Val				
35 40 45				
Ala Thr Ile Ser Ser Gly Gly Ser Tyr Pro Tyr Tyr Pro Asp Ser Val				
50 55 60				
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr				
65 70 75 80				
Leu Gln Met Ser Ser Leu Lys Ser Glu Asp Thr Ala Met Tyr Tyr Cys				
85 90 95				
Thr Arg Asp Val Tyr Asp Gly Tyr Ser Tyr Trp Gly Gln Gly Thr Thr				
100 105 110				

Leu Thr Val Ser Ser
115

<210> 260
<211> 318
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(318)
<223> SC16.114 VL

<220>
<221> CDS
<222> (1)..(318)

<400> 260
caa att gtt ctc tcc cag tct cca gca atc ctg tct gca tct cca ggg 48
Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
1 5 10 15

gag aag gtc aca atg act tgc agg gcc agc tca agt gta agt tac atg 96
Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

cac tgg tac cag cag aag cca gga tcc tcc ccc aaa ccc tgg att tat 144
His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
35 40 45

gcc aca tcc aac ctg gct tct gga gtc cct gct cgc ttc agt ggc agt 192
Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

ggg tct ggg acc tct tac tct ctc aca atc agc aga gtg gag gct gaa 240
Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
65 70 75 80

gat gct gcc act tat tac tgc cag cag tgg agt agt aac cca tac acg 288
Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Tyr Thr

	85	90	95	
ttc gga ggg ggg acc aag ctg gaa ata aaa				318
Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys				
	100	105		

$\langle 210 \rangle$	261
$\langle 211 \rangle$	106
$\langle 212 \rangle$	PRT
$\langle 213 \rangle$	Mus musculus

<400> 261

Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Tyr Thr
85 90 95

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

$\langle 210 \rangle$	262
$\langle 211 \rangle$	369

<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (369)
<223> SC16.114 VH

<220>
<221> CDS
<222> (1).. (369)

<400> 262
gag gtt cag ctg cag cag tct ggg gca gaa ctt gtg aag cca ggg gcc 48
Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Lys Pro Gly Ala
1 5 10 15

tca gtc aaa ttg tcc tgc aca gct tct ggc ttc aac att aaa gac acc 96
Ser Val Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Thr
20 25 30

tat ata cac tgg gtg aaa cag agg cct gaa cag ggc ctg gag tgg att 144
Tyr Ile His Trp Val Lys Gln Arg Pro Glu Gln Gly Leu Glu Trp Ile
35 40 45

gga agg att gat cct gcg aat ggt aat act aaa tat gac ccg aag ttc 192
Gly Arg Ile Asp Pro Ala Asn Gly Asn Thr Lys Tyr Asp Pro Lys Phe
50 55 60

cag ggc aag gcc act ata aca cca gac aca tcc tcc aac aca gcc tac 240
Gln Gly Lys Ala Thr Ile Thr Pro Asp Thr Ser Ser Asn Thr Ala Tyr
65 70 75 80

ctg cag ctc agc agc ctg aca tct gag gac act gcc gtc tat tac tgt 288
Leu Gln Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

gct aga agc tgg cga aac tac ggt agt agt ttc tgg tac ttc gat gtc 336
Ala Arg Ser Trp Arg Asn Tyr Gly Ser Ser Phe Trp Tyr Phe Asp Val
100 105 110

tgg ggc gca ggg acc acg gtc acc gtc tcc tca 369
Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser

115

120

<210> 263

<211> 123

<212> PRT

<213> Mus musculus

<400> 263

Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Thr
 20 25 30

Tyr Ile His Trp Val Lys Gln Arg Pro Glu Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Arg Ile Asp Pro Ala Asn Gly Asn Thr Lys Tyr Asp Pro Lys Phe
 50 55 60

Gln Gly Lys Ala Thr Ile Thr Pro Asp Thr Ser Ser Asn Thr Ala Tyr
 65 70 75 80

Leu Gln Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Ser Trp Arg Asn Tyr Gly Ser Ser Phe Trp Tyr Phe Asp Val
 100 105 110

Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser
 115 120

<210> 264

<211> 336

<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (336)
<223> SC16.115 VL

<220>
<221> CDS
<222> (1).. (336)

<400> 264
gat gtt gtg atg acc cag act cca ctc act ttg tcg gtt acc att gga 48
Asp Val Val Met Thr Gln Thr Pro Leu Thr Leu Ser Val Thr Ile Gly
1 5 10 15

caa cca gcc tcc atc tct tgc aag tca agt cag agc ctc tta gat agt 96
Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser
20 25 30

gat gga acg aca tat ttg aat tgg ttg tta cag agg cca ggc cag tct 144
Asp Gly Thr Thr Tyr Leu Asn Trp Leu Leu Gln Arg Pro Gly Gln Ser
35 40 45

cca aag cgc cta atc tat ctg gtg tct aaa ctg gac tct gga gtc cct 192
Pro Lys Arg Leu Ile Tyr Leu Val Ser Lys Leu Asp Ser Gly Val Pro
50 55 60

gac agg ttc act ggc agt gga tca ggg aca gat ttc aca ctg aaa atc 240
Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

agc aga gtg gag gct gag gat ttg gga gtt tat tat tgc tgg caa ggt 288
Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Trp Gln Gly
85 90 95

aca cat ttt ccg ctc acg ttc ggt gct ggg acc aag ctg gag ctg aaa 336
Thr His Phe Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105 110

<210> 265

<211> 112
<212> PRT
<213> Mus musculus

<400> 265

Asp Val Val Met Thr Gln Thr Pro Leu Thr Leu Ser Val Thr Ile Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser
20 25 30

Asp Gly Thr Thr Tyr Leu Asn Trp Leu Leu Gln Arg Pro Gly Gln Ser
35 40 45

Pro Lys Arg Leu Ile Tyr Leu Val Ser Lys Leu Asp Ser Gly Val Pro
50 55 60

Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Trp Gln Gly
85 90 95

Thr His Phe Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105 110

<210> 266
<211> 351
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(351)
<223> SC16.115 VH

<220>

<221> CDS

<222> (1)..(351)

<400> 266

gac	gtg	aag	ctg	gtg	gag	tct	ggg	gga	ggc	tta	gtg	aag	cct	gga	ggg	48
Asp	Val	Lys	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Lys	Pro	Gly	Gly	
1			5					10					15			

tcc	ctg	aaa	ctc	tcc	tgt	gca	gcc	tct	gga	ttc	act	ttc	agt	agc	tat	96
Ser	Leu	Lys	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Ser	Tyr	
		20					25					30				

acc	atg	tct	tgg	gtt	cgc	cag	act	ccg	gag	aag	agg	ctg	gag	tgg	gtc	144
Thr	Met	Ser	Trp	Val	Arg	Gln	Thr	Pro	Glu	Lys	Arg	Leu	Glu	Trp	Val	
		35				40					45					

gca	acc	att	agt	agt	ggt	ggt	agt	tac	ccc	tac	tat	cca	gac	agt	gtg	192
Ala	Thr	Ile	Ser	Ser	Gly	Gly	Ser	Tyr	Pro	Tyr	Tyr	Pro	Asp	Ser	Val	
	50				55						60					

aag	ggc	cga	ttc	acc	atc	tcc	aga	gac	aat	gcc	aag	aac	acc	ctg	tac	240
Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ala	Lys	Asn	Thr	Leu	Tyr	
65				70					75					80		

ctg	caa	atg	agc	agt	ctg	aag	tct	gag	gac	aca	gcc	atg	tat	tac	tgt	288
Leu	Gln	Met	Ser	Ser	Leu	Lys	Ser	Glu	Asp	Thr	Ala	Met	Tyr	Tyr	Cys	
			85					90					95			

aca	aga	gat	gtc	tat	gat	ggt	tac	tcc	tac	tgg	ggc	caa	ggc	acc	act	336
Thr	Arg	Asp	Val	Tyr	Asp	Gly	Tyr	Ser	Tyr	Trp	Gly	Gln	Gly	Thr	Thr	
		100					105					110				

ctc	aca	gtc	tcc	tca												351
Leu	Thr	Val	Ser	Ser												
		115														

<210> 267

<211> 117

<212> PRT

<213> Mus musculus

<400> 267

Asp Val Lys Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Thr Met Ser Trp Val Arg Gln Thr Pro Glu Lys Arg Leu Glu Trp Val
35 40 45

Ala Thr Ile Ser Ser Gly Gly Ser Tyr Pro Tyr Tyr Pro Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Ser Ser Leu Lys Ser Glu Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Thr Arg Asp Val Tyr Asp Gly Tyr Ser Tyr Trp Gly Gln Gly Thr Thr
100 105 110

Leu Thr Val Ser Ser
115

<210> 268

<211> 333

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1)..(333)

<223> SC16.116 VL

<220>

<221> CDS

<222> (1)..(333)

<400> 268

gac att gtg atg aca cag tct cca tcc tcc ctg act gtg aca gca gga	48
Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly	
1 5 10 15	

gag aag gtc act atg agc tgc acg tcc agt cag agt ctg tta acc agt	96
Glu Lys Val Thr Met Ser Cys Thr Ser Ser Gln Ser Leu Leu Thr Ser	
20 25 30	

gga aat caa aag aac tac ttg acc tgg tac cag cag aaa cca ggg cag	144
Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln	
35 40 45	

cct cct aaa ctg ttg atc tac tgg gca tcc act agg gaa tct ggg gtc	192
Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val	
50 55 60	

cct gat cgc ttc aca ggc agt gga tct gga aca gat ttc act ctc acc	240
Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr	
65 70 75 80	

atc agc agt ttg cag gct gaa gac ctg gca gtt tat tac tgt cag aat	288
Ile Ser Ser Leu Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn	
85 90 95	

gat tat agt ctc acg ttc ggt gct ggg acc aag ctg gag ctg aaa	333
Asp Tyr Ser Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys	
100 105 110	

<210> 269

<211> 111

<212> PRT

<213> Mus musculus

<400> 269

Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Thr Val Thr Ala Gly	
1 5 10 15	

Glu Lys Val Thr Met Ser Cys Thr Ser Ser Gln Ser Leu Leu Thr Ser
20 25 30

Gly Asn Gln Lys Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Leu Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
85 90 95

Asp Tyr Ser Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105 110

<210> 270
<211> 354
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (354)
<223> SC16.116 VH

<220>
<221> CDS
<222> (1).. (354)

<400> 270
cag gtg cag ctg aag cag tca gga cct ggc cga gtg cag ccc tca cag
Gln Val Gln Leu Lys Gln Ser Gly Pro Gly Arg Val Gln Pro Ser Gln

1	5	10	15	
agc ctg tcc atc acc tgc aca gtc tct ggt ttt tca tta act agc aat				96
Ser Leu Ser Ile Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Ser Asn				
20	25	30		
ggt gta cac tgg gtt cgc cag tct cca gga aag ggt ctg gag tgg ctg				144
Gly Val His Trp Val Arg Gln Ser Pro Gly Lys Gly Leu Glu Trp Leu				
35	40	45		
gga gtg cta tgg agt ggt gga agc aca gac tat aat gca gct ttc ata				192
Gly Val Leu Trp Ser Gly Gly Ser Thr Asp Tyr Asn Ala Ala Phe Ile				
50	55	60		
tcc aga ctg agc atc agc aag gac aat tac aag agc caa gtt ttc ttt				240
Ser Arg Leu Ser Ile Ser Lys Asp Asn Tyr Lys Ser Gln Val Phe Phe				
65	70	75	80	
aaa atg aac agt ctg caa gct aat gac aca gcc ata tat tac tgt gcc				288
Lys Met Asn Ser Leu Gln Ala Asn Asp Thr Ala Ile Tyr Tyr Cys Ala				
85	90	95		
aga aat aat aat agg tac gga gct atg gac tac tgg ggt caa gga acc				336
Arg Asn Asn Asn Arg Tyr Gly Ala Met Asp Tyr Trp Gly Gln Gly Thr				
100	105	110		
tca gtc acc gtc tcc tca				354
Ser Val Thr Val Ser Ser				
115				

<210> 271
 <211> 118
 <212> PRT
 <213> Mus musculus

<400> 271

Gln Val Gln Leu Lys Gln Ser Gly Pro Gly Arg Val Gln Pro Ser Gln
1 5 10 15

Ser Leu Ser Ile Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Ser Asn
20 25 30

Gly Val His Trp Val Arg Gln Ser Pro Gly Lys Gly Leu Glu Trp Leu
35 40 45

Gly Val Leu Trp Ser Gly Gly Ser Thr Asp Tyr Asn Ala Ala Phe Ile
50 55 60

Ser Arg Leu Ser Ile Ser Lys Asp Asn Tyr Lys Ser Gln Val Phe Phe
65 70 75 80

Lys Met Asn Ser Leu Gln Ala Asn Asp Thr Ala Ile Tyr Tyr Cys Ala
85 90 95

Arg Asn Asn Asn Arg Tyr Gly Ala Met Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Ser Val Thr Val Ser Ser
115

<210> 272
<211> 321
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(321)
<223> SC16.117 VL

<220>
<221> CDS
<222> (1)..(321)

<400> 272
gac atc cag atg aac cag tct cca tcc agt ctg tct gca tcc ctt gga
Asp Ile Gln Met Asn Gln Ser Pro Ser Ser Leu Ser Ala Ser Leu Gly

1	5	10	15	
gac aca att acc atc act tgc cat gtc agt cag aac att aat gtt tgg				96
Asp Thr Ile Thr Ile Thr Cys His Val Ser Gln Asn Ile Asn Val Trp				
	20	25	30	
tta agc tgg tac cag cag aaa cca gga aat att cct aaa cta ttg atc				144
Leu Ser Trp Tyr Gln Gln Lys Pro Gly Asn Ile Pro Lys Leu Leu Ile				
	35	40	45	
caa aag gct tcc aac ttg cac aca ggc gtc ccc tca agg ttt agt ggc				192
Gln Lys Ala Ser Asn Leu His Thr Gly Val Pro Ser Arg Phe Ser Gly				
	50	55	60	
agt gga tct gga aca ggt ttc aca tta acc atc agc agc ctg cag cct				240
Ser Gly Ser Gly Thr Gly Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro				
65		70	75	80
gaa gac att gcc act tac tac tgt caa cag ggt caa agt tat cca ttc				288
Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Gln Ser Tyr Pro Phe				
	85	90	95	
acg ttc ggc tcg ggg aca aag ttg gaa ata aaa				321
Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys				
	100	105		

<210> 273
 <211> 107
 <212> PRT
 <213> Mus musculus

<400> 273

Asp Ile Gln Met Asn Gln Ser Pro Ser Ser Leu Ser Ala Ser Leu Gly	
1	5 10 15
Asp Thr Ile Thr Ile Thr Cys His Val Ser Gln Asn Ile Asn Val Trp	
20	25 30
Leu Ser Trp Tyr Gln Gln Lys Pro Gly Asn Ile Pro Lys Leu Leu Ile	
35	40 45

Gln Lys Ala Ser Asn Leu His Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Gly Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Gln Ser Tyr Pro Phe
85 90 95

Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 274
<211> 351
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (351)
<223> SC16.117 VH

<220>
<221> CDS
<222> (1).. (351)

<400> 274
cag gtg cag ctg aag gag tca gga cct ggc ctg gtg gcg ccc tca cag 48
Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln
1 5 10 15

agc ctg tcc atc act tgc act gtc tct ggg ttt tca tta acc aac tat 96
Ser Leu Ser Ile Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Asn Tyr
20 25 30

ggt gta cac tgg gtt cgc cag cct cca gga aag ggt ctg gag tgg ctg 144
Gly Val His Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Leu

Ser Arg Leu Ser Ile Ser Glu Asp Asn Ser Lys Ser Gln Val Phe Leu
65 70 75 80

Lys Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Met Tyr Tyr Cys Ala
85 90 95

Arg Asn Leu Gly Pro Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser
100 105 110

Val Thr Val Ser Ser
115

<210> 276
<211> 333
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (333)
<223> SC16.118 VL

<220>
<221> CDS
<222> (1).. (333)

<400> 276
gac att gtg ctg acc caa tct cca gct tct ttg gct gtg tct cta ggg 48
Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

cag agg gcc acc atc tcc tgc aag gcc agc caa agt gtt gat tat gat 96
Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

ggt gat agt tat ttg acc tgg tac caa cag aaa cca gga cag cca ccc 144
Gly Asp Ser Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro

35	40	45	
aaa ctc ctc atc tat gct gca tcc aat cta gaa tct ggg atc cca gcc Lys Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala 50 55 60			192
agg ttt agt ggc agt ggg tct ggg aca gac ttc acc ctc aac atc cat Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His 65 70 75 80			240
cct gtg gag gag gag gac gct gca acc tat tac tgt cag caa agt aat Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Ser Asn 85 90 95			288
gag gat ccg tac acg ttc gga ggg ggg acc aag ctg gaa ata aaa Glu Asp Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys 100 105 110			333
<210> 277 <211> 111 <212> PRT <213> Mus musculus <400> 277			
Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly 1 5 10 15			
Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp 20 25 30			
Gly Asp Ser Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro 35 40 45			
Lys Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala 50 55 60			
Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His 65 70 75 80			

Pro	Val	Glu	Glu	Glu	Asp	Ala	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Ser	Asn
					85				90					95	

Glu	Asp	Pro	Tyr	Thr	Phe	Gly	Gly	Gly	Thr	Lys	Leu	Glu	Ile	Lys
			100					105					110	

<210> 278
 <211> 351
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1)..(351)
 <223> SC16.118 VH

<220>
 <221> CDS
 <222> (1)..(351)

<400>	278														
gag gtc cag ctg cag cag tct gga cct gac ctg gtg aag cct ggg gct		48													
Glu	Val	Gln	Leu	Gln	Gln	Ser	Gly	Pro	Asp	Leu	Val	Lys	Pro	Gly	Ala
1			5					10					15		
tca gtg aag ata tcc tgc aag gct tct ggt tac tca ttc act ggc tac		96													
Ser	Val	Lys	Ile	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Ser	Phe	Thr	Gly	Tyr
		20					25					30			
tac atg cac tgg gtg aag cag agc cat gga aag agc ctt gag tgg att		144													
Tyr	Met	His	Trp	Val	Lys	Gln	Ser	His	Gly	Lys	Ser	Leu	Glu	Trp	Ile
		35					40					45			
gga cgt gtt aat cct aac aat ggt ggt act agc tac aac cag aag ttc		192													
Gly	Arg	Val	Asn	Pro	Asn	Asn	Gly	Gly	Thr	Ser	Tyr	Asn	Gln	Lys	Phe
		50				55				60					
aag ggc aag gcc ata tta act gca gac aag tca tcc agc aca gcc tac		240													
Lys	Gly	Lys	Ala	Ile	Leu	Thr	Ala	Asp	Lys	Ser	Ser	Ser	Thr	Ala	Tyr

65	70	75	80	
atg gag ctc cgc agc ctg aca tct gag gac tct gcg gtc tat tac tgt				288
Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys				
	85	90	95	
gca aga ggg agt tat gat tac gcc gag ggc tgg ggc caa ggg act ctg				336
Ala Arg Gly Ser Tyr Asp Tyr Ala Glu Gly Trp Gly Gln Gly Thr Leu				
	100	105	110	
gtc act gtc tct gca				351
Val Thr Val Ser Ala				
	115			
<210> 279				
<211> 117				
<212> PRT				
<213> Mus musculus				
<400> 279				
Glu Val Gln Leu Gln Gln Ser Gly Pro Asp Leu Val Lys Pro Gly Ala				
1	5	10	15	
Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr				
	20	25	30	
Tyr Met His Trp Val Lys Gln Ser His Gly Lys Ser Leu Glu Trp Ile				
	35	40	45	
Gly Arg Val Asn Pro Asn Asn Gly Gly Thr Ser Tyr Asn Gln Lys Phe				
	50	55	60	
Lys Gly Lys Ala Ile Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr				
65	70	75	80	
Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys				
	85	90	95	

Ala Arg Gly Ser Tyr Asp Tyr Ala Glu Gly Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ala
115

<210> 280
<211> 339
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(339)
<223> SC16.120 VL

<220>
<221> CDS
<222> (1)..(339)

<400> 280
gac att gtg atg tca cag tct cca tcc tcc cta gct gtg tca gtt gga 48
Asp Ile Val Met Ser Gln Ser Pro Ser Ser Leu Ala Val Ser Val Gly
1 5 10 15

gag aag gtt act atg agc tgc aag tcc agt cag agc ctt tta tat agt 96
Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Tyr Ser
20 25 30

agc act caa aag aac tac ttg gcc tgg tac cag cag aaa cca ggg cag 144
Ser Thr Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

tct cct aaa ctg ctg att tac tgg gca tcc act agg gaa tct ggg gtc 192
Ser Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

cct gat cgc ttc aca ggc agt gga tct ggg aca gat ttc act ctc acc 240
Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr

65	70	75	80	
atc agc agt gtg aag gct gaa gac ctg gca gtt tat tac tgt cag caa				288
Ile Ser Ser Val Lys Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln				
	85	90	95	
tat tat agc tat ccg tac acg ttc gga ggg ggg acc aag ctg gaa ata				336
Tyr Tyr Ser Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile				
	100	105	110	
aaa				339
Lys				

<210> 281
 <211> 113
 <212> PRT
 <213> Mus musculus

<400> 281

Asp	Ile	Val	Met	Ser	Gln	Ser	Pro	Ser	Ser	Leu	Ala	Val	Ser	Val	Gly
1				5						10					15

Glu	Lys	Val	Thr	Met	Ser	Cys	Lys	Ser	Ser	Gln	Ser	Leu	Leu	Tyr	Ser
			20							25					30

Ser	Thr	Gln	Lys	Asn	Tyr	Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln
			35					40						45	

Ser	Pro	Lys	Leu	Leu	Ile	Tyr	Trp	Ala	Ser	Thr	Arg	Glu	Ser	Gly	Val
			50					55				60			

Pro	Asp	Arg	Phe	Thr	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr
65					70					75					80

Ile	Ser	Ser	Val	Lys	Ala	Glu	Asp	Leu	Ala	Val	Tyr	Tyr	Cys	Gln	Gln
				85						90				95	

Tyr Tyr Ser Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
100 105 110

Lys

<210> 282
<211> 351
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(351)
<223> SC16.120 VH

<220>
<221> CDS
<222> (1)..(351)

<400> 282
gag atc cag ctg cag cag tct gga cct gag ctg gtg aag cct ggg gct 48
Glu Ile Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1 5 10 15

tca gtg aag gta tcc tgc aag gct tct ggt tat gca ttc act agc tac 96
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Ser Tyr
20 25 30

aac atg tac tgg gtg atg cag agc cat gga aag agc ctt gag tgg att 144
Asn Met Tyr Trp Val Met Gln Ser His Gly Lys Ser Leu Glu Trp Ile
35 40 45

gga tat gtt gat cct tac aat ggt ggt act agc tac aac cag aag ttc 192
Gly Tyr Val Asp Pro Tyr Asn Gly Gly Thr Ser Tyr Asn Gln Lys Phe
50 55 60

aag ggc aag gcc aca ttg act gtt gac aag tcc tcc agc aca gcc tac 240
Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr

65	70	75	80	
atg cat ctc aac agc ctg aca tct gag gac tct gca gtc tat tac tgt				288
Met His Leu Asn Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys				
	85	90	95	
gca aga gaa aac tat agg tac ttt gac tac tgg ggc caa ggc acc act				336
Ala Arg Glu Asn Tyr Arg Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Thr				
	100	105	110	
ctc aca gtc tcc tca				351
Leu Thr Val Ser Ser				
	115			
<210> 283				
<211> 117				
<212> PRT				
<213> Mus musculus				
<400> 283				
Glu Ile Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala				
1	5	10	15	
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Ser Tyr				
	20	25	30	
Asn Met Tyr Trp Val Met Gln Ser His Gly Lys Ser Leu Glu Trp Ile				
	35	40	45	
Gly Tyr Val Asp Pro Tyr Asn Gly Gly Thr Ser Tyr Asn Gln Lys Phe				
	50	55	60	
Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr				
65	70	75	80	
Met His Leu Asn Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys				
	85	90	95	

Ala Arg Glu Asn Tyr Arg Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Thr
100 105 110

Leu Thr Val Ser Ser
115

<210> 284
<211> 318
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (318)
<223> SC16.121 VL

<220>
<221> CDS
<222> (1).. (318)

<400> 284
caa att gtt ctc acc cag tct cca gca atc atg tct gca tct cca ggg 48
Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1 5 10 15

gag aag gtc acc ata acc tgc agt gcc agc tca agt gta agt tac atg 96
Glu Lys Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

cac tgg ttc cag cag aag cca ggc act tct ccc aaa ctc tgg att tat 144
His Trp Phe Gln Gln Lys Pro Gly Thr Ser Pro Lys Leu Trp Ile Tyr
35 40 45

agc aca tcc aac ctg gct tct gga gtc cct gct cgc ttc agt ggc agt 192
Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

gga tct ggg acc tct tac tct ctc aca atc agc cga atg gag gct gaa 240
Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Met Glu Ala Glu

65	70	75	80	
gat gct gcc act tat tac tgc cag caa agg agt agt tac cca ccc acg				288
Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Arg Ser Ser Tyr Pro Pro Thr				
	85	90	95	

ttc gga ggg ggg acc aag ctg gaa ata aar				318
Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys				
	100	105		

<210> 285
 <211> 106
 <212> PRT
 <213> Mus musculus

<400> 285

Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

His Trp Phe Gln Gln Lys Pro Gly Thr Ser Pro Lys Leu Trp Ile Tyr
35 40 45

Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Met Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Arg Ser Ser Tyr Pro Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 286
 <211> 372
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1).. (372)
 <223> SC16.121 VH

<220>
 <221> CDS
 <222> (1).. (372)

<400> 286
 gag gtg cag ctt gtt gag tct ggt gga gga ttg gtg cag cct aaa ggg 48
 Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Lys Gly
 1 5 10 15

tca ttg aaa ctc tca tgt gca gcc tct gga ttc acc ttc aat acc tac 96
 Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Thr Tyr
 20 25 30

gcc atg aac tgg gtc cgc cag gct cca gga aag ggt ttg gaa tgg gtt 144
 Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

gct cgc ata aga att aaa agt aat aat tat gca aca tat tat gcc gat 192
 Ala Arg Ile Arg Ile Lys Ser Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
 50 55 60

tca gta aaa gac agg ttc acc atc tcc aga gat gat tca caa aac atg 240
 Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Gln Asn Met
 65 70 75 80

ctc tat ctg caa atg aac aac ttg aaa act gag gac aca gcc gtg tat 288
 Leu Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
 85 90 95

tac tgt gtg aga caa ggc tat agt tac gac tgg gga ccc tgg ttt gct 336
 Tyr Cys Val Arg Gln Gly Tyr Ser Tyr Asp Trp Gly Pro Trp Phe Ala

[illegible]

<210> 288
 <211> 321
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1)..(321)
 <223> SC16.122 VL

<220>
 <221> CDS
 <222> (1)..(321)

<400> 288
 gac att gtg atg acc cag tct caa aaa ttc atg tcc aca tca gta gga 48
 Asp Ile Val Met Thr Gln Ser Gln Lys Phe Met Ser Thr Ser Val Gly
 1 5 10 15

 gac agg gtc agc gtc acc tgc aag gcc agt cag aat gtg ggt act aat 96
 Asp Arg Val Ser Val Thr Cys Lys Ala Ser Gln Asn Val Gly Thr Asn
 20 25 30

 gta gcc tgg tat caa cag aaa cca ggg caa tct cct aaa gta ctg att 144
 Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Val Leu Ile
 35 40 45

 tac tgc gca tcc tac cgg tac agt gga gtc cct gat cgc ttc aca ggc 192
 Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr Gly
 50 55 60

 agt gga tct ggg aca gat ttc act ctc acc atc agc aat gtg cag tct 240
 Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Asn Val Gln Ser
 65 70 75 80

 gaa gac ttg gca gag ttt ttc tgt cag caa tat aac agc tat cct ctg 288
 Glu Asp Leu Ala Glu Phe Phe Cys Gln Gln Tyr Asn Ser Tyr Pro Leu
 85 90 95

 acg ttc ggt gga ggc acc aag ctg gaa atc aaa 321
 Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys

100

105

<210> 289

<211> 107

<212> PRT

<213> Mus musculus

<400> 289

Asp Ile Val Met Thr Gln Ser Gln Lys Phe Met Ser Thr Ser Val Gly
 1 5 10 15

Asp Arg Val Ser Val Thr Cys Lys Ala Ser Gln Asn Val Gly Thr Asn
 20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Val Leu Ile
 35 40 45

Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr Gly
 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Asn Val Gln Ser
 65 70 75 80

Glu Asp Leu Ala Glu Phe Phe Cys Gln Gln Tyr Asn Ser Tyr Pro Leu
 85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 100 105

<210> 290

<211> 354

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1).. (354)

<223> SC16.122 VH

<220>

<221> CDS

<222> (1).. (354)

<400> 290

gaa	gtg	cag	ctg	gtg	gag	tct	ggg	gga	ggc	tta	gtg	aag	cct	gga	ggg	48
Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Lys	Pro	Gly	Gly	
1				5					10					15		

tcc	ctg	aaa	ctc	tcc	tgt	gca	gcc	tct	gga	ttc	act	ttc	agt	gac	tat	96
Ser	Leu	Lys	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Asp	Tyr	
			20					25					30			

tac	atg	ttt	tgg	gtt	cgc	cag	act	ccg	gaa	aag	agg	ctg	gag	tgg	gtc	144
Tyr	Met	Phe	Trp	Val	Arg	Gln	Thr	Pro	Glu	Lys	Arg	Leu	Glu	Trp	Val	
		35				40					45					

gca	acc	att	agt	gat	ggg	ggg	agt	tac	acc	tac	ttt	cca	gac	agt	gtg	192
Ala	Thr	Ile	Ser	Asp	Gly	Gly	Ser	Tyr	Thr	Tyr	Phe	Pro	Asp	Ser	Val	
	50					55					60					

aag	ggg	cga	ttc	acc	atc	tcc	aga	gac	aat	gcc	cag	aac	aac	ctg	tac	240
Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ala	Gln	Asn	Asn	Leu	Tyr	
65					70					75				80		

ctg	caa	atg	agc	agt	ctg	aag	tct	gag	gac	aca	gcc	atg	tat	tac	tgt	288
Leu	Gln	Met	Ser	Ser	Leu	Lys	Ser	Glu	Asp	Thr	Ala	Met	Tyr	Tyr	Cys	
					85				90				95			

gca	aga	gcc	ggg	acc	ctc	tat	gct	atg	gac	tac	tgg	ggg	caa	gga	acc	336
Ala	Arg	Ala	Gly	Thr	Leu	Tyr	Ala	Met	Asp	Tyr	Trp	Gly	Gln	Gly	Thr	
		100					105					110				

tca	gtc	acc	gtc	tcc	tca											354
Ser	Val	Thr	Val	Ser	Ser											
						115										

<210> 291

<211> 118
<212> PRT
<213> Mus musculus

<400> 291

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Tyr Met Phe Trp Val Arg Gln Thr Pro Glu Lys Arg Leu Glu Trp Val
35 40 45

Ala Thr Ile Ser Asp Gly Gly Ser Tyr Thr Tyr Phe Pro Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Gln Asn Asn Leu Tyr
65 70 75 80

Leu Gln Met Ser Ser Leu Lys Ser Glu Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Ala Gly Thr Leu Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Ser Val Thr Val Ser Ser
115

<210> 292
<211> 324
<212> DNA
<213> Mus musculus

<220>

<221> misc_feature

<222> (1).. (324)

<223> SC16.123 VL

<220>

<221> CDS

<222> (1).. (324)

<400> 292

caa att gtt ctc acc cag tct cca gca atc atg tct gca tct cta ggg	48
Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Leu Gly	
1 5 10 15	

gaa cgg gtc acc atg acc tgc act gcc agc tca agt gta agt tcc agt	96
Glu Arg Val Thr Met Thr Cys Thr Ala Ser Ser Ser Val Ser Ser Ser	
20 25 30	

tac ttg cac tgg tac cag cag aag cca gga tcc tcc ccc aaa ctc tgg	144
Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Leu Trp	
35 40 45	

att tat agc aca tcc aac ctg gct tct gga gtc cca gct cgc ttc agt	192
Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser	
50 55 60	

ggc agt ggg tct ggg acc tct tac tct ctc aca atc agc agc atg gag	240
Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu	
65 70 75 80	

act gaa gat gct gcc act tat tac tgc cac cag tat cat cgt tcc ccc	288
Thr Glu Asp Ala Ala Thr Tyr Tyr Cys His Gln Tyr His Arg Ser Pro	
85 90 95	

ttc acg ttc ggc tcg ggg aca aag ttg gaa ata aaa	324
Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys	
100 105	

<210> 293

<211> 108

<212> PRT

<213> Mus musculus

<400> 293

Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Leu Gly
1 5 10 15

Glu Arg Val Thr Met Thr Cys Thr Ala Ser Ser Ser Val Ser Ser Ser
20 25 30

Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Leu Trp
35 40 45

Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu
65 70 75 80

Thr Glu Asp Ala Ala Thr Tyr Tyr Cys His Gln Tyr His Arg Ser Pro
85 90 95

Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 294

<211> 366

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1)..(366)

<223> SC16.123 VH

<220>

<221> CDS

<222> (1)..(366)

<400> 294

cag gtt gct ctg aaa gag tct ggc cct ggg ata ttg cag ccc tcc cag	48
Gln Val Ala Leu Lys Glu Ser Gly Pro Gly Ile Leu Gln Pro Ser Gln	
1 5 10 15	

acc ctc agt ctg act tgt tct ttc tct ggg ttt tca ctg agc act tct	96
Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser Thr Ser	
20 25 30	

ggc atg ggt gta ggc tgg att cgt cag cca tca ggg aag ggt ctg gag	144
Gly Met Gly Val Gly Trp Ile Arg Gln Pro Ser Gly Lys Gly Leu Glu	
35 40 45	

tgg ctg gca cac att tgg tgg gat gat gtc aag cgc tat aac cca gcc	192
Trp Leu Ala His Ile Trp Trp Asp Asp Val Lys Arg Tyr Asn Pro Ala	
50 55 60	

ctg aag agc cga ctg act atc tcc aag gat acc tcc agc agc cag gta	240
Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Ser Ser Gln Val	
65 70 75 80	

ttc ctc aag atc gcc agt gtg gac act gca gat act gcc aca tac tac	288
Phe Leu Lys Ile Ala Ser Val Asp Thr Ala Asp Thr Ala Thr Tyr Tyr	
85 90 95	

tgt gct cga atg gag gac tac ggt agt agc tcc tac ttt gac ttc tgg	336
Cys Ala Arg Met Glu Asp Tyr Gly Ser Ser Ser Tyr Phe Asp Phe Trp	
100 105 110	

ggc cac ggc acc act ctc aca gtc tcc tca	366
Gly His Gly Thr Thr Leu Thr Val Ser Ser	
115 120	

<210> 295

<211> 122

<212> PRT

<213> Mus musculus

<400> 295

Gln Val Ala Leu Lys Glu Ser Gly Pro Gly Ile Leu Gln Pro Ser Gln	
1 5 10 15	

Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser Thr Ser
20 25 30

Gly Met Gly Val Gly Trp Ile Arg Gln Pro Ser Gly Lys Gly Leu Glu
35 40 45

Trp Leu Ala His Ile Trp Trp Asp Asp Val Lys Arg Tyr Asn Pro Ala
50 55 60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Ser Ser Gln Val
65 70 75 80

Phe Leu Lys Ile Ala Ser Val Asp Thr Ala Asp Thr Ala Thr Tyr Tyr
85 90 95

Cys Ala Arg Met Glu Asp Tyr Gly Ser Ser Ser Tyr Phe Asp Phe Trp
100 105 110

Gly His Gly Thr Thr Leu Thr Val Ser Ser
115 120

<210> 296
<211> 321
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (321)
<223> SC16.124 VL

<220>
<221> CDS
<222> (1).. (321)

<400> 296

gac att cag atg acc cag tct cct gcc tcc cag tct gca tct ctg gga 48
Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Gln Ser Ala Ser Leu Gly
1 5 10 15

gaa agt gtc acc atc aca tgc ctg gca agt cag acc att ggt aca tgg 96
Glu Ser Val Thr Ile Thr Cys Leu Ala Ser Gln Thr Ile Gly Thr Trp
20 25 30

tta gca tgg tat cag cag aaa cca ggg aaa tct cct cag ctc ctg att 144
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ser Pro Gln Leu Leu Ile
35 40 45

tct gct gca acc agc ttg gca gat ggg gtc cca tca agg ttc agt ggt 192
Ser Ala Ala Thr Ser Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

agt gga tct ggc aca aaa ttt tct ttc aag atc agc agc cta cag gct 240
Ser Gly Ser Gly Thr Lys Phe Ser Phe Lys Ile Ser Ser Leu Gln Ala
65 70 75 80

gaa gat ttt gta agt tat tac tgt caa caa ctt tac agt act ccg tgg 288
Glu Asp Phe Val Ser Tyr Tyr Cys Gln Gln Leu Tyr Ser Thr Pro Trp
85 90 95

acg ttc ggt gga ggc acc aag ctg gaa atc aaa 321
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 297

<211> 107

<212> PRT

<213> Mus musculus

<400> 297

Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Gln Ser Ala Ser Leu Gly
1 5 10 15

Glu Ser Val Thr Ile Thr Cys Leu Ala Ser Gln Thr Ile Gly Thr Trp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ser Pro Gln Leu Leu Ile
35 40 45

Ser Ala Ala Thr Ser Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Lys Phe Ser Phe Lys Ile Ser Ser Leu Gln Ala
65 70 75 80

Glu Asp Phe Val Ser Tyr Tyr Cys Gln Gln Leu Tyr Ser Thr Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 298
<211> 369
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (369)
<223> SC16.124 VH

<220>
<221> CDS
<222> (1).. (369)

<400> 298
gag gtc cag ctg cag cag tct gga cct gag ctg gta aag cct ggg gct 48
Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1 5 10 15

tca gtg aag atg tcc tgc aag gct tct gga tac aca ttc act agc tat 96
Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr

20				25				30								
gtt	atg	cac	tgg	gtg	aag	cag	aag	cct	ggg	cag	ggc	ctt	gag	tgg	att	144
Val	Met	His	Trp	Val	Lys	Gln	Lys	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Ile	
35				40				45								
gga	tat	att	aat	cct	tac	aat	gat	ggt	act	aag	tac	aat	gag	aag	ttc	192
Gly	Tyr	Ile	Asn	Pro	Tyr	Asn	Asp	Gly	Thr	Lys	Tyr	Asn	Glu	Lys	Phe	
50				55				60								
aaa	ggc	aag	gcc	aca	ctg	act	tca	gac	aaa	tcc	tcc	agc	aca	gcc	tac	240
Lys	Gly	Lys	Ala	Thr	Leu	Thr	Ser	Asp	Lys	Ser	Ser	Ser	Thr	Ala	Tyr	
65				70				75				80				
atg	gag	ctc	agc	agc	ctg	acc	tct	gag	gac	tct	gcg	gtc	tat	tac	tgt	288
Met	Glu	Leu	Ser	Ser	Leu	Thr	Ser	Glu	Asp	Ser	Ala	Val	Tyr	Tyr	Cys	
				85				90				95				
gca	aga	ggg	gct	ctc	tac	tat	ggt	aac	tac	ctc	ggg	tac	ttc	gat	gtc	336
Ala	Arg	Gly	Ala	Leu	Tyr	Tyr	Gly	Asn	Tyr	Leu	Gly	Tyr	Phe	Asp	Val	
100				105				110								
tgg	ggc	gca	ggg	acc	acg	gtc	acc	gtc	tcc	tca						369
Trp	Gly	Ala	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser						
115				120												

Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Thr Lys Tyr Asn Glu Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ser Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Ala Leu Tyr Tyr Gly Asn Tyr Leu Gly Tyr Phe Asp Val
100 105 110

Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 300
<211> 321
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(321)
<223> SC16.125 VL

<220>
<221> CDS
<222> (1)..(321)

<400> 300
gac atc cag atg aac cag tct cca tcc agt ctg tct gca tcc ctt gga 48
Asp Ile Gln Met Asn Gln Ser Pro Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

gac aca att acc atc act tgc cat gcc agt cag aac att aat gtt tgg 96
Asp Thr Ile Thr Ile Thr Cys His Ala Ser Gln Asn Ile Asn Val Trp

Ser Gly Ser Gly Thr Gly Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Ser Cys Gln Gln Gly Gln Ser Tyr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 302
<211> 354
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (354)
<223> SC16.125 VH

<220>
<221> CDS
<222> (1).. (354)

<400> 302
gat gtg cag ctt cag gag tca gga cct gac ctg gtg aaa cct tct cag 48
Asp Val Gln Leu Gln Glu Ser Gly Pro Asp Leu Val Lys Pro Ser Gln
1 5 10 15

tca ctt tca ctc acc tgc act gtc act ggc tac tcc atc acc agt ggt 96
Ser Leu Ser Leu Thr Cys Thr Val Thr Gly Tyr Ser Ile Thr Ser Gly
20 25 30

tat agc tgg cac tgg atc cgg cag ttt cca gga aac aaa ctg gaa tgg 144
Tyr Ser Trp His Trp Ile Arg Gln Phe Pro Gly Asn Lys Leu Glu Trp
35 40 45

atg ggc tac ata cac tac agt ggt agc act aac tac aac cca tct ctc 192
Met Gly Tyr Ile His Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu

50	55	60	
aaa agt cga atc tct atc act cga gac aca tcc aag aac cag ttc ttc			240
Lys Ser Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe			
65	70	75	80
ctg cag ttc aaa tct gtg act act gaa gac tca gcc aca tat tac tgt			288
Leu Gln Phe Lys Ser Val Thr Thr Glu Asp Ser Ala Thr Tyr Tyr Cys			
	85	90	95
gcc cta gag ggg aat tac gac ggg ttt gct tac tgg ggc caa ggg act			336
Ala Leu Glu Gly Asn Tyr Asp Gly Phe Ala Tyr Trp Gly Gln Gly Thr			
	100	105	110
ctg gtc act gtc tct tcn			354
Leu Val Thr Val Ser Xaa			
	115		

<210> 303
 <211> 118
 <212> PRT
 <213> Mus musculus

 <220>
 <221> misc_feature
 <222> (118)..(118)
 <223> The 'Xaa' at location 118 stands for Ser.

 <400> 303

Asp Val Gln Leu Gln Glu Ser Gly Pro Asp Leu Val Lys Pro Ser Gln
1 5 10 15

Ser Leu Ser Leu Thr Cys Thr Val Thr Gly Tyr Ser Ile Thr Ser Gly
20 25 30

Tyr Ser Trp His Trp Ile Arg Gln Phe Pro Gly Asn Lys Leu Glu Trp
35 40 45

Met Gly Tyr Ile His Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu

50	55	60
Lys Ser Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe		
65	70	75 80
Leu Gln Phe Lys Ser Val Thr Thr Glu Asp Ser Ala Thr Tyr Tyr Cys		
	85	90 95
Ala Leu Glu Gly Asn Tyr Asp Gly Phe Ala Tyr Trp Gly Gln Gly Thr		
	100	105 110
Leu Val Thr Val Ser Xaa		
	115	

<210> 304
 <211> 321
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1).. (321)
 <223> SC16.126 VL

<220>
 <221> CDS
 <222> (1).. (321)

<400> 304	
gac atc cag atg aac cag tct cca tcc agt ctg tct gca tcc ctt gga	48
Asp Ile Gln Met Asn Gln Ser Pro Ser Ser Leu Ser Ala Ser Leu Gly	
1 5 10 15	
gac aca att acc atc act tgc cat gcc agt cag aac ata aat gtt tgg	96
Asp Thr Ile Thr Ile Thr Cys His Ala Ser Gln Asn Ile Asn Val Trp	
20 25 30	
tta agc tgg tac cag cag aaa cca gga aat att cct aaa cta ttg atc	144

Leu Ser Trp Tyr Gln Gln Lys Pro Gly Asn Ile Pro Lys Leu Leu Ile
35 40 45

tat aag get tcc aac ttg cac aca ggc gtc cca tca agg ttt agt ggc 192
Tyr Lys Ala Ser Asn Leu His Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

agt gga tct gga aca ggt ttc aca tta acc atc agc agc ctg cag cct 240
Ser Gly Ser Gly Thr Gly Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

gaa gac att gcc act tac tac tgt caa cag ggt caa agt tat cca ttc 288
Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Gln Ser Tyr Pro Phe
85 90 95

acg ttc ggc tcg ggg aca aag ttg gaa ata aaa 321
Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 305

<211> 107

<212> PRT

<213> Mus musculus

<400> 305

Asp Ile Gln Met Asn Gln Ser Pro Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

Asp Thr Ile Thr Ile Thr Cys His Ala Ser Gln Asn Ile Asn Val Trp
20 25 30

Leu Ser Trp Tyr Gln Gln Lys Pro Gly Asn Ile Pro Lys Leu Leu Ile
35 40 45

Tyr Lys Ala Ser Asn Leu His Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Gly Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro

65		70		75		80									
Glu	Asp	Ile	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Gly	Gln	Ser	Tyr	Pro	Phe
				85					90					95	

Thr	Phe	Gly	Ser	Gly	Thr	Lys	Leu	Glu	Ile	Lys
			100				105			

<210> 306
 <211> 348
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1)..(348)
 <223> SC16.126 VH

<220>
 <221> CDS
 <222> (1)..(348)

<400>	306															
cag	gtg	cag	atg	aag	gag	tca	gga	cct	ggc	ctg	gtg	gcg	ccc	tca	cag	48
Gln	Val	Gln	Met	Lys	Glu	Ser	Gly	Pro	Gly	Leu	Val	Ala	Pro	Ser	Gln	
1			5					10					15			

agc	ctg	tcc	atc	act	tgc	act	gtc	tct	ggg	tct	tca	tta	acc	aac	tat	96
Ser	Leu	Ser	Ile	Thr	Cys	Thr	Val	Ser	Gly	Ser	Ser	Leu	Thr	Asn	Tyr	
			20					25					30			

ggc	gta	cac	tgg	gtt	cgc	cag	cct	cca	gga	aag	ggc	cta	gag	tgg	ctg	144
Gly	Val	His	Trp	Val	Arg	Gln	Pro	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Leu	
		35				40					45					

gga	gta	ata	tgg	gct	ggc	gga	agc	aca	aat	tat	aat	tcg	gct	ctc	atg	192
Gly	Val	Ile	Trp	Ala	Gly	Gly	Ser	Thr	Asn	Tyr	Asn	Ser	Ala	Leu	Met	
		50				55					60					

tcc	aga	ctg	agt	atc	agc	aaa	gac	aac	tcc	aag	agc	caa	gtt	ttc	tta	240

Ser Arg Leu Ser Ile Ser Lys Asp Asn Ser Lys Ser Gln Val Phe Leu
65 70 75 80

aaa atg aac agt ctg caa act gat gac aca gcc atg tac tac tgt gcc 288
Lys Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Met Tyr Tyr Cys Ala
85 90 95

aga gac tgg gag ggc tgg ttt gct tac tgg ggc caa ggg act ctg gtc 336
Arg Asp Trp Glu Gly Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

act gtc tct gca 348
Thr Val Ser Ala
115

<210> 307

<211> 116

<212> PRT

<213> Mus musculus

<400> 307

Gln Val Gln Met Lys Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln
1 5 10 15

Ser Leu Ser Ile Thr Cys Thr Val Ser Gly Ser Ser Leu Thr Asn Tyr
20 25 30

Gly Val His Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Leu
35 40 45

Gly Val Ile Trp Ala Gly Gly Ser Thr Asn Tyr Asn Ser Ala Leu Met
50 55 60

Ser Arg Leu Ser Ile Ser Lys Asp Asn Ser Lys Ser Gln Val Phe Leu
65 70 75 80

Lys Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Met Tyr Tyr Cys Ala

85

90

95

Arg Asp Trp Glu Gly Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val
 100 105 110

Thr Val Ser Ala
 115

<210> 308
 <211> 321
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1)..(321)
 <223> SC16.129 VL

<220>
 <221> CDS
 <222> (1)..(321)

<400> 308
 gac att cag atg acc cag tct cct gcc tcc cag tct gca tct ctg gga 48
 Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Gln Ser Ala Ser Leu Gly
 1 5 10 15

gaa agt gtc acc atc aca tgc ctg gca agt cag acc att ggt aca tgg 96
 Glu Ser Val Thr Ile Thr Cys Leu Ala Ser Gln Thr Ile Gly Thr Trp
 20 25 30

tta gca tgg tat cag cag aaa cca ggg aaa tct cct cag ctc ctg att 144
 Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ser Pro Gln Leu Leu Ile
 35 40 45

tat gct gca acc agc ttg gca gat ggg gtc cca tca agg ttc agt ggt 192
 Tyr Ala Ala Thr Ser Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

agt gga tct ggc aca aaa ttt tct ttc aag atc agc agc cta cag gct 240

Ser Gly Ser Gly Thr Lys Phe Ser Phe Lys Ile Ser Ser Leu Gln Ala
65 70 75 80

gaa gat ttt gta agt tat tac tgt caa caa ctt tac agt act ccg tac 288
Glu Asp Phe Val Ser Tyr Tyr Cys Gln Gln Leu Tyr Ser Thr Pro Tyr
85 90 95

acg ttc gga ggg ggg acc aag ctg gaa ata aaa 321
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 309
<211> 107
<212> PRT
<213> Mus musculus

<400> 309

Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Gln Ser Ala Ser Leu Gly
1 5 10 15

Glu Ser Val Thr Ile Thr Cys Leu Ala Ser Gln Thr Ile Gly Thr Trp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ser Pro Gln Leu Leu Ile
35 40 45

Tyr Ala Ala Thr Ser Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Lys Phe Ser Phe Lys Ile Ser Ser Leu Gln Ala
65 70 75 80

Glu Asp Phe Val Ser Tyr Tyr Cys Gln Gln Leu Tyr Ser Thr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys

<210> 310
 <211> 348
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1).. (348)
 <223> SC16.129 VH

<220>
 <221> CDS
 <222> (1).. (348)

<400> 310

cag	gtg	cag	cta	aag	gag	tca	gga	cct	ggc	ctg	gtg	gcg	ccc	tca	cag	48
Gln	Val	Gln	Leu	Lys	Glu	Ser	Gly	Pro	Gly	Leu	Val	Ala	Pro	Ser	Gln	
1				5					10					15		

agc	ctg	tcc	atc	aca	tgc	act	gtc	tca	ggg	ttc	tca	tta	acc	gac	tat	96
Ser	Leu	Ser	Ile	Thr	Cys	Thr	Val	Ser	Gly	Phe	Ser	Leu	Thr	Asp	Tyr	
			20					25					30			

ggt	gta	agc	tgg	att	cgc	cag	cct	cca	gga	aag	ggt	ctg	gag	tgg	ctg	144
Gly	Val	Ser	Trp	Ile	Arg	Gln	Pro	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Leu	
		35				40						45				

gga	gta	ata	tgg	ggt	ggt	gga	agc	aca	tac	tat	aat	tca	gct	ctc	aaa	192
Gly	Val	Ile	Trp	Gly	Gly	Gly	Ser	Thr	Tyr	Tyr	Asn	Ser	Ala	Leu	Lys	
	50					55					60					

tcc	aga	ctg	agc	atc	agc	aag	gac	aac	tcc	aag	agc	caa	gtt	ttc	tta	240
Ser	Arg	Leu	Ser	Ile	Ser	Lys	Asp	Asn	Ser	Lys	Ser	Gln	Val	Phe	Leu	
65					70					75				80		

gaa	ctg	aac	agt	ctg	caa	act	gat	gac	aca	gcc	att	tac	tac	tgt	gcc	288
Glu	Leu	Asn	Ser	Leu	Gln	Thr	Asp	Asp	Thr	Ala	Ile	Tyr	Tyr	Cys	Ala	
				85					90					95		

aaa	cat	tat	ggt	cac	tac	gct	gct	tac	tgg	ggc	caa	ggg	act	ctg	gtc	336

Lys His Tyr Gly His Tyr Ala Ala Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

act gtc tct gca 348
Thr Val Ser Ala
115

<210> 311
<211> 116
<212> PRT
<213> Mus musculus

<400> 311

Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln
1 5 10 15

Ser Leu Ser Ile Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Asp Tyr
20 25 30

Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Leu
35 40 45

Gly Val Ile Trp Gly Gly Gly Ser Thr Tyr Tyr Asn Ser Ala Leu Lys
50 55 60

Ser Arg Leu Ser Ile Ser Lys Asp Asn Ser Lys Ser Gln Val Phe Leu
65 70 75 80

Glu Leu Asn Ser Leu Gln Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala
85 90 95

Lys His Tyr Gly His Tyr Ala Ala Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ala

<210> 312
 <211> 321
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1)..(321)
 <223> SC16.130 VL

<220>
 <221> CDS
 <222> (1)..(321)

<400> 312
 gac atc cag ttg act cag tct cca gcc tcc cta tct gca tct gtg gga 48
 Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Val Gly
 1 5 10 15
 gaa act gtc acc atc aca tgt cga gca agt ggg agt att cac aat tat 96
 Glu Thr Val Thr Ile Thr Cys Arg Ala Ser Gly Ser Ile His Asn Tyr
 20 25 30
 tta gca tgg tat cag cag aaa cag gga aag tct cct cag ctc ctg gtc 144
 Leu Ala Trp Tyr Gln Gln Lys Gln Gly Lys Ser Pro Gln Leu Leu Val
 35 40 45
 tat aat gca aaa acc tta gta gat ggt gtg cca tca agg ttc agt ggc 192
 Tyr Asn Ala Lys Thr Leu Val Asp Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60
 agt gga tca gga aca caa tat tct ctc aag atc aac agc ctg cag cct 240
 Ser Gly Ser Gly Thr Gln Tyr Ser Leu Lys Ile Asn Ser Leu Gln Pro
 65 70 75 80
 gaa gat ttt ggg tat tat tac tgt caa cat ttt tgg act act ccg tgg 288
 Glu Asp Phe Gly Tyr Tyr Tyr Cys Gln His Phe Trp Thr Thr Pro Trp
 85 90 95
 aca ttc ggt gga ggc acc aag ctg gaa atc aaa 321

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 313
<211> 107
<212> PRT
<213> Mus musculus

<400> 313

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Glu Thr Val Thr Ile Thr Cys Arg Ala Ser Gly Ser Ile His Asn Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Gln Gly Lys Ser Pro Gln Leu Leu Val
35 40 45

Tyr Asn Ala Lys Thr Leu Val Asp Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Gln Tyr Ser Leu Lys Ile Asn Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Gly Tyr Tyr Tyr Cys Gln His Phe Trp Thr Thr Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 314
<211> 360
<212> DNA
<213> Mus musculus

<220>

<221> misc_feature

<222> (1)..(360)

<223> SC16.130 VH

<220>

<221> CDS

<222> (1)..(360)

<400> 314

gag gtc cag ctg cag cag tct gga cct gag ctg gta aag cct ggg gct	48
Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala	
1 5 10 15	

tca gtg aag atg tcc tgc aag gct tct gga tac aca ttc act agc tat	96
Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr	
20 25 30	

gtt atg cac tgg gtg aag cag aag cct ggg cag ggc ctt gag tgg att	144
Val Met His Trp Val Lys Gln Lys Pro Gly Gln Gly Leu Glu Trp Ile	
35 40 45	

gga tat att aat cct tac aat gat ggt act gag tac aat gag aag ttc	192
Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Thr Glu Tyr Asn Glu Lys Phe	
50 55 60	

aaa ggc aag gcc aca ctg act tca gac aaa tcc tcc agc aca gcc tac	240
Lys Gly Lys Ala Thr Leu Thr Ser Asp Lys Ser Ser Ser Thr Ala Tyr	
65 70 75 80	

atg gag ctc agc agc ctg acc tct gag gac tct gcg gtc tat tac tgt	288
Met Glu Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys	
85 90 95	

gca aga ggg gtc tat gat ggt tac tct tac ttt gac tac tgg ggc caa	336
Ala Arg Gly Val Tyr Asp Gly Tyr Ser Tyr Phe Asp Tyr Trp Gly Gln	
100 105 110	

ggc acc act ctc aca gtc tcc tca	360
Gly Thr Thr Leu Thr Val Ser Ser	
115 120	

<210> 315
<211> 120
<212> PRT
<213> Mus musculus

<400> 315

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Val Met His Trp Val Lys Gln Lys Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Thr Glu Tyr Asn Glu Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ser Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Val Tyr Asp Gly Tyr Ser Tyr Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Thr Leu Thr Val Ser Ser
115 120

<210> 316
<211> 321
<212> DNA
<213> Mus musculus

<223> SC16.131 VL

 $\langle 222 \rangle \quad (1) \dots (321)$

acg ttc ggc tcg ggg aca aag ttg gaa ata aaa 321
Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
100 105

⟨213⟩ Mus musculus

<400> 317

Asp Ile Gln Met Asn Gln Ser Pro Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

Asp Thr Ile Thr Ile Thr Cys His Val Ser Gln Asn Ile Asn Val Trp
20 25 30

Leu Ser Trp Tyr Gln Gln Lys Pro Gly Asn Ile Pro Lys Leu Leu Ile
35 40 45

Gln Lys Ala Ser Asn Leu His Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Gly Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Gln Ser Tyr Pro Phe
85 90 95

Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 318

<211> 351

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1)..(351)

<223> SC16.131 VH

<220>

<221> CDS

<222> (1).. (351)

<400> 318

cag	gtg	cag	ctg	aag	gag	tca	gga	cct	ggc	ctg	gtg	gcg	ccc	tca	cag	48
Gln	Val	Gln	Leu	Lys	Glu	Ser	Gly	Pro	Gly	Leu	Val	Ala	Pro	Ser	Gln	
1				5					10					15		

agc	ctg	tcc	atc	act	tgc	act	gtc	tct	ggg	ttt	tca	tta	acc	aac	tat	96
Ser	Leu	Ser	Ile	Thr	Cys	Thr	Val	Ser	Gly	Phe	Ser	Leu	Thr	Asn	Tyr	
			20					25					30			

ggc	gta	cac	tgg	gtt	cgc	cag	cct	cca	gga	aag	ggc	ctg	gag	tgg	ctg	144
Gly	Val	His	Trp	Val	Arg	Gln	Pro	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Leu	
		35				40						45				

gga	gta	ata	tgg	gct	ggc	gga	atc	aca	aat	tat	aat	tgc	gct	ctc	atg	192
Gly	Val	Ile	Trp	Ala	Gly	Gly	Ile	Thr	Asn	Tyr	Asn	Ser	Ala	Leu	Met	
	50					55					60					

tcc	aga	ctg	agc	atc	agc	gaa	gac	aac	tcc	aag	agc	caa	gtt	ttc	tta	240
Ser	Arg	Leu	Ser	Ile	Ser	Glu	Asp	Asn	Ser	Lys	Ser	Gln	Val	Phe	Leu	
65					70					75				80		

aaa	atg	aac	agt	ctg	caa	act	gat	gac	aca	gcc	atg	tac	tac	tgt	gcc	288
Lys	Met	Asn	Ser	Leu	Gln	Thr	Asp	Asp	Thr	Ala	Met	Tyr	Tyr	Cys	Ala	
				85					90					95		

aga	aat	tta	ggc	ccc	tat	gct	atg	gac	tac	tgg	ggc	caa	gga	acc	tca	336
Arg	Asn	Leu	Gly	Pro	Tyr	Ala	Met	Asp	Tyr	Trp	Gly	Gln	Gly	Thr	Ser	
		100						105				110				

gtc	acc	gtc	tcc	tca												351
Val	Thr	Val	Ser	Ser												
				115												

<210> 319

<211> 117

<212> PRT

<213> Mus musculus

<400> 319

Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln

1	5	10	15												
Ser	Leu	Ser	Ile	Thr	Cys	Thr	Val	Ser	Gly	Phe	Ser	Leu	Thr	Asn	Tyr
			20					25					30		
Gly	Val	His	Trp	Val	Arg	Gln	Pro	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Leu
		35					40					45			
Gly	Val	Ile	Trp	Ala	Gly	Gly	Ile	Thr	Asn	Tyr	Asn	Ser	Ala	Leu	Met
	50					55					60				
Ser	Arg	Leu	Ser	Ile	Ser	Glu	Asp	Asn	Ser	Lys	Ser	Gln	Val	Phe	Leu
65					70					75				80	
Lys	Met	Asn	Ser	Leu	Gln	Thr	Asp	Asp	Thr	Ala	Met	Tyr	Tyr	Cys	Ala
				85					90					95	
Arg	Asn	Leu	Gly	Pro	Tyr	Ala	Met	Asp	Tyr	Trp	Gly	Gln	Gly	Thr	Ser
			100					105					110		
Val	Thr	Val	Ser	Ser											
			115												

<210> 320
 <211> 321
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1)..(321)
 <223> SC16.132 VL

<220>
 <221> CDS

<222> (1).. (321)

<400> 320

gac att cag atg acc cag tct cct gcc tcc cag tct gca tct ctg gga	48
Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Gln Ser Ala Ser Leu Gly	
1 5 10 15	

gaa agt gtc acc atc aca tgc ctg gca agt cag acc att ggt aca tgg	96
Glu Ser Val Thr Ile Thr Cys Leu Ala Ser Gln Thr Ile Gly Thr Trp	
20 25 30	

tta gca tgg tat cag cag aaa cca ggg aaa tct cct cag ctc ctg att	144
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ser Pro Gln Leu Leu Ile	
35 40 45	

tat gct gca acc agc ttg gca gat ggg gtc cca tca agg ttc agt ggt	192
Tyr Ala Ala Thr Ser Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly	
50 55 60	

agt gga tct ggc aca aaa ttt tct ttc aag atc agc agc cta cag gct	240
Ser Gly Ser Gly Thr Lys Phe Ser Phe Lys Ile Ser Ser Leu Gln Ala	
65 70 75 80	

gaa gat ttt gta agt tat tac tgt caa caa ctt tac agt act ccg tgg	288
Glu Asp Phe Val Ser Tyr Tyr Cys Gln Gln Leu Tyr Ser Thr Pro Trp	
85 90 95	

acg ttc ggt gga ggc acc aag ctg gag atc aaa	321
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys	
100 105	

<210> 321

<211> 107

<212> PRT

<213> Mus musculus

<400> 321

Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Gln Ser Ala Ser Leu Gly	
1 5 10 15	

Glu Ser Val Thr Ile Thr Cys Leu Ala Ser Gln Thr Ile Gly Thr Trp

20

25

30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ser Pro Gln Leu Leu Ile
 35 40 45

Tyr Ala Ala Thr Ser Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Lys Phe Ser Phe Lys Ile Ser Ser Leu Gln Ala
 65 70 75 80

Glu Asp Phe Val Ser Tyr Tyr Cys Gln Gln Leu Tyr Ser Thr Pro Trp
 85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 100 105

<210> 322

<211> 348

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1).. (348)

<223> SC16.132 VH

<220>

<221> CDS

<222> (1).. (348)

<400> 322

cag gtg cag ctg aag gag tca gga cct ggc ctg gtg gcg ccc tca cag 48
 Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln
 1 5 10 15

agc ctg tcc atc aca tgc act gtc tca ggg ttc tca tta acc gac tat 96

Ser Leu Ser Ile Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Asp Tyr
20 25 30

ggt gta agc tgg att cgc cag cct cca gga aag ggt ctg gag tgg ctg 144
Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Leu
35 40 45

gga gta gta tgg ggt ggt gga agc aca tac tat aat tcc gct ctc aaa 192
Gly Val Val Trp Gly Gly Gly Ser Thr Tyr Tyr Asn Ser Ala Leu Lys
50 55 60

tcc aga ctg agc atc acc aag gac aac tcc aag agc caa gtt ttc tta 240
Ser Arg Leu Ser Ile Thr Lys Asp Asn Ser Lys Ser Gln Val Phe Leu
65 70 75 80

aaa atg aac agt ctg caa act gat gac aca gcc atg tac tac tgt gcc 288
Lys Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Met Tyr Tyr Cys Ala
85 90 95

aaa cag agg ggt cag tac ggg gct tac tgg ggc caa ggg act ctg gtc 336
Lys Gln Arg Gly Gln Tyr Gly Ala Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

act gtc tct gca 348
Thr Val Ser Ala
115

<210> 323
<211> 116
<212> PRT
<213> Mus musculus

<400> 323

Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln
1 5 10 15

Ser Leu Ser Ile Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Asp Tyr
20 25 30

Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Leu

	35		40		45	
Gly	Val	Val	Trp	Gly	Gly	Gly
50				55		60
Ser	Arg	Leu	Ser	Ile	Thr	Lys
65				70		75
						80
Lys	Met	Asn	Ser	Leu	Gln	Thr
				85		90
						95
Lys	Gln	Arg	Gly	Gln	Tyr	Gly
			100			105
						110
Thr	Val	Ser	Ala			
			115			

<210> 324
 <211> 321
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1)..(321)
 <223> SC16.133 VL

<220>
 <221> CDS
 <222> (1)..(321)

<400>	324	
agt att gtg atg acc cag act ccc aaa ttc ctg ctt gtt tca gca gga		48
Ser Ile Val Met Thr Gln Thr Pro Lys Phe Leu Leu Val Ser Ala Gly		
1	5	10
		15
gac agg gtt acc ata acc tgc aag gcc agt cag agt gtg agt aat gat		96

Asp	Arg	Val	Thr	Ile	Thr	Cys	Lys	Ala	Ser	Gln	Ser	Val	Ser	Asn	Asp
			20					25					30		

gta	gct	tgg	tac	caa	cag	aag	cca	ggg	cag	tct	cct	aaa	ctg	ctg	ata	144
Val	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ser	Pro	Lys	Leu	Leu	Ile	
		35					40					45				

tac	tgt	gca	tcc	aat	cgc	tac	act	gga	gtc	cct	gat	cgc	ttc	act	ggc	192
Tyr	Cys	Ala	Ser	Asn	Arg	Tyr	Thr	Gly	Val	Pro	Asp	Arg	Phe	Thr	Gly	
	50					55				60						

agt	gga	tat	ggg	acg	gat	ttc	act	ttc	acc	atc	agc	act	gtg	cag	gct	240
Ser	Gly	Tyr	Gly	Thr	Asp	Phe	Thr	Phe	Thr	Ile	Ser	Thr	Val	Gln	Ala	
65					70				75					80		

gaa	gac	ctg	gca	gtt	tat	ttc	tgt	cag	cag	gat	tat	agc	tct	ccg	ctc	288
Glu	Asp	Leu	Ala	Val	Tyr	Phe	Cys	Gln	Gln	Asp	Tyr	Ser	Ser	Pro	Leu	
				85				90					95			

acg	ttc	ggt	gct	ggg	acc	aag	ctg	gag	ctg	aaa						321
Thr	Phe	Gly	Ala	Gly	Thr	Lys	Leu	Glu	Leu	Lys						
			100				105									

<210> 325
 <211> 107
 <212> PRT
 <213> Mus musculus

<400> 325

Ser	Ile	Val	Met	Thr	Gln	Thr	Pro	Lys	Phe	Leu	Leu	Val	Ser	Ala	Gly
1				5				10					15		

Asp	Arg	Val	Thr	Ile	Thr	Cys	Lys	Ala	Ser	Gln	Ser	Val	Ser	Asn	Asp
			20					25					30		

Val	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ser	Pro	Lys	Leu	Leu	Ile
		35					40					45			

Tyr	Cys	Ala	Ser	Asn	Arg	Tyr	Thr	Gly	Val	Pro	Asp	Arg	Phe	Thr	Gly

50 55 60

Ser Gly Tyr Gly Thr Asp Phe Thr Phe Thr Ile Ser Thr Val Gln Ala
65 70 75 80

Glu Asp Leu Ala Val Tyr Phe Cys Gln Gln Asp Tyr Ser Ser Pro Leu
85 90 95

Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105

<210> 326
<211> 357
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (357)
<223> SC16.133 VH

<220>
<221> CDS
<222> (1).. (357)

<400> 326
cag gtg cag ctg aag gag tca gga cct ggc ctg gtg gcg ccc tca cag 48
Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln
1 5 10 15

agc ctg tcc atc acc tgc aca gtc tct ggt ttc tca tta acc aac tat 96
Ser Leu Ser Ile Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Asn Tyr
20 25 30

gct gta cac tgg gtt cgc cag tct cca gga aag ggt ctg gag tgg ctg 144
Ala Val His Trp Val Arg Gln Ser Pro Gly Lys Gly Leu Glu Trp Leu
35 40 45

gga gtg ata tgg agt gat gga agc aca gac tat aat gca gct ttc ata 192

Gly Val Ile Trp Ser Asp Gly Ser Thr Asp Tyr Asn Ala Ala Phe Ile
50 55 60

tct aga ctg agc atc agc aag gac aac tcc aag agc caa gtt ttc ttt 240
Ser Arg Leu Ser Ile Ser Lys Asp Asn Ser Lys Ser Gln Val Phe Phe
65 70 75 80

aag atg aac agt ctg caa gct gat gac aca gcc atg tac tac tgt gcc 288
Lys Met Asn Ser Leu Gln Ala Asp Asp Thr Ala Met Tyr Tyr Cys Ala
85 90 95

cga aag aaa gga gga tgg ttt ccc tgg ttt gct tac tgg ggc caa ggg 336
Arg Lys Lys Gly Gly Trp Phe Pro Trp Phe Ala Tyr Trp Gly Gln Gly
100 105 110

act ctg gtc act gtc tct gca 357
Thr Leu Val Thr Val Ser Ala
115

<210> 327

<211> 119

<212> PRT

<213> Mus musculus

<400> 327

Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln
1 5 10 15

Ser Leu Ser Ile Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Asn Tyr
20 25 30

Ala Val His Trp Val Arg Gln Ser Pro Gly Lys Gly Leu Glu Trp Leu
35 40 45

Gly Val Ile Trp Ser Asp Gly Ser Thr Asp Tyr Asn Ala Ala Phe Ile
50 55 60

Ser Arg Leu Ser Ile Ser Lys Asp Asn Ser Lys Ser Gln Val Phe Phe

[illegible]

Lys Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
50 55 60

agg ttt agt ggc agt ggg tct ggg aca gac ttc acc ctc aac atc cat 240
Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

cct gtg gag gag gag gat gct gca acc tat tac tgt cag caa agt aat 288
Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Ser Asn
85 90 95

gag gat ccg tac acg ttc gga ggg ggg acc aag ctg gaa atc aaa 333
Glu Asp Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 329

<211> 111

<212> PRT

<213> Mus musculus

<400> 329

Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp His Ala
20 25 30

Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Ser Asn

85

90

95

Glu Asp Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 100 105 110

<210> 330

<211> 351

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1).. (351)

<223> SC16.134 VH

<220>

<221> CDS

<222> (1).. (351)

<400> 330

gag gtc cag ctg cag cag tct gga cct gac ctg gtg aag cct ggg gct 48
 Glu Val Gln Leu Gln Gln Ser Gly Pro Asp Leu Val Lys Pro Gly Ala
 1 5 10 15

tca gtg aag ata tcc tgc aag gct tct ggt tac tca ttc act ggc tac 96
 Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr
 20 25 30

tac atg cac tgg gtg aag cag agc cat gga aag agg ctt gag tgg att 144
 Tyr Met His Trp Val Lys Gln Ser His Gly Lys Arg Leu Glu Trp Ile
 35 40 45

gga cgt gtt aat cct aac aat ggt ggt act aac tac aac cag aaa ttc 192
 Gly Arg Val Asn Pro Asn Asn Gly Gly Thr Asn Tyr Asn Gln Lys Phe
 50 55 60

aag ggc aag gcc ata tta act gta gac aag tca tcc agc aca gcc tac 240
 Lys Gly Lys Ala Ile Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
 65 70 75 80

atg gag ctc cgc agc ctg aca tct gag gac tct gcg gtc tat tac tgt 288

Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

gca aga ggg agt tat gat aac gcc gag ggc tgg ggc caa ggg act ctg 336
Ala Arg Gly Ser Tyr Asp Asn Ala Glu Gly Trp Gly Gln Gly Thr Leu
100 105 110

gtc act gtc tct gca 351
Val Thr Val Ser Ala
115

<210> 331
<211> 117
<212> PRT
<213> Mus musculus

<400> 331

Glu Val Gln Leu Gln Gln Ser Gly Pro Asp Leu Val Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr
20 25 30

Tyr Met His Trp Val Lys Gln Ser His Gly Lys Arg Leu Glu Trp Ile
35 40 45

Gly Arg Val Asn Pro Asn Asn Gly Gly Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Gly Lys Ala Ile Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Ser Tyr Asp Asn Ala Glu Gly Trp Gly Gln Gly Thr Leu

100

105

110

Val Thr Val Ser Ala
115

<210> 332

<211> 321

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1)..(321)

<223> SC16.135 VL

<220>

<221> CDS

<222> (1)..(321)

<400> 332

gac atc aag atg acc cag tct cca tct tcc atg tat gca tct cta gga 48
Asp Ile Lys Met Thr Gln Ser Pro Ser Ser Met Tyr Ala Ser Leu Gly
1 5 10 15

gag aga gtc act atc act tgc aag gcg agt cag gac att aat agg tat 96
Glu Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Ile Asn Arg Tyr
20 25 30

tta agc tgg ttc cag cag aaa cca ggg aaa tct cct aag acc ctg atc 144
Leu Ser Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Thr Leu Ile
35 40 45

tat cgt gca aac aga ttg gta gat ggg gtc cca tca agg ttc agt ggc 192
Tyr Arg Ala Asn Arg Leu Val Asp Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

agt gga tct ggg caa gat tat tct ctc acc atc agc agc ctg gag tat 240
Ser Gly Ser Gly Gln Asp Tyr Ser Leu Thr Ile Ser Ser Leu Glu Tyr
65 70 75 80

gaa gat atg gga att tat tat tgt cta cag tat gat gag ttt cca ttc 288

Glu Asp Met Gly Ile Tyr Tyr Cys Leu Gln Tyr Asp Glu Phe Pro Phe
85 90 95

acg ttc ggc tcg ggg aca aag ttg gaa ata aaa 321
Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 333
<211> 107
<212> PRT
<213> Mus musculus

<400> 333

Asp Ile Lys Met Thr Gln Ser Pro Ser Ser Met Tyr Ala Ser Leu Gly
1 5 10 15

Glu Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Ile Asn Arg Tyr
20 25 30

Leu Ser Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Thr Leu Ile
35 40 45

Tyr Arg Ala Asn Arg Leu Val Asp Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Gln Asp Tyr Ser Leu Thr Ile Ser Ser Leu Glu Tyr
65 70 75 80

Glu Asp Met Gly Ile Tyr Tyr Cys Leu Gln Tyr Asp Glu Phe Pro Phe
85 90 95

Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 334

<211> 363
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(363)
<223> SC16.135 VH

<220>
<221> CDS
<222> (1)..(363)

<400> 334
cag gtc cag ttg cag cag tct gga gct gag ctg gta agg cct ggg act 48
Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Thr
1 5 10 15

tca gtg aag gtg tcc tgc aag gct tct gga tac gcc ttc act aat tac 96
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr
20 25 30

ttg ata gag tgg gta aag cag agg cct gga cag ggc ctt gag tgg att 144
Leu Ile Glu Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

ggg gtg att aat cct gga agt ggt ggt act aac tcc aat gag aag ttc 192
Gly Val Ile Asn Pro Gly Ser Gly Gly Thr Asn Ser Asn Glu Lys Phe
50 55 60

aag gcc aag gca aca ctg act gca gac aaa tcc tcc agc act gcc tac 240
Lys Ala Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

atg cag ctc agc agc ctg aca tct gct gac tct gcg gtc tat ttc tgt 288
Met Gln Leu Ser Ser Leu Thr Ser Ala Asp Ser Ala Val Tyr Phe Cys
85 90 95

gca aga tcg gac tat gat tac gcc ttc tat gct atg gac tac tgg ggt 336
Ala Arg Ser Asp Tyr Asp Tyr Ala Phe Tyr Ala Met Asp Tyr Trp Gly
100 105 110

caa gga acc tca gtc acc gtc tcc tca 363

Gln Gly Thr Ser Val Thr Val Ser Ser
115 120

<210> 335

<211> 121

<212> PRT

<213> Mus musculus

<400> 335

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Thr
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Asn Tyr
20 25 30

Leu Ile Glu Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Val Ile Asn Pro Gly Ser Gly Gly Thr Asn Ser Asn Glu Lys Phe
50 55 60

Lys Ala Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Ala Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Ser Asp Tyr Asp Tyr Ala Phe Tyr Ala Met Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Ser Val Thr Val Ser Ser
115 120

<210> 336

<211> 321
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1)..(321)
 <223> SC16.136 VL

<220>
 <221> CDS
 <222> (1)..(321)

<400> 336
 gac atc cag atg act cag tct cca gcc tcc cta tct gca tct gtg gga 48
 Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Val Gly
 1 5 10 15
 gaa act gtc acc atc aca tgt cga gca agt ggg aat att cac aat tat 96
 Glu Thr Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile His Asn Tyr
 20 25 30
 tta gca tgg tat cag cag aaa cag gga aaa tct cct cac ctc ctg gtc 144
 Leu Ala Trp Tyr Gln Gln Lys Gln Gly Lys Ser Pro His Leu Leu Val
 35 40 45
 tat aat gca aaa acc tta gca gat ggt gtg cca tca agg ttc agt ggc 192
 Tyr Asn Ala Lys Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60
 agt gga tca gga aca caa tat tct ctc aag atc aac agc ctg cag cct 240
 Ser Gly Ser Gly Thr Gln Tyr Ser Leu Lys Ile Asn Ser Leu Gln Pro
 65 70 75 80
 gaa gat ttt ggg agt tat tac tgt caa cat ttt tgg agt act ccg tgg 288
 Glu Asp Phe Gly Ser Tyr Tyr Cys Gln His Phe Trp Ser Thr Pro Trp
 85 90 95
 acg ttc ggt gga ggc acc aag ctg gaa atc aaa 321
 Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 100 105

<210> 337
<211> 107
<212> PRT
<213> Mus musculus

<400> 337

Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Glu Thr Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile His Asn Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Gln Gly Lys Ser Pro His Leu Leu Val
35 40 45

Tyr Asn Ala Lys Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Gln Tyr Ser Leu Lys Ile Asn Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Gly Ser Tyr Tyr Cys Gln His Phe Trp Ser Thr Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 338
<211> 366
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(366)

<210> 339

<400> 339

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Val Met His Trp Val Lys Gln Lys Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Thr Lys Tyr Asn Glu Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ser Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Ser Gly Tyr Glu Asp Tyr Tyr Gly Met Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Ser Val Thr Val Ser Ser
115 120

<210> 340

<211> 318

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1)..(318)

<223> SC16.137 VL

<220>

<221> CDS

<222> (1)..(318)

<400> 340

caa att gtt ctc acc cag tct cca gca atc atg tct gca tct cta ggg	48
Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Leu Gly	
1 5 10 15	

gag gag atc acc cta acc tgc agt gcc agc tcg agt gta agt tac atg	96
Glu Glu Ile Thr Leu Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met	
20 25 30	

cac tgg tac cag cag aag tca ggc act tct ccc aaa ctc ttg att tat	144
His Trp Tyr Gln Gln Lys Ser Gly Thr Ser Pro Lys Leu Leu Ile Tyr	
35 40 45	

agc aca tcc aac ctg gct tct gga gtc cct tct cgc ttc agt ggc agt	192
Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser	
50 55 60	

ggg tct ggg acc ttt tat tct ctc aca atc agc agt gtg gag gct gaa	240
Gly Ser Gly Thr Phe Tyr Ser Leu Thr Ile Ser Ser Val Glu Ala Glu	
65 70 75 80	

gat gct gcc gat tat tac tgc cat cag tgg agt agt tat cac acg ttc	288
Asp Ala Ala Asp Tyr Tyr Cys His Gln Trp Ser Ser Tyr His Thr Phe	
85 90 95	

gga ggg ggg acc aag ctg gaa ata aaa cgg	318
Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg	
100 105	

<210> 341

<211> 106

<212> PRT

<213> Mus musculus

<400> 341

Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Leu Gly

1	5	10	15												
Glu	Glu	Ile	Thr	Leu	Thr	Cys	Ser	Ala	Ser	Ser	Ser	Val	Ser	Tyr	Met
		20						25					30		
His	Trp	Tyr	Gln	Gln	Lys	Ser	Gly	Thr	Ser	Pro	Lys	Leu	Leu	Ile	Tyr
		35					40					45			
Ser	Thr	Ser	Asn	Leu	Ala	Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser
	50					55					60				
Gly	Ser	Gly	Thr	Phe	Tyr	Ser	Leu	Thr	Ile	Ser	Ser	Val	Glu	Ala	Glu
65					70				75					80	
Asp	Ala	Ala	Asp	Tyr	Tyr	Cys	His	Gln	Trp	Ser	Ser	Tyr	His	Thr	Phe
			85					90					95		
Gly	Gly	Gly	Thr	Lys	Leu	Glu	Ile	Lys	Arg						
		100					105								

<210> 342
 <211> 351
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1)..(351)
 <223> SC16.137 VH

<220>
 <221> CDS
 <222> (1)..(351)

<400> 342
 gag gtg cag ctg gtg gag tct ggg gga gac tta gtg aag cct gga ggg

20

25

30

Gly Met Ser Trp Val Arg Gln Thr Pro Asp Lys Arg Leu Glu Trp Val
 35 40 45

Ala Thr Ile Ser Ser Gly Gly Ser Tyr Thr Tyr Tyr Pro Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
 65 70 75 80

Leu Gln Met Ser Ser Leu Lys Ser Glu Asp Thr Ala Met Tyr Tyr Cys
 85 90 95

Ala Arg Arg Arg Ala Asp Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser
 100 105 110

Val Thr Val Ser Ser
 115

<210> 344
 <211> 321
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1)..(321)
 <223> SC16.138 VL

<220>
 <221> CDS
 <222> (1)..(321)

<400> 344
 gac att cag atg acc cag tct cct gcc tcc cag tct gca tct ctg gga

Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ala	Ser	Gln	Ser	Ala	Ser	Leu	Gly		
1				5				10						15			
gaa agt gtc acc atc aca tgc ctg gca agt cag acc att ggt aca tgg 96																	
Glu	Ser	Val	Thr	Ile	Thr	Cys	Leu	Ala	Ser	Gln	Thr	Ile	Gly	Thr	Trp		
		20						25					30				
tta gca tgg tat cag cag aaa cca ggg aaa tct cct cag ctc ctg att 144																	
Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ser	Pro	Gln	Leu	Leu	Ile		
		35					40					45					
tat tct gca acc agc ttg gca gat ggg gtc cca tca agg ttc agt ggt 192																	
Tyr	Ser	Ala	Thr	Ser	Leu	Ala	Asp	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly		
	50					55				60							
agt gga tct ggc aca aaa ttt tct ttc aag atc agc agc cta cag gct 240																	
Ser	Gly	Ser	Gly	Thr	Lys	Phe	Ser	Phe	Lys	Ile	Ser	Ser	Leu	Gln	Ala		
65					70					75				80			
gaa gat ttt gta agt tat tac tgt caa caa ctt tac agt act ccg tgg 288																	
Glu	Asp	Phe	Val	Ser	Tyr	Tyr	Cys	Gln	Gln	Leu	Tyr	Ser	Thr	Pro	Trp		
				85				90					95				
acg ttc ggt gga ggc acc aag ctg gaa atc aaa 321																	
Thr	Phe	Gly	Gly	Gly	Thr	Lys	Leu	Glu	Ile	Lys							
		100						105									

<210> 345
 <211> 107
 <212> PRT
 <213> Mus musculus

<400> 345

Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ala	Ser	Gln	Ser	Ala	Ser	Leu	Gly		
1				5				10						15			
Glu	Ser	Val	Thr	Ile	Thr	Cys	Leu	Ala	Ser	Gln	Thr	Ile	Gly	Thr	Trp		
		20						25					30				
Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ser	Pro	Gln	Leu	Leu	Ile		

35

40

45

Tyr Ser Ala Thr Ser Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Lys Phe Ser Phe Lys Ile Ser Ser Leu Gln Ala
 65 70 75 80

Glu Asp Phe Val Ser Tyr Tyr Cys Gln Gln Leu Tyr Ser Thr Pro Trp
 85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 100 105

<210> 346

<211> 348

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1).. (348)

<223> SC16.138 VH

<220>

<221> CDS

<222> (1).. (348)

<400> 346

cag gtg cag ctg aag gag tca gga cct ggc ctg gtg gcg ccc tca cag 48
 Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln
 1 5 10 15

agc ctg tcc atc aca tgc act gtc tca ggg ttc tca tta acc gac tat 96
 Ser Leu Ser Ile Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Asp Tyr
 20 25 30

ggt gta agc tgg att cgc cag cct cca gga aag ggt ctg gag tgg ctg 144

Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Leu
35 40 45

gga gta gta tgg ggt ggt gga agc aca tac tat aat tcc gct ctc aaa 192
Gly Val Val Trp Gly Gly Gly Ser Thr Tyr Tyr Asn Ser Ala Leu Lys
50 55 60

tcc aga ctg agc atc agc aag gac aac tcc aag agc caa gtt ttc tta 240
Ser Arg Leu Ser Ile Ser Lys Asp Asn Ser Lys Ser Gln Val Phe Leu
65 70 75 80

aaa atg aac agt ctg caa act gat gac aca gcc atg tac tac tgt gcc 288
Lys Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Met Tyr Tyr Cys Ala
85 90 95

aaa cag agg ggt cag tac ggg gct tac tgg ggc caa ggg act ctg gtc 336
Lys Gln Arg Gly Gln Tyr Gly Ala Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

act gtc tct gca 348
Thr Val Ser Ala
115

<210> 347
<211> 116
<212> PRT
<213> Mus musculus

<400> 347

Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln
1 5 10 15

Ser Leu Ser Ile Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Asp Tyr
20 25 30

Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Leu
35 40 45

Gly Val Val Trp Gly Gly Gly Ser Thr Tyr Tyr Asn Ser Ala Leu Lys

50 55 60

Ser Arg Leu Ser Ile Ser Lys Asp Asn Ser Lys Ser Gln Val Phe Leu
65 70 75 80

Lys Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Met Tyr Tyr Cys Ala
85 90 95

Lys Gln Arg Gly Gln Tyr Gly Ala Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ala
115

<210> 348
<211> 321
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(321)
<223> SC16.139 VL

<220>
<221> CDS
<222> (1)..(321)

<400> 348
gac att gtg atg acc cag tct cac aaa ttc atg tcc aca tca gta gga 48
Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly
1 5 10 15

gac agg gtc agc atc acc tgc aag gcc agt cag gat gtg aat act gct 96
Asp Arg Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Asn Thr Ala
20 25 30

gta ggc tgg tat caa cag aaa cca gga caa tct cct aaa cta ctg att 144

Val	Gly	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ser	Pro	Lys	Leu	Leu	Ile
	35						40					45			

tac	tcg	gca	tcc	tac	cgg	tac	act	gga	gtc	cct	gat	cgc	ttc	act	ggc	192
Tyr	Ser	Ala	Ser	Tyr	Arg	Tyr	Thr	Gly	Val	Pro	Asp	Arg	Phe	Thr	Gly	
	50					55					60					

agt	gga	tct	ggg	acg	gat	ttc	act	ttc	acc	atc	agc	agt	gtg	cag	gct	240
Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Phe	Thr	Ile	Ser	Ser	Val	Gln	Ala	
65					70					75				80		

gaa	gac	ctg	gca	gtt	tat	tac	tgt	cag	caa	cat	tat	agt	agt	ccg	tac	288
Glu	Asp	Leu	Ala	Val	Tyr	Tyr	Cys	Gln	Gln	His	Tyr	Ser	Ser	Pro	Tyr	
				85				90						95		

acg	ttc	gga	ggg	ggg	acc	aag	ctg	gaa	att	aaa	321
Thr	Phe	Gly	Gly	Gly	Thr	Lys	Leu	Glu	Ile	Lys	
		100					105				

<210> 349
 <211> 107
 <212> PRT
 <213> Mus musculus

 <400> 349

Asp	Ile	Val	Met	Thr	Gln	Ser	His	Lys	Phe	Met	Ser	Thr	Ser	Val	Gly
1			5					10						15	

Asp	Arg	Val	Ser	Ile	Thr	Cys	Lys	Ala	Ser	Gln	Asp	Val	Asn	Thr	Ala
		20					25					30			

Val	Gly	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ser	Pro	Lys	Leu	Leu	Ile
	35						40					45			

Tyr	Ser	Ala	Ser	Tyr	Arg	Tyr	Thr	Gly	Val	Pro	Asp	Arg	Phe	Thr	Gly
	50					55					60				

Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Phe	Thr	Ile	Ser	Ser	Val	Gln	Ala

65

70

75

80

Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Ser Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

$\langle 210 \rangle$ 350

<211> 357

⟨212⟩ DNA

⟨213⟩ Mus musculus

 $\langle 220 \rangle$

<221> misc feature

<222> (1).. (357)

<223> SC16.139 VH

 $\langle 220 \rangle$

〈221〉 CDS

⟨222⟩ (1)..(357)

$\langle 400 \rangle$ 350

gag gtc cag ctg cag cag tct gga cct gag ctg gta aag cct ggg gct 48
Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1 5 10 15

tca gtg aag atg tcc tgc aag gct tct gga tac aca ttc act aac tat 96
Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

gtt atg cac tgg gtg aag cag aag cct ggg cag ggc ctt gag tgg att 144
Val Met His Trp Val Lys Gln Lys Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

gga tat att aat cct tac aat gat ggt act aaa tac aat gag aag ttc 192
Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Thr Lys Tyr Asn Glu Lys Phe
50 55 60

aaa ggc aag gcc aca ctg act tca gac aaa tcc tcc acc aca gcc tac 240

Lys Gly Lys Ala Thr Leu Thr Ser Asp Lys Ser Ser Thr Thr Ala Tyr
65 70 75 80

atg gcg ctc agc agc ctg acc tct gag gac tct gcg gtc tat tac tgt 288
Met Ala Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

gca gta gcc tac tat agt aac tgg ggg ttt gct tac tgg ggc caa ggg 336
Ala Val Ala Tyr Tyr Ser Asn Trp Gly Phe Ala Tyr Trp Gly Gln Gly
100 105 110

act ctg gtc act gtc tct gca 357
Thr Leu Val Thr Val Ser Ala
115

<210> 351
<211> 119
<212> PRT
<213> Mus musculus

<400> 351

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Val Met His Trp Val Lys Gln Lys Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Tyr Asn Asp Gly Thr Lys Tyr Asn Glu Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ser Asp Lys Ser Ser Thr Thr Ala Tyr
65 70 75 80

Met Ala Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys

85

90

95

Ala Val Ala Tyr Tyr Ser Asn Trp Gly Phe Ala Tyr Trp Gly Gln Gly
 100 105 110

Thr Leu Val Thr Val Ser Ala
 115

<210> 352
 <211> 333
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1)..(333)
 <223> SC16.140 VL

<220>
 <221> CDS
 <222> (1)..(333)

<400> 352
 gac att gtg ctg aca cag tct ctt gct tcc tta gct gta tct ctg ggg 48
 Asp Ile Val Leu Thr Gln Ser Leu Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15

cag agg gcc acc atc tca tgc agg gcc agc aaa agt gtc agt aca tct 96
 Gln Arg Ala Thr Ile Ser Cys Arg Ala Ser Lys Ser Val Ser Thr Ser
 20 25 30

ggc tat agt tat atg cac tgg tac caa cag aaa cca gga cag cca ccc 144
 Gly Tyr Ser Tyr Met His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
 35 40 45

aaa ctc ctc att tat ctt gca tcc aac cta gaa tct ggg gtc cct gcc 192
 Lys Leu Leu Ile Tyr Leu Ala Ser Asn Leu Glu Ser Gly Val Pro Ala
 50 55 60

agg ttc agt ggc agt ggg tct ggg aca gac ttc acc ctc aac atc cat 240

Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Asn	Ile	His
65					70					75					80

cct	gtg	gaa	gac	gaa	gat	gct	gca	acc	tat	tac	tgt	cag	cac	agt	agg	288
Pro	Val	Glu	Asp	Glu	Asp	Ala	Ala	Thr	Tyr	Tyr	Cys	Gln	His	Ser	Arg	
				85					90					95		

gag	ctt	ccg	ttc	acg	ttc	gga	ggg	ggg	acc	aag	ctg	gaa	ata	aag	333
Glu	Leu	Pro	Phe	Thr	Phe	Gly	Gly	Gly	Thr	Lys	Leu	Glu	Ile	Lys	
			100					105					110		

<210> 353
 <211> 111
 <212> PRT
 <213> Mus musculus

<400> 353

Asp	Ile	Val	Leu	Thr	Gln	Ser	Leu	Ala	Ser	Leu	Ala	Val	Ser	Leu	Gly
1				5					10					15	

Gln	Arg	Ala	Thr	Ile	Ser	Cys	Arg	Ala	Ser	Lys	Ser	Val	Ser	Thr	Ser
			20					25					30		

Gly	Tyr	Ser	Tyr	Met	His	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Pro	Pro
		35					40					45			

Lys	Leu	Leu	Ile	Tyr	Leu	Ala	Ser	Asn	Leu	Glu	Ser	Gly	Val	Pro	Ala
	50					55					60				

Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Asn	Ile	His
65					70					75					80

Pro	Val	Glu	Asp	Glu	Asp	Ala	Ala	Thr	Tyr	Tyr	Cys	Gln	His	Ser	Arg
				85					90					95	

Glu	Leu	Pro	Phe	Thr	Phe	Gly	Gly	Gly	Thr	Lys	Leu	Glu	Ile	Lys

100

105

110

<210> 354

<211> 348

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1).. (348)

<223> SC16.140 VH

<220>

<221> CDS

<222> (1).. (348)

<400> 354

cag gtc caa ctg cag cag tct ggg cct gag ctg gtg agg cct ggg gct 48

Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Arg Pro Gly Ala

1 5 10 15

tca gtg aag atg tcc tgc aag gct tca ggc tat acc ttc acc agc tac 96

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr

20 25 30

tgg atg cac tgg gtg aaa cag agg cct gga caa ggc ctt gag tgg att 144

Trp Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile

35 40 45

ggc atg att gat cct tcc aat agt gaa act agg tta aat cag aag ttc 192

Gly Met Ile Asp Pro Ser Asn Ser Glu Thr Arg Leu Asn Gln Lys Phe

50 55 60

aag gac aag gcc aca ttg aat gta gac aaa tcc tcc aac aca gcc tac 240

Lys Asp Lys Ala Thr Leu Asn Val Asp Lys Ser Ser Asn Thr Ala Tyr

65 70 75 80

atg cag ctc agc agc ctg aca tct gag gac tct gca gtc tat tac tgt 288

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys

85 90 95

gca gta atg gac tac tac ttt gac tac tgg ggc caa ggc acc act ctc 336

Ala Val Met Asp Tyr Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Thr Leu
100 105 110

aca gtc tcc tca 348
Thr Val Ser Ser
115

<210> 355
<211> 116
<212> PRT
<213> Mus musculus

<400> 355

Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Arg Pro Gly Ala
1 5 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Trp Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Met Ile Asp Pro Ser Asn Ser Glu Thr Arg Leu Asn Gln Lys Phe
50 55 60

Lys Asp Lys Ala Thr Leu Asn Val Asp Lys Ser Ser Asn Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Val Met Asp Tyr Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Thr Leu
100 105 110

Thr Val Ser Ser

<210> 356
 <211> 321
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1)..(321)
 <223> SC16.141 VL

<220>
 <221> CDS
 <222> (1)..(321)

<400> 356
 gac atc aag atg acc cag tct cca tct tcc atg tat gca tct cta gga 48
 Asp Ile Lys Met Thr Gln Ser Pro Ser Ser Met Tyr Ala Ser Leu Gly
 1 5 10 15
 gag aga gtc act atc act tgc aag gcg agt cag gac att aat agc tat 96
 Glu Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Ile Asn Ser Tyr
 20 25 30
 tta agc tgg ttc cag cag aaa cca ggg aaa tct cct aag acc ctg atc 144
 Leu Ser Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Thr Leu Ile
 35 40 45
 tat cgt gca aac aga ttg gta gat ggg gtc cca tca agg ttc agt ggc 192
 Tyr Arg Ala Asn Arg Leu Val Asp Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60
 agt gga tct ggg caa gat tat tct ctc acc atc agc agc ctg gag tat 240
 Ser Gly Ser Gly Gln Asp Tyr Ser Leu Thr Ile Ser Ser Leu Glu Tyr
 65 70 75 80
 gaa gat atg gga att tat tat tgt cta cag tat gat gag ttt cca ttc 288
 Glu Asp Met Gly Ile Tyr Tyr Cys Leu Gln Tyr Asp Glu Phe Pro Phe
 85 90 95
 acg ttc ggc tcg ggg aca aag ttg gaa ata aaa 321

Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 357
<211> 107
<212> PRT
<213> Mus musculus

<400> 357

Asp Ile Lys Met Thr Gln Ser Pro Ser Ser Met Tyr Ala Ser Leu Gly
1 5 10 15

Glu Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Ile Asn Ser Tyr
20 25 30

Leu Ser Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Thr Leu Ile
35 40 45

Tyr Arg Ala Asn Arg Leu Val Asp Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Gln Asp Tyr Ser Leu Thr Ile Ser Ser Leu Glu Tyr
65 70 75 80

Glu Asp Met Gly Ile Tyr Tyr Cys Leu Gln Tyr Asp Glu Phe Pro Phe
85 90 95

Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 358
<211> 345
<212> DNA
<213> Mus musculus

<223> SC16.141 VH

 $\langle 222 \rangle \quad (1) \dots (345)$

gtc tcc tca 345
Val Ser Ser
115

<210> 359
<211> 115
<212> PRT
<213> Mus musculus

<400> 359

Gln Val Gln Leu Lys Gln Ser Gly Pro Gly Leu Val Ala Pro Ser Gln
1 5 10 15

Ser Leu Phe Ile Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Ser Tyr
20 25 30

Glu Ile Asn Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Leu
35 40 45

Gly Val Ile Trp Thr Gly Gly Ser Thr Asn Tyr Asn Ser Ala Leu Ile
50 55 60

Ser Arg Leu Ser Ile Ser Lys Asp Asn Ser Lys Ser Leu Val Phe Leu
65 70 75 80

Lys Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Val
85 90 95

Arg Gly Val Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr
100 105 110

Val Ser Ser
115

<210> 360
<211> 321
<212> DNA
<213> Mus musculus

<220>

<221> misc_feature

<222> (1)..(321)

<223> SC16.142 VL

<220>

<221> CDS

<222> (1)..(321)

<400> 360

gac atc aag atg acc cag tct cca tct tcc atg tat gca tct cta gga	48
Asp Ile Lys Met Thr Gln Ser Pro Ser Ser Met Tyr Ala Ser Leu Gly	
1 5 10 15	

gag aga gtc act atc act tgc aag gcg agt cag gac att aat aat tat	96
Glu Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Ile Asn Asn Tyr	
20 25 30	

tta agc tgg ttc cag cag aaa cca ggg aaa tct cct aag acc ctg atc	144
Leu Ser Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Thr Leu Ile	
35 40 45	

tat cgt gca aac aga ttg gta gat ggg gtc cca tca agg ttc agt ggc	192
Tyr Arg Ala Asn Arg Leu Val Asp Gly Val Pro Ser Arg Phe Ser Gly	
50 55 60	

agt gga tct ggg caa gat tat tct ctc acc atc agc agc ctg gag tat	240
Ser Gly Ser Gly Gln Asp Tyr Ser Leu Thr Ile Ser Ser Leu Glu Tyr	
65 70 75 80	

gaa gat atg gga att tat tat tgt cta cag tat gat gag ttt ccg tac	288
Glu Asp Met Gly Ile Tyr Tyr Cys Leu Gln Tyr Asp Glu Phe Pro Tyr	
85 90 95	

acg ttc gga ggg ggg acc aag ctg gaa ata aaa	321
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys	
100 105	

<210> 361

<211> 107

<212> PRT

<213> Mus musculus

<400> 361

Asp Ile Lys Met Thr Gln Ser Pro Ser Ser Met Tyr Ala Ser Leu Gly
1 5 10 15

Glu Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Ile Asn Asn Tyr
20 25 30

Leu Ser Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Thr Leu Ile
35 40 45

Tyr Arg Ala Asn Arg Leu Val Asp Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Gln Asp Tyr Ser Leu Thr Ile Ser Ser Leu Glu Tyr
65 70 75 80

Glu Asp Met Gly Ile Tyr Tyr Cys Leu Gln Tyr Asp Glu Phe Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 362

<211> 345

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1)..(345)

<223> SC16.142 VH

<220>

<221> CDS

$\langle 222 \rangle \quad (112) \dots (112)$

<223> The 'Xaa' at location 112 stands for Thr.

<220>

<221> misc_feature

<222> (114)..(114)

<223> The 'Xaa' at location 114 stands for Ser.

<220>

<221> misc_feature

<222> (115)..(115)

<223> The 'Xaa' at location 115 stands for Ser.

<400> 363

Glu	Val	Gln	Leu	Gln	Gln	Ser	Gly	Pro	Glu	Leu	Val	Lys	Pro	Gly	Ala
1			5					10					15		

Ser	Val	Lys	Ile	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Thr	Phe	Thr	Asp	Tyr
		20					25					30			

Asn	Met	His	Trp	Val	Lys	Gln	Ser	His	Gly	Lys	Ser	Leu	Glu	Trp	Ile
	35					40					45				

Gly	Phe	Phe	Tyr	Pro	Tyr	Asn	Gly	Asn	Thr	Val	Tyr	Ser	Gln	Lys	Phe
50					55				60						

Lys	Ser	Lys	Ala	Thr	Leu	Thr	Val	Asp	Asn	Ser	Ser	Ser	Thr	Ala	Tyr
65					70				75					80	

Met	Glu	Leu	Arg	Ser	Leu	Thr	Ser	Glu	Asp	Ser	Ala	Val	Tyr	Tyr	Cys
			85					90					95		

Ala	Arg	Leu	Asn	Trp	Glu	Gly	Tyr	Trp	Gly	Gln	Gly	Thr	Thr	Leu	Xaa
		100					105						110		

Val	Xaa	Xaa
	115	

<210> 364
 <211> 336
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1).. (336)
 <223> SC16.143 VL

<220>
 <221> CDS
 <222> (1).. (336)

<400> 364
 gat gtt ttg atg acc caa act cca ctc tcc ctg cct gtc agt ctt gga 48
 Asp Val Leu Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
 1 5 10 15

 gat caa gcc tcc atc tct tgc aga tct agt cag agc att gta cat agt 96
 Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Ile Val His Ser
 20 25 30

 aat gga aac acc tat tta gaa tgg tac ctg cag aaa cca ggc cag tct 144
 Asn Gly Asn Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
 35 40 45

 cca aag ctc ctg atc tac aaa gtt tcc aac cga ttt tct ggg gtc cca 192
 Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
 50 55 60

 gac agg ttc agt ggc agt gga tca ggg aca gat ttc aca ctc aag atc 240
 Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80

 agc aga gtg gag gct gag gat ctg gga gtt tat tac tgc ttt caa ggt 288
 Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Phe Gln Gly
 85 90 95

 tca cat gtt ccg ctc acg ttc ggt gct ggg acc aag ctg gag ctg aaa 336
 Ser His Val Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys

100

105

110

<210> 365

<211> 112

<212> PRT

<213> Mus musculus

<400> 365

Asp Val Leu Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
 1 5 10 15

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Ile Val His Ser
 20 25 30

Asn Gly Asn Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
 35 40 45

Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
 50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Phe Gln Gly
 85 90 95

Ser His Val Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
 100 105 110

<210> 366

<211> 357

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1).. (357)

<223> SC16.143 VH

<220>

<221> CDS

<222> (1).. (357)

<400> 366

cag gtc cag ctg cag cag tct gga cct gag ctg gtg aag cct ggg gct	48
Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala	
1 5 10 15	

tca gtg agg ata tcc tgc aag gct tct ggc tac acc ttc aca agc tac	96
Ser Val Arg Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr	
20 25 30	

tat ata cac tgg gtg aag cag agg cct gga cag gga ctt gag tgg att	144
Tyr Ile His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile	
35 40 45	

gga tgg att tat cct gga aat ggt aat act aag tac aat gag aag ttc	192
Gly Trp Ile Tyr Pro Gly Asn Gly Asn Thr Lys Tyr Asn Glu Lys Phe	
50 55 60	

aag ggc aag gcc aca ctg act gca gac aaa tcc tcc agc aca gcc tac	240
Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr	
65 70 75 80	

atg cag atc agc agc ctg acc tct gag gac tct gcg gtc tat ttc tgt	288
Met Gln Ile Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys	
85 90 95	

gca aga gag aga tgg tta cta cta tgg ttt gct tac tgg ggc caa ggg	336
Ala Arg Glu Arg Trp Leu Leu Leu Trp Phe Ala Tyr Trp Gly Gln Gly	
100 105 110	

act ctg gtc act gtc tct gca	357
Thr Leu Val Thr Val Ser Ala	
115	

<210> 367

<211> 119
<212> PRT
<213> Mus musculus

<400> 367

Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1 5 10 15

Ser Val Arg Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Tyr Ile His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Trp Ile Tyr Pro Gly Asn Gly Asn Thr Lys Tyr Asn Glu Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Ile Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Glu Arg Trp Leu Leu Leu Trp Phe Ala Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ala
115

<210> 368
<211> 321
<212> DNA
<213> Mus musculus

<220>

<221> misc_feature

<222> (1).. (321)

<223> SC16.144 VL

<220>

<221> CDS

<222> (1).. (321)

<400> 368

agt att gtg atg acc cag act ccc aaa ttc ctg ctt gta tca gca gga	48
Ser Ile Val Met Thr Gln Thr Pro Lys Phe Leu Leu Val Ser Ala Gly	
1 5 10 15	

gac agg gtt acc ata acc tgc aag gcc agt cag agt gtg agt aat gat	96
Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Ser Val Ser Asn Asp	
20 25 30	

gta ggt tgg tac caa cag aag cca ggg cag tct cct aaa ctg ctg ata	144
Val Gly Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile	
35 40 45	

tac tat gca tcc aat cgc tac aat gga gtc cct gat cgc ttc act ggc	192
Tyr Tyr Ala Ser Asn Arg Tyr Asn Gly Val Pro Asp Arg Phe Thr Gly	
50 55 60	

agt gga tat ggg acg gat ttc act ttc acc atc agc act gtg cag gct	240
Ser Gly Tyr Gly Thr Asp Phe Thr Phe Thr Ile Ser Thr Val Gln Ala	
65 70 75 80	

gaa gac ctg gca gtt tat ttc tgt cag cag gat tat agc tct ccg tgg	288
Glu Asp Leu Ala Val Tyr Phe Cys Gln Gln Asp Tyr Ser Ser Pro Trp	
85 90 95	

acg ttc ggt gga ggc acc aag ctg gaa atc aaa	321
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys	
100 105	

<210> 369

<211> 107

<212> PRT

<213> Mus musculus

<400> 369

Ser Ile Val Met Thr Gln Thr Pro Lys Phe Leu Leu Val Ser Ala Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Ser Val Ser Asn Asp
20 25 30

Val Gly Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Ala Ser Asn Arg Tyr Asn Gly Val Pro Asp Arg Phe Thr Gly
50 55 60

Ser Gly Tyr Gly Thr Asp Phe Thr Phe Thr Ile Ser Thr Val Gln Ala
65 70 75 80

Glu Asp Leu Ala Val Tyr Phe Cys Gln Gln Asp Tyr Ser Ser Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 370

<211> 354

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1)..(354)

<223> SC16.144 VH

<220>

<221> CDS

<222> (1)..(354)

cag atc cag ttg gtg cag tct gga cct gag ctg aag aag cct gga gag 48
Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1 5 10 15

aca gtc aag atc tcc tgc aag gct tct ggg tat acc ttc aca aac tat 96
Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

gga atg aac tgg gtg aag cag gct cca gga aag ggt tta aag tgg gtg 144
Gly Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Val
35 40 45

ggc tgg ata aac acc tac act gga gag cca aca tat gct gat gac ttc 192
Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe
50 55 60

aag gga cgg ttt gcc ttc tct ttg gaa acc tct gcc agc act gcc tat 240
Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

ttg cag atc gac aac ctc aaa aat gag gac acg gct aca tat ttc tgt 288
Leu Gln Ile Asp Asn Leu Lys Asn Glu Asp Thr Ala Thr Tyr Phe Cys
85 90 95

gca aga gtg ggg gat tac gtc ggc ttt gac tac tgg ggc caa ggc acc 336
Ala Arg Val Gly Asp Tyr Val Gly Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

act ctc aca gtc tcc tca 354
Thr Leu Thr Val Ser Ser
115

<210> 371

<211> 118

<212> PRT

⟨213⟩ Mus musculus

<400> 371

Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1 5 10 15

Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Val
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Leu Gln Ile Asp Asn Leu Lys Asn Glu Asp Thr Ala Thr Tyr Phe Cys
85 90 95

Ala Arg Val Gly Asp Tyr Val Gly Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Thr Leu Thr Val Ser Ser
115

<210> 372
<211> 321
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(321)
<223> SC16.147 VL

<220>
<221> CDS
<222> (1)..(321)

<400> 372

gat atc cag atg aca cag act gca tcc tcc ctg tct gcc tct ctg gga	48
Asp Ile Gln Met Thr Gln Thr Ala Ser Ser Leu Ser Ala Ser Leu Gly	
1 5 10 15	

gac aga gtc acc atc agt tgc agg gca agt cag gac att aac aat tat	96
Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Asn Asn Tyr	
20 25 30	

tta aac tgg tat cag cag aaa cca gat gga act gtt aaa ctc ctg atc	144
Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile	
35 40 45	

tac tac aca tca aga tta cac tca gga gtc cca tca agg ttc agt ggc	192
Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly	
50 55 60	

agt ggg tct gga aca gat tat tct ctc acc att agc atc ctg gaa caa	240
Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Ile Leu Glu Gln	
65 70 75 80	

gaa gat att gcc act tac ttt tgc caa cag ggt gat acg ctt ccg tgg	288
Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asp Thr Leu Pro Trp	
85 90 95	

acg ttc ggt gga ggc acc aag ctg gaa atc aaa	321
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys	
100 105	

<210> 373

<211> 107

<212> PRT

<213> Mus musculus

<400> 373

Asp Ile Gln Met Thr Gln Thr Ala Ser Ser Leu Ser Ala Ser Leu Gly	
1 5 10 15	

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Asn Asn Tyr	
20 25 30	

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Ile Leu Glu Gln
65 70 75 80

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asp Thr Leu Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 374
<211> 351
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(351)
<223> SC16.147 VH

<220>
<221> CDS
<222> (1)..(351)

<400> 374
cag atc cag ttg gtg cag tct gga cct gag ctg acg aag cct gga gag 48
Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Thr Lys Pro Gly Glu
1 5 10 15

aca gtc aag atc tcc tgc aag gcc tct gga tat acc ttc aca gac tat 96
Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr

	20						25						30							
tca ttg cac tgg gtg aag cag gct cta gga aag ggt tta aag tgg atg																			144	
Ser Leu His Trp Val Lys Gln Ala Leu Gly Lys Gly Leu Lys Trp Met																				
	35						40						45							
ggc tgg ata aac act gag act ggt gag cca gca tat gca gat gac ttc																			192	
Gly Trp Ile Asn Thr Glu Thr Gly Glu Pro Ala Tyr Ala Asp Asp Phe																				
	50						55						60							
aag gga cgg ttt gcc ttc tct ttg gaa acc tct gcc agc act gcc tat																			240	
Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr																				
	65						70						75						80	
ttg cag atc aac gac ctg aaa aat gag gac acg act aca tat ttc tgt																			288	
Leu Gln Ile Asn Asp Leu Lys Asn Glu Asp Thr Thr Thr Tyr Phe Cys																				
	85						90						95							
ggt att tac gac ggg tat gct atg gac tac tgg ggt caa gga acc tca																			336	
Gly Ile Tyr Asp Gly Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser																				
	100						105						110							
gtc acc gtc tcc tca																			351	
Val Thr Val Ser Ser																				
	115																			

Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Thr Lys Pro Gly Glu
1 5 10 15

Ser Leu His Trp Val Lys Gln Ala Leu Gly Lys Gly Leu Lys Trp Met
35 40 45

Gly Trp Ile Asn Thr Glu Thr Gly Glu Pro Ala Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Leu Gln Ile Asn Asp Leu Lys Asn Glu Asp Thr Thr Thr Tyr Phe Cys
85 90 95

Gly Ile Tyr Asp Gly Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser
100 105 110

Val Thr Val Ser Ser
115

<210> 376
<211> 318
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1).. (318)
<223> SC16.148 VL

<220>
<221> CDS
<222> (1).. (318)

<400> 376
caa att gtt ctc acc cag tct cca gca atc atg tct gca tct cca ggg 48
Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1 5 10 15

gag aag gtc acc atg acc tgc agt gcc agc tca agt gta agt tac atg 96
Glu Lys Val Thr Met Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met

Gly	Ser	Gly	Thr	Ser	Tyr	Ser	Leu	Thr	Ile	Ser	Arg	Met	Glu	Ala	Glu
65					70					75					80

Asp	Thr	Ala	Thr	Tyr	Tyr	Cys	Gln	Glu	Trp	Ser	Asn	Asn	Pro	Leu	Thr
				85					90					95	

Phe	Gly	Asp	Gly	Thr	Lys	Leu	Glu	Leu	Lys
			100					105	

<210> 378
 <211> 354
 <212> DNA
 <213> Mus musculus

<220>
 <221> misc_feature
 <222> (1).. (354)
 <223> SC16.148 VH

<220>
 <221> CDS
 <222> (1).. (354)

<400> 378																
cag	atc	cag	ttg	gtg	cag	tct	gga	cct	gag	ctg	aag	aag	cct	gga	gag	48
Gln	Ile	Gln	Leu	Val	Gln	Ser	Gly	Pro	Glu	Leu	Lys	Lys	Pro	Gly	Glu	
1			5						10					15		

aca	gtc	aag	atc	tcc	tgc	aag	gct	tct	ggg	tat	acc	ctc	aca	aac	tat	96
Thr	Val	Lys	Ile	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Thr	Leu	Thr	Asn	Tyr	
			20					25					30			

gga	atg	aac	tgg	gtg	aag	cag	gct	cca	gga	aag	ggt	tta	aag	tgg	atg	144
Gly	Met	Asn	Trp	Val	Lys	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Lys	Trp	Met	
		35				40					45					

ggc	tgg	ata	aac	acc	tac	act	gga	gag	cca	aca	tat	gct	gat	gac	ttc	192
Gly	Trp	Ile	Asn	Thr	Tyr	Thr	Gly	Glu	Pro	Thr	Tyr	Ala	Asp	Asp	Phe	

50	55	60	
aag gga cgg ttt gcc ttc tct ttg gaa acc tct gcc agg att gtc tat			240
Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Arg Ile Val Tyr			
65	70	75	80
ttg cag atc aac aac ctc aaa aat gag gac acg gct aca tat ttc tgt			288
Leu Gln Ile Asn Asn Leu Lys Asn Glu Asp Thr Ala Thr Tyr Phe Cys			
	85	90	95
gca aaa tat gag gcc cac gag ggg ttt gtt tat tgg ggc caa ggg act			336
Ala Lys Tyr Glu Ala His Glu Gly Phe Val Tyr Trp Gly Gln Gly Thr			
	100	105	110
ctg gtc act gtc tct gca			354
Leu Val Thr Val Ser Ala			
	115		
<210>	379		
<211>	118		
<212>	PRT		
<213>	Mus musculus		
<400>	379		
Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu			
1	5	10	15
Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Leu Thr Asn Tyr			
	20	25	30
Gly Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met			
	35	40	45
Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe			
	50	55	60
Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Arg Ile Val Tyr			
65	70	75	80

Leu Gln Ile Asn Asn Leu Lys Asn Glu Asp Thr Ala Thr Tyr Phe Cys
85 90 95

Ala Lys Tyr Glu Ala His Glu Gly Phe Val Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ala
115

<210> 380
<211> 321
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(321)
<223> SC16.149 VL

<220>
<221> CDS
<222> (1)..(321)

<400> 380
gac atc cag atg aac cag tct cca tcc agt ctg tct gca tcc ctt gga 48
Asp Ile Gln Met Asn Gln Ser Pro Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

gac aca att acc atc act tgc cat gcc agt cag aac att aat gtt tgg 96
Asp Thr Ile Thr Ile Thr Cys His Ala Ser Gln Asn Ile Asn Val Trp
20 25 30

tta agc tgg tac cag cag aaa cca gga aat att cca aaa cta ttg atc 144
Leu Ser Trp Tyr Gln Gln Lys Pro Gly Asn Ile Pro Lys Leu Leu Ile
35 40 45

tat aag gct tcc cac ttg cac aca ggc gtc cca tca agg ttg agt ggc 192
Tyr Lys Ala Ser His Leu His Thr Gly Val Pro Ser Arg Leu Ser Gly

50		55		60	
agt gga tct gga aca ggt ttc aca tta acc atc agc agc ctg cag cct					240
Ser Gly Ser Gly Thr Gly Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro					
65		70		75	80
gaa gac att gcc act tac tac tgt caa cag ggt caa agt tat cca ttc					288
Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Gln Ser Tyr Pro Phe					
	85		90		95
acg ttc ggc tcg ggg aca acg ttg gaa ata aaa					321
Thr Phe Gly Ser Gly Thr Thr Leu Glu Ile Lys					
	100		105		

$\langle 210 \rangle$	381
$\langle 211 \rangle$	107
$\langle 212 \rangle$	PRT
$\langle 213 \rangle$	Mus musculus

<400> 381

Asp Ile Gln Met Asn Gln Ser Pro Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

Asp Thr Ile Thr Ile Thr Cys His Ala Ser Gln Asn Ile Asn Val Trp
20 25 30

Leu Ser Trp Tyr Gln Gln Lys Pro Gly Asn Ile Pro Lys Leu Leu Ile
35 40 45

Tyr Lys Ala Ser His Leu His Thr Gly Val Pro Ser Arg Leu Ser Gly
50 55 60

Ser Gly Ser Gly Thr Gly Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Gln Ser Tyr Pro Phe
85 90 95

Thr Phe Gly Ser Gly Thr Thr Leu Glu Ile Lys
100 105

<210> 382
<211> 348
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(348)
<223> SC16.149 VH

<220>
<221> CDS
<222> (1)..(348)

<400> 382
cag gtg cag ctg aag gag tca gga cct ggc ctg gtg gcg ccc tca cag 48
Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln
1 5 10 15

agc ctg tcc atc act tgc gct gtc tct ggg ttt tca tta acc agc ttt 96
Ser Leu Ser Ile Thr Cys Ala Val Ser Gly Phe Ser Leu Thr Ser Phe
20 25 30

ggt gta cac tgg gtt cgc cag cct cca gga aag ggt ctg gag tgg ctg 144
Gly Val His Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Leu
35 40 45

gga gtt ata tgg gct ggt gga agc aca aat tat tat tcg gct ctc atg 192
Gly Val Ile Trp Ala Gly Gly Ser Thr Asn Tyr Tyr Ser Ala Leu Met
50 55 60

tcc aga ctg agc atc agc ata gac aac tcc aag agc caa gtt ttc tta 240
Ser Arg Leu Ser Ile Ser Ile Asp Asn Ser Lys Ser Gln Val Phe Leu
65 70 75 80

aag atg aac agt ctg caa act gat gac aca gcc atg tac tac tgt gcc 288
Lys Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Met Tyr Tyr Cys Ala

	85	90	95	
aga gac tgg gag ggc tgg ttt gct tac tgg ggc caa ggg act ctg gtc				336
Arg Asp Trp Glu Gly Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val				
	100	105	110	
act gtc tct gca				348
Thr Val Ser Ala				
	115			
<210>	383			
<211>	116			
<212>	PRT			
<213>	Mus musculus			
<400>	383			
Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln				
1	5	10	15	
Ser Leu Ser Ile Thr Cys Ala Val Ser Gly Phe Ser Leu Thr Ser Phe				
	20	25	30	
Gly Val His Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Leu				
	35	40	45	
Gly Val Ile Trp Ala Gly Gly Ser Thr Asn Tyr Tyr Ser Ala Leu Met				
	50	55	60	
Ser Arg Leu Ser Ile Ser Ile Asp Asn Ser Lys Ser Gln Val Phe Leu				
65	70	75	80	
Lys Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Met Tyr Tyr Cys Ala				
	85	90	95	
Arg Asp Trp Glu Gly Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val				
	100	105	110	

Thr Val Ser Ala
115

<210> 384
<211> 339
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(339)
<223> SC16.150 VL

<220>
<221> CDS
<222> (1)..(339)

<400> 384
gac att gtg atg tca cag tct cca tcc tcc cta act gtg tca gtt gga 48
Asp Ile Val Met Ser Gln Ser Pro Ser Ser Leu Thr Val Ser Val Gly
1 5 10 15

gag aag gtt act atg agc tgc atg tcc agt cag agc ctt tta tat agt 96
Glu Lys Val Thr Met Ser Cys Met Ser Ser Gln Ser Leu Leu Tyr Ser
20 25 30

agc act caa aag aac tac ttg gcc tgg tac cag cag aaa cca ggg cag 144
Ser Thr Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

tct cct aaa ctg ctg att tac tgg gca tcc act agg gaa tct ggg gtc 192
Ser Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

cct gat cgc ttc aca ggc agt gga tct ggg aca gat ttc act ctc acc 240
Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

atc agc agt gtg aag gct gaa gac ctg gca gtt tat tac tgt cag caa 288
Ile Ser Ser Val Lys Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln

	85	90	95	
tat tat agc tat ccg tac acg ttc gga ggg ggg acc aag ctg gaa ata				336
Tyr Tyr Ser Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile				
	100	105	110	

aaa		339
Lys		

<210> 385
 <211> 113
 <212> PRT
 <213> Mus musculus

<400> 385

Asp Ile Val Met Ser Gln Ser Pro Ser Ser Leu Thr Val Ser Val Gly
1 5 10 15

Glu Lys Val Thr Met Ser Cys Met Ser Ser Gln Ser Leu Leu Tyr Ser
20 25 30

Ser Thr Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Ser Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Val Lys Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln
85 90 95

Tyr Tyr Ser Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
100 105 110

Lys

<210> 386
<211> 351
<212> DNA
<213> Mus musculus

<220>
<221> misc_feature
<222> (1)..(351)
<223> SC16.150 VH

<220>
<221> CDS
<222> (1)..(351)

<400> 386
gag atc cag ctg cag cag tct gga cct gag ctg gtg aag cct ggg gct 48
Glu Ile Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1 5 10 15

tca gtg aag gta tcc tgc aag gct tct ggt tat gca ttc act agc tac 96
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Thr Ser Tyr
20 25 30

aac atg tac tgg gtg agt cag agc cat gga aag agc ctt gag tgg att 144
Asn Met Tyr Trp Val Ser Gln Ser His Gly Lys Ser Leu Glu Trp Ile
35 40 45

gga tat att gat cct tac aat ggt ggc act agc tac aac cag aag ttc 192
Gly Tyr Ile Asp Pro Tyr Asn Gly Gly Thr Ser Tyr Asn Gln Lys Phe
50 55 60

agg ggc aag gcc aca ttg act gtt gac aag tcc tca agc aca gcc tac 240
Arg Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

atg cat ctc aac agc ctg aca tct gag gac tcg gca gtc tat tat tgt 288
Met His Leu Asn Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys

Leu Thr Val Ser Ser
115

<210> 388
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<223> Humanized antibody sequence

<220>
<221> misc_feature
<222> (1).. (318)
<223> HSC16.13 VL

<220>
<221> CDS
<222> (1).. (318)

<400> 388
gac atc cag atg acc cag tct cca tcc tcc ctg tct gca tct gta gga 48
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

gac aga gtc acc atc act tgc agt gca agt agc agc gtt agc tat atg 96
Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

tat tgg tat cag cag aaa cca ggg aaa gcc cct aag ctc ctg atc tac 144
Tyr Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
35 40 45

ctc act agt aac ttg gca agt ggg gtc cca tca agg ttc agt ggc agt 192
Leu Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

gga tct ggg aca gat ttc act ctc acc atc agc agt ctg caa cct gaa 240
Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80

gat ttt gca act tac tac tgt caa cag tgg cgt agt aac cca ttc acg	288
Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Arg Ser Asn Pro Phe Thr	
85 90 95	

ttc ggc cag ggg aca aag ttg gaa ata aaa	318
Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys	
100 105	

<210> 389
 <211> 106
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 389

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

Tyr Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
35 40 45

Leu Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Arg Ser Asn Pro Phe Thr
85 90 95

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 390
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Humanized antibody sequence

<220>
<221> misc_feature
<222> (1)..(372)
<223> HSC16.13 VH

<220>
<221> CDS
<222> (1)..(372)

<400> 390
cag atc acc ttg aag gag tct ggt cct acg ctg gtg aaa ccc aca cag 48
Gln Ile Thr Leu Lys Glu Ser Gly Pro Thr Leu Val Lys Pro Thr Gln
1 5 10 15

acc ctc acg ctg acc tgc acc ttc tct ggg ttc tca ctc agc act agt 96
Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser
20 25 30

gga atg ggt gtg ggc tgg atc cgt cag ccc cca gga aag gcc ctg gag 144
Gly Met Gly Val Gly Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu
35 40 45

tgg ctt gca cac att tgg tgg gat gat gtt aag cgc tac agc cca tct 192
Trp Leu Ala His Ile Trp Trp Asp Asp Val Lys Arg Tyr Ser Pro Ser
50 55 60

ctg aag agc agg ctc acc atc acc aag gac acc tcc aaa aac cag gtg 240
Leu Lys Ser Arg Leu Thr Ile Thr Lys Asp Thr Ser Lys Asn Gln Val
65 70 75 80

gtc ctt aca atg acc aac atg gac cct gtg gac aca gcc aca tat tac 288

Val	Leu	Thr	Met	Thr	Asn	Met	Asp	Pro	Val	Asp	Thr	Ala	Thr	Tyr	Tyr
				85					90					95	

tgt	gca	cgc	ata	gtt	tcc	ttt	gat	aac	gac	gtt	gtc	tct	gct	atg	gac	336
Cys	Ala	Arg	Ile	Val	Ser	Phe	Asp	Asn	Asp	Val	Val	Ser	Ala	Met	Asp	
				100				105					110			

tac	tgg	ggc	caa	gga	acc	cta	gtc	acc	gtc	tcc	tcc	372
Tyr	Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser	
				115				120				

<210> 391
 <211> 124
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 391

Gln	Ile	Thr	Leu	Lys	Glu	Ser	Gly	Pro	Thr	Leu	Val	Lys	Pro	Thr	Gln
1				5					10					15	

Thr	Leu	Thr	Leu	Thr	Cys	Thr	Phe	Ser	Gly	Phe	Ser	Leu	Ser	Thr	Ser
				20				25					30		

Gly	Met	Gly	Val	Gly	Trp	Ile	Arg	Gln	Pro	Pro	Gly	Lys	Ala	Leu	Glu
				35			40					45			

Trp	Leu	Ala	His	Ile	Trp	Trp	Asp	Asp	Val	Lys	Arg	Tyr	Ser	Pro	Ser
				50			55				60				

Leu	Lys	Ser	Arg	Leu	Thr	Ile	Thr	Lys	Asp	Thr	Ser	Lys	Asn	Gln	Val
65					70				75					80	

Val	Leu	Thr	Met	Thr	Asn	Met	Asp	Pro	Val	Asp	Thr	Ala	Thr	Tyr	Tyr
				85					90					95	

Cys Ala Arg Ile Val Ser Phe Asp Asn Asp Val Val Ser Ala Met Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 392
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Humanized antibody sequence

<220>
<221> misc_feature
<222> (1)..(321)
<223> HSC16.15 VL

<220>
<221> CDS
<222> (1)..(321)

<400> 392
gcc atc cag ttg acc cag tct cca tcc tcc ctg tct gca tct gta gga 48
Ala Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

gac aga gtc acc atc act tgc cgg gca agt gag aac att tat tat aat 96
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Glu Asn Ile Tyr Tyr Asn
20 25 30

tta gcc tgg tat cag cag aaa cca ggg aaa gct cct aag ctc ctg atc 144
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

tat act gcc aat agt ttg gaa gat ggg gtc cca tca agg ttc agc ggc 192
Tyr Thr Ala Asn Ser Leu Glu Asp Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

agt gga tct ggg aca gat ttc act ctc acc atc agc agc ctg cag cct 240
 Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
 65 70 75 80

gaa gat ttt gca act tat ttt tgt aaa cag gct tat gac gtt cct ccg 288
Glu Asp Phe Ala Thr Tyr Phe Cys Lys Gln Ala Tyr Asp Val Pro Pro
85 90 95

acg ttc ggt gga ggc acc aag ctg gaa atc aaa 321
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

$\langle 210 \rangle$	393
$\langle 211 \rangle$	107
$\langle 212 \rangle$	PRT
$\langle 213 \rangle$	Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 393

Ala Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Glu Asn Ile Tyr Tyr Asn
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Thr Ala Asn Ser Leu Glu Asp Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Phe Cys Lys Gln Ala Tyr Asp Val Pro Pro
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 394
<211> 351
<212> DNA
<213> Artificial Sequence

<220>
<223> Humanized antibody sequence

<220>
<221> misc_feature
<222> (1)..(351)
<223> HSC16.15 VH

<220>
<221> CDS
<222> (1)..(351)

<400> 394
cag gtg cag ctg gtg cag tct ggg gct gag gtg aag aag cct ggg gcc 48
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

tca gtg aag gtt tcc tgc aag gca tct gga tac acc ttc acc agg tac 96
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

tgg ata cac tgg ata cga cag gcc cct gga caa ggg ctt gag tgg atg 144
Trp Ile His Trp Ile Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

gga tac atc aac cct aca act gtt tat act gag ttc aat cag aac ttc 192
Gly Tyr Ile Asn Pro Thr Thr Val Tyr Thr Glu Phe Asn Gln Asn Phe
50 55 60

aag gac aga gtc acc atg acc agg gac acg tcc acg agc aca gtc tac 240

Lys	Asp	Arg	Val	Thr	Met	Thr	Arg	Asp	Thr	Ser	Thr	Ser	Thr	Val	Tyr
65					70					75					80

atg	gag	ctg	agc	agc	ctg	aga	tct	gag	gac	acg	gcc	gtg	tat	tac	tgt	288
Met	Glu	Leu	Ser	Ser	Leu	Arg	Ser	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	
			85						90					95		

gcg	aga	ggc	ggt	agt	aac	ttc	ttt	gac	tac	tgg	ggc	caa	ggc	acc	act	336
Ala	Arg	Gly	Gly	Ser	Asn	Phe	Phe	Asp	Tyr	Trp	Gly	Gln	Gly	Thr	Thr	
			100						105					110		

gtc	aca	gtc	tcc	tca												351
Val	Thr	Val	Ser	Ser												

<210> 395
 <211> 117
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 395

Gln	Val	Gln	Leu	Val	Gln	Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Ala
1				5					10					15	

Ser	Val	Lys	Val	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Thr	Phe	Thr	Arg	Tyr
			20					25					30		

Trp	Ile	His	Trp	Ile	Arg	Gln	Ala	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Met
		35					40					45			

Gly	Tyr	Ile	Asn	Pro	Thr	Thr	Val	Tyr	Thr	Glu	Phe	Asn	Gln	Asn	Phe
	50						55				60				

Lys	Asp	Arg	Val	Thr	Met	Thr	Arg	Asp	Thr	Ser	Thr	Ser	Thr	Val	Tyr
65					70					75					80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Ser Asn Phe Phe Asp Tyr Trp Gly Gln Gly Thr Thr
100 105 110

Val Thr Val Ser Ser
115

<210> 396
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<223> Humanized antibody sequence

<220>
<221> misc_feature
<222> (1).. (318)
<223> HSC16.25 VL

<220>
<221> CDS
<222> (1).. (318)

<400> 396
gaa att gtg ctg act cag tct cca gac ttt cag tct gtg act cca aag 48
Glu Ile Val Leu Thr Gln Ser Pro Asp Phe Gln Ser Val Thr Pro Lys
1 5 10 15

gag aaa gtc acc atc acc tgc agt gcc agt agc agt gtg agc tac atg 96
Glu Lys Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

cac tgg tac cag cag aaa cca gat cag tct cca aag ctc ctc atc aag 144
His Trp Tyr Gln Gln Lys Pro Asp Gln Ser Pro Lys Leu Leu Ile Lys
35 40 45

gat agt tcc aaa ctc gcc tca ggg gtc ccc tcg agg ttc agt ggc agt	192
Asp Ser Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser	
50 55 60	

gga tct ggg aca gat ttc acc ctc acc atc aat agc ctg gaa gct gaa	240
Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Glu Ala Glu	
65 70 75 80	

gat gct gca acg tat tac tgt cag cag tgg agt agt aac ccg ctc acg	288
Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr	
85 90 95	

ttc ggt cag ggg acc aag ctg gag atc aaa	318
Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys	
100 105	

<210> 397
 <211> 106
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 397

Glu Ile Val Leu Thr Gln Ser Pro Asp Phe Gln Ser Val Thr Pro Lys
1 5 10 15

Glu Lys Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

His Trp Tyr Gln Gln Lys Pro Asp Gln Ser Pro Lys Leu Leu Ile Lys
35 40 45

Asp Ser Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 398
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Humanized antibody sequence

<220>
<221> misc_feature
<222> (1).. (372)
<223> HSC16.25 VH

<220>
<221> CDS
<222> (1).. (372)

<400> 398
cag atc acc ttg aag gag tct ggt cct acg ctg gtg aaa ccc aca cag 48
Gln Ile Thr Leu Lys Glu Ser Gly Pro Thr Leu Val Lys Pro Thr Gln
1 5 10 15

acc ctc acg ctg acc tgc acc ttc tct ggg ttc tca ctc agc act agt 96
Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser
20 25 30

gga atg ggt gtg ggc tgg atc cgt cag ccc cca gga aag gcc ctg gag 144
Gly Met Gly Val Gly Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu
35 40 45

tgg ctt aca gac att tgg tgg gat gat aat aag tac tac aac cca tct 192

Trp Leu Thr Asp Ile Trp Trp Asp Asp Asn Lys Tyr Tyr Asn Pro Ser
50 55 60

ctg aag agc agg ctc acc atc acc aag gac acc tcc aaa aac cag gtg 240
Leu Lys Ser Arg Leu Thr Ile Thr Lys Asp Thr Ser Lys Asn Gln Val
65 70 75 80

gtc ctt aca atg acc aac atg gac cct gtg gac aca gcc aca tat tac 288
Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
85 90 95

tgt gca cga aga gtt aac tat tat tac gac ccg tac tat gct atg gac 336
Cys Ala Arg Arg Val Asn Tyr Tyr Tyr Asp Pro Tyr Tyr Ala Met Asp
100 105 110

tac tgg ggt caa gga acc cta gtc acc gtc tcc tca 372
Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 399
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 399

Gln Ile Thr Leu Lys Glu Ser Gly Pro Thr Leu Val Lys Pro Thr Gln
1 5 10 15

Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser
20 25 30

Gly Met Gly Val Gly Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu
35 40 45

Trp Leu Thr Asp Ile Trp Trp Asp Asp Asn Lys Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Leu Thr Ile Thr Lys Asp Thr Ser Lys Asn Gln Val
65 70 75 80

Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
85 90 95

Cys Ala Arg Arg Val Asn Tyr Tyr Tyr Asp Pro Tyr Tyr Ala Met Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 400
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Humanized antibody sequence

<220>
<221> misc_feature
<222> (1)..(321)
<223> HSC16.34 VL

<220>
<221> CDS
<222> (1)..(321)

<400> 400
gac atc cag atg acc cag tct cca tcc tcc ctg tct gca tct gta gga 48
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

gac aga gtc acc atc act tgc aag gcg agt cag agc gtt agc aat gat 96
Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Ser Val Ser Asn Asp
20 25 30

gta gcc tgg tat cag cag aaa cca ggg aaa gtt cct aag ctc ctg atc	144
Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile	
35 40 45	

tat tat gca tcc aat agg tac tca ggg gtc cca tct cgg ttc agt ggc	192
Tyr Tyr Ala Ser Asn Arg Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly	
50 55 60	

agt gga tct ggg aca gat ttc act ctc acc atc agc agc ctg cag cct	240
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro	
65 70 75 80	

gaa gat gtt gca act tat ttc tgt cag cag gat tat agc tct ccg tgg	288
Glu Asp Val Ala Thr Tyr Phe Cys Gln Gln Asp Tyr Ser Ser Pro Trp	
85 90 95	

acg ttc ggt gga ggc acc aag gtg gaa atc aaa	321
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys	
100 105	

<210> 401
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 401

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Ser Val Ser Asn Asp
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile
35 40 45

Tyr Tyr Ala Ser Asn Arg Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Val Ala Thr Tyr Phe Cys Gln Gln Asp Tyr Ser Ser Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 402

<211> 354

<212> DNA

<213> Artificial Sequence

<220>

<223> Humanized antibody sequence

<220>

<221> misc_feature

<222> (1).. (354)

<223> HSC16.34 VH

<220>

<221> CDS

<222> (1).. (354)

<400> 402

cag gtc cag ctt gtg cag tct ggg gct gag gtg aag aag cct ggg gcc 48
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

tca gtg aag gtt tcc tgc aag gct tct gga tac acc ttc act aac tat 96
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

ggc atg aat tgg gtg cgc cag gcc ccc gga caa agg ctt gag tgg atg 144

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met	
35 40 45	
gga tgg atc aac act tac act ggt gac cca aca tat gca gat gat ttc	192
Gly Trp Ile Asn Thr Tyr Thr Gly Asp Pro Thr Tyr Ala Asp Asp Phe	
50 55 60	
aag ggc aga gtc acc att acc agg gac aca tcc gcg agc aca gcc tac	240
Lys Gly Arg Val Thr Ile Thr Arg Asp Thr Ser Ala Ser Thr Ala Tyr	
65 70 75 80	
atg gag ctg agc agc ctg aga tct gaa gac acg gct gtg tat tac tgt	288
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys	
85 90 95	
gcg aga att ggc ggt aat agt ccc tct gat tac tgg ggc caa ggc acc	336
Ala Arg Ile Gly Gly Asn Ser Pro Ser Asp Tyr Trp Gly Gln Gly Thr	
100 105 110	
act gtc aca gtc tcc tca	354
Thr Val Thr Val Ser Ser	
115	

<210> 403
 <211> 118
 <212> PRT
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<220>
 <223> Synthetic Construct

<400> 403

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala	
1 5 10 15	
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr	
20 25 30	
Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met	
35 40 45	

Gly Trp Ile Asn Thr Tyr Thr Gly Asp Pro Thr Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Val Thr Ile Thr Arg Asp Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ile Gly Gly Asn Ser Pro Ser Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Thr Val Thr Val Ser Ser
115

<210> 404
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (1).. (321)
<223> HSC16.56 VL

<220>
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<222> (1).. (321)

<400> 404
gag atc gtg atg acc cag tcc cct gcc aca ctg tcc gtg tcc cct gga
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1 5 10 15

gag agg gcc acc ctg tcc tgc aag gcc tcc cag tcc gtg tcc aac gac	96
Glu Arg Ala Thr Leu Ser Cys Lys Ala Ser Gln Ser Val Ser Asn Asp	
20 25 30	

gtg gtg tgg tac cag cag aag ccc gga cag gct ccc agg ctg ctg atc	144
Val Val Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile	
35 40 45	

tac tac gcc tcc aac agg tac acc ggc atc cct gcc agg ttc tcc gga	192
Tyr Tyr Ala Ser Asn Arg Tyr Thr Gly Ile Pro Ala Arg Phe Ser Gly	
50 55 60	

tcc gga tcc ggc acc gag ttc acc ctg acc atc tcc tcc ctg cag tcc	240
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser	
65 70 75 80	

gag gac ttc gcc gtg tac tac tgc cag cag gac tac acc tcc ccc tgg	288
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Asp Tyr Thr Ser Pro Trp	
85 90 95	

acc ttt ggc cag ggc acc aag ctg gag atc aag	321
Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys	
100 105	

<210> 405
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 405

Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Lys Ala Ser Gln Ser Val Ser Asn Asp
20 25 30

Val Val Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Tyr Ala Ser Asn Arg Tyr Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Asp Tyr Thr Ser Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 406
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (1).. (354)
<223> HSC16.56 VH

<220>
<221> CDS
<222> (1).. (354)

<400> 406
cag gtg cag ctg gtg cag tcc ggc gcc gaa gtg aag aaa ccc ggc gcc 48
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

tcc gtg aag gtg tcc tgc aag gcc tcc ggc tac acc ttc acc aac tac 96

Ser	Val	Lys	Val	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Thr	Phe	Thr	Asn	Tyr		
			20					25					30				
ggc	atg	aac	tgg	gtg	agg	cag	gct	cct	gga	cag	gga	ctg	gag	tgg	atg		144
Gly	Met	Asn	Trp	Val	Arg	Gln	Ala	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Met		
		35					40					45					
ggc	tgg	atc	aac	acc	tac	acc	ggc	gaa	ccc	acc	tac	gcc	gac	gac	ttc		192
Gly	Trp	Ile	Asn	Thr	Tyr	Thr	Gly	Glu	Pro	Thr	Tyr	Ala	Asp	Asp	Phe		
		50				55					60						
aag	ggc	agg	gtg	acc	atg	acc	acc	gac	acc	tcc	acc	tcc	acc	gcc	tac		240
Lys	Gly	Arg	Val	Thr	Met	Thr	Thr	Asp	Thr	Ser	Thr	Ser	Thr	Ala	Tyr		
65					70					75				80			
atg	gag	ctg	agg	tcc	ctg	agg	tcc	gac	gac	acc	gcc	gtg	tac	tac	tgc		288
Met	Glu	Leu	Arg	Ser	Leu	Arg	Ser	Asp	Asp	Thr	Ala	Val	Tyr	Tyr	Cys		
				85				90					95				
gct	agg	att	ggc	gac	tcc	tcc	ccc	tcc	gat	tac	tgg	gga	cag	ggc	acc		336
Ala	Arg	Ile	Gly	Asp	Ser	Ser	Pro	Ser	Asp	Tyr	Trp	Gly	Gln	Gly	Thr		
			100					105					110				
ctc	gtg	acc	gtc	tcc	tcc												354
Leu	Val	Thr	Val	Ser	Ser												
			115														

<210> 407
 <211> 118
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 407

Gln	Val	Gln	Leu	Val	Gln	Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Ala		
1				5					10					15			

Ser	Val	Lys	Val	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Thr	Phe	Thr	Asn	Tyr		
			20					25					30				

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ile Gly Asp Ser Ser Pro Ser Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> 408
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> HSC16.13 CDRL1

<400> 408

Ser Ala Ser Ser Ser Val Ser Tyr Met Tyr
1 5 10

<210> 409
<211> 7
<212> PRT
<213> Artificial Sequence

<220>

<223> HSC16.13 CDRL2

<400> 409

Leu Thr Ser Asn Leu Ala Ser

1 5

<210> 410

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> HSC16.13 CDRL3

<400> 410

Gln Gln Trp Arg Ser Asn Pro Phe Thr

1 5

<210> 411

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> HSC16.15 CDRL1

<400> 411

Arg Ala Ser Glu Asn Ile Tyr Tyr Asn Leu Ala

1 5 10

<210> 412

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> HSC16.15 CDRL2

<400> 412

Thr Ala Asn Ser Leu Glu Asp
1 5

<210> 413

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> HSC16.15 CDRL3

<400> 413

Lys Gln Ala Tyr Asp Val Pro Pro Thr
1 5

<210> 414

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> HSC16.25 CDRL1

<400> 414

Ser Ala Ser Ser Ser Val Ser Tyr Met His
1 5 10

<210> 415

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> HSC16.25 CDRL2

<400> 415

Asp Ser Ser Lys Leu Ala Ser
1 5

<210> 416

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> HSC16.25 CDRL3

<400> 416

Gln Gln Trp Ser Ser Asn Pro Leu Thr
1 5

<210> 417

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> HSC16.34 CDRL1

<400> 417

Lys Ala Ser Gln Ser Val Ser Asn Asp Val Ala
1 5 10

<210> 418

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> HSC16.34 CDRL2

<400> 418

Tyr Ala Ser Asn Arg Tyr Ser
1 5

<210> 419
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> HSC16.34 CDRL3

<400> 419

Gln Gln Asp Tyr Ser Ser Pro Trp Thr
1 5

<210> 420
<211> 11
<212> PRT
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<220>
<223> HSC16.56 CDRL1

<400> 420

Lys Ala Ser Gln Ser Val Ser Asn Asp Val Val
1 5 10

<210> 421
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> HSC16.56 CDRL2

<400> 421

Tyr Ala Ser Asn Arg Tyr Thr
1 5

<210> 422
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> HSC16.56 CDRL3

<400> 422

Gln Gln Asp Tyr Thr Ser Pro Trp Thr
1 5

<210> 423
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> HSC16.13 CDRH1

<400> 423

Thr Ser Gly Met Gly Val Gly
1 5

<210> 424
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> HSC16.13 CDRH2

<400> 424

His Ile Trp Trp Asp Asp Val Lys Arg Tyr Ser Pro Ser Leu Lys Ser
1 5 10 15

<210> 425
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> HSC16.13 CDRH3

<400> 425

Ile	Val	Ser	Phe	Asp	Asn	Asp	Val	Val	Ser	Ala	Met	Asp	Tyr
1				5					10				

<210> 426
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> HSC16.15 CDRH1

<400> 426

Arg	Tyr	Trp	Ile	His
1			5	

<210> 427
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> HSC16.15 CDRH2

<400> 427

Tyr	Ile	Asn	Pro	Thr	Thr	Val	Tyr	Thr	Glu	Phe	Asn	Gln	Asn	Phe	Lys
1				5					10					15	

Asp

<210> 428
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> HSC16.15 CDRH3

<400> 428

Gly Gly Ser Asn Phe Phe Asp Tyr
1 5

<210> 429
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> HSC16.25 CDRH1

<400> 429

Thr Ser Gly Met Gly Val Gly
1 5

<210> 430
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> HSC16.25 CDRH2

<400> 430

Asp Ile Trp Trp Asp Asp Asn Lys Tyr Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 431
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> HSC16.25 CDRH3

<400> 431

Arg	Val	Asn	Tyr	Tyr	Tyr	Asp	Pro	Tyr	Tyr	Ala	Met	Asp	Tyr
1				5						10			

<210> 432
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> HSC16.34 CDRH1

<400> 432

Asn	Tyr	Gly	Met	Asn
1				5

<210> 433
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> HSC16.34 CDRH2

<400> 433

Trp	Ile	Asn	Thr	Tyr	Thr	Gly	Asp	Pro	Thr	Tyr	Ala	Asp	Asp	Phe	Lys
1				5					10					15	

Gly

<210> 434
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> HSC16.34 CDRH3

<400> 434

Ile Gly Gly Asn Ser Pro Ser Asp Tyr
1 5

<210> 435
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> HSC16.56 CDRH1

<400> 435

Asn Tyr Gly Met Asn
1 5

<210> 436
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> HSC16.56 CDRH2

<400> 436

Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Asp Asp Phe Lys
1 5 10 15

Gly

<210> 437

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> HSC16.56 CDRH3

<400> 437

Ile Gly Asp Ser Ser Pro Ser Asp Tyr

1

5

摘要

本文提供了新的抗 DLL3 嵌合抗原受体及使用其用于治疗增生性障碍的方法。