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(54) Title: SELF-ASSEMBLING PROTEIN NANOSTRUCTURES DISPLAYING PARAMYXOVIRUS AND/OR PNEUMOVIRUS F PROTEINS AND THEIR USE

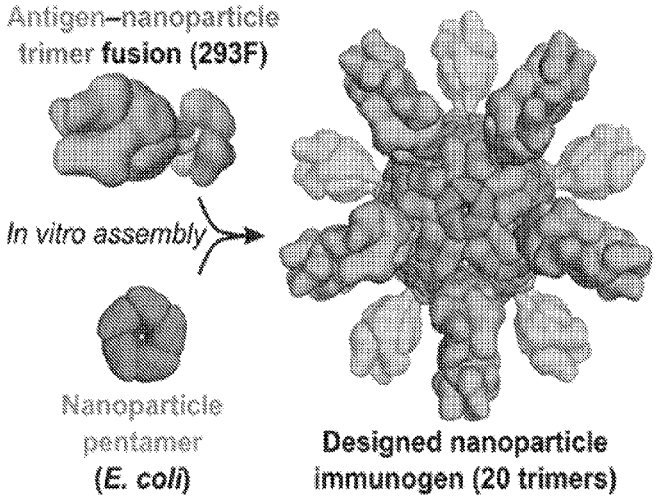

FIG. 1

(57) Abstract: Disclosed herein are nanostructures and their use, where the nanostructures include (a) a plurality of first assemblies, each first assembly comprising a plurality of identical first polypeptides; (b) a plurality of second assemblies, each second assembly comprising a plurality of identical second polypeptides, wherein the second polypeptide differs from the first polypeptide; wherein the plurality of first assemblies non-covalently interact with the plurality of second assemblies to form a nanostructures; and wherein the nanostructure displays multiple copies of one or more paramyxovirus and/or pneumovirus F proteins or antigenic fragments thereof, on an exterior of the nanostructure.

[Continued on next page]

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Self-assembling protein nanostructures displaying paramyxovirus and/or pneumovirus F proteins and their use

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This application claims priority to U.S. Provisional Patent Application Serial No. 62/481331 filed April 4, 2017, incorporated by reference herein in its entirety.

Background

Molecular self- and co-assembly of proteins into highly ordered, symmetric supramolecular complexes is an elegant and powerful means of patterning matter at the atomic scale. Recent years have seen advances in the development of self-assembling biomaterials, particularly those composed of nucleic acids. DNA has been used to create, for example, nanoscale shapes and patterns, molecular containers, and three-dimensional macroscopic crystals. Methods for designing self-assembling proteins have progressed more slowly, yet the functional and physical properties of proteins make them attractive as building blocks for the development of advanced functional materials.

Summary of the Invention

In a first aspect, the present invention provides a nanostructure, comprising:

(a) a plurality of first assemblies, each first assembly comprising a plurality of identical first polypeptides, wherein the first polypeptides comprise an amino acid sequence having at least 75% identity to the amino acid sequence of a polypeptide selected from the group consisting of SEQ ID NOS:1-51;

(b) a plurality of second assemblies, each second assembly comprising a plurality of identical second polypeptides, wherein the second polypeptides comprise an amino acid sequence having at least 75% identity to the amino acid sequence of a polypeptide selected from the group consisting of SEQ ID NOS:1-51, wherein the second polypeptide differs from the first polypeptide;

wherein the plurality of first assemblies non-covalently interact with the plurality of second assemblies to form a nanostructure; and

wherein the nanostructure displays multiple copies of one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof, on an exterior of the nanostructure.

In a second aspect, the present invention provides a recombinant nucleic acid encoding the first polypeptide fusion protein as recited in the first aspect.

2018249533 16 Dec 2021

In a third aspect, the present invention provides a recombinant expression vector comprising the recombinant nucleic acid of the second aspect.

In a fourth aspect, the present invention provides a recombinant host cell, comprising one or more recombinant expression vectors capable of expressing the first polypeptides and the second polypeptides of the first aspect, or the vector of the third aspect.

In a fifth aspect, the present invention provides an immunogenic composition comprising the nanostructure of the first aspect.

In a sixth aspect, the present invention provides a process for assembling the nanostructures of the first aspect in vitro, comprising mixing two or more nanostructure components in aqueous conditions to drive spontaneous assembly of the desired nanostructure.

In a seventh aspect, the present invention provides a nanostructure produced by the process of the sixth aspect.

In one aspect, nanostructures are provided comprising:

(a) a plurality of first assemblies, each first assembly comprising a plurality of identical first polypeptides;

(b) a plurality of second assemblies, each second assembly comprising a plurality of identical second polypeptides, wherein the second polypeptide differs from the first polypeptide;

wherein the plurality of first assemblies non-covalently interact with the plurality of second assemblies to form a nanostructure; and

wherein the nanostructure displays multiple copies of one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof, on an exterior of the nanostructure.

In one embodiment, (a) the first polypeptides comprise a polypeptide having at least 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or

100% identity along its full length to the amino acid sequence of a polypeptide selected from the group consisting of SEQ ID NOS:1-51; and

(b) the second polypeptides comprise a polypeptide having at least 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to the amino acid sequence of a polypeptide selected from the group consisting of SEQ ID NOS:1-51.

In another embodiment, the one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof, comprise a polypeptide having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to the amino acid sequence of a polypeptide selected from the group consisting of SEQ ID NOS: 53, 61-68, and 101.

In various embodiments:

(a) the first polypeptide comprises a polypeptide having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to the amino acid sequence of T33-31A (SEQ ID NO:51) and the second polypeptide comprises a polypeptide having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to the amino acid sequence of T33-09B/T33-31B (SEQ ID NO:44);

(b) the first polypeptide comprises a polypeptide having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to the amino acid sequence of T33-15B (SEQ ID NO:46) and the second polypeptide comprises a polypeptide having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to the amino acid sequence of T33-15A (SEQ ID NO:45);

(c) the first polypeptide has at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to the amino acid sequence of a polypeptide selected from the group consisting of I53-50A (SEQ ID NO:7), I53-50A.1 (SEQ ID NO:29), I53-50A.1NegT2 (SEQ ID NO:30), and I53-50A.1PosT1 (SEQ ID NO:31), and the second polypeptide has at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to the amino acid sequence of a polypeptide selected from the group consisting of I53-50B (SEQ ID NO:8), I53-50B.1 (SEQ ID NO:32), I53-50B.1NegT2 (SEQ ID NO:33), and I53-50B.4PosT1 (SEQ ID NO:34); or

(d) the first polypeptide comprises a polypeptide having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to the amino acid sequence of I32-28A (SEQ ID NO:21) and the second polypeptide comprises a polypeptide having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to the amino acid sequence of I32-28B (SEQ ID NO:22).

In one embodiment, the one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof, are expressed as a fusion protein with the first polypeptides. In one such embodiment, the plurality of first assemblies each comprise identical first polypeptides; in another such embodiment, the plurality of first assemblies in total comprise two or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof. In another embodiment, only a subset of the first polypeptides comprise a fusion protein with an F protein or antigenic fragment thereof. In a further embodiment, each first assembly comprises a homotrimer of the first polypeptide.

In another embodiment, the fusion protein comprises an amino acid linker positioned between the first polypeptide and the paramyxovirus and/or pneumovirus F proteins, or antigenic fragment thereof. In one such embodiment, the fusion protein comprises an amino acid linker positioned between the first polypeptide and the paramyxovirus F proteins, or antigenic fragment thereof.

In one embodiment the amino acid linker sequence comprises one or more trimerization domain; in another embodiment the amino acid linker sequence comprises a Gly-Ser linker.

In various embodiments, the first polypeptides comprise or consist of first polypeptides having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along their full length to the amino acid sequence of a polypeptide selected from the group consisting of DS-Cav1-foldon-T33-31A (SEQ ID NO:69), DS-Cav1-T33-31A (SEQ ID NO:70), DS-Cav1-foldon-T33-15B (SEQ ID NO:71), DS-Cav1-T33-15B (SEQ ID NO:72), DS-Cav1-foldon-I53-50A (SEQ ID NO:73), DS-Cav1-I53-50A (SEQ ID NO:74), and DS-Cav1-I32-28A (SEQ ID NO:75).

In other embodiments,

(a) when each first polypeptide has at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to the amino acid sequence of DS-Cav1-foldon-T33-31A (SEQ ID NO:69) or DS-Cav1-T33-31A (SEQ ID NO:70), each second polypeptide has at least 75%, 80%, 85%, 90%, 91%,

92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to the amino acid sequence of T33-31B (SEQ ID NO:44);

(b) when each first polypeptide has at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to the amino acid sequence of DS-Cav1-foldon-T33-15B (SEQ ID NO:71) or DS-Cav1-T33-15B (SEQ ID NO:72), each second polypeptide has at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to the amino acid sequence of T33-15A (SEQ ID NO:45);

(c) when each first polypeptide has at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to the amino acid sequence of DS-Cav1-foldon-I53-50A (SEQ ID NO:73) or DS-Cav1-I53-50A (SEQ ID NO:74), each second polypeptide has at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to the amino acid sequence of a polypeptide selected from the group consisting ofI53-50B (SEQ ID NO:8), I53-50B.1 (SEQ ID NO:32), I53-50B.1NegT2 (SEQ ID NO:33), or I53-50B.4PosT1 (SEQ ID NO:34); or

(d) when each first polypeptide has at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to the amino acid sequence of DS-Cav1-I32-28A (SEQ ID NO:75), each second polypeptide has at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to the amino acid sequence of I32-28B.

In one embodiment, the one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof comprises a polypeptide having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to the amino acid sequence of DS-Cav1(SEQ ID NO:53). In one such embodiment, each first polypeptide comprises a fusion polypeptide of a polypeptide having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to the amino acid sequence of DS-Cav1 linked via an amino acid linker to a polypeptide having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to the amino acid sequence of SEQ ID NO:7 (I53-50A). In another embodiment, the amino acid linker comprises a Gly-Ser linker. In a further embodiment, each fusion protein comprises a polypeptide having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to the amino acid

sequence selected from the group consisting of SEQ ID NOS:69-100. In a specific embodiment, each fusion protein comprises a polypeptide having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to the amino acid sequence of SEQ ID NO:76 (F10). In other embodiments, each second polypeptide comprises a polypeptide having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to the amino acid sequence selected from the group consisting of I53-50B (SEQ ID NO:8), I53-50B.1 (SEQ ID NO:32), I53-50B.1NegT2 (SEQ ID NO:33), or I53-50B.4PosT1 (SEQ ID NO:34). In a specific embodiment, each second polypeptide comprises a polypeptide having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to the amino acid sequence of I53-50B.4PosT1 (SEQ ID NO:34).

In other aspects, recombinant expression nucleic acids expressing the first polypeptide fusions, recombinant expression vectors comprising the recombinant nucleic acids linked to a promoter, and recombinant host cells comprising the recombinant expression vectors are provided.

Also provided are immunogenic compositions comprising the nanostructure of any embodiment or combination of embodiments disclosed herein, and a pharmaceutically acceptable carrier. In one embodiment, the immunogenic compositions may further comprise an adjuvant.

In other aspects, methods for generating an immune response to RSV F protein in a subject, or for treating or limiting a RSV infection in a subject are provided, comprising administering to the subject in need thereof an effective amount of the nanostructure or immunogenic composition of embodiment or combination of embodiments disclosed herein to generate the immune response or to treat or prevent RSV infection in the subject.

Also provided are processes assembling the nanostructures of any embodiment or combination of embodiments disclosed herein, comprising mixing two or more nanostructures components in aqueous conditions to drive spontaneous assembly of the desired nanostructures.

Brief Description of the Drawings

The foregoing aspects and many of the attendant advantages of this invention will become more readily appreciated as the same become better understood by reference to

the following detailed description, when taken in conjunction with the accompanying drawings.

FIG. 1 shows a schematic diagram of the production of antigen-bearing nanostructures by in vitro assembly. The two components or building blocks of a given nanostructure can be expressed and purified individually, which allows assembly of the nanostructure to be initiated by mixing the purified components in vitro, a process referred to as in vitro assembly. In some embodiments, the two components of the nanostructure may be expressed in different expression hosts (e.g., human HEK293F cells or bacterial E. coli cells). The figure schematically depicts assembly of a 120-subunit nanostructure bearing 20 trimeric antigens (60 antigen subunits) via in vitro assembly of an antigen-nanostructure trimer fusion protein produced in HEK293F cells and a nanostructure pentamer protein produced in E. coli.

FIG. 2 shows graphs illustrating detection of secreted DS-Cav1, DS-Cav1-foldon-T33-31A, and DS-Cav1-T33-31A fusion proteins in tissue culture supernatants. ELISA assays were performed on tissue culture supernatants from cells expressing DS-Cav1 (top), DS-Cav-1-foldon-T33-31A/T33-31B (bottom left), and DS-Cav-1-T33-31A/T33-31B (bottom right). Four different monoclonal antibodies that bind RSV F were used to evaluate the presence of DS-Cav1 or DS-Cav1 fusion proteins in the supernatants. The results confirm the secretion of proteins comprising well-folded RSV F antigen.

FIG. 3 shows size-exclusion chromatography of DS-Cav1-I53-50A. Protein purified from tissue culture supernatants by immobilized metal affinity chromatography was applied to a Superose^{TM} 6 10/300 GL size exclusion column. The protein eluted as a single, monodisperse species.

FIG. 4 shows size exclusion chromatography of in vitro-assembled DS-Cav1-I53-50 nanostructures. Purified DS-Cav1-I53-50A and I53-50B.4PT1 proteins were mixed at an approximately 1:1 molar ratio, incubated overnight at 4 °C, and then applied to a Sephacryl S-500 16/60 HR size exclusion column. The assembled nanostructure eluted as a single, monodisperse peak around 65 mL, while excess DS-Cav1-I53-50A trimeric component eluted around 90 mL.

FIG. 5 shows a negative stain electron micrograph and two-dimensional class averages of in vitro-assembled DS-Cav1-I53-50 nanostructures. In vitro-assembled DS-Cav1-I53-50 nanostructures, purified by size exclusion chromatography, were imaged by negative stain electron microscopy (top). Averaging many nanostructures yielded two-

dimensional class averages (bottom) that indicate that the I53-50 portion of the nanostructures is highly ordered and consistent, while the precise three-dimensional position of the displayed antigen varies slightly due to the flexible nature of the linker between the DS-Cav1 and I53-50A domains of the DS-Cav1-I53-50A fusion protein.

FIG. 6 shows a series of graphs depicting the antigenicity of DS-Cav1-I53-50 nanostructures. Analysis of purified DS-Cav1-I53-50 nanostructures by ELISA (A) using four RSV F-specific monoclonal antibodies, including the prefusion-specific antibodies MPE8, D25, and RSD5, indicated that the DS-Cav1 antigen is correctly folded and maintained in the prefusion state when multivalently displayed on DS-Cav1-I53-50 nanostructures. This finding was confirmed by surface plasmon resonance measurements using multiple RSV F-specific antibodies (B-C), which, when compared to trimeric DS-Cav1, further suggested that multivalent display of DS-Cav1 results in an avidity effect that reduces the dissociation rate of the antibodies.

FIG. 7 is a graph depicting DS-Cav1-specific serum antibody titers from mice immunized with DS-Cav1-I53-50 nanostructures. Groups of mice were immunized with I53-50 nanostructures lacking additional antigen, trimeric DS-Cav1, or I53-50 nanostructures bearing DS-Cav1 antigen at 33%, 66%, or 100% valency. DS-Cav1-specific serum antibody titers were measured by ELISA on plates coated with DS-Cav1. Serum antibody titers for each mouse are plotted as circles, with the geometric mean within each group plotted as a horizontal line.

FIG. 8 is a graph depicting serum neutralization activity elicited by immunization with DS-Cav1-I53-50 nanostructures. Groups of mice were immunized with I53-50 nanostructures lacking additional antigen, trimeric DS-Cav1, or I53-50 nanostructures bearing DS-Cav1 antigen at 33%, 66%, or 100% valency. Neutralization titers for each mouse are plotted as circles, with the geometric mean within each group plotted as a horizontal line.

FIG. 9 is a graph depicting immunogenicity in a primate immune system elicited by immunization with DS-Cav1-foldon I53-50 nanostructures. Rhesus macaques were injected at weeks 0 and 4 with either free DS-Cav1 trimer or DS-Cav1-foldon-I53-50 nanostructures displaying DS-Cav1 at 100% valency. In both cases, the dose of DS-Cav1 antigen was 50 μg, and the immunogens were formulated with the MF59-like, squalene-based oil-in-water emulsion adjuvant SWE. Sera obtained from the animals at weeks 6 and 16 were evaluated for anti-DS-Cav1 antibody titers (A) and RSV-neutralizing antibody titers (B).

FIG. 10 is a graph depicting the physical stability of DS-Cav1 when fused to I53-50A and/or when further assembled into the icosahedral nanostructure. Samples of trimeric DS-Cav1, trimeric DS-Cav1-foldon–I53-50A, and DS-Cav1-foldon–I53-50 nanostructures containing equivalent concentrations of DS-Cav1 were split into four aliquots and incubated at 20, 50, 70 or 80 °C for 1 hour. After cooling to room temperature, D25 binding was assayed by surface plasmon resonance (SPR).

FIG. 11 is a graph depicting physical stability of the nanostructures. Chemical denaturation in guanidine hydrochloride (GdnHCl), monitored by intrinsic tryptophan fluorescence, was used as a second, antibody-independent technique to evaluate physical stability of trimeric DS-Cav1 (A-B), DS-Cav1-foldon–I53-50A (C-D), DS-Cav1-foldon-I53-50 (E-F), I53-50 (G-H), and I53-50A (I-J). The data indicate superior physical stability of the DS-Cav1 antigen when genetically fused to the I53-50A nanostructure component.

Detailed Description of the Invention

All references cited are herein incorporated by reference in their entirety. Within this application, unless otherwise stated, the techniques utilized may be found in any of several well-known references such as: *Molecular Cloning: A Laboratory Manual* (Sambrook, et al., 1989, Cold Spring Harbor Laboratory Press), *Gene Expression Technology* (Methods in Enzymology, Vol. 185, edited by D. Goeddel, 1991. Academic Press, San Diego, CA), "Guide to Protein Purification" in *Methods in Enzymology* (M.P. Deutshcer, ed., (1990) Academic Press, Inc.); *PCR Protocols: A Guide to Methods and Applications* (Innis, et al. 1990. Academic Press, San Diego, CA), *Culture of Animal Cells: A Manual of Basic Technique, 2nd Ed.* (R.I. Freshney. 1987. Liss, Inc. New York, NY), *Gene Transfer and Expression Protocols*, pp. 109-128, ed. E.J. Murray, The Humana Press Inc., Clifton, N.J.), and the Ambion 1998 Catalog (Ambion, Austin, TX).

As used herein, the singular forms "a", "an" and "the" include plural referents unless the context clearly dictates otherwise. "And" as used herein is interchangeably used with "or" unless expressly stated otherwise.

As used herein, the amino acid residues are abbreviated as follows: alanine (Ala; A), asparagine (Asn; N), aspartic acid (Asp; D), arginine (Arg; R), cysteine (Cys; C), glutamic acid (Glu; E), glutamine (Gln; Q), glycine (Gly; G), histidine (His; H), isoleucine (Ile; I), leucine (Leu; L), lysine (Lys; K), methionine (Met; M), phenylalanine

(Phe; F), proline (Pro; P), serine (Ser; S), threonine (Thr; T), tryptophan (Trp; W), tyrosine (Tyr; Y), and valine (Val; V).

As used herein, "about" means +/- 5% of the recited parameter.

All embodiments of any aspect of the invention can be used in combination, unless the context clearly dictates otherwise.

Unless the context clearly requires otherwise, throughout the description and the claims, the words 'comprise', 'comprising', and the like are to be construed in an inclusive sense as opposed to an exclusive or exhaustive sense; that is to say, in the sense of "including, but not limited to". Words using the singular or plural number also include the plural and singular number, respectively. Additionally, the words "herein," "above," and "below" and words of similar import, when used in this application, shall refer to this application as a whole and not to any particular portions of the application.

The description of embodiments of the disclosure is not intended to be exhaustive or to limit the disclosure to the precise form disclosed. While the specific embodiments of, and examples for, the disclosure are described herein for illustrative purposes, various equivalent modifications are possible within the scope of the disclosure, as those skilled in the relevant art will recognize.

In a first aspect, the disclosure provides nanostructures, comprising:

(a) a plurality of first assemblies, each first assembly comprising a plurality of identical first polypeptides;

(b) a plurality of second assemblies, each second assembly comprising a plurality of identical second polypeptides, wherein the second polypeptide differs from the first polypeptide;

wherein the plurality of first assemblies non-covalently interact with the plurality of second assemblies to form a nanostructure; and

wherein the nanostructure displays multiple copies of one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof, on an exterior of the nanostructure.

Self-assembling polypeptide nanostructures are disclosed herein that multivalently display paramyxovirus and/or pneumovirus F proteins on the nanostructure exteriors. Multiple copies of pairs of first and second polypeptides are able to self-assemble to form nanostructures, such as icosahedral nanostructures. The nanostructures include symmetrically repeated, non-natural, non-covalent polypeptide-polypeptide interfaces that

orient a first assembly and a second assembly into a nanostructure, such as one with an icosahedral symmetry.

The nanostructures of the invention are synthetic, in that they are not naturally occurring. The first polypeptides and the second polypeptides are non-naturally occurring proteins that can be produced by any suitable means, including recombinant production or chemical synthesis. Each member of the plurality of first polypeptides is identical to each other (though when the first polypeptide is present as a fusion polypeptide with one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof, the F protein or antigenic fragment thereof may differ from one first polypeptide to another), and each member of the plurality of second polypeptides is identical to each other. The first proteins and the second proteins are different. There are no specific primary amino acid sequence requirements for the first and second polypeptides. US published patent application 20160122392 and published PCT application WO2014/124301 describe methods for designing synthetic nanostructures, where the nanostructures are not dependent on specific primary amino acid sequences of the first and second polypeptides.

A plurality (2, 3, 4, 5, 6, or more) of first polypeptides self-assemble to form a first assembly, and a plurality (2, 3, 4, 5, 6, or more) of second polypeptides self-assemble to form a second assembly. A plurality of these first and second assemblies then self-assemble non-covalently via the designed interfaces to produce the nanostructures.

The number of first polypeptides in the first assemblies may be the same or different than the number of second polypeptides in the second assemblies. In one exemplary embodiment, the first assembly comprises trimers of the first polypeptides, and the second assembly comprises dimers of the second polypeptides. In a further exemplary embodiment, the first assembly comprises trimers of the first polypeptides, and the second assembly comprises trimers of the second polypeptides. In a further exemplary embodiment, the first assembly comprises trimers of the first polypeptides, and the second assembly comprises pentamers of the second polypeptides.

The first and second polypeptides may be of any suitable length for a given purpose of the resulting nanostructure. In one embodiment, the first polypeptides and the second polypeptides are typically between 30-250 amino acids in length; the length of the first polypeptides and the second polypeptides may be the same or different. In various further embodiments, the first polypeptides and the second polypeptides are between 30-225, 30-200, 30-175, 50-250, 50-225, 50-200, 50-175, 75-250, 75-225, 75-200, 75-175,

100-250, 100-225, 100-200, 100-175, 125-250, 125-225, 125-200, 125-175, 150-250, 150-225, 150-200, and 150-175 amino acids in length.

The isolated polypeptides of SEQ ID NOS:1-51 were designed for their ability to self-assemble in pairs to form nanostructures, such as icosahedral nanostructures. The design involved design of suitable interface residues for each member of the polypeptide pair that can be assembled to form the nanostructure. The nanostructures so formed include symmetrically repeated, non-natural, non-covalent polypeptide-polypeptide interfaces that orient a first assembly and a second assembly into a nanostructure, such as one with an icosahedral symmetry. Thus, in one embodiment the first and second polypeptides are selected from the group SEQ ID NOS:1-51. In each case, the N-terminal methionine residue is optional.

Table 1

Name	Amino Acid Sequence	Identified interface residues
I53-34A SEQ ID NO:1	(M)EGMDPLAVLAESRLLPLLTVRGGEDLAGLATVLELMGV GALEITLRTEKGLEALKALRKSGLLLGAGTVRSPKEAEAAL EAGAAFLVSPGLLEEVAALAQARGVPYLPGVLTPTEVERAL ALGLSALKFFPAEPFQGVRVLRAYAEVFPEVRFLPTGGIKE EHLPHYAALPNLLAVGGSWLLQGDLAAVMKKVKAAKALLSP QAPG	I53-34A: 28,32,36,37,186,188,191,192,195
I53-34B SEQ ID NO:2	(M)TKKVGIVDTTFARVDMAEAAIRTLKALSPNIKIIRKTV PGIKDLPVACKKLLEEEGCDIVMALGMPGKAEKDKVCAHEA SLGLMLAQLMTNKHIIEVFVHEDEAKDDDELDILALVRAIE HAANVYYLLFKPEYLTRMAGKGLRQGREDAGPARE	I53-34B: 19,20,23,24,27,109,113,116,117,120,124,148
I53-40A SEQ ID NO:3	(M)TKKVGIVDTTFARVDMASAAILTLKMESPNIKIIRKTV PGIKDLPVACKKLLEEEGCDIVMALGMPGKAEKDKVCAHEA SLGLMLAQLMTNKHIIEVFVHEDEAKDDAELKILAARRAIE HALNVYYLLFKPEYLTRMAGKGLRQGFEDAGPARE	I53-40A: 20,23,24,27,28,109,112,113,116,120,124
I53-40B SEQ ID NO:4	(M)STINNQLKALKVIPVIAIDNAEDIIPLGKVLAENGLPA AEITFRSSAAVKAIMLLRSAQPEMLIGAGTILNGVQALAAK EAGATFVVSPGFNPNTVRACQIIGIDIVPGVNNPSTVEAAL EMGLTTLKFFPAEASGGISMVKSLVGPYGDIRLMPTGGITP SNIDNYLAIPQVLACGGTWMVDKKLVTNGEWDEIARLTREI VEQVNP	I53-40B: 47,51,54,58,74,102
I53-47A SEQ ID	(M)PIFTLNTNIKATDVPSDFLSLTSRLVGLILSKPGSYVA VHINTDQQLSFGGSTNPAAFGTLMSIGGIEPSKNRDHSAVL	I53-47A: 22,25,29,72,79,86,87

NO:5	FDHLNAMLGIPKNRMYIHFVNLNGDDVGWNGTTF	
I53-47B SEQ ID NO:6	(M)NQHSHKDYETVRIAVVRARWHADIVDACVEAFEIAMAA IGGDRFAVDVFDVPGAYEIPLHARTLAETGRYGAVLGTAFV VNGGIYRHEFVASAVIDGMMNVQLSTGVPVLSAVLTPHRYR DSAEHHRFFAAHFAVKGVEAARACIEILAAREKIAA	I53-47B: 28,31,35,36,39,131,132,135,139,146
I53-50A SEQ ID NO:7	(M)KMEELFKKHKIVAVLRANSVEEAIEKAVAVFAGGVHLI EITFTVPDADTVIKALSVLKEKGAIIGAGTVTSVEQCRKAV ESGAEFIVSPHLDEEISQFCKEKGVFYMPGVMTPTELVKAM KLGHTILKLFPGEVVGPQFVKAMKGPFPNVKFVPTGGVNLD NVCEWFKAGVLAVGVGSALVKGTPDEVREKAKAFVEKIRGC TE	I53-50A: 25,29,33,54,57
I53-50B SEQ ID NO:8	(M)NQHSHKDYETVRIAVVRARWHAEIVDACVSAFEAAMAD IGGDRFAVDVFDVPGAYEIPLHARTLAETGRYGAVLGTAFV VNGGIYRHEFVASAVIDGMMNVQLSTGVPVLSAVLTPHRYR DSDAHTLLFLALFAVKGMEAARACVEILAAREKIAA	I53-50B: 24,28,36,124,125,127,128, 129, 131,132,133,135,139
I53-51A SEQ ID NO:9	(M)FTKSGDDGNTNVINKRVGKDSPLVNFLGDLDELNSFIG FAISKIPWEDMKKDLERVQVELFEIGEDLSTQSSKKKIDES YVLWLLAATAIYRIESGPVKLFVIPGGSEEASVLHVTRSVA RRVERNAVKYTKELPEINRMIIVYLNRLSSLLFAMALVANK RRNQSEKIYEIGKSW	I53-51A: 80,83,86,87,88,90,91,94,166,172,176
I53-51B SEQ ID NO:10	(M)NQHSHKDYETVRIAVVRARWHADIVDQCVRAFEEAMAD AGGDRFAVDVFDVPGAYEIPLHARTLAETGRYGAVLGTAFV VNGGIYRHEFVASAVIDGMMNVQLSTGVPVLSAVLTPHRYR SSREHHEFFREHFMVKGVEAAAACITILAAREKIAA	I53-51B: 31,35,36,40,122,124,128,131,135,139,143,146,147
I52-03A SEQ ID NO:11	(M)GHTKGPTPQQHDGSALRIGIVHARWNKTIIMPLLIGTI AKLLECGVKASNIVVQSVPGSWELPIAVQRLYSASQLQTPS SGPSLSAGDLLGSSTTDLTALPTTTASSTGPFDALIAIGVL IKGETMHFEYIADSVSHGLMRVQLDTGVPVIFGVLTVLTDD QAKARAGVIEGSHNHGEDWGLAAVEMGVRRRDWAAGKTE	I52-03A: 28,32,36,39,44,49
I52-03B SEQ ID NO:12	(M)YEVDHADVYDLFYLGRGKDYAAEASDIADLVRSRTPEA SSLLDVACGTGTHLEHFTKEFGDTAGLELSEDMLTHARKRL PDATLHQGDMRDFQLGRKFSAVVSMFSSVGYLKTVAELGAA VASFAEHLEPGGVVVVEPWWFPETFADGWVSADVVRRDGRT VARVSHSVREGNATRMEVHFTVADPGKGVRHFSDVHLITLF HQREYEAAFMAAGLRVEYLEGGPSGRGLFVGVPA	I52-03B: 94,115,116,206,213
I52-32A SEQ ID NO:13	(M)GMKEKFVLIITHGDFGKGLLSGAEVIIGKQENVHTVGL NLGDNIEKVAKEVMRIIIAKLAEDKEIIIVVDLFGGSPFNI ALEMMKTFDVKVITGINMPMLVELLTSINVYDTTELLENIS KIGKDGIKVIEKSSLKM	I52-32A: 47,49,53,54,57,58,61,83,87,88
I52-32B	(M)KYDGSKLRIGILHARWNLEIIAALVAGAIKRLQEFGVK AENIIIETVPGSFELPYGSKLFVEKQKRLGKPLDAIIPIGV	I52-32B: 19,20,23,30,40

SEQ ID NO:14	LIKGSTMHFEYICDSTTHQLMKLNFELGIPVIFGVLTCLTD EQAEARAGLIEGKMHNHGEDWGAAAVEMATKFN	
I52-33A SEQ ID NO:15	(M)AVKGLGEVDQKYDGSKLRIGILHARWNRKIILALVAGA VLRLLEFGVKAENIIIETVPGSFELPYGSKLFVEKQKRLGK PLDAIIPIGVLIKGSTMHFEYICDSTTHQLMKLNFELGIPV IFGVLTCLTDEQAEARAGLIEGKMHNHGEDWGAAAVEMATK FN	I52-33A: 33,41,44,50
I52-33B SEQ ID NO:16	(M)GANWYLDNESSRLSFTSTKNADIAEVHRFLVLHGKVDP KGLAEVEVETESISTGIPLRDMLLRVLVFQVSKFPVAQINA QLDMRPINNLAPGAQLELRLPLTVSLRGKSHSYNAELLATR LDERRFQVVTLEPLVIHAQDFDMVRAFNALRLVAGLSAVSL SVPVGAVLIFTAR	I52-33B: 61,63,66,67,72,147,148,154,155
I32-06A SEQ ID NO:17	(M)TDYIRDGSAIKALSFAIILAEADLRHIPQDLQRLAVRV IHACGMVDVANDLAFSEGAGKAGRNALLAGAPILCDARMVA EGITRSRLPADNRVIYTLSDPSVPELAKKIGNTRSAAALDL WLPHIEGSIVAIGNAPTALFRLFELLDAGAPKPALIIGMPV GFVGAAESKDELAANSRGVPYVIVRGRRGGSAMTAAAVNAL ASERE	I32-06A: 9,12,13,14,20,30,33,34
I32-06B SEQ ID NO:18	(M)ITVFGLKSKLAPRREKLAEVIYSSLHLGLDIPKGKHAI RFLCLEKEDFYYPFDRSDDYTVIEINLMAGRSEETKMLLIF LLFIALERKLGIRAHDVEITIKEQPAHCWGFRGRTGDSARD LDYDIYV	I32-06B: 24,71,73,76,77,80,81,84,85,88,114,118
I32-19A SEQ ID NO:19	(M)GSDLQKLQRFSTCDISDGLLNVYNIPTGGYFPNLTAIS PPQNSSIVGTAYTVLFAPIDDPRPAVNYIDSVPPNSILVLA LEPHLQSQFHPFIKITQAMYGGLMSTRAQYLKSNGTVVFGR IRDVDEHRTLNHPVFAYGVGSCAPKAVVKAVGTNVQLKILT SDGVTQTICPGDYIAGDNNGIVRIPVQETDISKLVTYIEKS IEVDRLVSEAIKNGLPAKAAQTARRMVLKDYI	I32-19A: 208,213,218,222,225,226,229,233
I32-19B SEQ ID NO:20	(M)SGMRVYLGADHAGYELKQAIIAFLKMTGHEPIDCGALR YDADDDYPAFCIAAATRTVADPGSLGIVLGGSGNGEQIAAN KVPGARCALAWSVQTAALAREHNNAQLIGIGGRMHTLEEAL RIVKAFVTTPWSKAQRHQRRIDILAEYERTHEAPPVPGAPA	I32-19B: 20,23,24,27,117,118,122,125
I32-28A SEQ ID NO:21	(M)GDDARIAAIGDVDELNSQIGVLLAEPLPDDVRAALSAI QHDLFDLGGELCIPGHAAITEDHLLRLALWLVHYNGQLPPL EEFILPGGARGAALAHVCRTVCRRAERSIKALGASEPLNIA PAAYVNLLSDLLFVLARVLNRAAGGADVLWDRTRAH	I32-28A: 60,61,64,67,68,71,110,120,123,124,128
I32-28B SEQ ID NO:22	(M)ILSAEQSFTLRHPHGQAAALAFVREPAAALAGVQRLRG LDSDGEQVWGELLVRVPLLGEVDLPFRSEIVRTPQGAELRP LTLTGERAWVAVSGQATAAEGGEMAFAFQFQAHLATPEAEG EGGAAFEVMVQAAAGVTLLLVAMALPQGLAAGLPPA	I32-28B: 35,36,54,122,129,137,140,141,144,148

I53-40A.1 SEQ ID NO:23	(M)TKKVGIVDTTFARVDMASAAILTLKMESPNIKIIRKTV PGIKDLPVACKKLLEEEGCDIVMALGMPGKKEKDKVCAHEA SLGLMLAQLMTNKHIIEVFVHEDEAKDDAELKILAARRAIE HALNVYYLLFKPEYLTRMAGKGLRQGFEDAGPARE	I53-40A: 20,23,24,27,28,109,112,113,116,120,124
I53-40B.1 SEQ ID NO:24	(M)DDINNQLKRLKVIPVIAIDNAEDIIPLGKVLAENGLPA AEITFRSSAAVKAIMLLRSAQPEMLIGAGTILNGVQALAAK EAGADFVVSPGFNPNTVRACQIIGIDIVPGVNNPSTVEQAL EMGLTTLKFFPAEASGGISMVKSLVGPYGDIRLMPTGGITP DNIDNYLAIPQVLACGGTWMVDKKLVRNGEWDEIARLTREI VEQVNP	I53-40B: 47,51,54,58,74,102
I53-47A.1 SEQ ID NO:25	(M)PIFTLNTNIKADDVPSDFLSLTSRLVGLILSKPGSYVA VHINTDQQLSFGGSTNPAAFGTLMSIGGIEPDKNRDHSAVL FDHLNAMLGIPKNRMYIHFVNLNGDDVGWNGTTF	I53-47A: 22,25,29,72,79,86,87
I53-47A.1NegT2 SEQ ID NO:26	(M)PIFTLNTNIKADDVPSDFLSLTSRLVGLILSEPGSYVA VHINTDQQLSFGGSTNPAAFGTLMSIGGIEPDKNEDHSAVL FDHLNAMLGIPKNRMYIHFVDLDGDDVGWNGTTF	I53-47A: 22,25,29,72,79,86,87
I53-47B.1 SEQ ID NO:27	(M)NQHSHKDHETVRIAVVRARWHADIVDACVEAFEIAMAA IGGDRFAVDVFDVPGAYEIPLHARTLAETGRYGAVLGTAFV VNGGIYRHEFVASAVIDGMMNVQLDTGVPVLSAVLTPHRYR DSDEHHRFFAAHFAVKGVEAARACIEILNAREKIAA	I53-47B: 28,31,35,36,39,131,132,135,139,146
I53-47B.1NegT2 SEQ ID NO:28	(M)NQHSHKDHETVRIAVVRARWHADIVDACVEAFEIAMAA IGGDRFAVDVFDVPGAYEIPLHARTLAETGRYGAVLGTAFV VDGGIYDHEFVASAVIDGMMNVQLDTGVPVLSAVLTPHEYE DSDEDHEFFAAHFAVKGVEAARACIEILNAREKIAA	I53-47B: 28,31,35,36,39,131,132,135,139,146
I53-50A.1 SEQ ID NO:29	(M)KMEELFKKHKIVAVLRANSVEEAIEKAVAVFAGGVHLI EITFTVPDADTVIKALSVLKEKGAIIGAGTVTSVEQCRKAV ESGAEFIVSPHLDEEISQFCKEKGVFYMPGVMTPTELVKAM KLGHDILKLFPGEVVGPQFVKAMKGPFPNVKFVPTGGVNLD NVCEWFKAGVLAVGVGDALVKGDPDEVREKAKKFVEKIRGC TE	I53-50A: 25,29,33,54,57
I53-50A.1NegT2 SEQ ID	(M)KMEELFKKHKIVAVLRANSVEEAIEKAVAVFAGGVHLI EITFTVPDADTVIKALSVLKEKGAIIGAGTVTSVEQCRKAV ESGAEFIVSPHLDEEISQFCKEKGVFYMPGVMTPTELVKAM KLGHDILKLFPGEVVGPEFVEAMKGPFPNVKFVPTGGVDLD DVCEWFDAGVLAVGVGDALVEGDPDEVREDAKEFVEEIRGC	I53-50A: 25,29,33,54,57

NO:30	TE	
I53-50A.1PosT1 SEQ ID NO:31	(M)KMEELFKKHKIVAVLRANSVEEAIEKAVAVFAGGVHLIEITFTVPDADTVIKALSVLKEKGAIIGAGTVTSVEQCRKAVESGAEFIVSPHLDEEISQFCKEKGVFYMPGVMTPTELVKAMKLGHDILKLFPGEVVGPQFVKAMKGPFPNVKFVPTGGVNLDNVCKWFKAGVLAVGVGKALVKGKPDEVREKAKKFVKKIRGCTE	I53-50A: 25,29,33,54,57
I53-50B.1 SEQ ID NO:32	(M)NQHSHKDHETVRIAVVRARWHAEIVDACVSAFEAAMRDIGGDRFAVDVFDVPGAYEIPLHARTLAETGRYGAVLGTAFVVNGGIYRHEFVASAVIDGMMNVQLDTGVPVLSAVLTPHRYRDSDAHTLLFLALFAVKGMEAARACVEILAAREKIAA	I53-50B: 24,28,36,124,125,127,128,129,131,132,133,135,139
I53-50B.1NegT2 SEQ ID NO:33	(M)NQHSHKDHETVRIAVVRARWHAEIVDACVSAFEAAMRDIGGDRFAVDVFDVPGAYEIPLHARTLAETGRYGAVLGTAFVVDGGIYDHEFVASAVIDGMMNVQLDTGVPVLSAVLTPHEYEDSDADTLLFLALFAVKGMEAARACVEILAAREKIAA	I53-50B: 24,28,36,124,125,127,128,129,131,132,133,135,139
I53-50B.4PosT1 SEQ ID NO:34	(M)NQHSHKDHETVRIAVVRARWHAEIVDACVSAFEAAMRDIGGDRFAVDVFDVPGAYEIPLHARTLAETGRYGAVLGTAFVVNGGIYRHEFVASAVINGMMNVQLNTGVPVLSAVLTPHNYDKSKAHTLLFLALFAVKGMEAARACVEILAAREKIAA	I53-50B: 24,28,36,124,125,127,128,129,131,132,133,135,139

I53-40A genus (SEQ ID NO:35)

(M)TKKVGIVDTTFARVDMASAAILTLKMESPNIKIIRKTVPGIKDLPVACKKLLEEEGCDIVMALGMPGK(A/K)EKDKVCAHEASLGLMLAQLMTNKHIIEVFVHEDEAKDDAELKILAARRAIEHALNVYYLLFKPEYLTRMAGKGLRQGFEDAGPARE

I53-40B genus (SEQ ID NO:36)

(M)

(S/D)(T/D)INNQLK(A/R)LKVIPVIAIDNAEDIIPLGKVLAENGLPAAEITFRSSAAVKAIMLLRSAQPEMLIGAGTILNGVQALAAKEAGA(T/D)FVVSPGFNPNTVRACQIIGIDIVPGVNNPSTVE(A/Q)ALEMGLTTLKFFPAEASGGISMVKSLVGPYGDIRLMPTGGITP(S/D)NIDNYLAIPQVLACGGTWMVDKKLV(T/R)NGEWDEIARLTREIVEQVNP

I53-47A genus (SEQ ID NO:37)

(M)PIFTLNTNIKA(T/D)DVPSDFLSLTSRLVGLILS(K/E)PGSYVAVHINTDQQLSFGGSTN
PAAFGTLMSIGGIEP(S/D)KN(R/E)DHSAVLFDHLNAMLGIPKNRMYIHFV(N/D)L(N/D)G
DDVGWNGTTF

I53-47B genus (SEQ ID NO:38)

(M)NQHSHKD(Y/H)ETVRIAVVRARWHADIVDACVEAFEIAMAAIGGDRFAVDVFDVPGAYEIP
LHARTLAETGRYGAVLGTAFVV(N/D)GGIY(R/D)HEFVASAVIDGMMNVQL(S/D)TGVPVLS
AVLTPH(R/E)Y(R/E)DS(A/D)E(H/D)H(R/E)FFAAHFAVKGVEAARACIEIL(A/N)ARE
KIAA

I53-50A genus (SEQ ID NO:39)

(M)KMEELFKKHKIVAVLRANSVEEAIEKAVAVFAGGVHLIEITFTVPDADTVIKALSVLKEKGA
IIGAGTVTSVEQCRKAVESGAEFIVSPHLDEEISQFCKEKGVFYMPGVMTPTELVKAMKLGH(T/
D)ILKLFPGEVVGP(Q/E)FV(K/E)AMKGPFPNVKFVPTGGV(N/D)LD(N/D)VC(E/K)WF(
K/D)AGVLAVGVG(S/K/D)ALV(K/E)G(T/D/K)PDEVRE(K/D)AK(A/E/K)FV(E/K)(K
/E)IRGCTE

I53-50B genus (SEQ ID NO:40)

(M)NQHSHKD(Y/H)ETVRIAVVRARWHAEIVDACVSAFEAAM(A/R)DIGGDRFAVDVFDVPGA
YEIPLHARTLAETGRYGAVLGTAFVV(N/D)GGIY(R/D)HEFVASAVI(D/N)GMMNVQL(S/D
/N)TGVPVLSAVLTPH(R/E/N)Y(R/D/E)(D/K)S(D/K)A(H/D)TLLFLALFAVKGMEAAR
ACVEILAAREKIAA

T32-28A (SEQ ID NO:41)

(M)GEVPIGDPKELNGMEIAAVYLQPIEMEPRGIDLAASLADIHLEADIHALKNNPNGFPEGFWM
PYLTIAYALANADTGAIKTGTLMPMVADDGPHYGANIAMEKDKKGGFGVGTYALTFLISNPEKQG
FGRHVDEETGVGKWFEPFVVTYFFKYTGTPK

T32-28B (SEQ ID NO:42)

(M)SQAIGILELTSIAKGMELGDAMLKSANVDLLVSKTISPGKFLLMLGGDIGAIQQAIETGTSQ
AGEMLVDSLVLANIHPSVLPAISGLNSVDKRQAVGIVETWSVAACISAADLAVKGSNVTLVRVHM
AFGIGGKCYMVVAGDVLDVAAAVATASLAAGAKGLLVYASIIPRPHEAMWRQMVEG

T33-09A (SEQ ID NO:43)

(M)EEVVLITVPSALVAVKIAHALVEERLAACVNIVPGLTSIYRWQGSVVSDHELLLLVKTTTHA
FPKLKERVKALHPYTVPEIVALPIAEGNREYLDWLRENTG

T33-09B (SEQ ID NO:44)

(M)VRGIRGAITVEEDTPAAILAATIELLLKMLEANGIQSYEELAAVIFTVTEDLTSAFPAEAAR
LIGMHRVPLLSAREVPVPGSLPRVIRVLALWNTDTPQDRVRHVYLNEAVRLRPDLESAQ

T33-15A (SEQ ID NO:45)

(M)SKAKIGIVTVSDRASAGITADISGKAIILALNLYLTSEWEPIYQVIPDEQDVIETTLIKMAD
EQDCCLIVTTGGTGPAKRDVTPEATEAVCDRMMPGFGELMRAESLKEVPTAILSRQTAGLRGDSL
IVNLPGDPASISDCLLAVFPAIPYCIDLMEGPYLECNEAMIKPFRPKAK

T33-15B (SEQ ID NO:46)

(M)VRGIRGAITVNSDTPTSIIIATILLLEKMLEANGIQSYEELAAVIFTVTEDLTSAFPAEAAR
QIGMHRVPLLSAREVPVPGSLPRVIRVLALWNTDTPQDRVRHVYLSEAVRLRPDLESAQ

T33-21A (SEQ ID NO:47)

(M)RITTKVGDKGSTRLFGGEEVWKDSPIIEANGTLDELTSFIGEAKHYVDEEMKGILEEIQNDI
YKIMGEIGSKGKIEGISEERIAWLLKLILRYMEMVNLKSFVLPGGTLESAKLDVCRTIARRALRK
VLTVTREFGIGAEAAAYLLALSDLLFLLARVIEIEKNKLKEVRS

T33-21B (SEQ ID NO:48)

(M)PHLVIEATANLRLETSPGELLEQANKALFASGQFGEADIKSRFVTLEAYRQGTAAVERAYLH
ACLSILDGRDIATRTLLGASLCAVLAEAVAGGGEEGVQVSVEVREMERLSYAKRVVARQR

T33-28A (SEQ ID NO:49)

(M)ESVNTSFLSPSLVTIRDFDNGQFAVLRIGRTGFPADKGDIDLCLDKMIGVRAAQIFLGDDTE
DGFKGPHIRIRCVDIDDKHTYNAMVYVDLIVGTGASEVERETAEEEAKLALRVALQVDIADEHSC
VTQFEMKLREELLSSDSFHPDKDEYYKDFL

T33-28B (SEQ ID NO:50)

(M)PVIQTFVSTPLDHHKRLLLAIIYRIVTRVVLGKPEDLVMMTFHDSTPMHFFGSTDPVACVRV
EALGGYGPSEPEKVTSIVTAAITAVCGIVADRIFVLYFSPLHCGWNGTNF

T33-31A (SEQ ID NO:51)

(M)EEVVLITVPSALVAVKIAHALVEERLAACVNIVPGLTSIYREEGSVVSDHELLLLVKTTTDA
FPKLKERVKELHPYEVPEIVALPIAEGNREYLDWLRENTG

Table 1 provides the amino acid sequence of the first and second polypeptides; the right hand column in Table 1 identifies the residue numbers in each exemplary polypeptide that were identified as present at the interface of resulting assembled nanostructures (i.e.: "identified interface residues"). As can be seen, the number of interface residues for the exemplary polypeptides of SEQ ID NO:1-34 range from 4-13. In various embodiments, the first and second polypeptides comprise an amino acid sequence that is at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical over its length, and identical at least at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13 identified interface positions (depending on the number of interface residues for a given polypeptide), to the amino acid sequence of a polypeptide selected from the group consisting of SEQ ID NOS: 1-34. In other embodiments, the first and second polypeptides comprise an amino acid sequence that is at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical over its length, and identical at least at 20%, 25%, 33%, 40%, 50%, 60%, 70%, 75%, 80%, 90%, or 100% of the identified interface positions, to the amino acid sequence of a polypeptide selected from the group consisting of SEQ ID NOS:1-51.

As is the case with proteins in general, the polypeptides are expected to tolerate some variation in the designed sequences without disrupting subsequent assembly into nanostructures: particularly when such variation comprises conservative amino acid substitutions. As used here, "conservative amino acid substitution" means that: hydrophobic amino acids (Ala, Cys, Gly, Pro, Met, See, Sme, Val, Ile, Leu) can only be substituted with other hydrophobic amino acids; hydrophobic amino acids with bulky side chains (Phe, Tyr, Trp) can only be substituted with other hydrophobic amino acids with bulky side chains; amino acids with positively charged side chains (Arg, His, Lys) can only be substituted with other amino acids with positively charged side chains; amino acids with negatively charged side chains (Asp, Glu) can only be substituted with other amino acids with negatively charged side chains; and amino acids with polar uncharged side chains (Ser, Thr, Asn, Gln) can only be substituted with other amino acids with polar uncharged side chains.

Table 2 lists surface amino acid residue numbers for each exemplary polypeptide of the invention denoted by SEQ ID NOS: 1-34. Thus, in various embodiments, 1 or more (at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47,

48, 49, 50, or more) of these surface residues may be modified in the polypeptides of the invention. Residues in parentheses are optional.

Table 2

Name	Amino Acid Sequence	Surface residues not near interface
I53-34A SEQ ID NO:1	(M)EGMDPLAVLAESRLLPLLTVRGGEDLAGLATVLELMGV GALEITLRTEKGLEALKALRKSGLLLGAGTVRSPKEAEAAL EAGAAFLVSPGLLEEVAALAQARGVPYLPGVLTPTEVERAL ALGLSALKFFPAEPFQGVRVLRAYAEVFPEVRFLPTGGIKE EHLPHYAALPNLLAVGGSWLLQGDLAAVMKKVKAAKALLSP QAPG	I53-34A: 6,8,9,12,14,22,25,48,49,50, 52,53,56,73,74,81,94,95,10 1,102,103, 104,119,122,137,140,143,1 47, 150,151,153,161,162,163,1 64, 166,167,170,172,184,193,1 98, 199,200,202
I53-34B SEQ ID NO:2	(M)TKKVGIVDTTFARVDMAEAAIRTLKALSPNIKIIRKTV PGIKDLPVACKKLLEEEGCDIVMALGMPGKAEKDKVCAHEA SLGLMLAQLMTNKHIIEVFVHEDEAKDDDELDILALVRAIE HAANVYYLLFKPEYLTRMAGKGLRQGREDAGPARE	I53-34B: 3,12,31,33,35,36,51,54,55, 56,59,69,70,71,74,93,103,1 06,107,108,131,132,133,13 4,138,142,153
I53-40A SEQ ID NO:3	(M)TKKVGIVDTTFARVDMASAAILTLKMESPNIKIIRKTV PGIKDLPVACKKLLEEEGCDIVMALGMPGKAEKDKVCAHEA SLGLMLAQLMTNKHIIEVFVHEDEAKDDAELKILAARRAIE HALNVYYLLFKPEYLTRMAGKGLRQGFEDAGPARE	I53-40A: 3,4,31,33,35,36,37,51,54,5 5,56, 57,59,69,70,71,74,93,103,1 06, 118,127,128,131,132,133,1 34, 135,138,139,142,150,153
I53-40B SEQ ID NO:4	(M)STINNQLKALKVIPVIAIDNAEDIIPLGKVLAENGLPA AEITFRSSAAVKAIMLLRSAQPEMLIGAGTILNGVQALAAK EAGATFVVSPGFNPNTVRACQIIGIDIVPGVNNPSTVEAAL EMGLTTLKFFPAEASGGISMVKSLVGPYGDIRLMPTGGITP SNIDNYLAIPQVLACGGTWMVDKKLVTNGEWDEIARLTREI VEQVNP	I53-40B: 2,3,7,9,10,12,20,21,23,26,2 7,30, 34,38,45,60,62,75,85,94,95 ,122, 124,126,134,139,143,151,1 53, 161,163,166,167,170,172,1 80, 184,185,186,189,190,192,1 93, 194,195,198,201,202,205,2 08, 209
I53-47A SEQ ID NO:5	(M)PIFTLNTNIKATDVPSDFLSLTSRLVGLILSKPGSYVA VHINTDQQLSFGGSTNPAAFGTLMSIGGIEPSKNRDHSAVL FDHLNAMLGIPKNRMYIHFVNLNGDDVGWNGTTF	I53-47A: 11,13,14,17,34,36,37,45,47 ,54,55,56,65,69,70,71,74,9 1,92,93,101,103,105,109,1 10,112,114
I53-47B SEQ ID	(M)NQHSHKDYETVRIAVVRARWHADIVDACVEAFEIAMAA IGGDRFAVDVFDVPGAYEIPLHARTLAETGRYGAVLGTAFV VNGGIYRHEFVASAVIDGMMNVQLSTGVPVLSAVLTPHRYR	I53-47B: 6,7,8,9,10,11,13,18,20,21,2 4,43,44,51,63,67,70,85,87,

NO:6	DSAEHHRFFAAHFAVKGVEAARACIEILAAREKIAA	101,105,122,123,124,125,126,147,152,153,154
I53-50A SEQ ID NO:7	(M)KMEELFKKHKIVAVLRANSVEEAIEKAVAVFAGGVHLIEITFTVPDADTVIKALSVLKEKGAIIGAGTVTSVEQCRKAVESGAEFIVSPHLDEEISQFCKEKGVFYMPGVMTPTELVKAMKLGHTILKLFPGEVVGPQFVKAMKGPFPNVKFVPTGGVNLDNVCEWFKAGVLAVGVGSALVKGTPDEVREKAKAFVEKIRGCTE	I53-50A: 4,5,6,8,9,11,17,19,23,37,46,47,59,74,77,78,81,94,95,98,101,102, 103,106,119,122,126,139,142,145,149,150,152,160,161,162,163,166,169,179,183,185,188,191,192,194,198,199
I53-50B SEQ ID NO:8	(M)NQHSHKDYETVRIAVVRARWHAEIVDACVSAFEAAMADIGGDRFAVDVFDVPGAYEIPLHARTLAETGRYGAVLGTAFVVNGGIYRHEFVASAVIDGMMNVQLSTGVPVLSAVLTPHRYRDSDAHTLLFLALFAVKGMEAARACVEILAAREKIAA	I53-50B: 6,7,8,9,10,11,13,18,20,21,34,38,39,40,43,44,48,51,63,67,70,87,101,105,118,143,147,152,153,154
I53-51A SEQ ID NO:9	(M)FTKSGDDGNTNVINKRVGKDSPLVNFLGDLDELNSFIGFAISKIPWEDMKKDLERVQVELFEIGEDLSTQSSKKKIDESYVLWLLAATAIYRIESGPVKLFVIPGGSEEASVLHVTRSVARRVERNAVKYTKELPEINRMIIVYLNRLSSLLFAMALVANKRRNQSEKIYEIGKSW	I53-51A: 19,20,24,28,46,47,51,70,71,73,74,75,76,102,122,130,133,134,135,136,137,140,162,163,164,165, 169,175,177
I53-51B SEQ ID NO:10	(M)NQHSHKDYETVRIAVVRARWHADIVDQCVRAFEEAMADAGGDRFAVDVFDVPGAYEIPLHARTLAETGRYGAVLGTAFVVNGGIYRHEFVASAVIDGMMNVQLSTGVPVLSAVLTPHRYRSSREHHEFFREHFMVKGVEAAAACITILAAREKIAA	I53-51B: 6,7,8,9,10,11,13,18,21,27,34,38, 43,48,63,67,70,85,87,101,118, 125,126,129,152,153,154
I52-03A SEQ ID NO:11	(M)GHTKGPTPQQHDGSALRIGIVHARWNKTIIMPLLIGTIAKLLECGVKASNIVVQSVPGSWELPIAVQRLYSASQLQTPSSGPSLSAGDLLGSSTTDLTALPTTTASSTGPFDALIAIGVLIKGETMHFEYIADSVSHGLMRVQLDTGVPVIFGVLTVLTDDQAKARAGVIEGSHNHGEDWGLAAVEMGVRRRDWAAGKTE	I52-03A: 6,9,10,11,13,15,16,26,48,69,75, 76,78,79,111,125,127,142,146, 159,160,161,162,171,175,193, 194,196,197,199,200
I52-03B SEQ ID NO:12	(M)YEVDHADVYDLFYLGRGKDYAAEASDIADLVRSRTPEASSLLDVACGTGTHLEHFTKEFGDTAGLELSEDMLTHARKRLPDATLHQGDMRDFQLGRKFSAVVSMFSSVGYLKTVAELGAAVASFAEHLEPGGVVVVEPWWFPETFADGWVSADVVRRDGRTVARVSHSVREGNATRMEVHFTVADPGKGVRHFSDVHLITLFHQREYEAAFMAAGLRVEYLEGGPSGRGLFVGVPA	I52-03B: 2,3,5,6,8,15,17,20,22,23,26,27, 30,33,34,35,37,38,40,54,55,57,58,59,61,62,68,70,71,74,77,78,79, 81,82,84,86,87,91,96,97,98,111, 127,130,131,132,141,144,145, 148,150,154,157,158,159,160, 161,171,172,173,174,177,187, 189,192,198,199,222,223,224, 236
I52-32A	(M)GMKEKFVLIITHGDFGKGLLSGAEVIIGKQENVHTVGL	I52-32A: 3,5,15,18,30,32,35,40,41,4

SEQ ID NO:13	NLGDNIEKVAKEVMRIIIAKLAEDKEIIIVVDLFGGSPFNI ALEMMKTFDVKVITGINMPMLVELLTSINVYDTTELLENIS KIGKDGIKVIEKSSLKM	2,44, 45,65,73,79,91,103,106,10 9,110,111,112,114,115,118 ,122,123, 125,126,129,131
I52-32B SEQ ID NO:14	(M)KYDGSKLRIGILHARWNLEIIAALVAGAIKRLQEFGVK AENIIIETVPGSFELPYGSKLFVEKQKRLGKPLDAIIPIGV LIKGSTMHFEYICDSTTHQLMKLNFELGIPVIFGVLTCLTD EQAEARAGLIEGKMHNHGEDWGAAAVEMATKFN	I52-32B: 4,6,7,9,17,32,35,42,59,63,6 4,66, 67,68,69,70,71,73,83,85,90 ,106, 119,120,121,122,125,131,1 33, 134,135,136,154
I52-33A SEQ ID NO:15	(M)AVKGLGEVDQKYDGSKLRIGILHARWNRKIILALVAGA VLRLLEFGVKAENIIIETVPGSFELPYGSKLFVEKQKRLGK PLDAIIPIGVLIKGSTMHFEYICDSTTHQLMKLNFELGIPV IFGVLTCLTDEQAEARAGLIEGKMHNHGEDWGAAAVEMATK FN	I52-33A: 12,14,16,17,19,26,27,46,69 ,73,74,76,77,78,80,81,83,9 3,95,100,116,129,130,131, 132,145,164
I52-33B SEQ ID NO:16	(M)GANWYLDNESSRLSFTSTKNADIAEVHRFLVLHGKVDP KGLAEVEVETESISTGIPLRDMLLRVLVFQVSKFPVAQINA QLDMRPINNLAPGAQLELRLPLTVSLRGKSHSYNAELLATR LDERRFQVVTLEPLVIHAQDFDMVRAFNALRLVAGLSAVSL SVPVGAVLIFTAR	I52-33B: 4,6,10,20,21,23,24,31,32,3 4,36, 39,40,42,44,46,48,56,73,77 ,79, 81,83,85,88,89,91,92,96,97 ,99, 101,103,109,110,111,112,1 14, 124,125,138,140,143,158,1 75
I32-06A SEQ ID NO:17	(M)TDYIRDGSAIKALSFAIILAEADLRHIPQDLQRLAVRV IHACGMVDVANDLAFSEGAGKAGRNALLAGAPILCDARMVA EGITRSRLPADNRVIYTLSDPSVPELAKKIGNTRSAAALDL WLPHIEGSIVAIGNAPTALFRLFELLDAGAPKPALIIGMPV GFVGAAESKDELAANSRGVPYVIVRGRRGGSAMTAAAVNAL ASERE	I32-06A: 24,26,27,41,47,50,51,56,60 ,63,64,67,68,77,84,85,86,9 1,93,98,99, 100,101,102,105,108,109,1 14, 123,124,125,127,135,142,1 45, 148,149,152,153,169,172,1 73, 176,177,180,187,189
I32-06B SEQ ID NO:18	(M)ITVFGLKSKLAPRREKLAEVIYSSLHLGLDIPKGKHAI RFLCLEKEDFYYPFDRSDDYTVIEINLMAGRSEETKMLLIF LLFIALERKLGIRAHDVEITIKEQPAHCWGFRGRTGDSARD LDYDIYV	I32-06B: 8,9,10,13,14,15,16,17,20,3 4,36, 45,46,47,50,51,53,54,57,67 ,70,91,93,95,105,112
I32-19A SEQ ID NO:19	(M)GSDLQKLQRFSTCDISDGLLNVYNIPTGGYFPNLTAIS PPQNSSIVGTAYTVLFAPIDDPRPAVNYIDSVPPNSILVLA LEPHLQSQFHPFIKITQAMYGGLMSTRAQYLKSNGTVVFGR IRDVDEHRTLNHPVFAYGVGSCAPKAVVKAVGTNVQLKILT SDGVTQTICPGDYIAGDNNGIVRIPVQETDISKLVTYIEKS IEVDRLVSEAIKNGLPAKAAQTARRMVLKDYI	I32-19A: 3,4,6,7,9,10,25,27,36,40,42 ,43,44,49,58,59,61,62,63,7 0,72,73,74, 82,84,88,89,109,110,112,1 26,127,129,130,132,146,15 5,156,157, 159,166,169,172,189,190,1 92, 194,195,198,201,204,215,2

		32
I32-19B SEQ ID NO:20	(M) SGMRVYLGADHAGYELKQAIIAFLKMTGHEPIDCGALR YDADDDYPAFCIAAATRTVADPGSLGIVLGGSGNGEQIAAN KVPGARCALAWSVQTAALAREHNNAQLIGIGGRMHTLEEAL RIVKAFVTTPWSKAQRHQRRIDILAEYERTHEAPPVPGAPA	I32-19B: 4,5,31,33,38,41,42,43,55,5 6,59, 61,62,83,93,94,101,104,11 3,119,129,131,134,136,137 ,139,140, 143,144,146,147,150,152,1 53, 156,158,159
I32-28A SEQ ID NO:21	(M) GDDARIAAIGDVDELNSQIGVLLAEPLPDDVRAALSAI QHDLFDLGGELCIPGHAAITEDHLLRLALWLVHYNGQLPPL EEFILPGGARGAALAHVCRTVCRRAERSIKALGASEPLNIA PAAYVNLLSDLLFVLARVLNRAAGGADVLWDRTRAH	I32-28A: 4,6,7,10,14,27,30,31,33,34, 41,44,45,51,52,53,54,55,56 ,59,76,78,79,80,81,82,83,9 0,103,111,115,116,131,134 ,142,145,147,150
I32-28B SEQ ID NO:22	(M) ILSAEQSFTLRHPHGQAAALAFVREPAAALAGVQRLRG LDSDGEQVWGELLVRVPLLGEVDLPFRSEIVRTPQGAELRP LTLTGERAWVAVSGQATAAEGGEMAFAFQFQAHLATPEAEG EGGAAFEVMVQAAAGVTLLLVAMALPQGLAAGLPPA	I32-28B: 3,4,6,8,12,15,17,18,22,26,2 8,32, 38,39,41,43,45,46,48,50,60 ,66,68,71,73,74,79,81,82,8 3,84,86,87, 95,100,103,105,109,111,11 3,151,152,155,156,157
I53-40A.1 SEQ ID NO:23	(M) TKKVGIVDTTFARVDMASAAILTLKMESPNIKIIRKTV PGIKDLPVACKKLLEEEGCDIVMALGMPGKKEKDKVCAHEA SLGLMLAQLMTNKHIIEVFVHEDEAKDDAELKILAARRAIE HALNVYYLLFKPEYLTRMAGKGLRQGFEDAGPARE	I53-40A: 3,4,31,33,35,36,37,51,54,5 5,56, 57,59,69,70,71,74,93,103,1 06, 118,127,128,131,132,133,1 34, 135,138,139,142,150,153
I53-40B.1 SEQ ID NO:24	(M) DDINNQLKRLKVIPVIAIDNAEDIIPLGKVLAENGLPA AEITFRSSAAVKAIMLLRSAQPEMLIGAGTILNGVQALAAK EAGADFVVSPGFNPNTVRACQIIGIDIVPGVNNPSTVEQAL EMGLTTLKFFPAEASGGISMVKSLVGPYGDIRLMPTGGITP DNIDNYLAIPQVLACGGTWMVDKKLVRNGEWDEIARLTREI VEQVNP	I53-40B: 2,3,7,9,10,12,20,21,23,26,2 7,30, 34,38,45,60,62,75,85,94,95 ,122, 124,126,134,139,143,151,1 53, 161,163,166,167,170,172,1 80, 184,185,186,189,190,192,1 93, 194,195,198,201,202,205,2 08, 209
I53-47A.1 SEQ ID NO:25	(M) PIFTLNTNIKADDVPSDFLSLTSRLVGLILSKPGSYVA VHINTDQQLSFGGSTNPAAFGTLMSIGGIEPDKNRDHSAVL FDHLNAMLGIPKNRMYIHFVNLNGDDVGWNGTTF	I53-47A: 11,13,14,17,34,36,37,45,47 ,54,55,56,65,69,70,71,74,9 1,92,93,101,103,105,109,1 10,112,114
I53-47A.1Ne	(M) PIFTLNTNIKADDVPSDFLSLTSRLVGLILSEPGSYVA VHINTDQQLSFGGSTNPAAFGTLMSIGGIEPDKNEDHSAVL	I53-47A: 11,13,14,17,34,36,37,45,47 ,54,55,56,65,69,70,71,74,9

gT2 SEQ ID NO:26	FDHLNAMLGIPKNRMYIHFVDLDGDDVGWNGTTF	1,92,93,101,103,105,109,110,112,114
I53-47B.1 SEQ ID NO:27	(M)NQHSHKDHETVRIAVVRARWHADIVDACVEAFEIAMAA IGGDRFAVDVFDVPGAYEIPLHARTLAETGRYGAVLGTAFV VNGGIYRHEFVASAVIDGMMNVQLDTGVPVLSAVLTPHRYR DSDEHHRFFAAHFAVKGVEAARACIEILNAREKIAA	I53-47B: 6,7,8,9,10,11,13,18,20,21,24,43,44,51,63,67,70,85,87,101,105,122,123,124,125,126,147,152,153, 154
I53-47B.1NegT2 SEQ ID NO:28	(M)NQHSHKDHETVRIAVVRARWHADIVDACVEAFEIAMAA IGGDRFAVDVFDVPGAYEIPLHARTLAETGRYGAVLGTAFV VDGGIYDHEFVASAVIDGMMNVQLDTGVPVLSAVLTPHEYE DSDEDHEFFAAHFAVKGVEAARACIEILNAREKIAA	I53-47B: 6,7,8,9,10,11,13,18,20,21,24,43,44,51,63,67,70,85,87,101,105,122,123,124,125,126,147,152,153, 154
I53-50A.1 SEQ ID NO:29	(M)KMEELFKKHKIVAVLRANSVEEAIEKAVAVFAGGVHLI EITFTVPDADTVIKALSVLKEKGAIIGAGTVTSVEQCRKAV ESGAEFIVSPHLDEEISQFCKEKGVFYMPGVMTPTELVKAM KLGHDILKLFPGEVVGPQFVKAMKGPFPNVKFVPTGGVNLD NVCEWFKAGVLAVGVGDALVKGDPDEVREKAKKFVEKIRGC TE	I53-50A: 4,5,6,8,9,11,17,19,23,37,46,47,59,74,77,78,81,94,95,98,101,102,103,106,119,122,126,139,142,145,149,150,152,160,161,162,163,166,169,179,183,185,188,191,192,194,198,199
I53-50A.1NegT2 SEQ ID NO:30	(M)KMEELFKKHKIVAVLRANSVEEAIEKAVAVFAGGVHLI EITFTVPDADTVIKALSVLKEKGAIIGAGTVTSVEQCRKAV ESGAEFIVSPHLDEEISQFCKEKGVFYMPGVMTPTELVKAM KLGHDILKLFPGEVVGPEFVEAMKGPFPNVKFVPTGGVDLD DVCEWFDAGVLAVGVGDALVEGDPDEVREDAKEFVEEIRGC TE	I53-50A: 4,5,6,8,9,11,17,19,23,37,46,47,59,74,77,78,81,94,95,98,101,102,103,106,119,122,126,139,142,145,149,150,152,160,161,162,163,166,169,179,183,185,188,191,192,194,198,199
I53-50A.1PosT1 SEQ ID NO:31	(M)KMEELFKKHKIVAVLRANSVEEAIEKAVAVFAGGVHLI EITFTVPDADTVIKALSVLKEKGAIIGAGTVTSVEQCRKAV ESGAEFIVSPHLDEEISQFCKEKGVFYMPGVMTPTELVKAM KLGHDILKLFPGEVVGPQFVKAMKGPFPNVKFVPTGGVNLD NVCKWFKAGVLAVGVGKALVKGKPDEVREKAKKFVKKIRGC TE	I53-50A: 4,5,6,8,9,11,17,19,23,37,46,47,59,74,77,78,81,94,95,98,101,102,103,106,119,122,126,139,142,145,149,150,152,160,161,162,163,166,169,179,183,185,188,191,192,194,198,199
I53-50B.1 SEQ ID NO:32	(M)NQHSHKDHETVRIAVVRARWHAEIVDACVSAFEAAMRD IGGDRFAVDVFDVPGAYEIPLHARTLAETGRYGAVLGTAFV VNGGIYRHEFVASAVIDGMMNVQLDTGVPVLSAVLTPHRYR DSDAHTLLFLALFAVKGMEAARACVEILAAREKIAA	I53-50B: 6,7,8,9,10,11,13,18,20,21,34,38,39,40,43,44,48,51,63,67,70,87,101,105,118,143,147,152,153,154
I53-50B.1NegT2 SEQ ID	(M)NQHSHKDHETVRIAVVRARWHAEIVDACVSAFEAAMRD IGGDRFAVDVFDVPGAYEIPLHARTLAETGRYGAVLGTAFV VDGGIYDHEFVASAVIDGMMNVQLDTGVPVLSAVLTPHEYE DSDADTLLFLALFAVKGMEAARACVEILAAREKIAA	I53-50B: 6,7,8,9,10,11,13,18,20,21,34,38,39,40,43,44,48,51,63,67,70,87,101,105,118,143,147,152,153,154

NO:33		
I53-50B.4PosT1 SEQ ID NO:34	(M)NQHSHKDHETVRIAVVRARWHAEIVDACVSAFEAAMRD IGGDRFAVDVFDVPGAYEIPLHARTLAETGRYGAVLGTAFV VNGGIYRHEFVASAVINGMMNVQLNTGVPVLSAVLTPHNYD KSKAHTLLFLALFAVKGMEAARACVEILAAREKIAA	I53-50B: 6,7,8,9,10,11,13,18,20,21,34,38,39,40,43,44,48,51,63,67,70,87,101,105,118,143,147,152,153,154

In various embodiments of the nanostructure of the invention, the first polypeptides and the second polypeptides comprise polypeptides with the amino acid sequence selected from the following pairs, or modified versions thereof (i.e.: permissible modifications as disclosed for the polypeptides of the invention: isolated polypeptides comprising an amino acid sequence that is at least 75% 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical over its length, and/or identical at least at one identified interface position, to the amino acid sequence indicated by the SEQ ID NO.):

SEQ ID NO:1 and SEQ ID NO:2 (I53-34A and I53-34B);

SEQ ID NO:3 and SEQ ID NO:4 (I53-40A and I53-40B);

SEQ ID NO:3 and SEQ ID NO:24 (I53-40A and I53-40B.1);

SEQ ID NO:23 and SEQ ID NO:4 (I53-40A.1 and I53-40B);

SEQ ID NO:35 and SEQ ID NO:36 (I53-40A genus and I53-40B genus);

SEQ ID NO:5 and SEQ ID NO:6 (I53-47A and I53-47B);

SEQ ID NO:5 and SEQ ID NO:27 (I53-47A and I53-47B.1);

SEQ ID NO:5 and SEQ ID NO:28 (I53-47A and I53-47B.1NegT2);

SEQ ID NO:25 and SEQ ID NO:6 (I53-47A.1 and I53-47B);

SEQ ID NO:25 and SEQ ID NO:27 (I53-47A.1 and I53-47B.1);

SEQ ID NO:25 and SEQ ID NO:28 (I53-47A.1 and I53-47B.1NegT2);

SEQ ID NO:26 and SEQ ID NO:6 (I53-47A.1NegT2 and I53-47B);

SEQ ID NO:26 and SEQ ID NO:27 (I53-47A.1NegT2 and I53-47B.1);

SEQ ID NO:26 and SEQ ID NO:28 (I53-47A.1NegT2 and I53-47B.1NegT2);

SEQ ID NO:37 and SEQ ID NO:38 (I53-47A genus and I53-47B genus);

SEQ ID NO:7 and SEQ ID NO:8 (I53-50A and I53-50B);

SEQ ID NO:7 and SEQ ID NO:32 (I53-50A and I53-50B.1);

SEQ ID NO:7 and SEQ ID NO:33 (I53-50A and I53-50B.1NegT2);

SEQ ID NO:7 and SEQ ID NO:34 (I53-50A and I53-50B.4PosT1);

SEQ ID NO:29 and SEQ ID NO:8 (I53-50A.1 and I53-50B);
SEQ ID NO:29 and SEQ ID NO:32 (I53-50A.1 and I53-50B.1);
SEQ ID NO:29 and SEQ ID NO:33 (I53-50A.1 and I53-50B.1NegT2);
SEQ ID NO:29 and SEQ ID NO:34 (I53-50A.1 and I53-50B.4PosT1);
SEQ ID NO:30 and SEQ ID NO:8 (I53-50A.1NegT2 and I53-50B);
SEQ ID NO:30 and SEQ ID NO:32 (I53-50A.1NegT2 and I53-50B.1);
SEQ ID NO:30 and SEQ ID NO:33 (I53-50A.1NegT2 and I53-50B.1NegT2);
SEQ ID NO:30 and SEQ ID NO:34 (I53-50A.1NegT2 and I53-50B.4PosT1);
SEQ ID NO:31 and SEQ ID NO:8 (I53-50A.1PosT1 and I53-50B);
SEQ ID NO:31 and SEQ ID NO:32 (I53-50A.1PosT1 and I53-50B.1);
SEQ ID NO:31 and SEQ ID NO:33 (I53-50A.1PosT1 and I53-50B.1NegT2);
SEQ ID NO:31 and SEQ ID NO:34 (I53-50A.1PosT1 and I53-50B.4PosT1);
SEQ ID NO:39 and SEQ ID NO:40 (I53-50A genus and I53-50B genus);
SEQ ID NO:9 and SEQ ID NO:10 (I53-51A and I53-51B);
SEQ ID NO:11 and SEQ ID NO:12 (I52-03A and I52-03B);
SEQ ID NO:13 and SEQ ID NO:14 (I52-32A and I52-32B);
SEQ ID NO:15 and SEQ ID NO:16 (I52-33A and I52-33B)
SEQ ID NO:17 and SEQ ID NO:18 (I32-06A and I32-06B);
SEQ ID NO:19 and SEQ ID NO:20 (I32-19A and I32-19B);
SEQ ID NO:21 and SEQ ID NO:22 (I32-28A and I32-28B);
SEQ ID NO:23 and SEQ ID NO:24 (I53-40A.1 and I53-40B.1);
SEQ ID NO:41 and SEQ ID NO:42 (T32-28A and T32-28B);
SEQ ID NO:43 and SEQ ID NO:44 (T33-09A and T33-09B);
SEQ ID NO:45 and SEQ ID NO:46 (T33-15A and T33-15B);
SEQ ID NO:47 and SEQ ID NO:48 (T33-21A and T33-21B);
SEQ ID NO:49 and SEQ ID NO:50 (T33-28A and T32-28B); and
SEQ ID NO:51 and SEQ ID NO:44 (T33-31A and T33-09B (also referred to as T33-31B))

In one embodiment, the one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof, are expressed as a fusion protein with the first and/or second polypeptides. In these embodiments, it is preferred that the one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof are present at the N terminus of the fusion protein, whenever this configuration can facilitate

presentation of the one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof on an exterior of the nanostructure. This preference for the presence of the paramyxovirus and/or pneumovirus F protein at the N terminus of the fusion protein derives from the location of the C terminus of the paramyxovirus and/or pneumovirus F proteins at one extreme (the "bottom") of the F protein trimer; by locating the genetic fusion at this point, the majority of the F protein structure will be displayed and accessible on the nanostructure exterior. In a further embodiment, the nanostructures comprise one or more copies of a fusion protein comprising at least two domains—a paramyxovirus and/or pneumovirus F protein, or an antigenic fragment thereof, and a trimeric assembly domain (i.e.: each first assembly is a homotrimer of the first polypeptide)—and one or more copies of a second oligomeric block (i.e.: each second assembly is an oligomer of two or more copies of the second polypeptide). In another embodiment, the first and or second polypeptides may be modified to permit the one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof, to be covalently linked to the first and/or second polypeptides. In one non-limiting example, the first and/or second polypeptides can be modified, such as by introduction of various cysteine residues at defined positions to facilitate linkage one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof.

In other embodiments, the one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof are attached to the first or second polypeptides via any suitable technique, including but not limited to covalent chemical cross-linking (via any suitable cross-linking technique) and non-covalent attachment including engineered electrostatic interactions.

Trimeric assembly domains

In one embodiment of a trimeric assembly that comprises a trimeric paramyxovirus and/or pneumovirus F protein, or antigenic fragments thereof, the paramyxovirus and/or pneumovirus F protein, or antigenic fragment thereof is genetically fused to the first polypeptides that self-assemble into the trimeric assembly. The trimeric assembly comprises a protein-protein interface that induces three copies of the first polypeptides to self-associate to form trimeric building blocks. Each copy of the first polypeptides further comprises a surface-exposed interface that interacts with a complementary surface-exposed interface on a second assembly domain. As described in King et al. (Nature 510, 103–108, 2014), Bale et al. (Science 353, 389–394, 2016), and

patent publications WO2014124301 A1 and US20160122392 A1, the complementary protein-protein interface between the trimeric assembly domain and second assembly domain drives the assembly of multiple copies of the trimeric assembly domain and second assembly domain to a target nanostructure. In some embodiments, each copy of the trimeric assembly domains of the nanostructure bears a paramyxovirus and/or pneumovirus F proteins, or antigenic fragment thereof, as a genetic fusion; these nanostructures display the F proteins at full valency. In other embodiments, the nanostructures of the invention comprise one or more copies of trimeric assembly domains bearing paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof as genetic fusions as well as one or more trimeric assembly domains that do not bear F proteins as genetic fusions; these nanostructures display the F proteins at partial valency. The trimeric assembly domain can be any polypeptide sequence that forms a trimer and interacts with a second assembly domain to drive assembly to a target nanostructure.

In one specific embodiment, the first polypeptides comprise polypeptides having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along their full length to the amino acid sequence of T33-31A (SEQ ID NO:51) and the second polypeptides comprise polypeptides having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along their full length to the amino acid sequence of T33-09B/T33-31B (SEQ ID NO:44) (residues in parentheses are optional)

T33-31A (SEQ ID NO:51)

(M)EEVVLITVPSALVAVKIAHALVEERLAACVNIVPGLTSIYREEGSVVSDHELLLLVKTTTDA
FPKLKERVKELHPYEVPEIVALPIAEGNREYLDWLRENTG

>T33-31B (SEQ ID NO:44)

(M)VRGIRGAITVEEDTPAAILAATIELLLKMLEANGIQSYEELAAVIFTVTEDLTSAFPAEAAR
LIGMHRVPLLSAREVPVPGSLPRVIRVLALWNTDTPQDRVRHVYLNEAVRLRPDLESAQ

In another specific embodiment, the first polypeptides comprise polypeptides having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along their full length to the amino acid sequence of T33-15A (SEQ ID NO:45) and the second polypeptides comprise polypeptides having at least 75%, 80%,

85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along their full length to the amino acid sequence of T33-15B (SEQ ID NO:46).

In various further specific embodiments, the first polypeptides comprise polypeptides having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along their full length to the amino acid sequence of a polypeptides selected from the group consisting of I53-50A (SEQ ID NO:7), I53-50A.1 (SEQ ID NO:29), I53-50A.1NegT2 (SEQ ID NO:30), and I53-50A.1PosT1 (SEQ ID NO:31), and the second polypeptides comprise polypeptides having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along their full length to the amino acid sequence of a polypeptide selected from the group consisting of I53-50B (SEQ ID NO:8), I53-50B.1 (SEQ ID NO:32), I53-50B.1NegT2 (SEQ ID NO:33), and I53-50B.4PosT1 (SEQ ID NO:34).

In another specific embodiment, the first polypeptides comprise polypeptides having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along their full length to the amino acid sequence of I32-28A (SEQ ID NO:21) and the second polypeptides comprise polypeptides having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along their full length to the amino acid sequence of I32-28B (SEQ ID NO:22).

The nanostructures of the invention display multiple copies (i.e.: 2, 3, or more) of one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof, on an exterior of the nanostructure. Exemplary paramyxovirus and/or pneumovirus include, but are not limited to, respiratory syncytial virus (RSV) and Human metapneumovirus (hMPV).(C. L. Afonso et al., Taxonomy of the order Mononegavirales: update 2016. Arch. Virol. 161, 2351–2360 (2016)).

As used herein, "on an exterior of the nanostructure" means that an antigenic portion of the one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof, must be accessible for binding by B cell receptors, antibodies, or antibody fragments and not buried within the nanostructure.

The one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof, may comprise any suitable native F proteins, post-fusion, or pre-fusion (preF) antigens, or mutants thereof capable of inducing an immune response that will generate antibodies that bind to paramyxovirus and/or pneumovirus F proteins. A nanostructure may display more than one F protein; thus, in some embodiments the one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof

comprise 1, 2, 3, 4, or more F proteins or antigenic fragments thereof. In one embodiment, the one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof may be as defined in patent publication number US 2016/0046675 A1. In some embodiments, the one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof, are selected from the group consisting of SEQ ID NOS: 1-350, 370-382, 389-693, 698-1026, 1429-1442, 1456-1468, and 1474-1478 as disclosed in US published patent application 2016/0046675. In other embodiments, the one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof may be as defined in WO2012158613, US 20160102123, US20140141037, WO2014079842, WO2014160463, US20140271699, EP2970393, WO2014174018, US20140271699, US20160176932, US20160122398, WO2017040387, WO2017109629, WO2017172890, WO2017207477, Krarup et al. (2015) Nature Communications 6:8143, and WO2017207480.

In a specific embodiment, the one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof, comprise a polypeptide having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to the amino acid sequence of DS-Cav1 shown below (residues in parentheses are optional; note that the N-terminal residues in parentheses are cleaved from the protein during secretion—the mature N terminus begins with QNITEEF... (SEQ ID NO:52)). DS-Cav1 comprises a prefusion-stabilized form of the fusion (F) glycoprotein, which elicits improved protective responses against respiratory syncytial virus (RSV) in mice and macaques compared to postfusion RSV F (McLellan et al. (2013) *Science* **342**:592-8).

DS-Cav1 (SEQ ID NO:53):

(MELLILKANAITTILTAVTFCFASG)QNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIEL
SNIKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPATNNRARRELPRFMNYTLNNAKKTN
VTLSKKRKRRFLGFLLGVGSAIASGVAVCKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTFK
VLDLKNYIDKQLLPILNKQSCSISNIETVIEFQQKNNRLLEITREFSVNAGVTTPVSTYMLTNSE
LLSLINDMPITNDQKKLMSNNVQIVRQQSYSIMCIIKEEVLAYVVQLPLYGVIDTPCWKLHTSPL
CTTNTKEGSNICLTRTDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNVDI
FNPKYDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGIIKTFSNGCDYVSNKGVDTVS
VGNTLYYVNKQEGKSLYVKGEPIINFYDPLVFPSDEFDASISQVNEKINQSLAFIR(KSDELL)

In other embodiments, the F protein may comprise a polypeptide having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to a polypeptide selected from:

RSV F

sc9-10 DS-Cav1 A149C Y458C (SEQ ID NO:61)

(MELLILKANAITTILTAVTFCFASG)QNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSN
IKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPATGSGSAICSGVAVCKVLHLEGEVNKI
KSALLSTNKAVVSLSNGVSVLTFKVLDLKNYIDKQLLPILNKQSCSISNIETVIEFQQKNNRLLE
ITREFSVNAGVTTPVSTYMLTNSELLSLINDMPITNDQKKLMSNNVQIVRQQSYSIMCIIKEEVL
AYVVQLPLYGVIDTPCWKLHTSPLCTTNTKEGSNICLTRTDRGWYCDNAGSVSFFPQAETCKVQS
NRVFCDTMNSRTLPSEVNLCNVDIFNPKYDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNK
NRGIIKTFSNGCDYVSNKGVDTVSVGNTLYCVNKQEGKSLYVKGEPIINFYDPLVFPSDEFDASI
SQVNEKINQSLAFIR(KSDELL)

sc9-10 DS-Cav1 A149C Y458C S46G K465Q S215P E92D (SEQ ID NO:62)

(MELLILKANAITTILTAVTFCFASG)QNITEEFYQSTCSAVSKGYLGALRTGWYTSVITIELSN
IKENKCNGTDAKVKLIKQELDKYKNAVTDLQLLMQSTPATGSGSAICSGVAVCKVLHLEGEVNKI
KSALLSTNKAVVSLSNGVSVLTFKVLDLKNYIDKQLLPILNKQSCSIPNIETVIEFQQKNNRLLE
ITREFSVNAGVTTPVSTYMLTNSELLSLINDMPITNDQKKLMSNNVQIVRQQSYSIMCIIKEEVL
AYVVQLPLYGVIDTPCWKLHTSPLCTTNTKEGSNICLTRTDRGWYCDNAGSVSFFPQAETCKVQS
NRVFCDTMNSRTLPSEVNLCNVDIFNPKYDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNK
NRGIIKTFSNGCDYVSNKGVDTVSVGNTLYCVNKQEGQSLYVKGEPIINFYDPLVFPSDEFDASI
SQVNEKINQSLAFIR(KSDELL)

SEQ ID NO:61-62 represent second-generation stabilized DS-Cav1 immunogens; mutations relative to DS-Cav1 are noted and it should be noted that the present disclosure contemplates the use of DS-Cav1 mutants that differ by a single one of the noted amino acid substitutions in SEQ ID NO:61 or 62 above, or two or more of the amino acid substitutions noted. In other embodiments, the F protein may comprise one or more of the following, each of which may additionally include 1, 2, or more of the noted amino acid substitutions in SEQ ID NO:61 or 62 above:

RSV F SC-DM (N67I, S215P) (SEQ ID NO:63)

(MELLILKANAITTILTAVTFCFASG)QNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSN
IKKIKCNGTDAKIKLIKQELDKYKNAVTELQLLMQSTPATNNQARGSGSGRSLGFLLGVGSAIAS
GVAVSKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSKVLDLKNYIDKQLLPIVNKQSCSIP
NIETVIEFQQKNNRLLEITREFSVNAGVTTPVSTYMLTNSELLSLINDMPITNDQKKLMSNNVQI

VRQQSYSIMSIIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTNTKEGSNICLTRTDRGWYCDN
AGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNVDIFNPKYDCKIMTSKTDVSSSVITSL
GAIVSCYGKTKCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVGNTLYYVNKQEGKSLYVKGEPII
NFYDPLVFPSDEFDASISQVNEKINQSLAFIR(KSDELLSAIG**GYIPEAPRDGQAYVRKDGEWVL**
LSTFL)

SC-TM (N67I, S215P, and E487Q) (SEQ ID NO:64)

(MELLILKANAITTILTAVTFCFASG)QNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSN
IKKIKCNGTDAKIKLIKQELDKYKNAVTELQLLMQSTPATNNQARGSGSGRSLGFLLGVGSAIAS
GVAVSKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSKVLDLKNYIDKQLLPIVNKQSCSIP
NIETVIEFQQKNNRLLEITREFSVNAGVTTPVSTYMLTNSELLSLINDMPITNDQKKLMSNNVQI
VRQQSYSIMSIIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTNTKEGSNICLTRTDRGWYCDN
AGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNVDIFNPKYDCKIMTSKTDVSSSVITSL
GAIVSCYGKTKCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVGNTLYYVNKQEGKSLYVKGEPII
NFYDPLVFPSDQFDASISQVNEKINQSLAFIR(KSDELLSAIG**GYIPEAPRDGQAYVRKDGEWVL**
LSTFL)

HMPV F protein, strain CAN97-83 (A2) (SEQ ID NO:65)

(MSWKVVIIFSLLITPQHG)LKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVGDVENLTCSDG
PSLIKTELDLTKSALRELKTVSADQLAREEQIENPRQSRFVLGAIALGVATAAAVTAGVAIAKTI
RLESEVTAIKNALKTTNEAVSTLGNGVRVLATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSF
SQFNRRFLNVVRQFSDNAGITPAISLDLMTDAELARAVSNMPTSAGQIKLMLENRAMVRRKGFGI
LIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSGKKGNYACLLREDQGWYCQNAGSTVYYPNE
KDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPCKVSTGRHPISMVALSPLGALVACYKGV
SCSIGSNRVGIIKQLNKGCSYITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPE
DQFNVALDQVFENIENSQALVDQSNRILSSAEKGNTG

HMPVF with A113C, A339C, T160F, I177L (SEQ ID NO:66)

(MSWKVVIIFSLLITPQHG)LKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVGDVENLTCSDG
PSLIKTELDLTKSALRELKTVSADQLAREEQIENPRQSRFVLGAIALGVCTAAAVTAGVAIAKTI
RLESEVTAIKNALKTTNEAVSTLGNGVRVLAFAVRELKDFVSKNLTRALNKNKCDIDDLKMAVSF
SQFNRRFLNVVRQFSDNAGITPAISLDLMTDAELARAVSNMPTSAGQIKLMLENRAMVRRKGFGI
LIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSGKKGNYACLLREDQGWYCQNAGSTVYYPNE
KDCETRGDHVFCDTACGINVAEQSKECNINISTTNYPCKVSTGRHPISMVALSPLGALVACYKGV
SCSIGSNRVGIIKQLNKGCSYITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPE
DQFNVALDQVFENIENSQALVDQSNRILSSAEKGNTG

HMPV F with A113C, A120C, A339C, T160F, I177L, and Q426C (SEQ ID NO:67)

(MSWKVVIIFSLLITPQHG)LKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVGDVENLTCSDG
PSLIKTELDLTKSALRELKTVSADQLAREEQIENPRQSRFVLGAIALGVCTAAAVTCGVAIAKTI
RLESEVTAIKNALKTTNEAVSTLGNGVRVLAFAVRELKDFVSKNLTRALNKNKCDIDDLKMAVSF
SQFNRRFLNVVRQFSDNAGITPAISLDLMTDAELARAVSNMPTSAGQIKLMLENRAMVRRKGFGI
LIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSGKKGNYACLLREDQGWYCQNAGSTVYYPNE
KDCETRGDHVFCDTACGINVAEQSKECNINISTTNYPCKVSTGRHPISMVALSPLGALVACYKGV
SCSIGSNRVGIIKQLNKGCSYITNQDADTVTIDNTVYCLSKVEGEQHVIKGRPVSSSFDPIKFPE
DQFNVALDQVFENIENSQALVDQSNRILSSAEKGNTG

HMPV F_>AAK62968.2 fusion protein [Human metapneumovirus] (SEQ ID NO:101)

(MSWKVVIIFSLLITPQHG)LKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVGDVENLTCADG
PSLIKTELDLTKSALRELRTVSADQLAREEQIENPRQSRFVLGAIALGVATAAAVTAGVAIAKTI
RLESEVTAIKNALKKTNEAVSTLGNGVRVLATAVRELKDFVSKNLTRAINKNKCDIADLKMAVSF
SQFNRRFLNVVRQFSDNAGITPAISLDLMTDAELARAVSNMPTSAGQIKLMLENRAMVRRKGFGF
LIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSGKKGNYACLLREDQGWYCQNAGSTVYYPNE
KDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPCKVSTGRHPISMVALSPLGALVACYKGV
SCSIGSNRVGIIKQLNKGCSYITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPVKFPE
DQFNVALDQVFESIENSQALVDQSNRILSSAEKGNTG

115-BV (A185P) (SEQ ID NO:68)

(MSWKVVIIFSLLITPQHG)LKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVGDVENLTCADG
PSLIKTELDLTKSALRELRTVSADQLAREEQIENPRRRRFVLGAIALGVATAAAVTAGVAIAKTI
RLESEVTAIKNALKKTNEAVSTLGNGVRVLATAVRELKDFVSKNLTRAINKNKCDIPDLKMAVSF
SQFNRRFLNVVRQFSDNAGITPAISLDLMTDAELARAVSNMPTSAGQIKLMLENRAMVRRKGFGI
LIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYCQNAGSTVYYPNE
KDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPCKVSTGRHPISMVALSPLGALVACYKGV
SCSIGSNRVGIIKQLNKGCSYITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPVKFPE
DQFNVALDQVFESIENSQALVDQSNRILSSAEKGNT(SGRENLYFQGGGGSGYIPEAPRDGQAYV
RKDGEWVLLSTFLGGIEGRHHHHHH)

In other embodiments, the one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof, may comprise a polypeptide having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to an RSV F protein or mutant thereof selected from the group consisting of SEQ ID NO:53 and 61-64, wherein the polypeptide includes one or more of the following residues: 67I, 149C, 458C, 46G, 465Q, 215P, 92D, and 487Q.

In other embodiments, the one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof, may comprise a polypeptide having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity along its full length to an MPV F protein or mutant thereof selected from the group consisting of SEQ ID NO:65-68 and 101, wherein the polypeptide includes one or more of the following residues: 113C, 120C, 339C, 160F, 177L, 185P, and 426C.

Linker between F proteins and trimeric assembly domains and geometric requirements

In the nanostructures of the invention, the F protein and the trimeric assembly domain may be genetically fused such that they are both present in a single polypeptide. Preferably, the linkage between the F protein and the trimeric assembly domain allows the F protein, or antigenic fragment thereof, to be displayed on the exterior of the nanostructures of the invention. As such, the point of connection to the trimeric assembly domain should be on the exterior of the nanostructure formed by the trimeric assembly domain and the second assembly domain in the absence of any F protein. As will be understood by those of skill in the art, a wide variety of polypeptide sequences can be used to link the paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof and the trimeric assembly domain. These polypeptide sequences are referred to as linkers. Any suitable linker can be used; there is no amino acid sequence requirement to serve as an appropriate linker. There is no requirement that the linker impose a rigid relative orientation of the F protein or antigenic fragment thereof to the trimeric assembly domain beyond enabling the F protein or antigenic fragment thereof to be displayed on the exterior of the nanostructures of the invention. In some embodiments, the linker includes additional trimerization domains (e.g., the foldon domain of T4 fibritin) that assist in stabilizing the trimeric form of the F protein.

T4 fibritin foldon domain (optional in the linker region) (SEQ ID NO:54)
GYIPEAPRDGQAYVRKDGEWVLLSTFL

In other embodiments, the linker may comprise a Gly-Ser linker (i.e.: a linker consisting of glycine and serine residues) of any suitable length. In various embodiments, the Gly-Ser linker may be 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or more amino acids in length. In various embodiments, the Gly-Ser linker may comprise or consist of the amino acid sequence of GSGGSGSGSGGSGSG (SEQ ID NO:55), GGSGGSGS (SEQ ID NO:56) or GSGGSGSG (SEQ ID NO:57).

In further embodiments the linker may comprise a helical extension domain that may serve to extend the N-terminal helix of the first polypeptide, when expressed as a fusion polypeptide with the one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof, so that it is located at the exterior of the nanostructure surface. The helical extension may be present in combination with the other linker components described herein, or may be absent. The helical extension may be of any suitable length (i.e.: 7, 8, 9, 10, 11, 12, or more amino acids) and comprise any suitable primary amino acid sequence. In one embodiment, the helical extension may comprise or consist of the amino acid sequence EKAAKAEEAAR (SEQ ID NO:58).

Thus, in various non-limiting embodiments in which the F protein is present as a fusion protein with the first polypeptide and a linker is used, the F protein-linker sequence may comprise the following (exemplified by DS-Cav1 as the F protein in these non-limiting embodiments). Residues in parentheses are optional and the amino acid sequence MELLILKANAITTILTAVTFCFASG (SEQ ID NO:59) represents the N-terminal DS-Cav1 signal peptide that is cleaved during processing:

DS-Cav1-foldon (SEQ ID NO:60):

(MELLILKANAITTILTAVTFCFASG)QNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSN
IKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPATNNRARRELPRFMNYTLNNAKKTNVT
LSKKRKRRFLGFLLGVGSAIASGVAVCKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTFKVL
DLKNYIDKQLLPILNKQSCSISNIETVIEFQQKNNRLLEITREFSVNAGVTTPVSTYMLTNSELL
SLINDMPITNDQKKLMSNNVQIVRQQSYSIMCIIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCT
TNTKEGSNICLTRTDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNVDIFN
PKYDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVG
NTLYYVNKQEGKSLYVKGEPIINFYDPLVFPSDEFDASISQVNEKINQSLAFIRKSDELL**GYIPE**
APRDGQAYVRKDGEWVLLSTFL

In various further embodiments, the first polypeptides comprise or consist of fusion polypeptides of first polypeptides fused to an F protein, where the fusion protein has a sequence selected from the following (optional residues in parentheses):

DS-Cav1-foldon-T33-31A (SEQ ID NO:69)

(MELLILKANVIATILTAVTFCFASS)QNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSN
IKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPATNNRARRELPRFMNYTLNNAKKTNVT
LSKKRKRRFLGFLLGVGSAIASGVAVCKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTFKVL
DLKNYIDKQLLPILNKQSCSISNIETVIEFQQKNNRLLEITREFSVNAGVTTPVSTYMLTNSELL
SLINDMPITNDQKKLMSNNVQIVRQQSYSIMCIIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCT

TNTKEGSNICLTRTDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNVDIFN
PKYDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVG
NTLYYVNKQEGKSLYVKGEPIINFYDPLVFPSDEFDASISQVNEKINQSLAFIRKSDELLGYIPE
APRDGQAYVRKDGEWVLLSTFLGGSMEEVVLITVPSALVAVKIAHALVEERLAACVNIVPGLTSI
YREEGSVVSDHELLLLVKTTTDAFPKLKERVKELHPYEVPEIVALPIAEGNREYLDWLRENTG

DS-Cav1-T33-31A (SEQ ID NO:70)

(MELLILKANVIATILTAVTFCFASS)QNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSN
IKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPATNNRARRELPRFMNYTLNNAKKTNVT
LSKKRKRRFLGFLLGVGSAIASGVAVCKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTFKVL
DLKNYIDKQLLPILNKQSCSISNIETVIEFQQKNNRLLEITREFSVNAGVTTPVSTYMLTNSELL
SLINDMPITNDQKKLMSNNVQIVRQQSYSIMCIIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCT
TNTKEGSNICLTRTDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNVDIFN
PKYDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVG
NTLYYVNKQEGKSLYVKGEPIINFYDPLVFPSDEFDASISQVNEKINQSLAFIRKSDELLGGSME
EVVLITVPSALVAVKIAHALVEERLAACVNIVPGLTSIYREEGSVVSDHELLLLVKTTTDAFPKL
KERVKELHPYEVPEIVALPIAEGNREYLDWLRENTG

DS-Cav1-foldon-T33-15B (SEQ ID NO:71)

(MELLILKANVIATILTAVTFCFASS)QNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSN
IKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPATNNRARRELPRFMNYTLNNAKKTNVT
LSKKRKRRFLGFLLGVGSAIASGVAVCKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTFKVL
DLKNYIDKQLLPILNKQSCSISNIETVIEFQQKNNRLLEITREFSVNAGVTTPVSTYMLTNSELL
SLINDMPITNDQKKLMSNNVQIVRQQSYSIMCIIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCT
TNTKEGSNICLTRTDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNVDIFN
PKYDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVG
NTLYYVNKQEGKSLYVKGEPIINFYDPLVFPSDEFDASISQVNEKINQSLAFIRKSDELLGYIPE
APRDGQAYVRKDGEWVLLSTFLGGSMVRGIRGAITVNSDTPTSIIIATILLLEKMLEANGIQSYE
ELAAVIFTVTEDLTSAFPAEAARQIGMHRVPLLSAREVPVPGSLPRVIRVLALWNTDTPQDRVRH
VYLSEAVRLRPDLESAQ

DS-Cav1-T33-15B (SEQ ID NO:72)

(MELLILKANVIATILTAVTFCFASS)QNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSN
IKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPATNNRARRELPRFMNYTLNNAKKTNVT
LSKKRKRRFLGFLLGVGSAIASGVAVCKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTFKVL
DLKNYIDKQLLPILNKQSCSISNIETVIEFQQKNNRLLEITREFSVNAGVTTPVSTYMLTNSELL
SLINDMPITNDQKKLMSNNVQIVRQQSYSIMCIIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCT

TNTKEGSNICLTRTDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNVDIFN
PKYDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVG
NTLYYVNKQEGKSLYVKGEPIINFYDPLVFPSDEFDASISQVNEKINQSLAFIRKSDELLGGSMV
RGIRGAITVNSDTPTSIIIATILLLEKMLEANGIQSYEELAAVIFTVTEDLTSAFPAEAARQIGM
HRVPLLSAREVPVPGSLPRVIRVLALWNTDTPQDRVRHVYLSEAVRLRPDLESAQ

DS-Cav1-foldon-I53-50A (SEQ ID NO:73)

(MELLILKANAITTILTAVTFCFASG)QNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSN
IKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPATNNRARRELPRFMNYTLNNAKKTNVT
LSKKRKRRFLGFLLGVGSAIASGVAVCKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTFKVL
DLKNYIDKQLLPILNKQSCSISNIETVIEFQQKNNRLLEITREFSVNAGVTTPVSTYMLTNSELL
SLINDMPITNDQKKLMSNNVQIVRQQSYSIMCIIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCT
TNTKEGSNICLTRTDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNVDIFN
PKYDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVG
NTLYYVNKQEGKSLYVKGEPIINFYDPLVFPSDEFDASISQVNEKINQSLAFIRGYIPEAPRDGQ
AYVRKDGEWVLLSTFLGSGSHHHHHHHHGGSGGSGSEKAAKAEEAARKMEELFKKHKIVAVLRAN
SVEEAIEKAVAVFAGGVHLIEITFTVPDADTVIKALSVLKEKGAIIGAGTVTSVEQCRKAVESGA
EFIVSPHLDEEISQFCKEKGVFYMPGVMTPTELVKAMKLGHTILKLFPGEVVGPQFVKAMKGPFP
NVKFVPTGGVNLDNVCEWFKAGVLAVGVGSALVKGTPDEVREKAKAFVEKIRGCTE

DS-Cav1-I53-50A (SEQ ID NO:74)

(MELLILKANVIATILTAVTFCFASS)QNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSN
IKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPATNNRARRELPRFMNYTLNNAKKTNVT
LSKKRKRRFLGFLLGVGSAIASGVAVCKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTFKVL
DLKNYIDKQLLPILNKQSCSISNIETVIEFQQKNNRLLEITREFSVNAGVTTPVSTYMLTNSELL
SLINDMPITNDQKKLMSNNVQIVRQQSYSIMCIIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCT
TNTKEGSNICLTRTDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNVDIFN
PKYDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVG
NTLYYVNKQEGKSLYVKGEPIINFYDPLVFPSDEFDASISQVNEKINQSLAFIRGGSGGSGSEKA
AKAEEAARKMEELFKKHKIVAVLRANSVEEAIEKAVAVFAGGVHLIEITFTVPDADTVIKALSVL
KEKGAIIGAGTVTSVEQCRKAVESGAEFIVSPHLDEEISQFCKEKGVFYMPGVMTPTELVKAMKL
GHTILKLFPGEVVGPQFVKAMKGPFPNVKFVPTGGVNLDNVCEWFKAGVLAVGVGSALVKGTPDE
VREKAKAFVEKIRGCTE

DS-Cav1-I32-28A (SEQ ID NO:75)

(MELLILKANAITTILTAVTFCFASG)QNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSN
IKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPATNNRARRELPRFMNYTLNNAKKTNVT

LSKKRKRRFLGFLLGVGSAIASGVAVCKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTFKVL
DLKNYIDKQLLPILNKQSCSISNIETVIEFQQKNNRLLEITREFSVNAGVTTPVSTYMLTNSELL
SLINDMPITNDQKKLMSNNVQIVRQQSYSIMCIIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCT
TNTKEGSNICLTRTDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNVDIFN
PKYDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVG
NTLYYVNKQEGKSLYVKGEPIINFYDPLVFPSDEFDASISQVNEKINQSLAFIRKSDELLGGSGG
SGSDDARIAAIGDVDELNSQIGVLLAEPLPDDVRAALSAIQHDLFDLGGELCIPGHAAITEDHLL
RLALWLVHYNGQLPPLEEFILPGGARGAALAHVCRTVCRRAERSIKALGASEPLNIAPAAYVNLL
SDLLFVLARVLNRAAGGADVLWDRTRAH

DS-Cav1-8GS-HelExt-I53-50A (F10) (SEQ ID NO:76)

(MELLILKANAITTILTAVTFCFASG)QNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSN
IKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPATNNRARRELPRFMNYTLNNAKKTNVT
LSKKRKRRFLGFLLGVGSAIASGVAVCKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTFKVL
DLKNYIDKQLLPILNKQSCSISNIETVIEFQQKNNRLLEITREFSVNAGVTTPVSTYMLTNSELL
SLINDMPITNDQKKLMSNNVQIVRQQSYSIMCIIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCT
TNTKEGSNICLTRTDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNVDIFN
PKYDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVG
NTLYYVNKQEGKSLYVKGEPIINFYDPLVFPSDEFDASISQVNEKINQSLAFIRGSGGSGSGEKA
AKAEEAARKMEELFKKHKIVAVLRANSVEEAIEKAVAVFAGGVHLIEITFTVPDADTVIKALSVL
KEKGAIIGAGTVTSVEQCRKAVESGAEFIVSPHLDEEISQFCKEKGVFYMPGVMTPTELVKAMKL
GHTILKLFPGEVVGPQFVKAMKGPFPNVKFVPTGGVNLDNVCEWFKAGVLAVGVGSALVKGTPDE
VREKAKAFVEKIRGCTE

DS-Cav1-foldon-15GS-HelExt-I53-50A (F14) (SEQ ID NO:77)

(MELLILKANAITTILTAVTFCFASG)QNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSN
IKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPATNNRARRELPRFMNYTLNNAKKTNVT
LSKKRKRRFLGFLLGVGSAIASGVAVCKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTFKVL
DLKNYIDKQLLPILNKQSCSISNIETVIEFQQKNNRLLEITREFSVNAGVTTPVSTYMLTNSELL
SLINDMPITNDQKKLMSNNVQIVRQQSYSIMCIIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCT
TNTKEGSNICLTRTDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNVDIFN
PKYDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVG
NTLYYVNKQEGKSLYVKGEPIINFYDPLVFPSDEFDASISQVNEKINQSLAFIRGYIPEAPRDGQ
AYVRKDGEWVLLSTFLGSGGSGSGSGGSGSGEKAAKAEEAARKMEELFKKHKIVAVLRANSVEEA
IEKAVAVFAGGVHLIEITFTVPDADTVIKALSVLKEKGAIIGAGTVTSVEQCRKAVESGAEFIVS
PHLDEEISQFCKEKGVFYMPGVMTPTELVKAMKLGHTILKLFPGEVVGPQFVKAMKGPFPNVKFV
PTGGVNLDNVCEWFKAGVLAVGVGSALVKGTPDEVREKAKAFVEKIRGCTE

HMPV F wt_CAN97-83 strain-I53-50A (SEQ ID NO:78)

(MSWKVVIIFSLLITPQHG)LKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVGDVENLTCSDG
PSLIKTELDLTKSALRELKTVSADQLAREEQIENPRQSRFVLGAIALGVATAAAVTAGVAIAKTI
RLESEVTAIKNALKTTNEAVSTLGNGVRVLATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSF
SQFNRRFLNVVRQFSDNAGITPAISLDLMTDAELARAVSNMPTSAGQIKLMLENRAMVRRKGFGI
LIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSGKKGNYACLLREDQGWYCQNAGSTVYYPNE
KDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPCKVSTGRHPISMVALSPLGALVACYKGV
SCSIGSNRVGIIKQLNKGCSYITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPE
DQFNVALDQVFENIENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSIFIIIKKTK
KPTGAPPELSGVTNNGFIPHSGSGSHHHHHHHHGGSGGSGSEKAAKAEEAARKMEELFKKHKIVA
VLRANSVEEAIEKAVAVFAGGVHLIEITFTVPDADTVIKALSVLKEKGAIIGAGTVTSVEQCRKA
VESGAEFIVSPHLDEEISQFCKEKGVFYMPGVMTPTELVKAMKLGHTILKLFPGEVVGPQFVKAM
KGPFPNVKFVPTGGVNLDNVCEWFKAGVLAVGVGSALVKGTPDEVREKAKAFVEKIRGCTE

HMPV F A113C_A339C_T160F_I177L-I53-50A (SEQ ID NO:79)

(MSWKVVIIFSLLITPQHG)LKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVGDVENLTCSDG
PSLIKTELDLTKSALRELKTVSADQLAREEQIENPRQSRFVLGAIALGVCTAAAVTAGVAIAKTI
RLESEVTAIKNALKTTNEAVSTLGNGVRVLAFAVRELKDFVSKNLTRALNKNKCDIDDLKMAVSF
SQFNRRFLNVVRQFSDNAGITPAISLDLMTDAELARAVSNMPTSAGQIKLMLENRAMVRRKGFGI
LIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSGKKGNYACLLREDQGWYCQNAGSTVYYPNE
KDCETRGDHVFCDTACGINVAEQSKECNINISTTNYPCKVSTGRHPISMVALSPLGALVACYKGV
SCSIGSNRVGIIKQLNKGCSYITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPE
DQFNVALDQVFENIENSQALVDQSNRILSSAEKGNTGGSGSHHHHHHHHGGSGGSGSEKAAKAEE
AARKMEELFKKHKIVAVLRANSVEEAIEKAVAVFAGGVHLIEITFTVPDADTVIKALSVLKEKGA
IIGAGTVTSVEQCRKAVESGAEFIVSPHLDEEISQFCKEKGVFYMPGVMTPTELVKAMKLGHTIL
KLFPGEVVGPQFVKAMKGPFPNVKFVPTGGVNLDNVCEWFKAGVLAVGVGSALVKGTPDEVREKA
KAFVEKIRGCTE

HMPV F A113C_A339C_T160F_I177L_A120C, Q426C mutations-I53-50A (SEQ ID NO:80)

(MSWKVVIIFSLLITPQHG)LKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVGDVENLTCSDG
PSLIKTELDLTKSALRELKTVSADQLAREEQIENPRQSRFVLGAIALGVCTAAAVTCGVAIAKTI
RLESEVTAIKNALKTTNEAVSTLGNGVRVLAFAVRELKDFVSKNLTRALNKNKCDIDDLKMAVSF
SQFNRRFLNVVRQFSDNAGITPAISLDLMTDAELARAVSNMPTSAGQIKLMLENRAMVRRKGFGI
LIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSGKKGNYACLLREDQGWYCQNAGSTVYYPNE
KDCETRGDHVFCDTACGINVAEQSKECNINISTTNYPCKVSTGRHPISMVALSPLGALVACYKGV
SCSIGSNRVGIIKQLNKGCSYITNQDADTVTIDNTVYCLSKVEGEQHVIKGRPVSSSFDPIKFPE
DQFNVALDQVFENIENSQALVDQSNRILSSAEKGNTGGSGSHHHHHHHHGGSGGSGSEKAAKAEE
AARKMEELFKKHKIVAVLRANSVEEAIEKAVAVFAGGVHLIEITFTVPDADTVIKALSVLKEKGA

IIGAGTVTSVEQCRKAVESGAEFIVSPHLDEEISQFCKEKGVFYMPGVMTPTELVKAMKLGHTIL
KLFPGEVVGPQFVKAMKGPFPNVKFVPTGGVNLDNVCEWFKAGVLAVGVGSALVKGTPDEVREKA
KAFVEKIRGCTE

sc-DS2-I53-50A (SEQ ID NO:81)

(MELLILKANAITTILTAVTFCFASG)QNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSN
IKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPATGSGSCIASGVAVCKVLHLEGEVNKI
KSALLSTNKAVVSLSNGVSVLTFKVLDLKNYIDKQLLPILNKQSCSISNIETVIEFQQKNNRLLE
ITREFSVNAGVTTPVSTYMLTNSELLSLINDMPITNDQKKLMSNNVQIVRQQSYSIMCIIKEEVL
AYVVQLPLYGVIDTPCWKLHTSPLCTTNTKEGSNICLTRTDRGWYCDNAGSVSFFPQAETCKVQS
NRVFCDTMNSLTLPSEVNLCNVDIFNPKYDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNK
NRGIIKTFSNGCDYVSNKGVDTVSVGNTLYCVNKQEGKSLYVKGEPIINFYDPLVFPSDEFDASI
SQVNEKINQSLAFIRGSGSHHHHHHHHGGSGGSGSEKAAKAEEAARKMEELFKKHKIVAVLRANS
VEEAIEKAVAVFAGGVHLIEITFTVPDADTVIKALSVLKEKGAIIGAGTVTSVEQCRKAVESGAE
FIVSPHLDEEISQFCKEKGVFYMPGVMTPTELVKAMKLGHTILKLFPGEVVGPQFVKAMKGPFPN
VKFVPTGGVNLDNVCEWFKAGVLAVGVGSALVKGTPDEVREKAKAFVEKIRGCTE

tc-DS2-I53-50A (SEQ ID NO:82)

(MELLILKANAITTILTAVTFCFASG)QNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSN
IKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPATNNRARRELPRFMNYTLNNAKKTNVT
LSKKRKRRFLGFLLGVGSCIASGVAVCKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTFKVL
DLKNYIDKQLLPILNKQSCSISNIETVIEFQQKNNRLLEITREFSVNAGVTTPVSTYMLTNSELL
SLINDMPITNDQKKLMSNNVQIVRQQSYSIMCIIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCT
TNTKEGSNICLTRTDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNVDIFN
PKYDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVG
NTLYCVNKQEGKSLYVKGEPIINFYDPLVFPSDEFDASISQVNEKINQSLAFIRGSGSHHHHHHH
HGGSGGSGSEKAAKAEEAARKMEELFKKHKIVAVLRANSVEEAIEKAVAVFAGGVHLIEITFTVP
DADTVIKALSVLKEKGAIIGAGTVTSVEQCRKAVESGAEFIVSPHLDEEISQFCKEKGVFYMPGV
MTPTELVKAMKLGHTILKLFPGEVVGPQFVKAMKGPFPNVKFVPTGGVNLDNVCEWFKAGVLAVG
VGSALVKGTPDEVREKAKAFVEKIRGCTE

DS-Cav1-12GS-HelExt-I53-50A (F11) (SEQ ID NO:83)

(MELLILKANAITTILTAVTFCFASG)QNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSN
IKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPATNNRARRELPRFMNYTLNNAKKTNVT
LSKKRKRRFLGFLLGVGSAIASGVAVCKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTFKVL
DLKNYIDKQLLPILNKQSCSISNIETVIEFQQKNNRLLEITREFSVNAGVTTPVSTYMLTNSELL
SLINDMPITNDQKKLMSNNVQIVRQQSYSIMCIIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCT
TNTKEGSNICLTRTDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNVDIFN

PKYDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVG
NTLYYVNKQEGKSLYVKGEPIINFYDPLVFPSDEFDASISQVNEKINQSLAFIRGSGGSGSGSGG
SEKAAKAEEAARKMEELFKKHKIVAVLRANSVEEAIEKAVAVFAGGVHLIEITFTVPDADTVIKA
LSVLKEKGAIIGAGTVTSVEQCRKAVESGAEFIVSPHLDEEISQFCKEKGVFYMPGVMTPTELVK
AMKLGHTILKLFPGEVVGPQFVKAMKGPFPNVKFVPTGGVNLDNVCEWFKAGVLAVGVGSALVKG
TPDEVREKAKAFVEKIRGCTE

DS-Cav1-16GS-HelExt-I53-50A (F12) (SEQ ID NO:84)

(MELLILKANAITTILTAVTFCFASG)QNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSN
IKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPATNNRARRELPRFMNYTLNNAKKTNVT
LSKKRKRRFLGFLLGVGSAIASGVAVCKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTFKVL
DLKNYIDKQLLPILNKQSCSISNIETVIEFQQKNNRLLEITREFSVNAGVTTPVSTYMLTNSELL
SLINDMPITNDQKKLMSNNVQIVRQQSYSIMCIIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCT
TNTKEGSNICLTRTDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNVDIFN
PKYDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVG
NTLYYVNKQEGKSLYVKGEPIINFYDPLVFPSDEFDASISQVNEKINQSLAFIRGSGGSGSGSGG
SGSGGEKAAKAEEAARKMEELFKKHKIVAVLRANSVEEAIEKAVAVFAGGVHLIEITFTVPDADT
VIKALSVLKEKGAIIGAGTVTSVEQCRKAVESGAEFIVSPHLDEEISQFCKEKGVFYMPGVMTPT
ELVKAMKLGHTILKLFPGEVVGPQFVKAMKGPFPNVKFVPTGGVNLDNVCEWFKAGVLAVGVGSA
LVKGTPDEVREKAKAFVEKIRGCTE

DS-Cav1-foldon-10GS-HelExt-I53-50A (F13 (SEQ ID NO:85)

(MELLILKANAITTILTAVTFCFASG)QNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSN
IKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPATNNRARRELPRFMNYTLNNAKKTNVT
LSKKRKRRFLGFLLGVGSAIASGVAVCKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTFKVL
DLKNYIDKQLLPILNKQSCSISNIETVIEFQQKNNRLLEITREFSVNAGVTTPVSTYMLTNSELL
SLINDMPITNDQKKLMSNNVQIVRQQSYSIMCIIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCT
TNTKEGSNICLTRTDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNVDIFN
PKYDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVG
NTLYYVNKQEGKSLYVKGEPIINFYDPLVFPSDEFDASISQVNEKINQSLAFIRGYIPEAPRDGQ
AYVRKDGEWVLLSTFLGSGGSGSGSGEKAAKAEEAARKMEELFKKHKIVAVLRANSVEEAIEKAV
AVFAGGVHLIEITFTVPDADTVIKALSVLKEKGAIIGAGTVTSVEQCRKAVESGAEFIVSPHLDE
EISQFCKEKGVFYMPGVMTPTELVKAMKLGHTILKLFPGEVVGPQFVKAMKGPFPNVKFVPTGGV
NLDNVCEWFKAGVLAVGVGSALVKGTPDEVREKAKAFVEKIRGCTE

DS-Cav1-foldon-20GS-HelExt-I53-50A (F15) (SEQ ID NO:86)

(MELLILKANAITTILTAVTFCFASG)QNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSN
IKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPATNNRARRELPRFMNYTLNNAKKTNVT

LSKKRKRRFLGFLLGVGSAIASGVAVCKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTFKVL
DLKNYIDKQLLPILNKQSCSISNIETVIEFQQKNNRLLEITREFSVNAGVTTPVSTYMLTNSELL
SLINDMPITNDQKKLMSNNVQIVRQQSYSIMCIIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCT
TNTKEGSNICLTRTDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNVDIFN
PKYDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVG
NTLYYVNKQEGKSLYVKGEPIINFYDPLVFPSDEFDASISQVNEKINQSLAFIRGYIPEAPRDGQ
AYVRKDGEWVLLSTFLGSGGSGSGSGGSGSGGSSGSEKAAKAEEAARKMEELFKKHKIVAVLRAN
SVEEAIEKAVAVFAGGVHLIEITFTVPDADTVIKALSVLKEKGAIIGAGTVTSVEQCRKAVESGA
EFIVSPHLDEEISQFCKEKGVFYMPGVMTPTELVKAMKLGHTILKLFPGEVVGPQFVKAMKGPFP
NVKFVPTGGVNLDNVCEWFKAGVLAVGVGSALVKGTPDEVREKAKAFVEKIRGCTE

sc9-10 DS-Cav1 A149C Y458C-foldon-I53-50A embodiment (SEQ ID NO:87)

(MELLILKANAITTILTAVTFCFASG)QNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSN
IKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPATGSGSAICSGVAVCKVLHLEGEVNKI
KSALLSTNKAVVSLSNGVSVLTFKVLDLKNYIDKQLLPILNKQSCSISNIETVIEFQQKNNRLLE
ITREFSVNAGVTTPVSTYMLTNSELLSLINDMPITNDQKKLMSNNVQIVRQQSYSIMCIIKEEVL
AYVVQLPLYGVIDTPCWKLHTSPLCTTNTKEGSNICLTRTDRGWYCDNAGSVSFFPQAETCKVQS
NRVFCDTMNSRTLPSEVNLCNVDIFNPKYDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNK
NRGIIKTFSNGCDYVSNKGVDTVSVGNTLYCVNKQEGKSLYVKGEPIINFYDPLVFPSDEFDASI
SQVNEKINQSLAFIR(KSDELL)GYIPEAPRDGQAYVRKDGEWVLLSTFLGSGSHHHHHHHHGGS
GGSGSEKAAKAEEAARKMEELFKKHKIVAVLRANSVEEAIEKAVAVFAGGVHLIEITFTVPDADT
VIKALSVLKEKGAIIGAGTVTSVEQCRKAVESGAEFIVSPHLDEEISQFCKEKGVFYMPGVMTPT
ELVKAMKLGHTILKLFPGEVVGPQFVKAMKGPFPNVKFVPTGGVNLDNVCEWFKAGVLAVGVGSA
LVKGTPDEVREKAKAFVEKIRGCTE

sc9-10 DS-Cav1 A149C Y458C-I53-50A - F10 embodiment (SEQ ID NO:88)

(MELLILKANAITTILTAVTFCFASG)QNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSN
IKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQSTPATGSGSAICSGVAVCKVLHLEGEVNKI
KSALLSTNKAVVSLSNGVSVLTFKVLDLKNYIDKQLLPILNKQSCSISNIETVIEFQQKNNRLLE
ITREFSVNAGVTTPVSTYMLTNSELLSLINDMPITNDQKKLMSNNVQIVRQQSYSIMCIIKEEVL
AYVVQLPLYGVIDTPCWKLHTSPLCTTNTKEGSNICLTRTDRGWYCDNAGSVSFFPQAETCKVQS
NRVFCDTMNSRTLPSEVNLCNVDIFNPKYDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNK
NRGIIKTFSNGCDYVSNKGVDTVSVGNTLYCVNKQEGKSLYVKGEPIINFYDPLVFPSDEFDASI
SQVNEKINQSLAFIR(KSDELL)GSGGSGSGEKAAKAEEAARKMEELFKKHKIVAVLRANSVEEA
IEKAVAVFAGGVHLIEITFTVPDADTVIKALSVLKEKGAIIGAGTVTSVEQCRKAVESGAEFIVS
PHLDEEISQFCKEKGVFYMPGVMTPTELVKAMKLGHTILKLFPGEVVGPQFVKAMKGPFPNVKFV
PTGGVNLDNVCEWFKAGVLAVGVGSALVKGTPDEVREKAKAFVEKIRGCTE

sc9-10 DS-Cav1 A149C Y458C S46G K465Q S215P E92D-foldon-I53-50A embodiment (SEQ ID NO:89)

(MELLILKANAITTILTAVTFCFASG)QNITEEFYQSTCSAVSKGYLGALRTGWYTSVITIELSN
IKENKCNGTDAKVKLIKQELDKYKNAVTDLQLLMQSTPATGSGSAICSGVAVCKVLHLEGEVNKI
KSALLSTNKAVVSLSNGVSVLTFKVLDLKNYIDKQLLPILNKQSCSIPNIETVIEFQQKNNRLLE
ITREFSVNAGVTTPVSTYMLTNSELLSLINDMPITNDQKKLMSNNVQIVRQQSYSIMCIIKEEVL
AYVVQLPLYGVIDTPCWKLHTSPLCTTNTKEGSNICLTRTDRGWYCDNAGSVSFFPQAETCKVQS
NRVFCDTMNSRTLPSEVNLCNVDIFNPKYDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNK
NRGIIKTFSNGCDYVSNKGVDTVSVGNTLYCVNKQEGQSLYVKGEPIINFYDPLVFPSDEFDASI
SQVNEKINQSLAFIR(KSDELL)GYIPEAPRDGQAYVRKDGEWVLLSTFLGSGSHHHHHHHHGGS
GGSGSEKAAKAEEAARKMEELFKKHKIVAVLRANSVEEAIEKAVAVFAGGVHLIEITFTVPDADT
VIKALSVLKEKGAIIGAGTVTSVEQCRKAVESGAEFIVSPHLDEEISQFCKEKGVFYMPGVMTPT
ELVKAMKLGHTILKLFPGEVVGPQFVKAMKGPFPNVKFVPTGGVNLDNVCEWFKAGVLAVGVGSA
LVKGTPDEVREKAKAFVEKIRGCTE

sc9-10 DS-Cav1 A149C Y458C S46G K465Q S215P E92D-I53-50A - F10 embodiment (SEQ ID NO:90)

(MELLILKANAITTILTAVTFCFASG)QNITEEFYQSTCSAVSKGYLGALRTGWYTSVITIELSN
IKENKCNGTDAKVKLIKQELDKYKNAVTDLQLLMQSTPATGSGSAICSGVAVCKVLHLEGEVNKI
KSALLSTNKAVVSLSNGVSVLTFKVLDLKNYIDKQLLPILNKQSCSIPNIETVIEFQQKNNRLLE
ITREFSVNAGVTTPVSTYMLTNSELLSLINDMPITNDQKKLMSNNVQIVRQQSYSIMCIIKEEVL
AYVVQLPLYGVIDTPCWKLHTSPLCTTNTKEGSNICLTRTDRGWYCDNAGSVSFFPQAETCKVQS
NRVFCDTMNSRTLPSEVNLCNVDIFNPKYDCKIMTSKTDVSSSVITSLGAIVSCYGKTKCTASNK
NRGIIKTFSNGCDYVSNKGVDTVSVGNTLYCVNKQEGQSLYVKGEPIINFYDPLVFPSDEFDASI
SQVNEKINQSLAFIR(KSDELL)GSGGSGSGEKAAKAEEAARKMEELFKKHKIVAVLRANSVEEA
IEKAVAVFAGGVHLIEITFTVPDADTVIKALSVLKEKGAIIGAGTVTSVEQCRKAVESGAEFIVS
PHLDEEISQFCKEKGVFYMPGVMTPTELVKAMKLGHTILKLFPGEVVGPQFVKAMKGPFPNVKFV
PTGGVNLDNVCEWFKAGVLAVGVGSALVKGTPDEVREKAKAFVEKIRGCTE

SC-DM (N67I, S215P) - foldon-I53-50A embodiment (SEQ ID NO:91)

(MELLILKANAITTILTAVTFCFASG)QNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSN
IKKIKCNGTDAKIKLIKQELDKYKNAVTELQLLMQSTPATNNQARGSGSGRSLGFLLGVGSAIAS
GVAVSKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSKVLDLKNYIDKQLLPIVNKQSCSIP
NIETVIEFQQKNNRLLEITREFSVNAGVTTPVSTYMLTNSELLSLINDMPITNDQKKLMSNNVQI
VRQQSYSIMSIIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTNTKEGSNICLTRTDRGWYCDN
AGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNVDIFNPKYDCKIMTSKTDVSSSVITSL
GAIVSCYGKTKCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVGNTLYYVNKQEGKSLYVKGEPII

NFYDPLVFPSDEFDASISQVNEKINQSLAFIR(KSDELL)GYIPEAPRDGQAYVRKDGEWVLLST
FLGSGSHHHHHHHHGGSGGSGSEKAAKAEEAARKMEELFKKHKIVAVLRANSVEEAIEKAVAVFA
GGVHLIEITFTVPDADTVIKALSVLKEKGAIIGAGTVTSVEQCRKAVESGAEFIVSPHLDEEISQ
FCKEKGVFYMPGVMTPTELVKAMKLGHTILKLFPGEVVGPQFVKAMKGPFPNVKFVPTGGVNLDN
VCEWFKAGVLAVGVGSALVKGTPDEVREKAKAFVEKIRGCTE

SC-DM (N67I, S215P)-I53-50A - F10 embodiment (SEQ ID NO:92)

(MELLILKANAITTILTAVTFCFASG)QNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSN
IKKIKCNGTDAKIKLIKQELDKYKNAVTELQLLMQSTPATNNQARGSGSGRSLGFLLGVGSAIAS
GVAVSKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSKVLDLKNYIDKQLLPIVNKQSCSIP
NIETVIEFQQKNNRLLEITREFSVNAGVTTPVSTYMLTNSELLSLINDMPITNDQKKLMSNNVQI
VRQQSYSIMSIIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTNTKEGSNICLTRTDRGWYCDN
AGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNVDIFNPKYDCKIMTSKTDVSSSVITSL
GAIVSCYGKTKCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVGNTLYYVNKQEGKSLYVKGEPII
NFYDPLVFPSDEFDASISQVNEKINQSLAFIR(KSDELL)GSGGSGSGEKAAKAEEAARKMEELF
KKHKIVAVLRANSVEEAIEKAVAVFAGGVHLIEITFTVPDADTVIKALSVLKEKGAIIGAGTVTS
VEQCRKAVESGAEFIVSPHLDEEISQFCKEKGVFYMPGVMTPTELVKAMKLGHTILKLFPGEVVG
PQFVKAMKGPFPNVKFVPTGGVNLDNVCEWFKAGVLAVGVGSALVKGTPDEVREKAKAFVEKIRG
CTE

SC-TM (N67I, S215P, and E487Q) - foldon-I53-50A embodiment (SEQ ID NO:93)

(MELLILKANAITTILTAVTFCFASG)QNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSN
IKKIKCNGTDAKIKLIKQELDKYKNAVTELQLLMQSTPATNNQARGSGSGRSLGFLLGVGSAIAS
GVAVSKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSKVLDLKNYIDKQLLPIVNKQSCSIP
NIETVIEFQQKNNRLLEITREFSVNAGVTTPVSTYMLTNSELLSLINDMPITNDQKKLMSNNVQI
VRQQSYSIMSIIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTNTKEGSNICLTRTDRGWYCDN
AGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNVDIFNPKYDCKIMTSKTDVSSSVITSL
GAIVSCYGKTKCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVGNTLYYVNKQEGKSLYVKGEPII
NFYDPLVFPSDQFDASISQVNEKINQSLAFIR(KSDELL)GYIPEAPRDGQAYVRKDGEWVLLST
FLGSGSHHHHHHHHGGSGGSGSEKAAKAEEAARKMEELFKKHKIVAVLRANSVEEAIEKAVAVFA
GGVHLIEITFTVPDADTVIKALSVLKEKGAIIGAGTVTSVEQCRKAVESGAEFIVSPHLDEEISQ
FCKEKGVFYMPGVMTPTELVKAMKLGHTILKLFPGEVVGPQFVKAMKGPFPNVKFVPTGGVNLDN
VCEWFKAGVLAVGVGSALVKGTPDEVREKAKAFVEKIRGCTE

SC-TM (N67I, S215P, and E487Q)-I53-50A - F10 embodiment (SEQ ID NO:94)

(MELLILKANAITTILTAVTFCFASG)QNITEEFYQSTCSAVSKGYLSALRTGWYTSVITIELSN
IKKIKCNGTDAKIKLIKQELDKYKNAVTELQLLMQSTPATNNQARGSGSGRSLGFLLGVGSAIAS
GVAVSKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSKVLDLKNYIDKQLLPIVNKQSCSIP

NIETVIEFQQKNNRLLEITREFSVNAGVTTPVSTYMLTNSELLSLINDMPITNDQKKLMSNNVQI
VRQQSYSIMSIIKEEVLAYVVQLPLYGVIDTPCWKLHTSPLCTTNTKEGSNICLTRTDRGWYCDN
AGSVSFFPQAETCKVQSNRVFCDTMNSLTLPSEVNLCNVDIFNPKYDCKIMTSKTDVSSSVITSL
GAIVSCYGKTKCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVGNTLYYVNKQEGKSLYVKGEPII
NFYDPLVFPSDQFDASISQVNEKINQSLAFIR(KSDELL)GSGGSGSGEKAAKAEEAARKMEELF
KKHKIVAVLRANSVEEAIEKAVAVFAGGVHLIEITFTVPDADTVIKALSVLKEKGAIIGAGTVTS
VEQCRKAVESGAEFIVSPHLDEEISQFCKEKGVFYMPGVMTPTELVKAMKLGHTILKLFPGEVVG
PQFVKAMKGPFPNVKFVPTGGVNLDNVCEWFKAGVLAVGVGSALVKGTPDEVREKAKAFVEKIRG
CTE

HMPV-F with A113C, A339C, T160F, I177L - foldon-I53-50A embodiment (SEQ ID NO:95)

(MSWKVVIIFSLLITPQHG)LKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVGDVENLTCSDG
PSLIKTELDLTKSALRELKTVSADQLAREEQIENPRQSRFVLGAIALGVCTAAAVTAGVAIAKTI
RLESEVTAIKNALKTTNEAVSTLGNGVRVLAFAVRELKDFVSKNLTRALNKNKCDIDDLKMAVSF
SQFNRRFLNVVRQFSDNAGITPAISLDLMTDAELARAVSNMPTSAGQIKLMLENRAMVRRKGFGI
LIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSGKKGNYACLLREDQGWYCQNAGSTVYYPNE
KDCETRGDHVFCDTACGINVAEQSKECNINISTTNYPCKVSTGRHPISMVALSPLGALVACYKGV
SCSIGSNRVGIIKQLNKGCSYITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPE
DQFNVALDQVFENIENSQALVDQSNRILSSAEKGNTGGYIPEAPRDGQAYVRKDGEWVLLSTFLG
SGSHHHHHHHHGGSGGSGSEKAAKAEEAARKMEELFKKHKIVAVLRANSVEEAIEKAVAVFAGGV
HLIEITFTVPDADTVIKALSVLKEKGAIIGAGTVTSVEQCRKAVESGAEFIVSPHLDEEISQFCK
EKGVFYMPGVMTPTELVKAMKLGHTILKLFPGEVVGPQFVKAMKGPFPNVKFVPTGGVNLDNVCE
WFKAGVLAVGVGSALVKGTPDEVREKAKAFVEKIRGCTE

HMPV-F with A113C, A339C, T160F, I177L-I53-50A F10 embodiment (SEQ ID NO:96)

(MSWKVVIIFSLLITPQHG)LKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVGDVENLTCSDG
PSLIKTELDLTKSALRELKTVSADQLAREEQIENPRQSRFVLGAIALGVCTAAAVTAGVAIAKTI
RLESEVTAIKNALKTTNEAVSTLGNGVRVLAFAVRELKDFVSKNLTRALNKNKCDIDDLKMAVSF
SQFNRRFLNVVRQFSDNAGITPAISLDLMTDAELARAVSNMPTSAGQIKLMLENRAMVRRKGFGI
LIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSGKKGNYACLLREDQGWYCQNAGSTVYYPNE
KDCETRGDHVFCDTACGINVAEQSKECNINISTTNYPCKVSTGRHPISMVALSPLGALVACYKGV
SCSIGSNRVGIIKQLNKGCSYITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPE
DQFNVALDQVFENIENSQALVDQSNRILSSAEKGNTGGSGGSGSGEKAAKAEEAARKMEELFKKH
KIVAVLRANSVEEAIEKAVAVFAGGVHLIEITFTVPDADTVIKALSVLKEKGAIIGAGTVTSVEQ
CRKAVESGAEFIVSPHLDEEISQFCKEKGVFYMPGVMTPTELVKAMKLGHTILKLFPGEVVGPQF
VKAMKGPFPNVKFVPTGGVNLDNVCEWFKAGVLAVGVGSALVKGTPDEVREKAKAFVEKIRGCTE

HMPV-F with A113C, A120C, A339C, T160F, I177L, and Q426C - foldon-I53-50A embodiment (SEQ ID NO:97)

(MSWKVVIIFSLLITPQHG)LKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVGDVENLTCSDG
PSLIKTELDLTKSALRELKTVSADQLAREEQIENPRQSRFVLGAIALGVCTAAAVTCGVAIAKTI
RLESEVTAIKNALKTTNEAVSTLGNGVRVLAFAVRELKDFVSKNLTRALNKNKCDIDDLKMAVSF
SQFNRRFLNVVRQFSDNAGITPAISLDLMTDAELARAVSNMPTSAGQIKLMLENRAMVRRKGFGI
LIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSGKKGNYACLLREDQGWYCQNAGSTVYYPNE
KDCETRGDHVFCDTACGINVAEQSKECNINISTTNYPCKVSTGRHPISMVALSPLGALVACYKGV
SCSIGSNRVGIIKQLNKGCSYITNQDADTVTIDNTVYCLSKVEGEQHVIKGRPVSSSFDPIKFPE
DQFNVALDQVFENIENSQALVDQSNRILSSAEKGNTGGYIPEAPRDGQAYVRKDGEWVLLSTFLG
SGSHHHHHHHHGGSGGSGSEKAAKAEEAARKMEELFKKHKIVAVLRANSVEEAIEKAVAVFAGGV
HLIEITFTVPDADTVIKALSVLKEKGAIIGAGTVTSVEQCRKAVESGAEFIVSPHLDEEISQFCK
EKGVFYMPGVMTPTELVKAMKLGHTILKLFPGEVVGPQFVKAMKGPFPNVKFVPTGGVNLDNVCE
WFKAGVLAVGVGSALVKGTPDEVREKAKAFVEKIRGCTE

HMPV-F with A113C, A120C, A339C, T160F, I177L, and Q426C - F10 embodiment (SEQ ID NO:98)

(MSWKVVIIFSLLITPQHG)LKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVGDVENLTCSDG
PSLIKTELDLTKSALRELKTVSADQLAREEQIENPRQSRFVLGAIALGVCTAAAVTCGVAIAKTI
RLESEVTAIKNALKTTNEAVSTLGNGVRVLAFAVRELKDFVSKNLTRALNKNKCDIDDLKMAVSF
SQFNRRFLNVVRQFSDNAGITPAISLDLMTDAELARAVSNMPTSAGQIKLMLENRAMVRRKGFGI
LIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSGKKGNYACLLREDQGWYCQNAGSTVYYPNE
KDCETRGDHVFCDTACGINVAEQSKECNINISTTNYPCKVSTGRHPISMVALSPLGALVACYKGV
SCSIGSNRVGIIKQLNKGCSYITNQDADTVTIDNTVYCLSKVEGEQHVIKGRPVSSSFDPIKFPE
DQFNVALDQVFENIENSQALVDQSNRILSSAEKGNTGGSGGSGSGEKAAKAEEAARKMEELFKKH
KIVAVLRANSVEEAIEKAVAVFAGGVHLIEITFTVPDADTVIKALSVLKEKGAIIGAGTVTSVEQ
CRKAVESGAEFIVSPHLDEEISQFCKEKGVFYMPGVMTPTELVKAMKLGHTILKLFPGEVVGPQF
VKAMKGPFPNVKFVPTGGVNLDNVCEWFKAGVLAVGVGSALVKGTPDEVREKAKAFVEKIRGCTE

HMPV-F 115-BV (A185P) -foldon-I53-50A embodiment (SEQ ID NO:99)

(MSWKVVIIFSLLITPQHG)LKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVGDVENLTCADG
PSLIKTELDLTKSALRELRTVSADQLAREEQIENPRRRRFVLGAIALGVATAAAVTAGVAIAKTI
RLESEVTAIKNALKKTNEAVSTLGNGVRVLATAVRELKDFVSKNLTRAINKNKCDIPDLKMAVSF
SQFNRRFLNVVRQFSDNAGITPAISLDLMTDAELARAVSNMPTSAGQIKLMLENRAMVRRKGFGI
LIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYCQNAGSTVYYPNE
KDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPCKVSTGRHPISMVALSPLGALVACYKGV
SCSIGSNRVGIIKQLNKGCSYITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPVKFPE

DQFNVALDQVFESIENSQALVDQSNRILSSAEKGNTGYIPEAPRDGQAYVRKDGEWVLLSTFLGS
GSHHHHHHHHGGSGGSGSEKAAKAEEAARKMEELFKKHKIVAVLRANSVEEAIEKAVAVFAGGVH
LIEITFTVPDADTVIKALSVLKEKGAIIGAGTVTSVEQCRKAVESGAEFIVSPHLDEEISQFCKE
KGVFYMPGVMTPTELVKAMKLGHTILKLFPGEVVGPQFVKAMKGPFPNVKFVPTGGVNLDNVCEW
FKAGVLAVGVGSALVKGTPDEVREKAKAFVEKIRGCTE

HMPV-F 115-BV (A185P)-I53-50A - F10 embodiment (SEQ ID NO:100)

(MSWKVVIIFSLLITPQHG)LKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVGDVENLTCADG
PSLIKTELDLTKSALRELRTVSADQLAREEQIENPRRRRFVLGAIALGVATAAAVTAGVAIAKTI
RLESEVTAIKNALKKTNEAVSTLGNGVRVLATAVRELKDFVSKNLTRAINKNKCDIPDLKMAVSF
SQFNRRFLNVVRQFSDNAGITPAISLDLMTDAELARAVSNMPTSAGQIKLMLENRAMVRRKGFGI
LIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYCQNAGSTVYYPNE
KDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPCKVSTGRHPISMVALSPLGALVACYKGV
SCSIGSNRVGIIKQLNKGCSYITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPVKFPE
DQFNVALDQVFESIENSQALVDQSNRILSSAEKGNTGSGGSGSGEKAAKAEEAARKMEELFKKHK
IVAVLRANSVEEAIEKAVAVFAGGVHLIEITFTVPDADTVIKALSVLKEKGAIIGAGTVTSVEQC
RKAVESGAEFIVSPHLDEEISQFCKEKGVFYMPGVMTPTELVKAMKLGHTILKLFPGEVVGPQFV
KAMKGPFPNVKFVPTGGVNLDNVCEWFKAGVLAVGVGSALVKGTPDEVREKAKAFVEKIRGCTE

Second assemblies

The nanostructures of the invention may comprise multiple copies of a trimeric first assembly and multiple copies of a second assembly. The second assembly comprises a protein-protein interface that induces multiple copies of the second polypeptide to self-associate to form the second assemblies. Multiple oligomeric states of the second assembly may be compatible with nanostructure formation, including dimeric (two copies), trimeric (three copies), tetrameric (four copies), pentameric (five copies), hexameric (six copies), or higher oligomeric states. Each copy of the second assembly further comprises a surface-exposed interface that interacts with a complementary surface-exposed interface on a trimeric assembly domain. As described in King et al., Bale et al., and patent publications WO2014124301 A1 and US20160122392 A1, the complementary interface between the trimeric assembly domain and second assembly domain drives the assembly of multiple copies of the trimeric assembly domain and second assembly domain to a target nanostructure. In various specific embodiments:

(a) when each first polypeptide is DS-Cav1-foldon-T33-31A (SEQ ID NO:69) or DS-Cav1-T33-31A (SEQ ID NO:70), each second polypeptide is T33-31B (SEQ ID NO:44);

(b) when each first polypeptide is DS-Cav1-foldon-T33-15B (SEQ ID NO:71) or DS-Cav1-T33-15B (SEQ ID NO:72), each second polypeptide is T33-15A (SEQ ID NO:45);

(c) when each first polypeptide is DS-Cav1-foldon-I53-50A (SEQ ID NO:73) or DS-Cav1-I53-50A (SEQ ID NO:74), each second polypeptide is I53-50B (SEQ ID NO:8), I53-50B.1 (SEQ ID NO:32), I53-50B.1NegT2 (SEQ ID NO:33), or I53-50B.4PosT1 (SEQ ID NO:34);

(d) when each first polypeptide is DS-Cav1-I32-28A (SEQ ID NO:75), each second polypeptide is I32-28B.

Assembly of full valency nanostructures by in vitro assembly of two components

In some embodiments, each trimeric first assembly of the nanostructure bears an identical F protein as a genetic fusion; these nanostructures display the F protein at full (100%) valency. Such nanostructures are produced from purified first polypeptides and second polypeptides in a process called in vitro assembly. Purified trimeric first polypeptides comprising an F protein, are mixed with appropriate second polypeptides in an approximately 1:1 molar ratio in aqueous conditions (see Fig. 1). The second assembly interacts with the trimeric first assembly in order to drive assembly of the target nanostructure. Successful assembly of the target nanostructure can be confirmed by analyzing the in vitro assembly reaction by common biochemical or biophysical methods used to assess the physical size of proteins or protein assemblies, including but not limited to size exclusion chromatography, native (non-denaturing) gel electrophoresis, dynamic light scattering, multi-angle light scattering, analytical ultracentrifugation, negative stain electron microscopy, cryo-electron microscopy, or X-ray crystallography. If necessary, the assembled nanostructure can be purified from other species or molecules present in the in vitro assembly reaction using preparative techniques commonly used to isolate proteins by their physical size, including but not limited to size exclusion chromatography, preparative ultracentrifugation, tangential flow filtration, or preparative gel electrophoresis. The presence of the F protein in the nanostructure can be assessed by techniques commonly used to determine the identity of protein molecules in aqueous solutions, including but not limited to SDS-PAGE, mass spectrometry, protein sequencing, or amino acid analysis. The accessibility of the F protein on the exterior of the particle, as well as its conformation or antigenicity, can be assessed by techniques commonly used to detect the presence and conformation of an antigen, including but not

limited to binding by monoclonal antibodies, conformation-specific monoclonal antibodies, or anti-sera specific to the antigen.

In vitro assembly of partial valency nanostructures

In other embodiments, the nanostructures of the invention comprise one or more copies of trimeric first assemblies bearing F proteins as genetic fusions as well as one or more trimeric first assemblies that do not bear F proteins as genetic fusions; these nanostructures display the F proteins at partial valency. These partial valency nanostructures are produced by performing in vitro assembly with mixtures of first polypeptides in which the fraction of trimeric first assemblies bearing an F protein as a genetic fusion is equal to the desired valency of the antigen in the resulting nanostructure. The in vitro assembly reaction typically contains an approximately 1:1 molar ratio of total first polypeptides to total second polypeptides. By way of non-limiting example, performing an in vitro assembly reaction with a mixture of trimeric assemblies in which one half of the first polypeptides bear an F protein as a genetic fusion would yield an assembled nanostructure with an F protein valency of 50%. That is, 50% of the possible sites for F protein display on the nanostructure would be occupied. By way of non-limiting example, if the nanostructure is a 120-subunit assembly with icosahedral symmetry, the nanostructure comprises 20 total trimeric building blocks, and a 50% valency nanostructure displays 10 of the possible 20 F protein trimers. In this way, the ratio of F protein-bearing first polypeptides to first polypeptides lacking F proteins in an in vitro assembly reaction can be used to precisely tune the F protein valency of the resulting nanostructures. It will be understood by those of skill in the art that it is the average valency that can be tuned in this manner; the valency of individual nanostructures in the mixture will be a distribution centered around the average. Successful assembly of such partial valency nanostructures can be assessed using the techniques described above for evaluating full-valency nanostructures, and, if necessary, the partial valency nanostructures can be purified using the methods described for purifying full-valency nanostructures. The average valency of F protein-bearing first polypeptides in a given sample can be assessed by quantitative analysis using the techniques described above for evaluating the presence of F proteins in full-valency nanostructures.

In vitro assembly of nanostructures co-displaying multiple F proteins

In other embodiments, the nanostructures of the invention comprise two or more distinct first polypeptides bearing different F proteins as genetic fusions; these nanostructures co-display multiple different F proteins on the same nanostructure. These multi-antigen nanostructures are produced by performing in vitro assembly with mixtures of first polypeptides in which each first polypeptide bears one of two or more distinct F proteins as a genetic fusion. The fraction of each first polypeptide in the mixture determines the average valency of each F protein in the resulting nanostructures. The in vitro assembly reaction typically contains an approximately 1:1 molar ratio of total trimeric first polypeptides to total second polypeptides. The presence and average valency of each F protein-bearing first polypeptides in a given sample can be assessed by quantitative analysis using the techniques described above for evaluating the presence of F proteins in full-valency nanostructures.

In various embodiments, the nanostructures are between about 20 nanometers (nm) to about 40 nm in diameter, with interior lumens between about 15 nm to about 32 nm across and pore sizes in the protein shells between about 1 nm to about 14 nm in their longest dimensions.

In one embodiment, the nanostructure has icosahedral symmetry. In this embodiment, the nanostructure may comprise 60 copies of the first polypeptide and 60 copies of the second polypeptide. In one such embodiment, the number of identical first polypeptides in each first assembly is different than the number of identical second polypeptides in each second assembly. For example, in one embodiment, the nanostructure comprises twelve first assemblies and twenty second assemblies; in this embodiment, each first assembly may, for example, comprise five copies of the identical first polypeptide, and each second assembly may, for example, comprise three copies of the identical second polypeptide. In another embodiment, the nanostructure comprises twelve first assemblies and thirty second assemblies; in this embodiment, each first assembly may, for example, comprise five copies of the identical first polypeptide, and each second assembly may, for example, comprise two copies of the identical second polypeptide. In a further embodiment, the nanostructure comprises twenty first assemblies and thirty second assemblies; in this embodiment, each first assembly may, for example, comprise three copies of the identical first polypeptide, and each second assembly may, for example, comprise two copies of the identical second polypeptide. All of these embodiments are capable of forming synthetic nanomaterials with regular

icosahedral symmetry. In various further embodiments, oligomeric states of the first and second polypeptides are as follows:

I53-34A: trimer + I53-34B: pentamer;

I53-40A: pentamer + I53-40B: trimer;

I53-47A: trimer + I53-47B: pentamer;

I53-50A: trimer + I53-50B: pentamer;

I53-51A: trimer + I53-51B: pentamer;

I32-06A: dimer + I32-06B: trimer;

I32-19A: trimer + I32-19B: dimer;

I32-28A: trimer + I32-28B: dimer;

I52-03A: pentamer + I52-03B: dimer;

I52-32A: dimer + I52-32B: pentamer; and

I52-33A: pentamer + I52-33B: dimer

In another embodiment, the nanostructure of any embodiment or combination of embodiments of the invention has one or more of the following characteristics, each as demonstrated in the examples that follow:

(a) binds prefusion F-specific antibodies including but not limited to monoclonal antibody D25;

(b) forms a symmetrical structure, including but not limited to an icosahedral structure;

(c) is stable at 50°C; and/or

(d) is stable in 2.25M guanidine hydrochloride.

In another aspect, the present invention provides isolated nucleic acids encoding a fusion protein of the present invention. The isolated nucleic acid sequence may comprise RNA or DNA. As used herein, "isolated nucleic acids" are those that have been removed from their normal surrounding nucleic acid sequences in the genome or in cDNA sequences. Such isolated nucleic acid sequences may comprise additional sequences useful for promoting expression and/or purification of the encoded protein, including but not limited to polyA sequences, modified Kozak sequences, and sequences encoding epitope tags, export signals, and secretory signals, nuclear localization signals, and plasma membrane localization signals. It will be apparent to those of skill in the art, based on the teachings herein, what nucleic acid sequences will encode the proteins of the invention.

In a further aspect, the present invention provides recombinant expression vectors comprising the isolated nucleic acid of any embodiment or combination of embodiments of the invention operatively linked to a suitable control sequence. "Recombinant expression vector" includes vectors that operatively link a nucleic acid coding region or gene to any control sequences capable of effecting expression of the gene product. "Control sequences" operably linked to the nucleic acid sequences of the invention are nucleic acid sequences capable of effecting the expression of the nucleic acid molecules. The control sequences need not be contiguous with the nucleic acid sequences, so long as they function to direct the expression thereof. Thus, for example, intervening untranslated yet transcribed sequences can be present between a promoter sequence and the nucleic acid sequences and the promoter sequence can still be considered "operably linked" to the coding sequence. Other such control sequences include, but are not limited to, polyadenylation signals, termination signals, and ribosome binding sites. Such expression vectors can be of any type known in the art, including but not limited to plasmid and viral-based expression vectors. The control sequence used to drive expression of the disclosed nucleic acid sequences in a mammalian system may be constitutive (driven by any of a variety of promoters, including but not limited to, CMV, SV40, RSV, actin, EF) or inducible (driven by any of a number of inducible promoters including, but not limited to, tetracycline, ecdysone, steroid-responsive). The construction of expression vectors for use in transfecting prokaryotic cells is also well known in the art, and thus can be accomplished via standard techniques. (See, for example, Sambrook, Fritsch, and Maniatis, in: Molecular Cloning, A Laboratory Manual, Cold Spring Harbor Laboratory Press, 1989; Gene Transfer and Expression Protocols, pp. 109-128, ed. E.J. Murray, The Humana Press Inc., Clifton, N.J.), and the Ambion 1998 Catalog (Ambion, Austin, TX). The expression vector must be replicable in the host organisms either as an episome or by integration into host chromosomal DNA. In a preferred embodiment, the expression vector comprises a plasmid. However, the invention is intended to include other expression vectors that serve equivalent functions, such as viral vectors.

In another aspect, the present invention provides host cells that have been transfected with the recombinant expression vectors disclosed herein, wherein the host cells can be either prokaryotic or eukaryotic, such as mammalian cells. The cells can be transiently or stably transfected. Such transfection of expression vectors into prokaryotic and eukaryotic cells can be accomplished via any technique known in the art, including but not limited to standard bacterial transformations, calcium phosphate co-precipitation,

electroporation, or liposome mediated-, DEAE dextran mediated-, polycationic mediated-, or viral mediated transfection. (See, for example, Molecular Cloning: A Laboratory Manual (Sambrook, et al., 1989, Cold Spring Harbor Laboratory Press; Culture of Animal Cells: A Manual of Basic Technique, 2nd Ed. (R.I. Freshney. 1987. Liss, Inc. New York, NY). A method of producing a polypeptide according to the invention is an additional part of the invention. The method comprises the steps of (a) culturing a host according to this aspect of the invention under conditions conducive to the expression of the polypeptide, and (b) optionally, recovering the expressed polypeptide.

In a further aspect, the invention provides an immunogenic composition comprising an effective amount of the nanostructure of any embodiment or combination of embodiments of the invention and a pharmaceutically acceptable carrier. The composition may comprise (a) a lyoprotectant; (b) a surfactant; (c) a bulking agent; (d) a tonicity adjusting agent; (e) a stabilizer; (f) a preservative and/or (g) a buffer.

In some embodiments, the buffer in the pharmaceutical composition is a Tris buffer, a histidine buffer, a phosphate buffer, a citrate buffer or an acetate buffer. The composition may also include a lyoprotectant, e.g. sucrose, sorbitol or trehalose. In certain embodiments, the composition includes a preservative e.g. benzalkonium chloride, benzethonium, chlorohexidine, phenol, m-cresol, benzyl alcohol, methylparaben, propylparaben, chlorobutanol, o-cresol, p-cresol, chlorocresol, phenylmercuric nitrate, thimerosal, benzoic acid, and various mixtures thereof. In other embodiments, the composition includes a bulking agent, like glycine. In yet other embodiments, the composition includes a surfactant e.g., polysorbate-20, polysorbate-40, polysorbate- 60, polysorbate-65, polysorbate-80 polysorbate-85, poloxamer-188, sorbitan monolaurate, sorbitan monopalmitate, sorbitan monostearate, sorbitan monooleate, sorbitan trilaurate, sorbitan tristearate, sorbitan trioleaste, or a combination thereof. The composition may also include a tonicity adjusting agent, e.g., a compound that renders the formulation substantially isotonic or isoosmotic with human blood. Exemplary tonicity adjusting agents include sucrose, sorbitol, glycine, methionine, mannitol, dextrose, inositol, sodium chloride, arginine and arginine hydrochloride. In other embodiments, the composition additionally includes a stabilizer, e.g., a molecule which substantially prevents or reduces chemical and/or physical instability of the nanostructure, in lyophilized or liquid form. Exemplary stabilizers include sucrose, sorbitol, glycine, inositol, sodium chloride, methionine, arginine, and arginine hydrochloride.

The nanostructure may be the sole active agent in the composition, or the composition may further comprise one or more other agents suitable for an intended use, including but not limited to adjuvants to stimulate the immune system generally and improve immune responses overall. Any suitable adjuvant can be used. The term "adjuvant" refers to a compound or mixture that enhances the immune response to an antigen. Exemplary adjuvants include, but are not limited to, Adju-Phos™, Adjumer™, albumin-heparin microparticles, Algal Glucan, Algammulin, Alum, Antigen Formulation, AS-2 adjuvant, autologous dendritic cells, autologous PBMC, Avridine™, B7-2, BAK, BAY R1005, Bupivacaine, Bupivacaine-HCl, BWZL, Calcitriol, Calcium Phosphate Gel, CCR5 peptides, CFA, Cholera holotoxin (CT) and Cholera toxin B subunit (CTB), Cholera toxin A1-subunit-Protein A D-fragment fusion protein, CpG, CRL1005, Cytokine-containing Liposomes, D-Murapalmitine, DDA, DHEA, Diphtheria toxoid, DL-PGL, DMPC, DMPG, DOC/Alum Complex, Fowlpox, Freund's Complete Adjuvant, Gamma Inulin, Gerbu Adjuvant, GM-CSF, GMDP, hGM-CSF, hIL-12 (N222L), hTNF-alpha, IFA, IFN-gamma in pcDNA3, IL-12 DNA, IL-12 plasmid, IL-12/GMCSF plasmid (Sykes), IL-2 in pcDNA3, IL-2/Ig plasmid, IL-2/Ig protein, IL-4, IL-4 in pcDNA3, Imiquimod™, ImmTher™, Immunoliposomes Containing Antibodies to Costimulatory Molecules, Interferon-gamma, Interleukin-1 beta, Interleukin-12, Interleukin-2, Interleukin-7, ISCOM(s)™, Iscoprep 7.0.3™, Keyhole Limpet Hemocyanin, Lipid-based Adjuvant, Liposomes, Loxoribine, LT(R192G), LT-OA or LT Oral Adjuvant, LT-R192G, LTK63, LTK72, MF59, MONTANIDE ISA 51, MONTANIDE ISA 720, MPL.TM., MPL-SE, MTP-PE, MTP-PE Liposomes, Murametide, Murapalmitine, NAGO, nCT native Cholera Toxin, Non-Ionic Surfactant Vesicles, non-toxic mutant E112K of Cholera Toxin mCT-E112K, p-Hydroxybenzoique acid methyl ester, pCIL-10, pCIL12, pCMVmCAT1, pCMVN, Peptomer-NP, Pleuran, PLG, PLGA, PGA, and PLA, Pluronic L121, PMMA, PODDS™, Poly rA: Poly rU, Polysorbate 80, Protein Cochleates, QS-21, Quadri A saponin, Quil-A, Rehydragel HPA, Rehydragel LV, RIBI, Ribilike adjuvant system (MPL, TMD, CWS), S-28463, SAF-1, Sclavo peptide, Sendai Proteoliposomes, Sendai-containing Lipid Matrices, Span 85, Specol, Squalane 1, Squalene 2, Stearyl Tyrosine, Tetanus toxoid (TT), Theramide™, Threonyl muramyl dipeptide (TMDP), Ty Particles, and Walter Reed Liposomes. Selection of an adjuvant depends on the subject to be treated. Preferably, a pharmaceutically acceptable adjuvant is used.

In another aspect, the invention provides methods for generating an immune response to paramyxovirus and/or pneumovirus F protein in a subject, comprising

administering to the subject an effective amount of the immunogenic composition of any embodiment or combination of embodiments of the invention to generate the immune response. In a further aspect, the invention provides methods for treating or preventing a paramyxovirus and/or pneumovirus infection in a subject, comprising administering to the subject an effective amount of the immunogenic composition of any embodiment or combination of embodiments of the invention, thereby treating or preventing paramyxovirus and/or pneumovirus infection in the subject.

In one embodiment, the paramyxovirus and/or pneumovirus comprises respiratory syncytial virus. "Respiratory Syncytial Virus" and "RSV" refer to a negative-sense, single-stranded RNA virus that causes a respiratory disease, especially in children. When the method comprises treating an RSV infection, the immunogenic compositions are administered to a subject that has already been infected with the RSV, and/or who is suffering from symptoms (including but not limited to lower respiratory tract infections, upper respiratory tract infections, bronchiolitis, pneumonia, fever, listlessness, diminished appetite, recurrent wheezing, and asthma) indicating that the subject is likely to have been infected with the RSV. As used herein, "treat" or "treating" includes, but is not limited to accomplishing one or more of the following: (a) reducing paramyxovirus and/or pneumovirus titer in the subject; (b) limiting any increase of paramyxovirus and/or pneumovirus titer in the subject; (c) reducing the severity of paramyxovirus and/or pneumovirus symptoms; (d) limiting or preventing development of paramyxovirus and/or pneumovirus symptoms after infection; (e) inhibiting worsening of paramyxovirus and/or pneumovirus symptoms; (f) limiting or preventing recurrence of paramyxovirus and/or pneumovirus symptoms in subjects that were previously symptomatic for paramyxovirus and/or pneumovirus infection; and/or promoting maternal transmission of paramyxovirus and/or pneumovirus antibodies to infants (after maternal immunization).

When the method comprises limiting a paramyxovirus and/or pneumovirus infection, the immunogenic compositions are administered prophylactically to a subject that is not known to be infected, but may be at risk of exposure to the paramyxovirus and/or pneumovirus. As used herein, "limiting" means to limit RSV infection in subjects at risk of RSV infection. Groups at particularly high risk include children under age 18 (particularly infants 3 years or younger), adults over the age of 65, and individuals suffering from any type of immunodeficiency.

As used herein, an "effective amount" refers to an amount of the immunogenic composition that is effective for treating and/or limiting RSV infection. The immunogenic

compositions are typically formulated as a pharmaceutical composition, such as those disclosed above, and can be administered via any suitable route, including orally, parentally, by inhalation spray, rectally, or topically in dosage unit formulations containing conventional pharmaceutically acceptable carriers, adjuvants, and vehicles. The term parenteral as used herein includes, subcutaneous, intravenous, intra-arterial, intramuscular, intrasternal, intratendinous, intraspinal, intracranial, intrathoracic, infusion techniques or intraperitoneally. Polypeptide compositions may also be administered via microspheres, liposomes, immune-stimulating complexes (ISCOMs), or other microparticulate delivery systems or sustained release formulations introduced into suitable tissues (such as blood). Dosage regimens can be adjusted to provide the optimum desired response (e.g., a therapeutic or prophylactic response). A suitable dosage range may, for instance, be 0.1 ug/kg-100 mg/kg body weight of the F protein or antigenic fragment thereof. The composition can be delivered in a single bolus, or may be administered more than once (e.g., 2, 3, 4, 5, or more times) as determined by attending medical personnel.

In one embodiment, the administering results in production of paramyxovirus and/or pneumovirus neutralizing antibodies in the subject. In another embodiment, the neutralizing antibodies are present in sera of the subject at a titer ($1/ID_{50}$) of at least 1,000; in other embodiments, the neutralizing antibodies are present in sera of the subject at a titer of 2,000 or 5,000.

Examples

Methods:

Expression and screening of trimeric building blocks comprising an F protein and a trimeric assembly domain

Human codon-optimized sequences for trimeric building blocks including and lacking DS-Cav1 fusions were ordered from Genscript. Building blocks for single-component nanostructures (i.e., I3-01) were cloned into the pcDNA3.1 vector (ThermoFisher Scientific) containing one CMV promoter, while building blocks for two-component nanostructures (e.g., I53-50) were cloned into the pBudCE4.1™ vector (ThermoFisher Scientific) containing both CMV and EF-1α promoters. Recombinant proteins were expressed by transient transfection of Expi293F™ cells (ThermoFisher Scientific) using polyethylenimine (PEI). Cell cultures were harvested five days post-

transfection by centrifugation. Secreted proteins were analyzed by ELISA, using either direct coating of the cell supernatants or by sandwich ELISA. Briefly, 96-well MaxiSorp™ plates (Nunc) were coated with cell supernatant for direct ELISA or murine anti-His tag monoclonal antibody (ThermoFisher Scientific) for sandwich ELISA. Secreted proteins were detected using the human Palivizumab, MPE8, RSD5, and D25 monoclonal antibodies. Transfected Expi293F cells were fixed and permeabilized with BD cytofix/cytoperm (BD Biosciences), incubated with human Palivizumab, MPE8, and D25 monoclonal antibodies, and stained with Alexa Fluor 647-conjugated anti-human IgG antibody (Jackson ImmunoResearch). Stained cells were counted with a FACS Fortessa™ flow cytometer (BD Biosciences). Analysis was performed with FlowJo™ software. Cell lines were routinely tested for mycoplasma contamination.

Expression and purification of DS-Cav1-I53-50A

Lentivirus was produced by transient transfection of 293T (ATCC) cells using linear 25-kDa polyethyleneimine (PEI; Polysciences). Briefly, 4×10^6 cells were plated onto 10 cm tissue culture plates. After 24 h, 3 µg of psPAX2, 1.5 µg of pMD2G (Addgene™ plasmid #12260 and #12259, respectively) and 6 µg of lentiviral vector plasmid were mixed in 500 µl diluent (5 mM HEPES, 150 mM NaCl, pH = 7.05) and 42 µl of PEI (1 mg/ml) and incubated for 15 min. The DNA/PEI complex was then added to the plate drop-wise. Lentivirus was harvested 48 h post-transfection and concentrated 100-fold by low-speed centrifugation at 8000g for 18 h. Transduction of the target cell line was carried out in 125 mL shake flasks containing 10×10^6 cells in 10 mL of growth media. 100 uL of 100x lentivirus was added to the flask and the cells were incubated with shaking (225 rpm) at 37 °C, in 8% CO_2 for 4–6 h. 20 mL of growth media was added to the shake flask after 4–6 h.

Transduced cells were expanded every other day to a density of 1×10^6 cells/ml until a final culture size of 4 L was reached. The media was harvested after 17 days of total incubation after measuring final cell concentration (~5×10^6 cells/mL) and viability (~90% viable). Culture supernatant was harvested by low-speed centrifugation to remove cells from the supernatant. NaCl and NaN_3 were added to final concentrations of 250 mM and 0.02%, respectively. The supernatant was loaded over one 5 mL HisTrap™ FF Crude column (GE Healthsciences) at 5 ml/min by an AKTA Pure™ (GE Healthsciences). The nickel elution was applied to a HiLoad™ 16/600 Superdex 200 pg column (GE Healthsciences) to further purify the target protein by size-exclusion chromatography.

The size-exclusion purified target protein was snap frozen in liquid nitrogen and stored at -80 °C.

In vitro assembly of DS-Cav1-bearing nanostructures

100% valency particles (20 DS-Cav1 trimers per icosahedral nanostructure) were prepared by mixing DS-Cav1-foldon-I53-50A trimers and I53-50B.4PT1 pentamers at 50 μM each and incubating with rocking overnight at 4 °C. In some cases, assembled nanostructures were purified from excess components remaining in the in vitro assembly reaction using a GE Sephacryl S-500 HR 16/60 column in a buffer comprising 25 mM Tris pH 8, 250 mM NaCl, 5% glycerol. Sample load and SEC fractions were analyzed by SDS-PAGE in the presence and absence of reducing agent. Peak fractions were pooled, concentrated using a GE Vivaspin™ 20 30kDa MWCO centrifugal filter, and quantified using an Agilent 8454 spectrophotometer.

66% valency particles (~14 DS-Cav1 trimers per icosahedral nanostructure) were prepared by mixing DS-Cav1-foldon-I53-50A trimers, I53-50A trimers, and I53-50B.4PosT1 pentamers at 50, 25, and 75 μM, respectively. 33% valency particles (~7 DS-Cav1 trimers per icosahedral nanostructure) were prepared by mixing DS-Cav1-foldon-I53-50A trimers, I53-50A trimers, and I53-50B.4PosT1 pentamers at 25, 50, and 75 μM, respectively. The *in vitro* assembly reactions were allowed to incubate with rocking overnight at 4 °C. In some cases, assembled nanostructures were purified from excess components remaining in the in vitro assembly reaction using a GE Sephacryl™ S-500 HR 16/60 column in a buffer comprising 25 mM Tris pH 8, 250 mM NaCl, 5% glycerol. Sample load and SEC fractions were analyzed by SDS-PAGE in the presence and absence of reducing agent. Peak fractions were pooled, concentrated using a GE Vivaspin™ 20 30kDa MWCO centrifugal filter, and quantified using an Agilent 8454 spectrophotometer after centrifuging at ~21,000 g for 10 minutes at 4 °C. Samples were then transferred to cryogenic tubes in 1 mL aliquots at 1.1 mg/mL for the 33% valency particles and 0.6 mg/mL for the 66% valency particles, flash frozen in liquid nitrogen, and stored at -80 °C.

Electron microscopy of DS-Cav1-bearing nanostructures

Samples were prepared for negative stain EM by diluting to 0.01 mg/mL using 25 mM Tris pH 8, 250 mM NaCl, 5% glycerol and 3.5 μL was incubated on a glow-discharged, copper, carbon-coated grid for 20 seconds before blotting away the liquid

with a piece of Whatman No. 1 filter paper. Within seconds of blotting away the sample, a 3.5 µL droplet of stain (2% w/v uranyl formate) was deposited and blotted away immediately, and then a second cycle of staining/blotting was performed.

Circular dichroism (CD) spectropolarimetry

CD spectra from F proteins (0.5 mg ml^{-1}) were recorded on a Chirascan™ spectropolarimeter (Applied Photophysics) over the wavelength range of 195 to 260 nm at a bandwidth of 1 nm, step size of 0.5 nm, and 1 s per step. The spectra in the far-ultraviolet region required an average of three scans and were subtracted from blank spectra performed with buffer. Thermal denaturation was monitored by performing scans at intervals of 1 °C, after equilibration for 1 min at each temperature. Data were fitted to a simple first order curve. The values of ΔA222 are represented on the y axis as the percentage of the values recorded at 20 °C.

Enzyme-linked immunosorbent assay (ELISA)

To test specific binding of antibody or sera, 96-well MaxiSorp™ plates (Nunc) were coated with serial dilutions of tissue culture supernatants from cells expressing trimeric building blocks comprising F proteins and a trimeric assembly domain or 2 µg ml^{-1} of the following purified proteins: Ds-Cav1 with foldon, Ds-Cav1 fused to a trimeric first polypeptide or DS-Cav1-displaying nanostructures. Plates were blocked with 1% bovine serum albumin (BSA) and incubated with titrated antibodies (D25, MPE8, Palivizumab, RSD5) or murine sera followed by AP-conjugated goat anti-human IgG (Southern Biotech, 2040-04) or goat anti-mouse IgG (Southern Biotech, 1030-04). Plates were then washed with PBS buffer (Gibco, Invitrogen), 0.05% Tween-20 and substrate (p-NPP, Sigma) was added and plates were read at 405 nm.

Surface plasmon resonance (SPR)

The experiments were carried out at 25 °C on a ProteON™ XPR-36 instrument (Bio-Rad Laboratories) in a PBS buffer (Gibco, Invitrogen), 0.05% Tween-20. The D25 mAb was immobilized on a GLM sensor chip surface through amine coupling at 1000 response units (RU) and a blank surface with no protein was created under identical coupling conditions for use as a reference. Monoclonal antibodies (D25, MPE8, Palivizumab and 131-2a) were injected at a flow rate of 100 µl/min, at concentrations of 50 nM in different sensor channels. The data were processed using Proteon software and

double referenced by subtraction of the blank surface and buffer only injection before local fitting of the data.

Vaccination and Serological Analysis

Female BALB/c mice 6–9 weeks of age were obtained from ENVIGO Laboratories (Italy). All proteins were formulated with AddaVax™ adjuvant (Invivogen) according to the manufacturer's instruction. Mice were immunized subcutaneously (s.c) with a total protein dose corresponding to 5 µg of the DS-Cav1 antigen equivalent on day 0, 14, and 28 in 50% AddaVax™ in PBS. Mice were bled on day 24 and 40. Recovered sera were used to measure binding and neutralizing titers. Binding titers were measured by coating 3 µg/ml of DS-Cav1, I53-50 nanostructures or I53-50 nanostructure subunits.

Virus neutralization assay and microscopy analysis

Neutralization of RSV infection by sera was measured using a micro-neutralization flow cytometry-based assay. Serial dilutions of sera were pre-incubated with RSV for 1 hour at 37 °C and added to 10000 HEp-2 (ATCC® CCL-23™) cells/well in 96-well flat-bottom plates (MOI of 1). After 24 hours, cells were washed, detached and fixed with 2% formaldehyde. Percentage of GFP positive cells were measured by High throughput FACS with an Intellicyt coupled to an automated platform. The Tissue Culture Inhibiting Dilution (TCID) neutralizing 50% of the Infection ($TCID_{50}$) was calculated by nonlinear regression with Prism 7 (GraphPad Software).

Non-human primate (NHP) immunization

Rhesus macaques were immunized i.m. (right quadriceps) at weeks 0 and 4 with trimeric DS-Cav1 (50 µg; n=4) or DS-Cav1-foldon–I53-50 nanostructures (96 µg, comprising 50 µg of displayed DS-Cav1; n=5) formulated in the MF59-like adjuvant SWE. Sera were obtained at weeks 6 and 16 for serological analysis.

Stability of DS-Cav1-bearing nanostructures by relative binding to D25

Experiments were carried out at 20 °C on a ProteON™ XPR-36 instrument (Bio-Rad Laboratories) in a PBS buffer (Gibco, Thermo Fisher Scientific) and 0.05% Tween-20 (Sigma). 100 nM D25 antibody was immobilized on a GLM sensor chip surface through amine coupling (EDC/NHS chemistry) and a blank surface with no antibody was created under identical coupling conditions for use as a reference. Analyte proteins

(soluble DS-Cav1, soluble DS-Cav1–I53-50A and DS-Cav1-foldon–I53-50 nanostructures), heat stressed at different temperatures (20, 50, 70 or 80°C) for 1 h, were injected at a flow rate of 100 µl/ min, at a concentration of 50 nM in the different sensor channels. Data were processed using Proteon software and double referenced by subtraction of the blank surface and buffer-only injection before local fitting of the data.

Chemical denaturation of nanostructure-related proteins

Trimeric DS-Cav1, DS-Cav1–I53-50A, DS-Cav1–I53-50, I53-50, trimeric I53-50A, or pentameric I53-50B.4PT1 was diluted to a final concentration of 2.5 µM in 25 mM Tris pH 8, 250 mM NaCl, 5% glycerol with varying concentrations of guanidine hydrochloride, ranging from 0 M to 6.5 M, increasing in 0.25 M increments. Samples were prepared in triplicate and incubated for 16 hours at ambient temperature. On a Cary Eclipse Fluorescence Spectrophotometer, intrinsic fluorescence was measured for each guanidine hydrochloride concentration of each protein and of each replicate. A Peltier controller was used in the cell holder to maintain a temperature of 25 °C throughout all experiments. Using a 10 mm cell (Agilent Cuvette, part # 6610021600), fluorescence spectra were collected, exciting at 290 nm and scanning emission from 310 nm to 510 nm at a rate of 60 nm/ minute with a bandpass of 1 nm.

Statistical analysis

No statistical methods were used to predetermine sample size. Data were analyzed with Prism 6 (GraphPad™ Software) using the two-tailed non-parametric Mann-Whitney U test for two groups' comparison, or Kruskall-Wallis test (and Dunn's posttest) when three or more groups were compared.

Results

Trimeric building blocks comprising an F protein and a trimeric assembly domain

Several trimeric building blocks, each comprising an F protein genetically fused to a trimeric assembly domain, were found to be secreted from HEK293F cells with their F proteins in a well-folded, prefusion conformation as judged by prefusion-specific monoclonal antibody binding in ELISA assays. Fig. 2 shows an example of ELISA data analyzing the supernatant of HEK293F cells expressing DS-Cav1-foldon, DS-Cav1-

foldon-T33-31A, and DS-Cav1-T33-31A. Several other trimeric building blocks yielded detectable secretion of well-folded, prefusion F proteins.

Expression and purification of DS-Cav1-foldon-I53-50A

A lentiviral vector encoding DS-Cav1-foldon-I53-50A was used to transduce HEK293F cells for large-scale expression. The secreted protein was purified from tissue culture supernatants by immobilized metal affinity chromatography and size exclusion chromatography. Size exclusion chromatograms (Fig. 3) indicated that the purified protein formed a single, monodisperse species.

Expression and purification of I53-50B.4PT1

I53-50B.4PT1, a pentameric protein comprising a second assembly domain that interacts with the trimeric assembly domain in I53-50A or DS-Cav1-foldon-I53-50A to drive assembly of icosahedral I53-50-based nanostructures, was expressed and purified as described in Bale et al. and patent publication US20160122392 A1.

In vitro assembly and characterization of DS-Cav1-bearing I53-50 nanostructures

I53-50 is a 120-subunit two-component nanostructure with icosahedral symmetry comprising 20 trimeric (I53-50A) and 12 pentameric (I53-50B) building blocks, as recently described by Bale et al. The N terminus of I53-50A is exposed on the exterior of the I53-50 nanostructure, which enables the display of antigens on the nanostructure exterior through genetic fusion to the I53-530A N terminus. Purified DS-Cav1-foldon-I53-50A and I53-50B.4PT1 were assembled in vitro to form 120-subunit icosahedral nanostructures displaying various amounts of DS-Cav1 on the nanostructure exteriors by mixing the two purified proteins in various molar ratios. In separate preparations, nanostructures displaying DS-Cav1 at valencies of 100% (20 trimers), 66% (~14 trimers), and 33% (~7 trimers) were prepared as described above. The species present in the in vitro assembly reactions after overnight incubation were assessed by several techniques, including size exclusion chromatography-multi-angle light scattering (SEC-MALS), dynamic light scattering, and UV/vis spectroscopy. Assembled, 120-subunit nanostructures were purified from the in vitro assembly reactions using size exclusion chromatography (an example chromatogram obtained using the 100% valency nanostructures is presented in Fig. 4). The purified nanostructures were characterized by negative stain electron microscopy, which revealed fields of monodisperse particles in

which DS-Cav1 was clearly visible as spikes projecting outward from the core icosahedral I53-50 assembly (an example micrograph obtained using the 100% valency particles is presented in Fig. 5). ELISA assays using monoclonal antibodies specific to the prefusion conformation confirmed that the DS-Cav1 thus displayed on the nanostructure exteriors was well-folded and antigenically intact (Fig. 6). Surface plasmon resonance experiments evaluating the kinetics of monoclonal antibody binding revealed that antibody dissociation from the 100% valency DS-Cav1-foldon-I53-50 nanostructures was slower than from DS-Cav1-foldon trimers, likely due to avidity effects deriving from the multivalent presentation of DS-Cav1 on the nanostructure exterior (Fig. 6). Together, these experiments confirmed that the DS-Cav1-foldon-I53-50 nanostructures formed monodisperse, icosahedral nanostructures that display well-folded, antigenically intact DS-Cav1 trimers on their exteriors. These findings motivated experiments to evaluate the utility of the DS-Cav1-foldon-I53-50 nanostructures as immunogens for inducing humoral immune responses against DS-Cav1 in animals.

Immunogenicity of DS-Cav1-foldon-I53-50 nanostructures

The DS-Cav1-foldon-I53-50 nanostructures displaying DS-Cav1 at 33%, 66%, and 100% valency were injected into mice using a prime-boost strategy as described above. Additional groups of mice were injected with trimeric DS-Cav1-foldon as a benchmark for the humoral immune response induced against DS-Cav1 by the nanostructures or I53-50 nanostructures lacking displayed DS-Cav1 as negative controls for a DS-Cav1 specific response. ELISA assays of serum extracted from the mice at defined time points after the injections were used to measure DS-Cav1 specific antibody titers present in the sera of the injected animals (Fig. 7). As expected, sera from animals injected with the I53-50 nanostructures lacking displayed DS-Cav1 did not contain antibodies specific to DS-Cav1. Trimeric DS-Cav1-foldon induced DS-Cav1-specific antibodies, in accordance with previous results (McClellan et al.). The 33%, 66%, and 100% valency DS-Cav1 nanostructures all induced higher DS-Cav1-specific antibody titers than trimeric DS-Cav1-foldon, with the antibody titers increasing with increasing DS-Cav1 valency. DS-Cav1-specific titers were roughly 2.5-fold higher on average in mice injected with 100% valency DS-Cav1-foldon-I53-50 nanostructures compared to DS-Cav1. These results demonstrate that immunogens in which paramyxovirus F proteins are multivalently displayed on self-assembling protein nanostructures can induce higher humoral immune responses when injected into animals.

The sera from the mice injected with the series of immunogens described above was also evaluated for the presence of neutralizing antibody titers using the standard neutralization assay in HEp-2 cells (Fig. 8). The trend in serum neutralizing antibody titers correlated highly with the trend observed in DS-Cav1-specific binding antibody titers. Sera from animals injected with the I53-50 nanostructures lacking displayed DS-Cav1 did not neutralize virus, consistent with the lack of DS-Cav1-specific antibodies in these sera. The sera from animals injected with trimeric DS-Cav-1-foldon neutralized virus with an average titer ($1/ID_{50}$) of 3,030. The 33%, 66%, and 100% valency DS-Cav1-I53-50 nanostructures induced higher neutralizing antibody titers than trimeric DS-Cav1-foldon, with average titers of 9,400, 20,000, and 30,500, respectively. These results demonstrate that the higher humoral response induced by immunogens in which paramyxovirus F proteins are multivalently displayed on self-assembling protein nanostructures result in more effective virus neutralization.

The DS-Cav1-foldon-I53-50 nanostructures were also injected into Rhesus macaques to evaluate their immunogenicity in a primate immune system. The animals were injected intramuscularly at weeks 0 and 4 with either free DS-Cav1 trimer or DS-Cav1-foldon-I53-50 nanostructures displaying DS-Cav1 at 100% valency. In both cases, the dose of DS-Cav1 antigen was 50 μg, and the immunogens were formulated with the MF59-like, squalene-based oil-in-water emulsion adjuvant SWE. Sera obtained from the animals at weeks 6 and 16 were evaluated for anti-DS-Cav1 antibody titers and RSV-neutralizing antibody titers (Fig. 9). The results mirrored those obtained in mice. At week 16, the mean anti-DS-Cav1 antibody titer was 4-fold higher in animals injected with the DS-Cav1-foldon-I53-50 nanostructure compared to animals injected with trimeric DS-Cav1. The mean RSV-neutralizing antibody titer at week 16 was 16-fold higher in animals injected with the DS-Cav1-foldon-I53-50 nanostructure compared to animals injected with trimeric DS-Cav1. These results demonstrate, in a primate immune system, that immunogens in which paramyxovirus F proteins are multivalently displayed on self-assembling protein nanostructures induce more robust humoral immune responses, including high levels of virus-neutralizing antibodies, than the trimeric paramyxovirus F proteins alone.

Physical stabilization of DS-Cav1 by fusion to I53-50A

Given the key antigenic properties of prefusion F, we used two orthogonal approaches to measure the physical stability of DS-Cav1 when fused to I53-50A and/or

when further assembled into the icosahedral nanostructure. The first assay measured the retention of binding by a prefusion-specific mAb (D25) after thermal stress, an approach that has been used previously to characterize prefusion F stability (McLellan et al. 2013; Joyce et al. 2016; Krarup et al. 2015). Samples of trimeric DS-Cav1, trimeric DS-Cav1–I53-50A, and DS-Cav1–I53-50 nanostructures containing equivalent concentrations (50 nM) of DS-Cav1 were split into four aliquots and incubated at 20, 50, 70 or 80 °C for 1 hour. After cooling to room temperature, D25 binding was assayed by surface plasmon resonance (SPR). We found that all samples bound D25 equivalently at 20 and 50 °C, but lost most of their reactivity to D25 after 1 hour at 80 °C as previously reported for DS-Cav1 (McLellan et al. 2013; Joyce et al. 2016) (Fig. 10). Interestingly, while D25 was also unable to bind trimeric DS-Cav1 incubated at 70 °C for 1 hour, trimeric DS-Cav1–I53-50A and the DS-Cav1–I53-50 nanostructures retained 50 and 80% of their respective binding signals (Fig. 10). While the multivalent nature of the DS-Cav1–I53-50 nanostructures complicates direct quantitative comparisons to trimeric DS-Cav1, these results indicate that genetic fusion to the I53-50A trimer further stabilizes the prefusion conformation of DS-Cav1, and suggest that this increased stability is maintained in the context of the assembled nanostructure immunogen.

We used chemical denaturation in guanidine hydrochloride (GdnHCl), monitored by intrinsic tryptophan fluorescence, as a second, antibody-independent technique to evaluate physical stability. Analyzing fluorescence emission from DS-Cav1 incubated in 0–6.5 M GdnHCl revealed that the protein undergoes two subtly distinct transitions, one between 0.25 and 2.25 M GdnHCl and another between 2.25 and 5.75 M (Fig. 11). In contrast, only a single transition is apparent for trimeric DS-Cav1–I53-50A, occurring between 2.25 and 6.25 M GdnHCl (Fig. 11). It is unclear at present whether the transition at lower [GdnHCl] observed for DS-Cav1 is absent from trimeric DS-Cav1–I53-50A or simply shifted to higher [GdnHCl]. However, it is clear that the native conformation of DS-Cav1 is stabilized by genetic fusion to trimeric I53-50A, mirroring the results obtained by measuring D25 binding after thermal stress. Comparing the data for the DS-Cav1–I53-50 nanostructure and the I53-50 nanostructure alone (lacking fused DS-Cav1) indicated that the stabilization is maintained upon assembly to the icosahedral nanostructure (Fig. 11). The source of this effect is likely the extreme stability of the I53-50A trimer. I53-50A is derived from the KDPG aldolase of the hyperthermophilic

bacterium *T. maritima* and only began to exhibit changes in fluorescence at very high (≥ 5.75 M) GdnHCl concentrations (Fig. 11).

We made addition constructs to assess the number of GS repeats and the need for a stabilization domain such as the Foldon moiety.

Sequence Information

IPD Name	MS (Da)	Construct Information
RSV_F-10	74005.38	DS-Cav1-8GS-HelExt-50A
RSV_F-11	74293.64	DS-Cav1-12GS-HelExt-50A
RSV_F-12	74551.87	DS-Cav1-16GS-HelExt-50A
RSV_F-13	77212.97	DS-Cav1-foldon-10GS-HelExt-50A
RSV_F-14	77558.28	DS-Cav1-foldon-15GS-HelExt-50A
RSV_F-15	77933.62	DS-Cav1-foldon-20GS-HelExt-50A

Studies were based on expression yield in a small-scale transient transfection. Plasmids capable of expressing the relevant constructs were transformed into NEB 5α *E. coli* cells and selected on LB + carbenicillin agar plates. 1 mL cultures were prepared by inoculating TB media with a bacterial colony and again selecting with 50 ug/mL carbenicillin. A Qiagen Mini Prep kit was used to purify plasmid from the *E. coli* cultures in accordance with their protocol. Expi293F™ Cells (ThermoFisher) were cultured in Expi293™ Expression Medium (ThermoFisher) supplemented with penicillin (100 u/mL) and streptomycin (100 µg/mL) at 8% CO_2, 37° C, and 125 rpm shaking.

On the day prior to transfection, cells were seeded at a concentration of 2E6 cells/mL. On the day of transfection, cells were counted by a Countess II (ThermoFisher) with trypan blue to determine cell viability. Cell concentration was adjusted to 2.5E6 cells/mL, and cells where plated into untreated 12-well plates (Corning) in 1 mL volumes. 1 µg of DNA plasmid were transfected per each well using Expifectamine™ (ThermoFisher), following the manufacturer's directions. Enhancers, components of ThermoFisher's Expifectamine™ Transfection Kit, were added 18 hours after transfection. The 1 mL cultures were harvested 5 days post-transfection, and the cells were pelleted from the supernatant by centrifugation at 1,500xg for 5 minutes at 4° C. Supernatants were filtered through a 0.45 µM filter with a PVDF membrane.

Filtered supernatants containing DS-Cav1–I53-50A constructs were denatured and boiled for 10 minutes at 95° C for 10 minutes in 2x Laemmli buffer with 2-mercaptoethanol. SDS-PAGE separated the sample fractions, which were then transferred to a nitrocellulose membrane and probed with palivizumab, followed with a

secondary antibody, anti-human conjugated to HRP. Blot was imaged using Clarity Western ECL Blotting Substrate (Bio-Rad).

Filtered supernatants containing DS-Cav1–I53-50A constructs were bound to Nunc MaxiSorp™ 96-well plates in a two-fold dilution series. The pre-fusion conformation-specific antibody D25 was used to detect DS-Cav1–I53-50A, followed by a secondary anti-human antibody conjugated to HRP. Protein yield was determined colorimetrically via the substrate TMB and absorbances were collected at 450 nm.

The expression yields and binding of the prefusion-specific mAb D25 (data not shown) indicate that all constructs express well and are in the prefusion conformation. Those of skill in the art would have expected that a heterologous trimerization domain (such as the foldon) would be required for proper expression and folding of prefusion F constructs. Our results indicate that the I53-50A nanostructure component can support the expression and proper folding of DS-Cav1 without the use of a trimerization domain like the foldon. Binding of D25 to these constructs suggests that they are antigenically intact and would be expected to induce potent immune responses, including neutralizing antibodies, similarly to nanostructures comprising the DS-Cav1-foldon–I53-50 fusion polypeptide.

CLAIMS:

1. A nanostructure, comprising:

(a) a plurality of first assemblies, each first assembly comprising a plurality of identical first polypeptides, wherein the first polypeptides comprise an amino acid sequence having at least 75% identity to the amino acid sequence of a polypeptide selected from the group consisting of SEQ ID NOS:1-51;

(b) a plurality of second assemblies, each second assembly comprising a plurality of identical second polypeptides, wherein the second polypeptides comprise an amino acid sequence having at least 75% identity to the amino acid sequence of a polypeptide selected from the group consisting of SEQ ID NOS:1-51, wherein the second polypeptide differs from the first polypeptide;

wherein the plurality of first assemblies non-covalently interact with the plurality of second assemblies to form a nanostructure; and

wherein the nanostructure displays multiple copies of one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof, on an exterior of the nanostructure.

2. The nanostructure of claim 1, wherein:

(a) the first polypeptides comprise an amino acid sequence having at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to the amino acid sequence of a polypeptide selected from the group consisting of SEQ ID NOS:1-51; and

(b) the second polypeptides comprise an amino acid sequence having at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to the amino acid sequence of a polypeptide selected from the group consisting of SEQ ID NOS:1-51.

3. The nanostructure of claim 1 or 2, wherein each of the one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof, comprises

(a) an amino acid sequence having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to the amino acid sequence of a polypeptide selected from the group consisting of SEQ ID NOS:53, 61-68, and 101;

(b) an amino acid sequence having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to the amino acid sequence of an RSV F protein or mutant thereof selected from the group consisting of SEQ ID NO:53 and 61-64, wherein the protein

includes one or more of the following residues: 67I, 149C, 458C, 46G, 465Q, 215P, 92D, and 487Q; or

(c) an amino acid sequence having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to the amino acid sequence of an MPV F protein or mutant thereof selected from the group consisting of SEQ ID NO:65-68 and 101, wherein the protein includes one or more of the following residues: 113C, 120C, 339C, 160F, 177L, 185P, and 426C.

4. The nanostructure of any one of claims 1-3, wherein the first polypeptides and the second polypeptides comprise an amino acid sequence having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to the amino acid sequences selected from the following pairs:

SEQ ID NO:1 and SEQ ID NO:2 (I53-34A and I53-34B);
SEQ ID NO:3 and SEQ ID NO:4 (I53-40A and I53-40B);
SEQ ID NO:3 and SEQ ID NO:24 (I53-40A and I53-40B.1);
SEQ ID NO:23 and SEQ ID NO:4 (I53-40A.1 and I53-40B);
SEQ ID NO:35 and SEQ ID NO:36 (I53-40A genus and I53-40B genus);
SEQ ID NO:5 and SEQ ID NO:6 (I53-47A and I53-47B);
SEQ ID NO:5 and SEQ ID NO:27 (I53-47A and I53-47B.1);
SEQ ID NO:5 and SEQ ID NO:28 (I53-47A and I53-47B.1NegT2);
SEQ ID NO:25 and SEQ ID NO:6 (I53-47A.1 and I53-47B);
SEQ ID NO:25 and SEQ ID NO:27 (I53-47A.1 and I53-47B.1);
SEQ ID NO:25 and SEQ ID NO:28 (I53-47A.1 and I53-47B.1NegT2);
SEQ ID NO:26 and SEQ ID NO:6 (I53-47A.1NegT2 and I53-47B);
SEQ ID NO:26 and SEQ ID NO:27 (I53-47A.1NegT2 and I53-47B.1);
SEQ ID NO:26 and SEQ ID NO:28 (I53-47A.1NegT2 and I53-47B.1NegT2);
SEQ ID NO:37 and SEQ ID NO:38 (I53-47A genus and I53-47B genus);
SEQ ID NO:7 and SEQ ID NO:8 (I53-50A and I53-50B);
SEQ ID NO:7 and SEQ ID NO:32 (I53-50A and I53-50B.1);
SEQ ID NO:7 and SEQ ID NO:33 (I53-50A and I53-50B.1NegT2);
SEQ ID NO:7 and SEQ ID NO:34 (I53-50A and I53-50B.4PosT1);
SEQ ID NO:29 and SEQ ID NO:8 (I53-50A.1 and I53-50B);

SEQ ID NO:29 and SEQ ID NO:32 (I53-50A.1 and I53-50B.1);
SEQ ID NO:29 and SEQ ID NO:33 (I53-50A.1 and I53-50B.1NegT2);
SEQ ID NO:29 and SEQ ID NO:34 (I53-50A.1 and I53-50B.4PosT1);
SEQ ID NO:30 and SEQ ID NO:8 (I53-50A.1NegT2 and I53-50B);
SEQ ID NO:30 and SEQ ID NO:32 (I53-50A.1NegT2 and I53-50B.1);
SEQ ID NO:30 and SEQ ID NO:33 (I53-50A.1NegT2 and I53-50B.1NegT2);
SEQ ID NO:30 and SEQ ID NO:34 (I53-50A.1NegT2 and I53-50B.4PosT1);
SEQ ID NO:31 and SEQ ID NO:8 (I53-50A.1PosT1 and I53-50B);
SEQ ID NO:31 and SEQ ID NO:32 (I53-50A.1PosT1 and I53-50B.1);
SEQ ID NO:31 and SEQ ID NO:33 (I53-50A.1PosT1 and I53-50B.1NegT2);
SEQ ID NO:31 and SEQ ID NO:34 (I53-50A.1PosT1 and I53-50B.4PosT1);
SEQ ID NO:39 and SEQ ID NO:40 (I53-50A genus and I53-50B genus);
SEQ ID NO:9 and SEQ ID NO:10 (I53-51A and I53-51B);
SEQ ID NO:11 and SEQ ID NO:12 (I52-03A and I52-03B);
SEQ ID NO:13 and SEQ ID NO:14 (I52-32A and I52-32B);
SEQ ID NO:15 and SEQ ID NO:16 (I52-33A and I52-33B)
SEQ ID NO:17 and SEQ ID NO:18 (I32-06A and I32-06B);
SEQ ID NO:19 and SEQ ID NO:20 (I32-19A and I32-19B);
SEQ ID NO:21 and SEQ ID NO:22 (I32-28A and I32-28B);
SEQ ID NO:23 and SEQ ID NO:24 (I53-40A.1 and I53-40B.1);
SEQ ID NO:41 and SEQ ID NO:42 (T32-28A and T32-28B);
SEQ ID NO:43 and SEQ ID NO:44 (T33-09A and T33-09B);
SEQ ID NO:45 and SEQ ID NO:46 (T33-15A and T33-15B);
SEQ ID NO:47 and SEQ ID NO:48 (T33-21A and T33-21B);
SEQ ID NO:49 and SEQ ID NO:50 (T33-28A and T32-28B); and
SEQ ID NO:51 and SEQ ID NO:44 (T33-31B and T33-09B (also referred to as T33-31B)).

5. The nanostructure of any one of claims 1-4, wherein the first polypeptides comprise polypeptides having at least 95%, 96%, 97%, 98%, 99%, or 100% identity along their full length to the amino acid sequence of I53-50A (SEQ ID NO: 7) and the second polypeptides comprise polypeptides having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%,

99%, or 100% identity along their full length to the amino acid sequence of I53-50B (SEQ ID NO: 34).

6. The nanostructure of any one of claims 1-5, wherein the one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof, are expressed as a fusion protein with the first polypeptides.

7. The nanostructure of claim 6, wherein
(a) the plurality of first assemblies each comprise identical fusion proteins; or
(b) the plurality of first assemblies in total comprise two or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof.

8. The nanostructure of claim 7, wherein only a subset of the first polypeptides comprise a fusion protein with an F protein or antigenic fragment thereof.

9. The nanostructure of any one of claims 1-8, wherein each first assembly comprises a homotrimer of the first polypeptide.

10. The nanostructure of any one of claims 1-9, wherein the one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof comprises an amino acid sequence having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to the amino acid sequence of DS-Cav1 (SEQ ID NO:53).

11. The nanostructure of any one of claims 1-10, wherein the one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragments thereof comprises an amino acid sequence having at least 95% identity to the amino acid sequence of DS-Cav1 (SEQ ID NO:53).

12. The nanostructure of any one of claims 5-11, wherein each fusion protein comprises an amino acid linker positioned between the first polypeptide and the one or more paramyxovirus and/or pneumovirus F proteins, or antigenic fragment thereof.

13. The nanostructure of claim 12, wherein the amino acid linker sequence comprises one or more trimerization domain.

14. The nanostructure of claim 12 or 13, wherein the amino acid linker sequence (a) comprises the amino acid sequence GYIPEAPRDGQAYVRKDGEWVLLSTFL (SEQ ID NO:54) or (b) comprises a Gly-Ser linker.

15. The nanostructure of any one of claims 6-14, wherein the fusion protein comprises an amino acid sequence having at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to the amino acid sequence selected from the group consisting of SEQ ID NOS:69-100.

16. The nanostructure of claim 11, wherein each first polypeptide comprises a fusion protein of DS-Cav1 (SEQ ID NO:53) linked to SEQ ID NO:7 (I53-50A) via an amino acid linker.

17. The nanostructure of claim 16, wherein the amino acid linker comprises a Gly-Ser linker and/or a helical extension domain.

18. A recombinant nucleic acid encoding the first polypeptide fusion protein as recited in any one of claims 6-17.

19. A recombinant expression vector comprising the recombinant nucleic acid of claim 18 operatively linked to a promoter.

20. A recombinant host cell, comprising one or more recombinant expression vectors capable of expressing the first polypeptides and the second polypeptides of any one of claims 1-17, or the vector of claim 19.

21. An immunogenic composition comprising the nanostructure of any one of claims 1-17, and a pharmaceutically acceptable carrier.

22. The immunogenic composition of claim 21, further comprising an adjuvant.

23. A process for assembling the nanostructures of any one of claims 1-17 in vitro, comprising mixing two or more nanostructure components in aqueous conditions to drive spontaneous assembly of the desired nanostructure.

24. A nanostructure produced by the process of claim 23.

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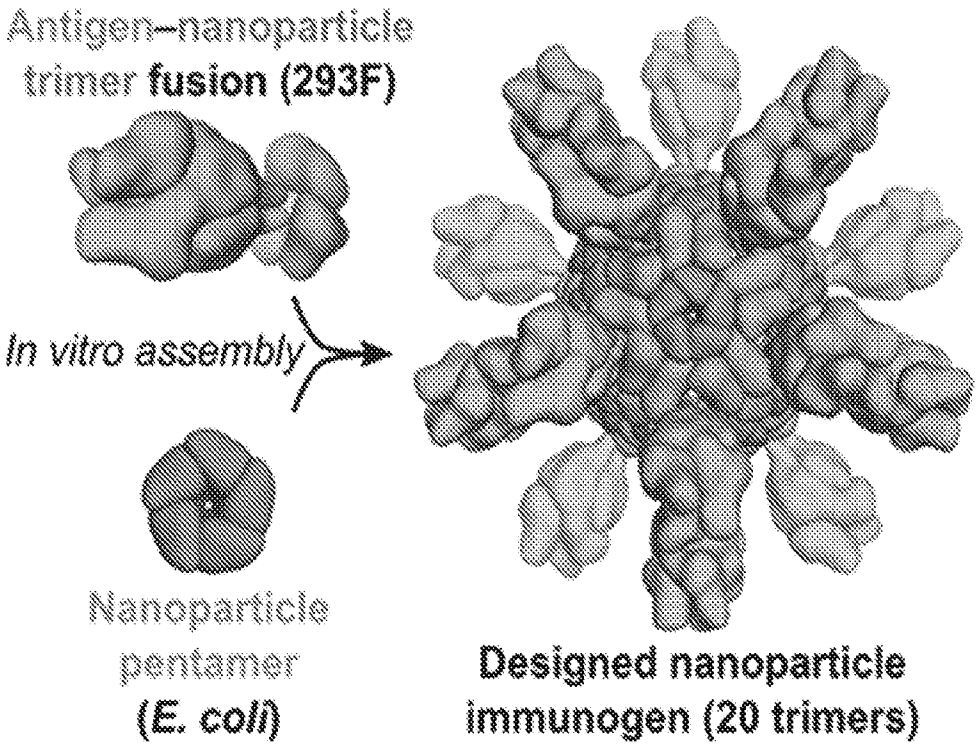
Antigen–nanoparticle
trimer fusion (293F)
In vitro assembly
Nanoparticle
pentamer
(E. coli)
Designed nanoparticle
immunogen (20 trimers)

FIG. 1

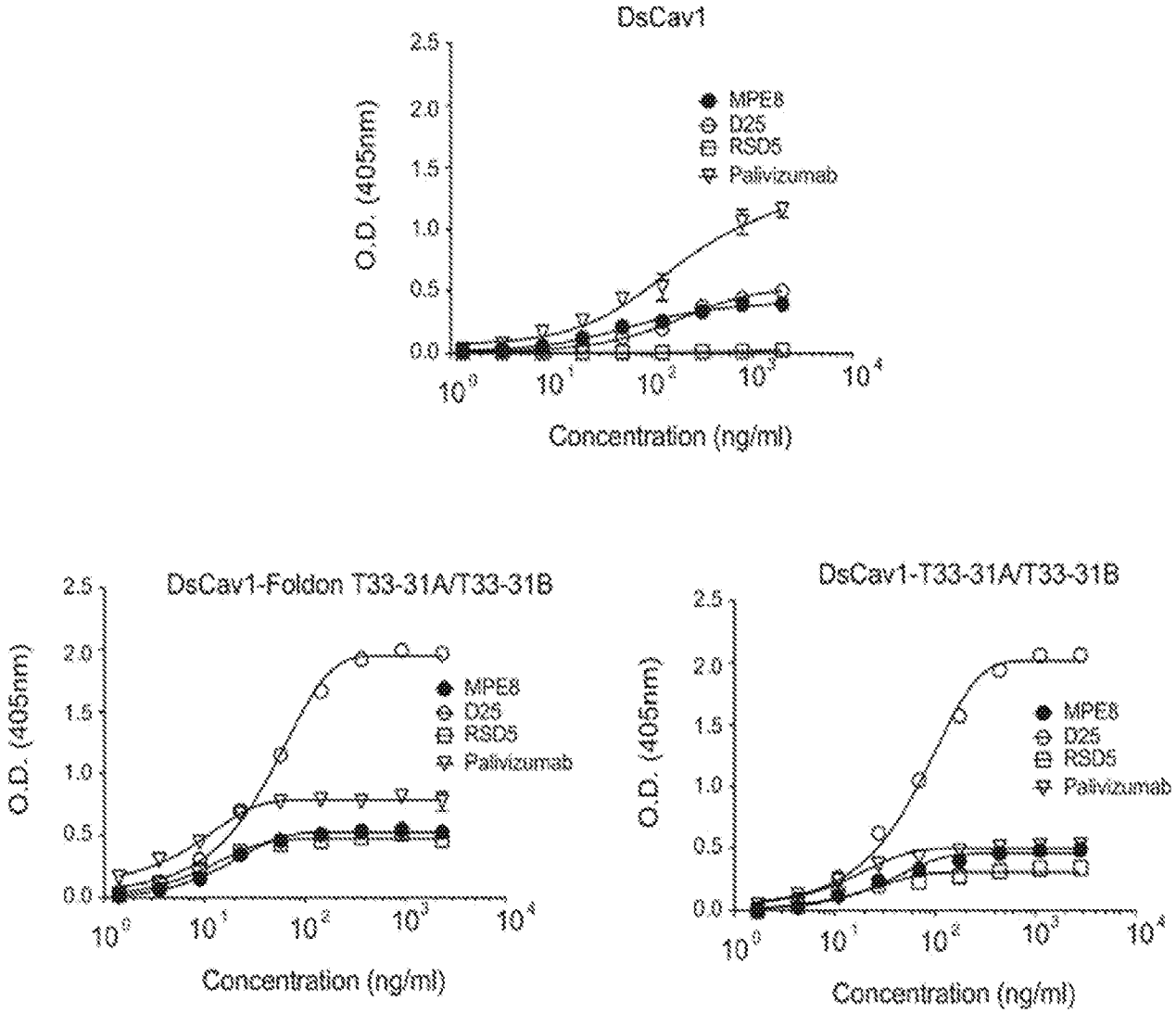
DsCav1
O.D. (405nm)
Concentration (ng/ml)
MPE8
D25
RSD5
Palivizumab
DsCav1-Foldon T33-31A/T33-31B
DsCav1-T33-31A/T33-31B

FIG. 2

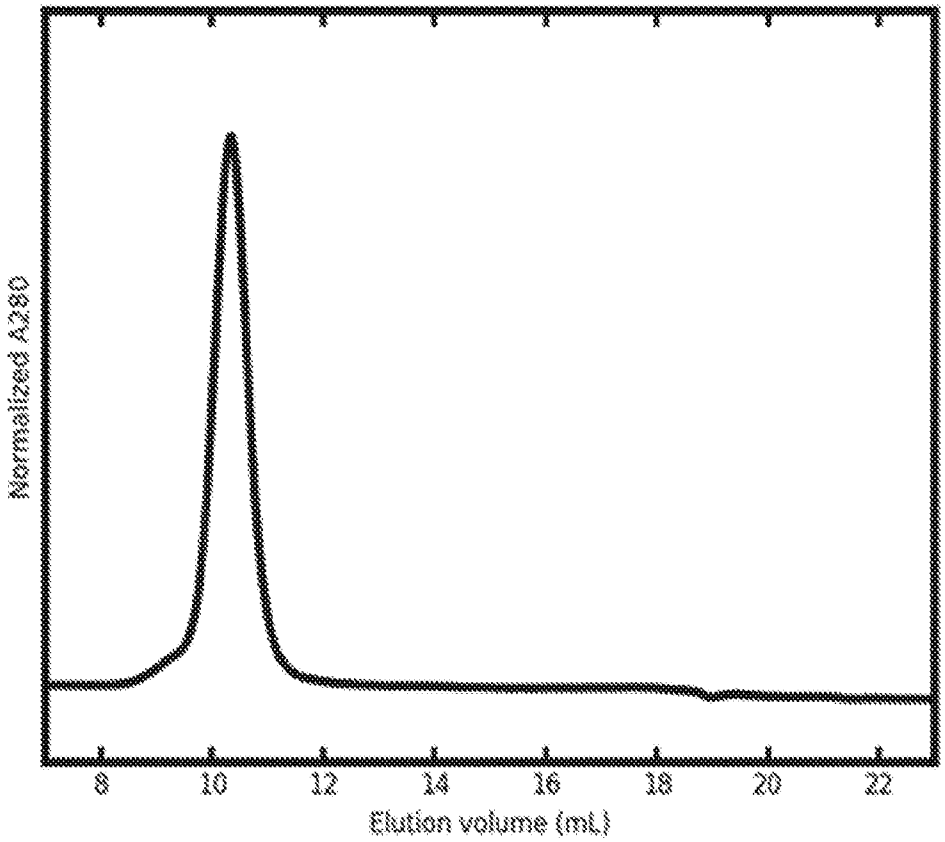

FIG. 3

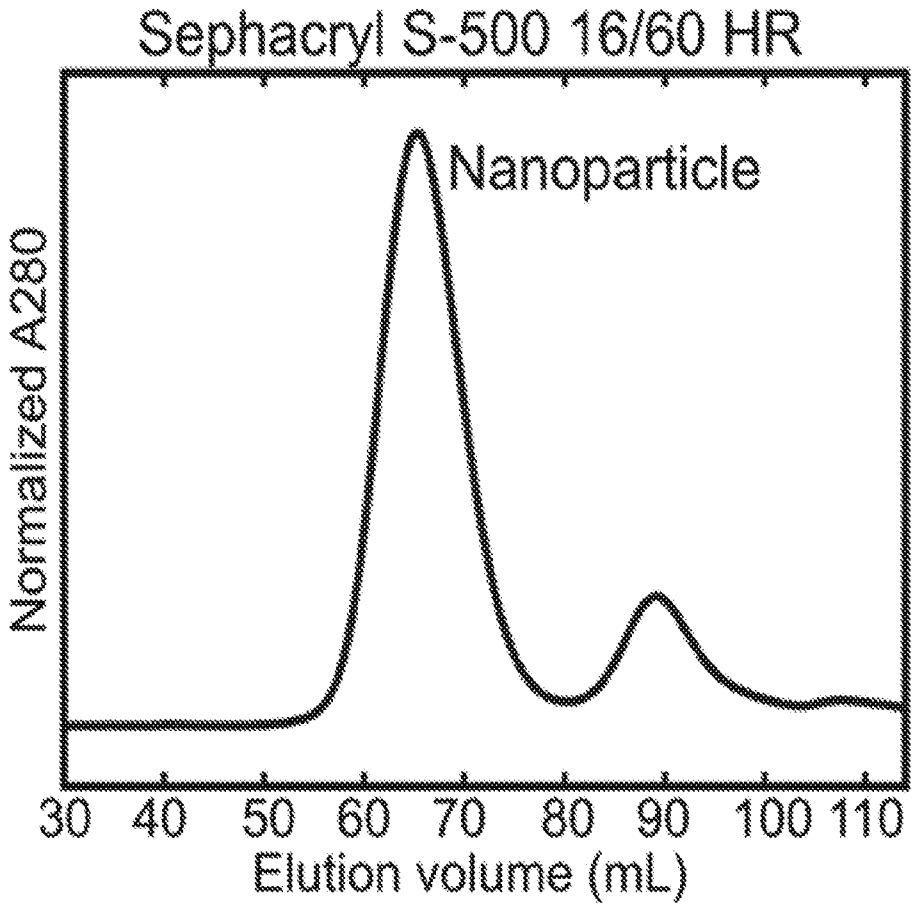
Sephacryl S-500 16/60 HR
Nanoparticle
Normalized A280
30 40 50 60 70 80 90 100 110
Elution volume (mL)

FIG. 4

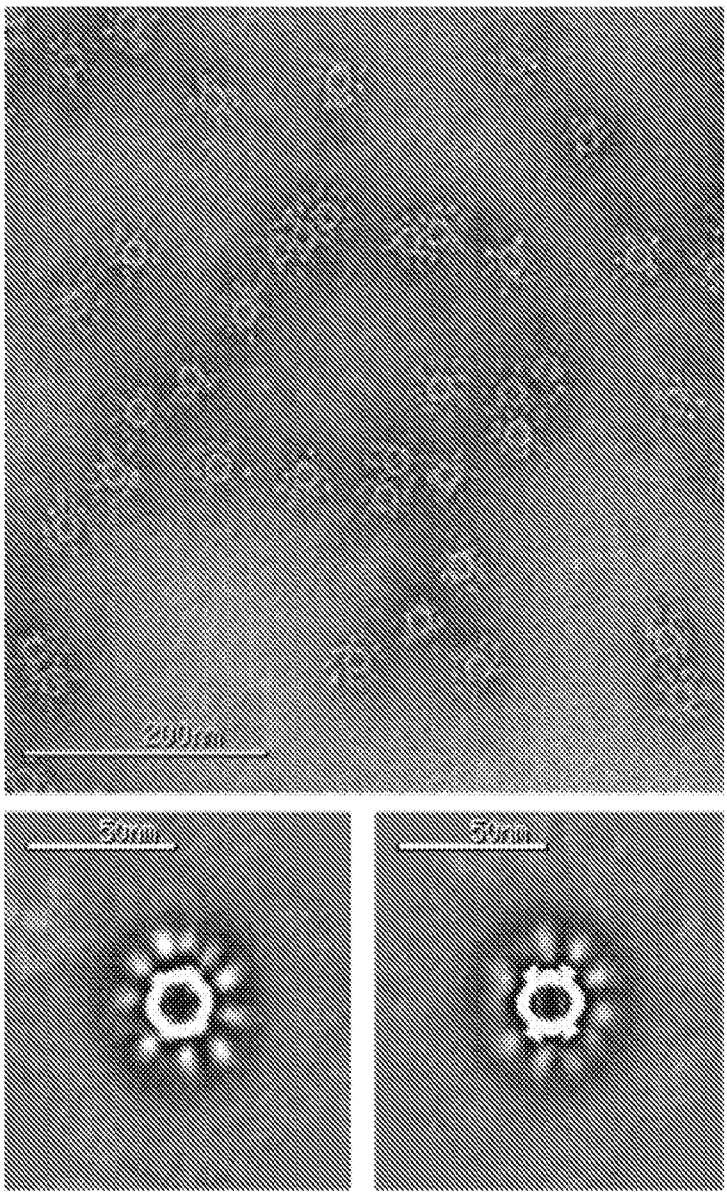

FIG. 5

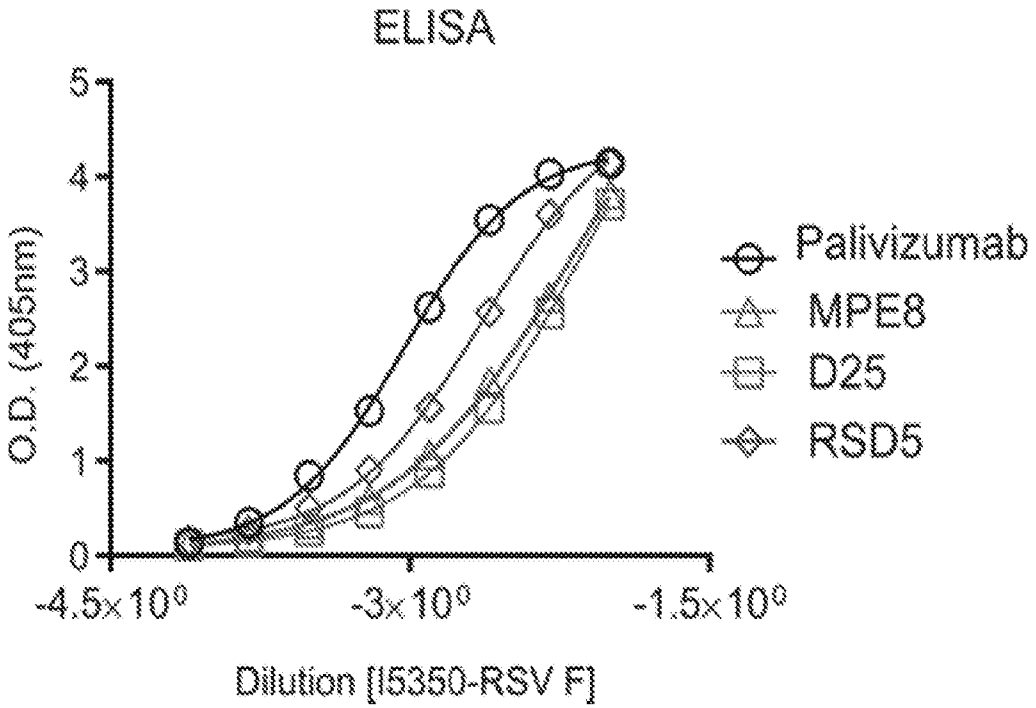
ELISA
O.D. (405nm)
5
4
3
2
1
0
-4.5×10⁰
-3×10⁰
-1.5×10⁰
Dilution [I5350-RSV F]
Palivizumab
MPE8
D25
RSD5

FIG. 6a

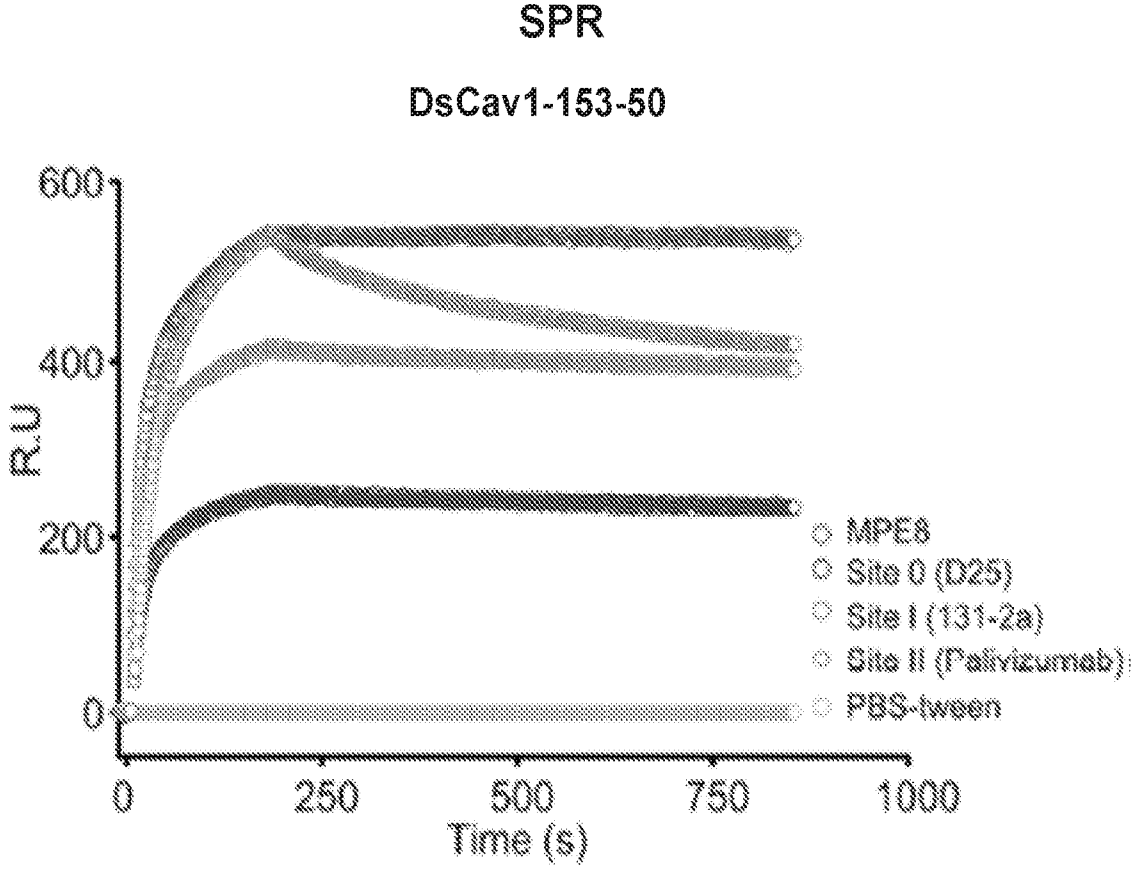
SPR
DsCav1-153-50
600
400
200
0
RU
0
250
500
750
1000
Time (s)
MPE8
Site 0 (D25)
Site I (131-2a)
Site II (Palivizumab)
PBS-tween

FIG. 6b

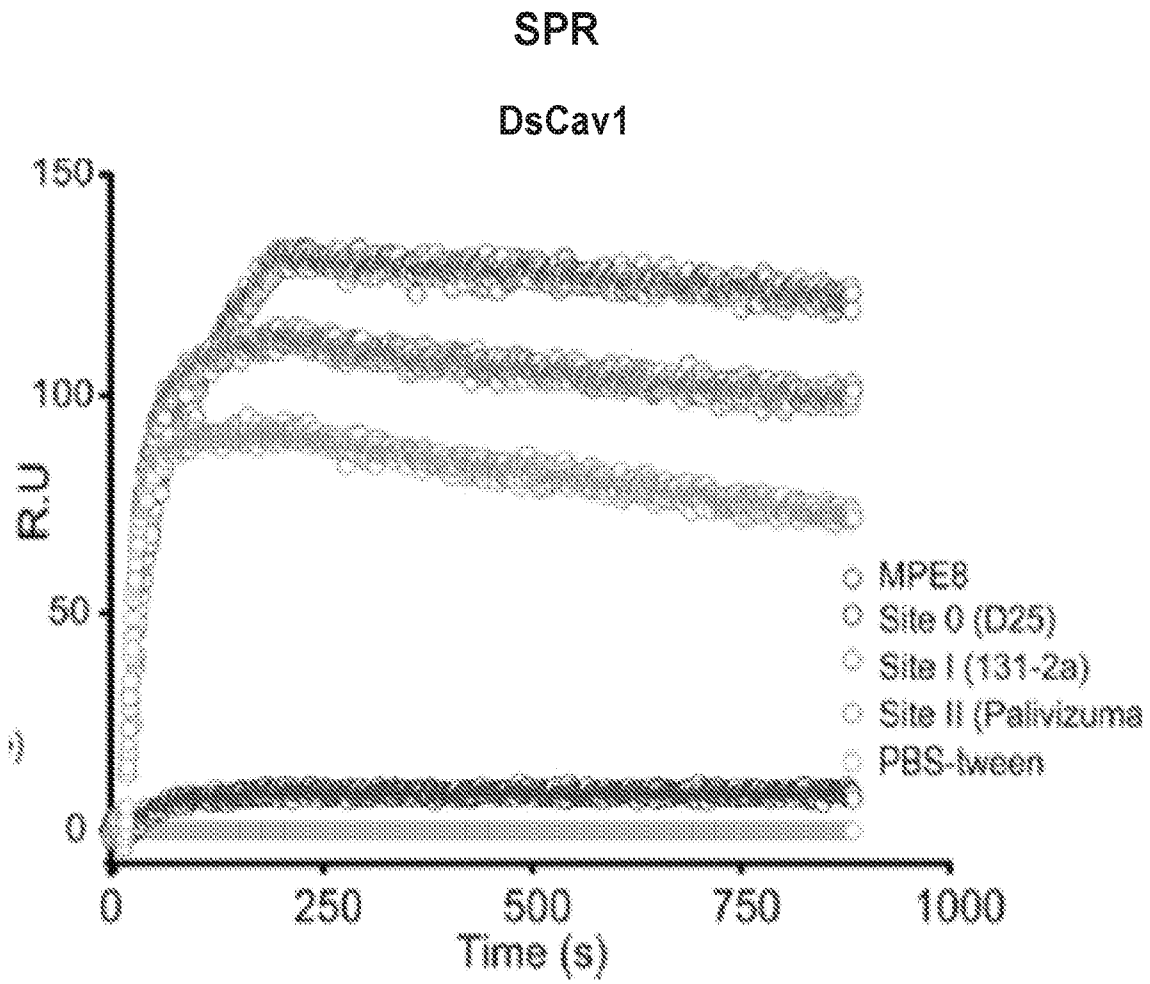
SPR
DsCav1
150
100
50
0
R.U
0
250
500
750
1000
Time (s)
MPE8
Site 0 (D25)
Site I (131-2a)
Site II (Palivizuma
PBS-tween

FIG. 6c

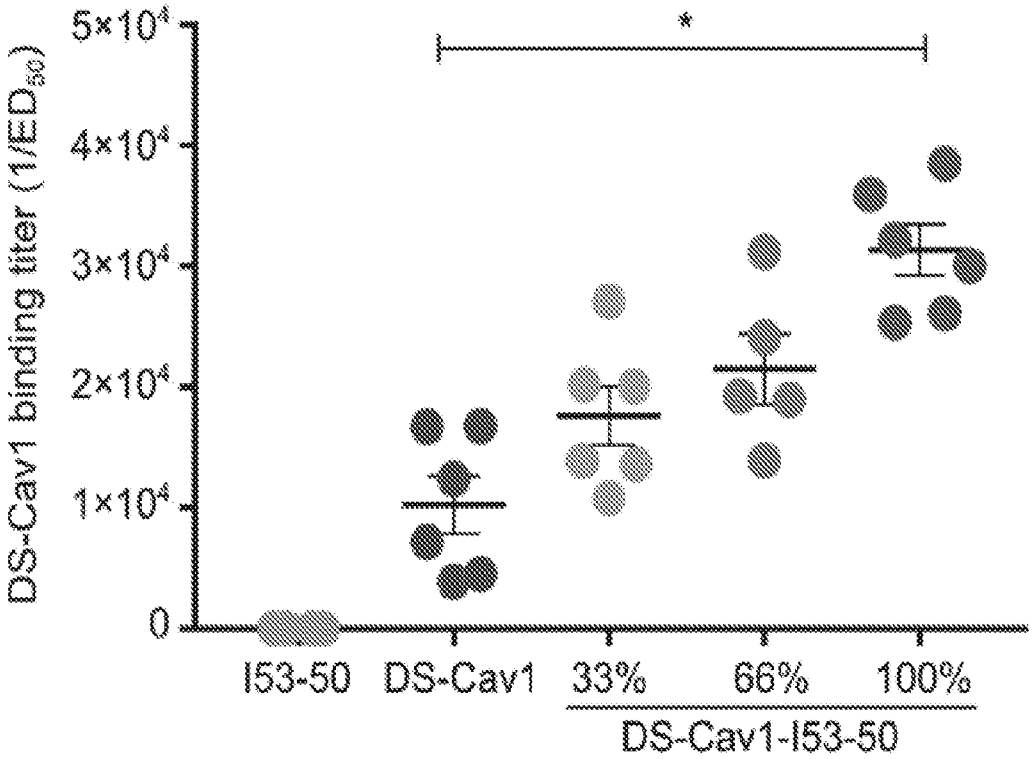
DS-Cav1 binding titer (1/ED50)
5×10⁴
4×10⁴
3×10⁴
2×10⁴
1×10⁴
0
*
I53-50
DS-Cav1
33%
66%
100%
DS-Cav1-I53-50

FIG. 7

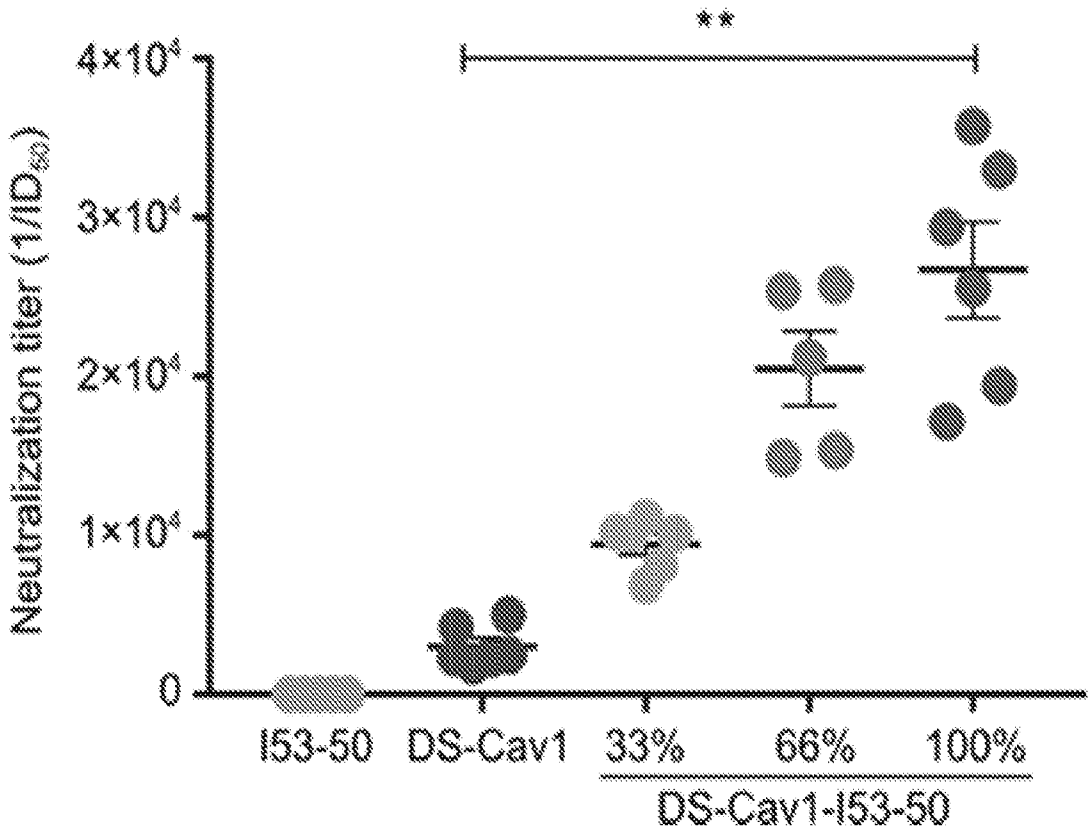
**
4×10⁴
3×10⁴
2×10⁴
1×10⁴
0
Neutralization titer (1/ID50)
I53-50
DS-Cav1
33%
66%
100%
DS-Cav1-I53-50

FIG. 8

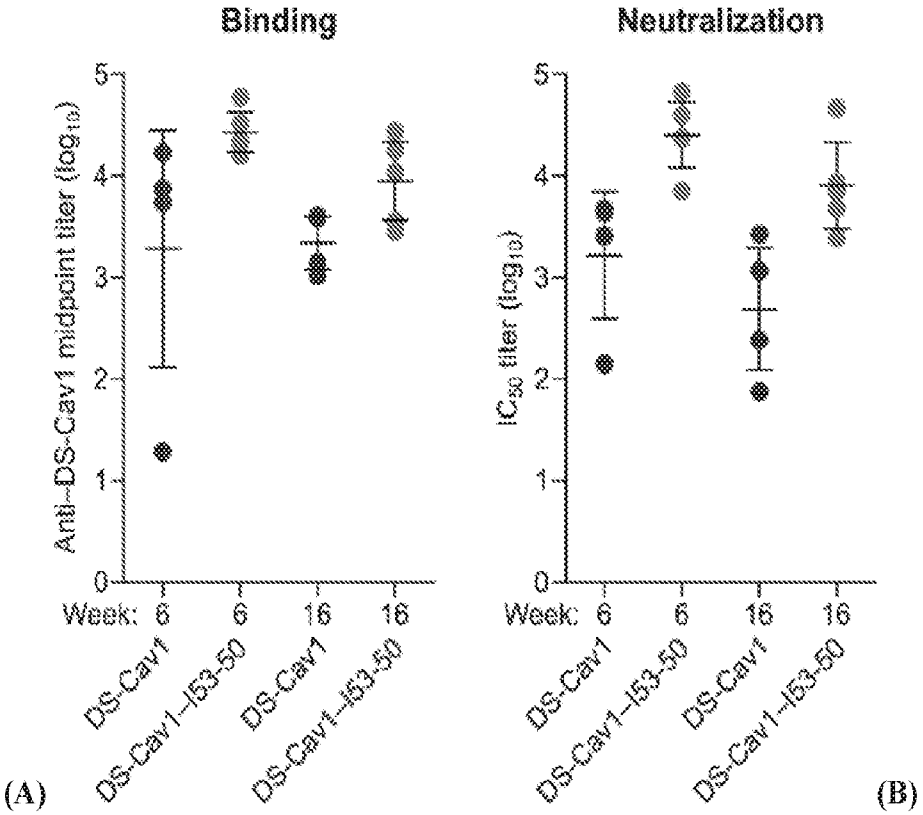
Binding
Neutralization
Anti-DS-Cav1 midpoint titer (log_{10})
IC_{50} titer (log_{10})
0
1
2
3
4
5
Week: 6 6 16 16
DS-Cav1
DS-Cav1-I53-50
DS-Cav1
DS-Cav1-I53-50
(A)
(B)

FIG. 9

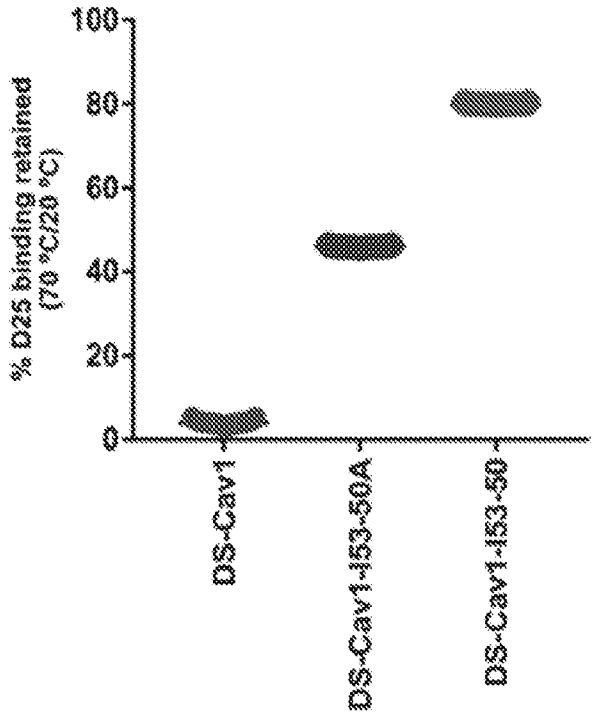
% D25 binding retained (70 °C/20 °C)
0
20
40
60
80
100
DS-Cav1
DS-Cav1-I53-50A
DS-Cav1-I53-50

FIG. 10

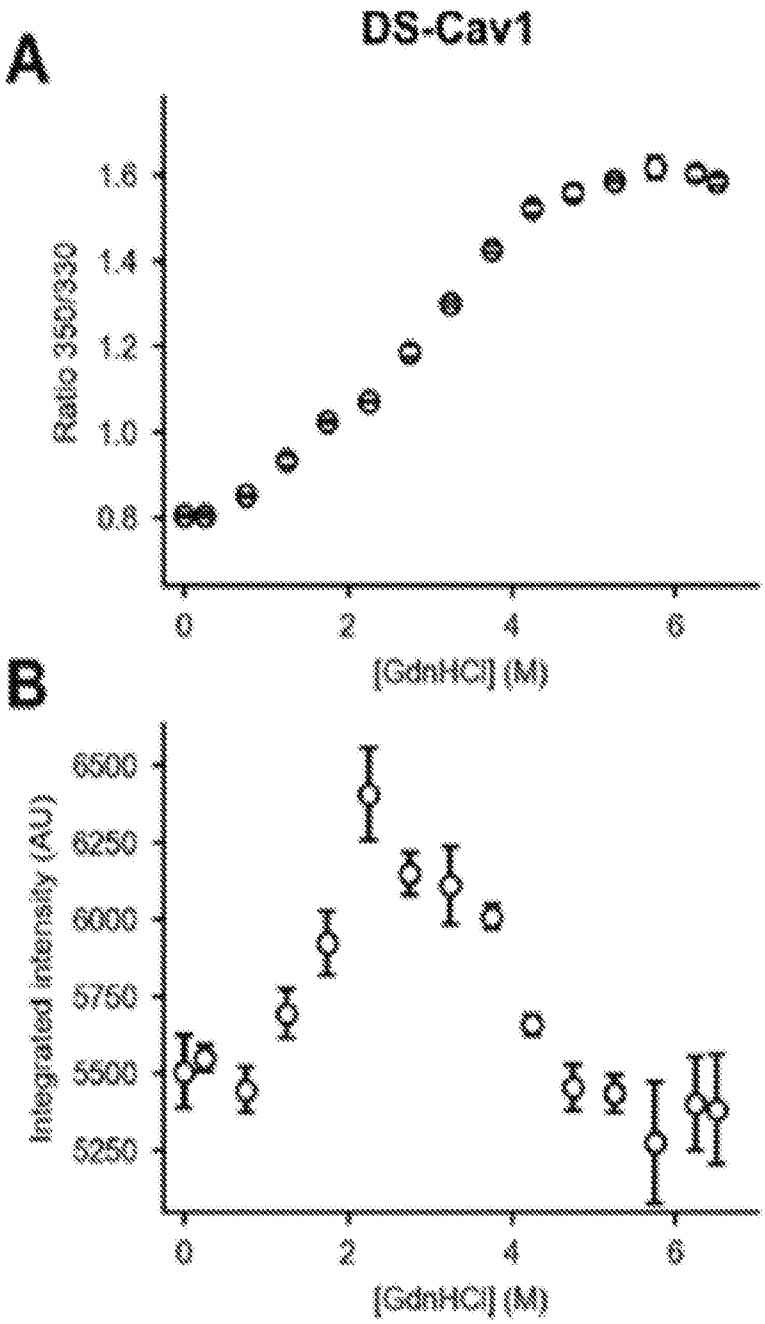
A
DS-Cav1
Ratio 350/330
1.6
1.4
1.2
1.0
0.8
0
2
4
6
[GdnHCl] (M)
B
Integrated intensity (AU)
6500
6250
6000
5750
5500
5250
0
2
4
6
[GdnHCl] (M)

FIG. 11a – 11b

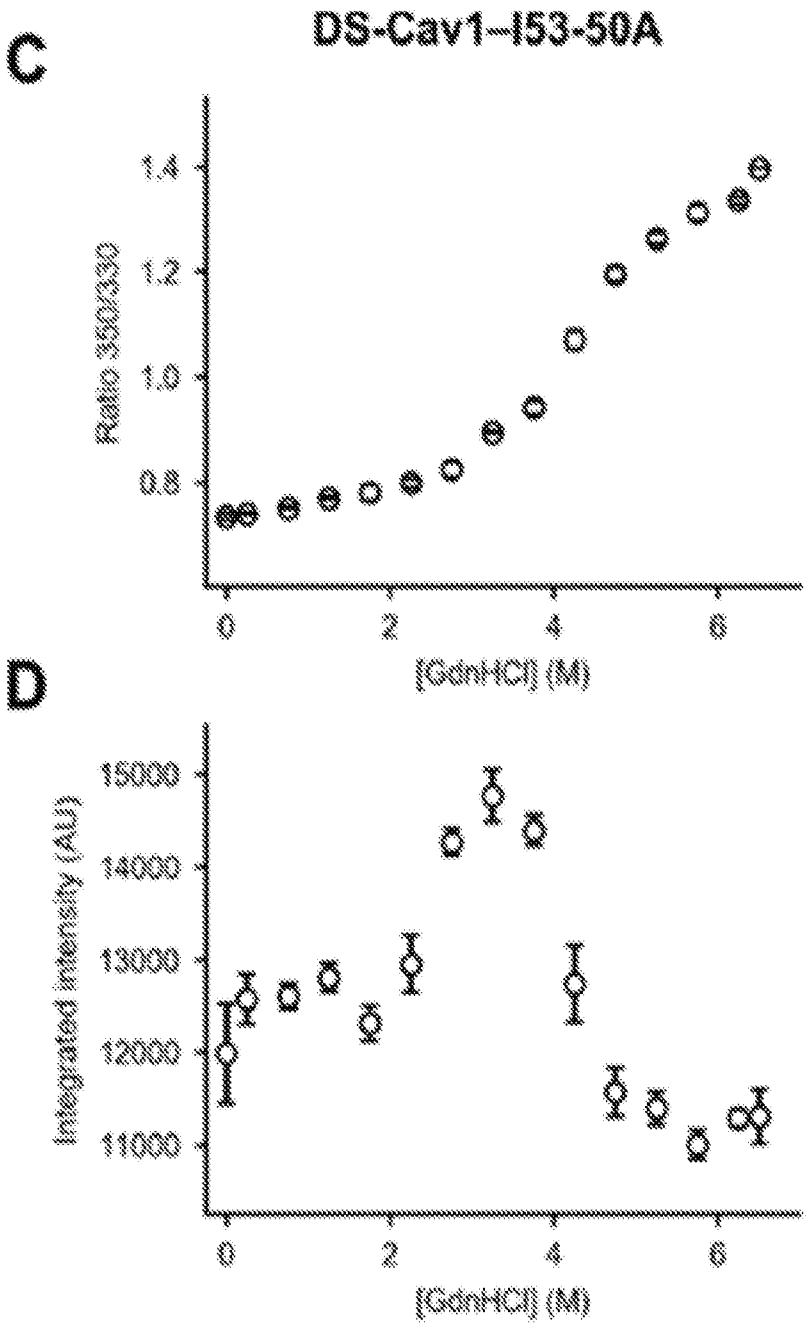
C
DS-Cav1–I53-50A
Ratio 350/330
1.4
1.2
1.0
0.8
0
2
4
6
[GdnHCl] (M)
D
Integrated intensity (AU)
15000
14000
13000
12000
11000
0
2
4
6
[GdnHCl] (M)

FIG. 11c – 11d

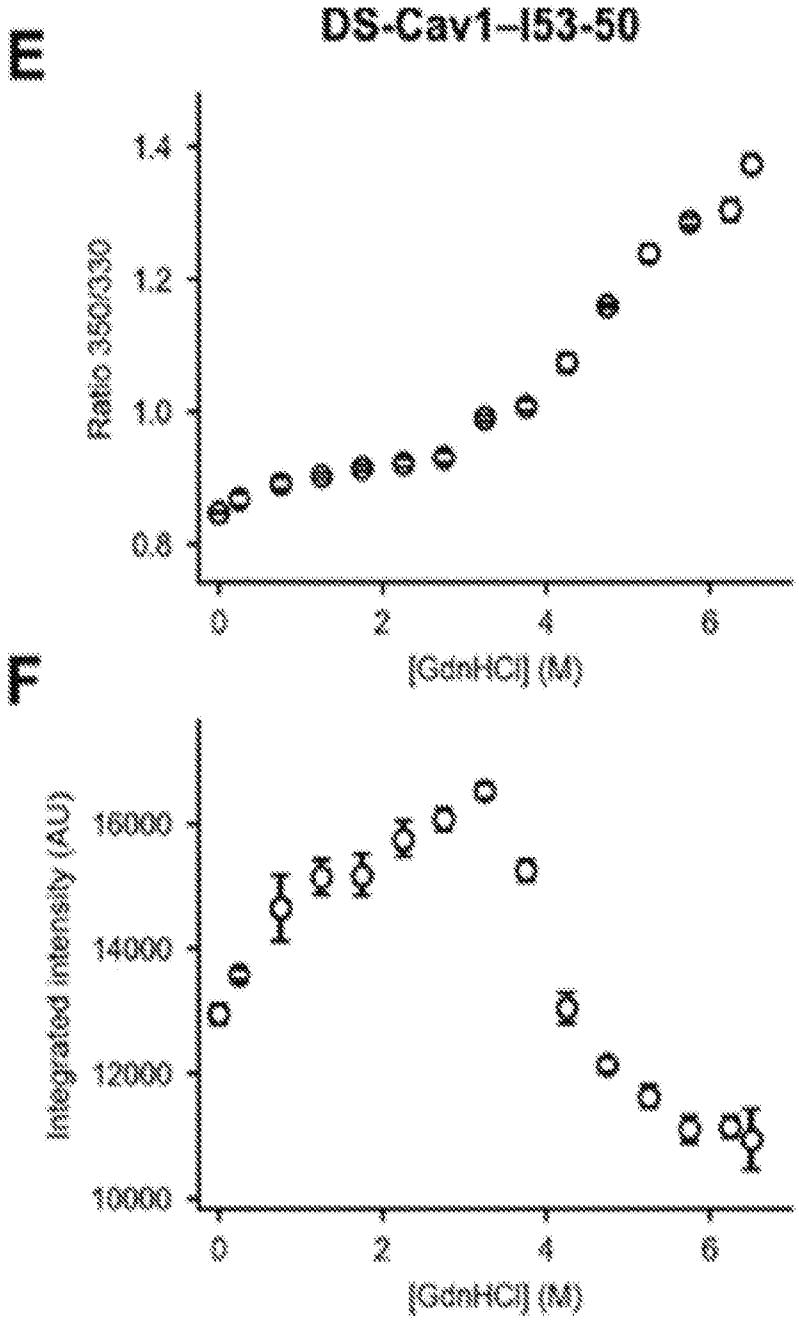
E
DS-Cav1–I53-50
Ratio 350/330
1.4
1.2
1.0
0.8
0
2
4
6
[GdnHCl] (M)
F
Integrated intensity (AU)
16000
14000
12000
10000
0
2
4
6
[GdnHCl] (M)

FIG. 11e -11f

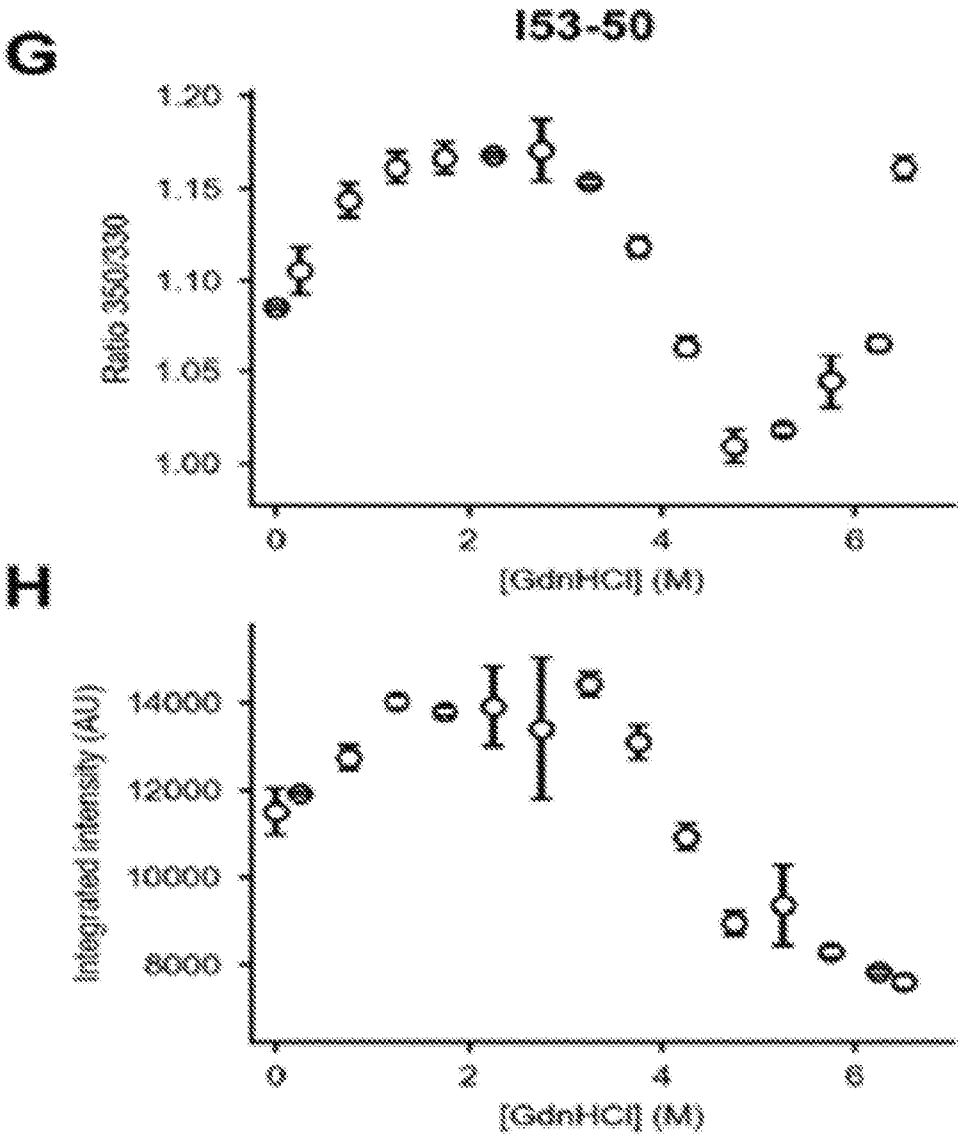
G
I53-50
1.20
1.15
1.10
1.05
1.00
Ratio 350/330
0
2
4
6
[GdnHCl] (M)
H
14000
12000
10000
8000
Integrated intensity (AU)
0
2
4
6
[GdnHCl] (M)

FIG. 11g – 11h

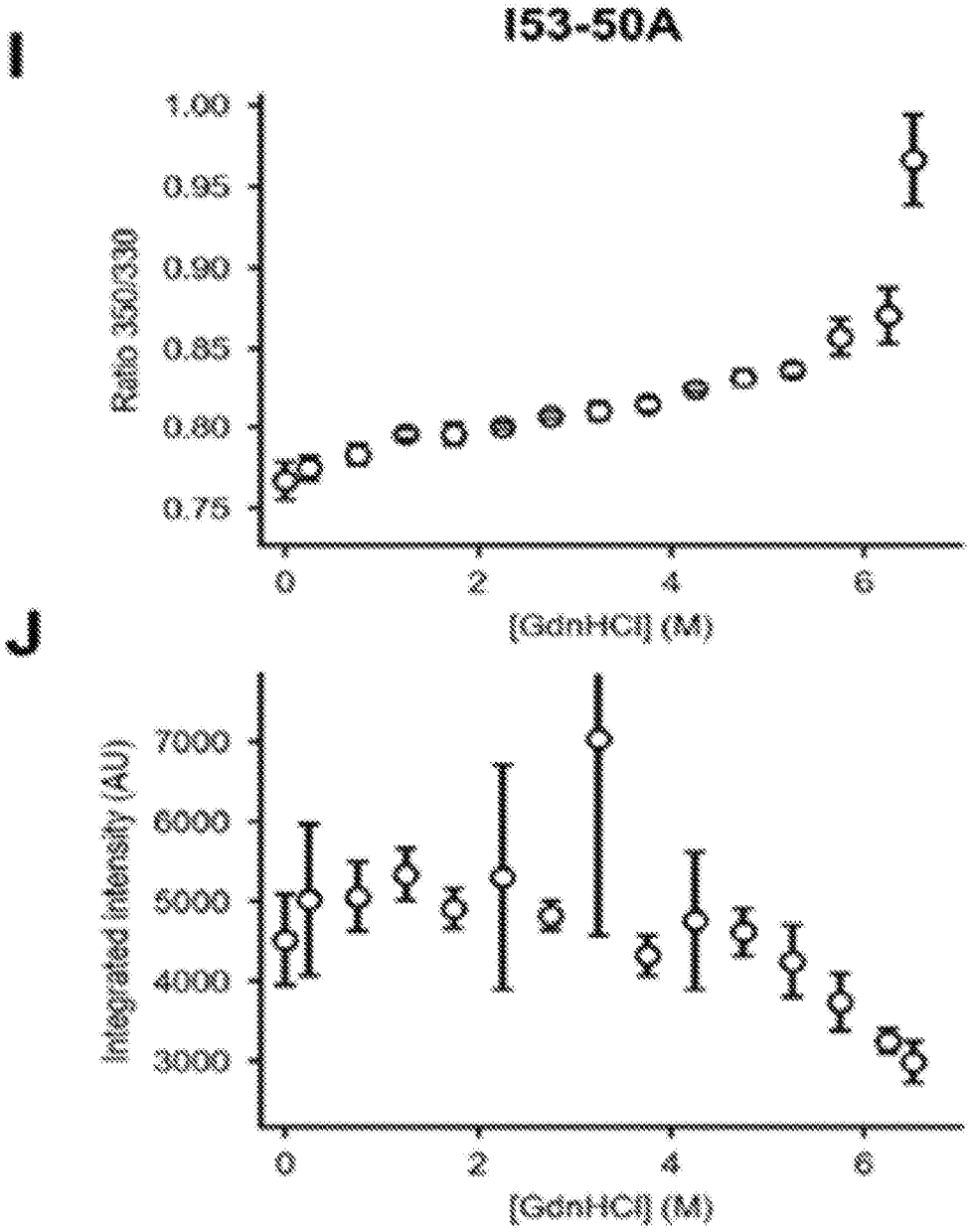
I
I53-50A
1.00
0.95
0.90
0.85
0.80
0.75
Ratio 350/330
0
2
4
6
[GdnHCl] (M)
J
7000
6000
5000
4000
3000
Integrated Intensity (AU)
0
2
4
6
[GdnHCl] (M)

FIG. 11i -11j

SEQUENCE LISTING

<110> University of Washington
Institute for Research in Biomedicine
KING, Neil P
BAKER, David
NICKERSON, Brooke
STEWART, Lance J
PEREZ, Laurent
LANZAVECCHIA, Antonio
MARCANDALLI, Jessica

<120> Self-assembling protein nanostructures displaying paramyxovirus and/or pneumovirus F proteins and their use

<130> 17-341-PCT

<150> US 62/481,331
<151> 2017-04-01

<160> 101

<170> PatentIn version 3.5

<210> 1
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<223> optionally absent

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Met Glu Gly Met Asp Pro Leu Ala Val Leu Ala Glu Ser Arg Leu Leu
1 5 10 15

Pro Leu Leu Thr Val Arg Gly Gly Glu Asp Leu Ala Gly Leu Ala Thr
20 25 30

Val Leu Glu Leu Met Gly Val Gly Ala Leu Glu Ile Thr Leu Arg Thr
35 40 45

```
Glu Lys Gly Leu Glu Ala Leu Lys Ala Leu Arg Lys Ser Gly Leu Leu
    50                  55                  60

Leu Gly Ala Gly Thr Val Arg Ser Pro Lys Glu Ala Glu Ala Ala Leu
65                  70                  75                  80

Glu Ala Gly Ala Ala Phe Leu Val Ser Pro Gly Leu Leu Glu Glu Val
                85                  90                  95

Ala Ala Leu Ala Gln Ala Arg Gly Val Pro Tyr Leu Pro Gly Val Leu
            100                 105                 110

Thr Pro Thr Glu Val Glu Arg Ala Leu Ala Leu Gly Leu Ser Ala Leu
        115                 120                 125

Lys Phe Phe Pro Ala Glu Pro Phe Gln Gly Val Arg Val Leu Arg Ala
    130                 135                 140

Tyr Ala Glu Val Phe Pro Glu Val Arg Phe Leu Pro Thr Gly Gly Ile
145                 150                 155                 160

Lys Glu Glu His Leu Pro His Tyr Ala Ala Leu Pro Asn Leu Leu Ala
                165                 170                 175

Val Gly Gly Ser Trp Leu Leu Gln Gly Asp Leu Ala Ala Val Met Lys
            180                 185                 190

Lys Val Lys Ala Ala Lys Ala Leu Leu Ser Pro Gln Ala Pro Gly
        195                 200                 205


<210>  2
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<223>  I53-34B


<220>
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<223> optionally absent

<400> 2

Met Thr Lys Lys Val Gly Ile Val Asp Thr Thr Phe Ala Arg Val Asp
1 5 10 15

Met Ala Glu Ala Ala Ile Arg Thr Leu Lys Ala Leu Ser Pro Asn Ile
20 25 30

Lys Ile Ile Arg Lys Thr Val Pro Gly Ile Lys Asp Leu Pro Val Ala
35 40 45

Cys Lys Lys Leu Leu Glu Glu Glu Gly Cys Asp Ile Val Met Ala Leu
50 55 60

Gly Met Pro Gly Lys Ala Glu Lys Asp Lys Val Cys Ala His Glu Ala
65 70 75 80

Ser Leu Gly Leu Met Leu Ala Gln Leu Met Thr Asn Lys His Ile Ile
85 90 95

Glu Val Phe Val His Glu Asp Glu Ala Lys Asp Asp Asp Glu Leu Asp
100 105 110

Ile Leu Ala Leu Val Arg Ala Ile Glu His Ala Ala Asn Val Tyr Tyr
115 120 125

Leu Leu Phe Lys Pro Glu Tyr Leu Thr Arg Met Ala Gly Lys Gly Leu
130 135 140

Arg Gln Gly Arg Glu Asp Ala Gly Pro Ala Arg Glu
145 150 155

<210> 3
<211> 156
<212> PRT
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<220>
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<220>
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<222> (1)..(1)
<223> optionally absent

<400> 3

```
Met Thr Lys Lys Val Gly Ile Val Asp Thr Thr Phe Ala Arg Val Asp
1               5                  10                  15


Met Ala Ser Ala Ala Ile Leu Thr Leu Lys Met Glu Ser Pro Asn Ile
            20                  25                  30


Lys Ile Ile Arg Lys Thr Val Pro Gly Ile Lys Asp Leu Pro Val Ala
        35                  40                  45


Cys Lys Lys Leu Leu Glu Glu Glu Gly Cys Asp Ile Val Met Ala Leu
    50                  55                  60


Gly Met Pro Gly Lys Ala Glu Lys Asp Lys Val Cys Ala His Glu Ala
65                  70                  75                  80


Ser Leu Gly Leu Met Leu Ala Gln Leu Met Thr Asn Lys His Ile Ile
                85                  90                  95


Glu Val Phe Val His Glu Asp Glu Ala Lys Asp Asp Ala Glu Leu Lys
            100                 105                 110


Ile Leu Ala Ala Arg Arg Ala Ile Glu His Ala Leu Asn Val Tyr Tyr
        115                 120                 125


Leu Leu Phe Lys Pro Glu Tyr Leu Thr Arg Met Ala Gly Lys Gly Leu
    130                 135                 140


Arg Gln Gly Phe Glu Asp Ala Gly Pro Ala Arg Glu
145                 150                 155
```

<210> 4
<211> 209
<212> PRT
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<223> optionally absent

<400> 4

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


Ile Ala Ile Asp Asn Ala Glu Asp Ile Ile Pro Leu Gly Lys Val Leu
            20                  25                  30


Ala Glu Asn Gly Leu Pro Ala Ala Glu Ile Thr Phe Arg Ser Ser Ala
        35                  40                  45


Ala Val Lys Ala Ile Met Leu Leu Arg Ser Ala Gln Pro Glu Met Leu
    50                  55                  60


Ile Gly Ala Gly Thr Ile Leu Asn Gly Val Gln Ala Leu Ala Ala Lys
65                  70                  75                  80


Glu Ala Gly Ala Thr Phe Val Val Ser Pro Gly Phe Asn Pro Asn Thr
                85                  90                  95


Val Arg Ala Cys Gln Ile Ile Gly Ile Asp Ile Val Pro Gly Val Asn
            100                 105                 110


Asn Pro Ser Thr Val Glu Ala Ala Leu Glu Met Gly Leu Thr Thr Leu
        115                 120                 125


Lys Phe Phe Pro Ala Glu Ala Ser Gly Gly Ile Ser Met Val Lys Ser
    130                 135                 140


Leu Val Gly Pro Tyr Gly Asp Ile Arg Leu Met Pro Thr Gly Gly Ile
145                 150                 155                 160
```

Thr Pro Ser Asn Ile Asp Asn Tyr Leu Ala Ile Pro Gln Val Leu Ala
165 170 175

Cys Gly Gly Thr Trp Met Val Asp Lys Lys Leu Val Thr Asn Gly Glu
180 185 190

Trp Asp Glu Ile Ala Arg Leu Thr Arg Glu Ile Val Glu Gln Val Asn
195 200 205

Pro

<210> 5
<211> 114
<212> PRT
<213> Artificial Sequence

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<223> optionally absent

<400> 5

Met Pro Ile Phe Thr Leu Asn Thr Asn Ile Lys Ala Thr Asp Val Pro
1 5 10 15

Ser Asp Phe Leu Ser Leu Thr Ser Arg Leu Val Gly Leu Ile Leu Ser
20 25 30

Lys Pro Gly Ser Tyr Val Ala Val His Ile Asn Thr Asp Gln Gln Leu
35 40 45

Ser Phe Gly Gly Ser Thr Asn Pro Ala Ala Phe Gly Thr Leu Met Ser
50 55 60

Ile Gly Gly Ile Glu Pro Ser Lys Asn Arg Asp His Ser Ala Val Leu
65 70 75 80

Phe Asp His Leu Asn Ala Met Leu Gly Ile Pro Lys Asn Arg Met Tyr
85 90 95

Ile His Phe Val Asn Leu Asn Gly Asp Asp Val Gly Trp Asn Gly Thr
100 105 110

Thr Phe

<210> 6
<211> 157
<212> PRT
<213> Artificial Sequence

<220>
<223> I53-47B

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> optionally absent

<400> 6

Met Asn Gln His Ser His Lys Asp Tyr Glu Thr Val Arg Ile Ala Val
1 5 10 15

Val Arg Ala Arg Trp His Ala Asp Ile Val Asp Ala Cys Val Glu Ala
20 25 30

Phe Glu Ile Ala Met Ala Ala Ile Gly Gly Asp Arg Phe Ala Val Asp
35 40 45

Val Phe Asp Val Pro Gly Ala Tyr Glu Ile Pro Leu His Ala Arg Thr
50 55 60

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

Val Asn Gly Gly Ile Tyr Arg His Glu Phe Val Ala Ser Ala Val Ile
85 90 95

```
Asp Gly Met Met Asn Val Gln Leu Ser Thr Gly Val Pro Val Leu Ser
            100                 105                 110


Ala Val Leu Thr Pro His Arg Tyr Arg Asp Ser Ala Glu His His Arg
        115                 120                 125


Phe Phe Ala Ala His Phe Ala Val Lys Gly Val Glu Ala Ala Arg Ala
    130                 135                 140


Cys Ile Glu Ile Leu Ala Ala Arg Glu Lys Ile Ala Ala
145                 150                 155


<210>  7
<211>  205
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  I53-50A


<220>
<221>  MISC_FEATURE
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<223>  optionally absent

<400>  7

Met Lys Met Glu Glu Leu Phe Lys Lys His Lys Ile Val Ala Val Leu
1               5                   10                  15


Arg Ala Asn Ser Val Glu Glu Ala Ile Glu Lys Ala Val Ala Val Phe
            20                  25                  30


Ala Gly Gly Val His Leu Ile Glu Ile Thr Phe Thr Val Pro Asp Ala
        35                  40                  45


Asp Thr Val Ile Lys Ala Leu Ser Val Leu Lys Glu Lys Gly Ala Ile
    50                  55                  60


Ile Gly Ala Gly Thr Val Thr Ser Val Glu Gln Cys Arg Lys Ala Val
65                  70                  75                  80
```

```
Glu Ser Gly Ala Glu Phe Ile Val Ser Pro His Leu Asp Glu Glu Ile
                85                  90                  95


Ser Gln Phe Cys Lys Glu Lys Gly Val Phe Tyr Met Pro Gly Val Met
            100                 105                 110


Thr Pro Thr Glu Leu Val Lys Ala Met Lys Leu Gly His Thr Ile Leu
        115                 120                 125


Lys Leu Phe Pro Gly Glu Val Val Gly Pro Gln Phe Val Lys Ala Met
    130                 135                 140


Lys Gly Pro Phe Pro Asn Val Lys Phe Val Pro Thr Gly Gly Val Asn
145                 150                 155                 160


Leu Asp Asn Val Cys Glu Trp Phe Lys Ala Gly Val Leu Ala Val Gly
                165                 170                 175


Val Gly Ser Ala Leu Val Lys Gly Thr Pro Asp Glu Val Arg Glu Lys
            180                 185                 190


Ala Lys Ala Phe Val Glu Lys Ile Arg Gly Cys Thr Glu
        195                 200                 205


<210>  8
<211>  157
<212>  PRT
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<220>
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<220>
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<222>  (1)..(1)
<223>  optionally absent

<400>  8

Met Asn Gln His Ser His Lys Asp Tyr Glu Thr Val Arg Ile Ala Val
1               5                   10                  15
```

```
Val Arg Ala Arg Trp His Ala Glu Ile Val Asp Ala Cys Val Ser Ala
            20                  25                  30


Phe Glu Ala Ala Met Ala Asp Ile Gly Gly Asp Arg Phe Ala Val Asp
        35                  40                  45


Val Phe Asp Val Pro Gly Ala Tyr Glu Ile Pro Leu His Ala Arg Thr
    50                  55                  60


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


Val Asn Gly Gly Ile Tyr Arg His Glu Phe Val Ala Ser Ala Val Ile
                85                  90                  95


Asp Gly Met Met Asn Val Gln Leu Ser Thr Gly Val Pro Val Leu Ser
            100                 105                 110


Ala Val Leu Thr Pro His Arg Tyr Arg Asp Ser Asp Ala His Thr Leu
        115                 120                 125


Leu Phe Leu Ala Leu Phe Ala Val Lys Gly Met Glu Ala Ala Arg Ala
    130                 135                 140


Cys Val Glu Ile Leu Ala Ala Arg Glu Lys Ile Ala Ala
145                 150                 155


<210>  9
<211>  177
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  I53-51A


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<223>  optionally absent

<400>  9
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```
Met Phe Thr Lys Ser Gly Asp Asp Gly Asn Thr Asn Val Ile Asn Lys
1               5                  10                  15

Arg Val Gly Lys Asp Ser Pro Leu Val Asn Phe Leu Gly Asp Leu Asp
            20                  25                  30

Glu Leu Asn Ser Phe Ile Gly Phe Ala Ile Ser Lys Ile Pro Trp Glu
        35                  40                  45

Asp Met Lys Lys Asp Leu Glu Arg Val Gln Val Glu Leu Phe Glu Ile
    50                  55                  60

Gly Glu Asp Leu Ser Thr Gln Ser Ser Lys Lys Lys Ile Asp Glu Ser
65                  70                  75                  80

Tyr Val Leu Trp Leu Leu Ala Ala Thr Ala Ile Tyr Arg Ile Glu Ser
                85                  90                  95

Gly Pro Val Lys Leu Phe Val Ile Pro Gly Gly Ser Glu Glu Ala Ser
            100                 105                 110

Val Leu His Val Thr Arg Ser Val Ala Arg Arg Val Glu Arg Asn Ala
        115                 120                 125

Val Lys Tyr Thr Lys Glu Leu Pro Glu Ile Asn Arg Met Ile Ile Val
    130                 135                 140

Tyr Leu Asn Arg Leu Ser Ser Leu Leu Phe Ala Met Ala Leu Val Ala
145                 150                 155                 160

Asn Lys Arg Arg Asn Gln Ser Glu Lys Ile Tyr Glu Ile Gly Lys Ser
                165                 170                 175

Trp
```

<210> 10
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<212> PRT
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<220>
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<222> (1)..(1)
<223> optionally absent

<400> 10

```
Met Asn Gln His Ser His Lys Asp Tyr Glu Thr Val Arg Ile Ala Val
1               5                   10                  15


Val Arg Ala Arg Trp His Ala Asp Ile Val Asp Gln Cys Val Arg Ala
            20                  25                  30


Phe Glu Glu Ala Met Ala Asp Ala Gly Gly Asp Arg Phe Ala Val Asp
        35                  40                  45


Val Phe Asp Val Pro Gly Ala Tyr Glu Ile Pro Leu His Ala Arg Thr
    50                  55                  60


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


Val Asn Gly Gly Ile Tyr Arg His Glu Phe Val Ala Ser Ala Val Ile
                85                  90                  95


Asp Gly Met Met Asn Val Gln Leu Ser Thr Gly Val Pro Val Leu Ser
            100                 105                 110


Ala Val Leu Thr Pro His Arg Tyr Arg Ser Ser Arg Glu His His Glu
        115                 120                 125


Phe Phe Arg Glu His Phe Met Val Lys Gly Val Glu Ala Ala Ala Ala
    130                 135                 140


Cys Ile Thr Ile Leu Ala Ala Arg Glu Lys Ile Ala Ala
145                 150                 155
```

<210> 11
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<220>
<223> I52-03A

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<222> (1)..(1)
<223> optionally absent

<400> 11

```
Met Gly His Thr Lys Gly Pro Thr Pro Gln Gln His Asp Gly Ser Ala
1               5                   10                  15


Leu Arg Ile Gly Ile Val His Ala Arg Trp Asn Lys Thr Ile Ile Met
            20                  25                  30


Pro Leu Leu Ile Gly Thr Ile Ala Lys Leu Leu Glu Cys Gly Val Lys
        35                  40                  45


Ala Ser Asn Ile Val Val Gln Ser Val Pro Gly Ser Trp Glu Leu Pro
    50                  55                  60


Ile Ala Val Gln Arg Leu Tyr Ser Ala Ser Gln Leu Gln Thr Pro Ser
65                  70                  75                  80


Ser Gly Pro Ser Leu Ser Ala Gly Asp Leu Leu Gly Ser Ser Thr Thr
                85                  90                  95


Asp Leu Thr Ala Leu Pro Thr Thr Thr Ala Ser Ser Thr Gly Pro Phe
            100                 105                 110


Asp Ala Leu Ile Ala Ile Gly Val Leu Ile Lys Gly Glu Thr Met His
        115                 120                 125


Phe Glu Tyr Ile Ala Asp Ser Val Ser His Gly Leu Met Arg Val Gln
    130                 135                 140
```

```
Leu Asp Thr Gly Val Pro Val Ile Phe Gly Val Leu Thr Val Leu Thr
145                 150                 155                 160


Asp Asp Gln Ala Lys Ala Arg Ala Gly Val Ile Glu Gly Ser His Asn
                165                 170                 175


His Gly Glu Asp Trp Gly Leu Ala Ala Val Glu Met Gly Val Arg Arg
            180                 185                 190


Arg Asp Trp Ala Ala Gly Lys Thr Glu
        195                 200


<210>  12
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Met Tyr Glu Val Asp His Ala Asp Val Tyr Asp Leu Phe Tyr Leu Gly
1               5                   10                  15


Arg Gly Lys Asp Tyr Ala Ala Glu Ala Ser Asp Ile Ala Asp Leu Val
            20                  25                  30


Arg Ser Arg Thr Pro Glu Ala Ser Ser Leu Leu Asp Val Ala Cys Gly
        35                  40                  45


Thr Gly Thr His Leu Glu His Phe Thr Lys Glu Phe Gly Asp Thr Ala
    50                  55                  60


Gly Leu Glu Leu Ser Glu Asp Met Leu Thr His Ala Arg Lys Arg Leu
65                  70                  75                  80
```

```
Pro Asp Ala Thr Leu His Gln Gly Asp Met Arg Asp Phe Gln Leu Gly
                85                  90                  95

Arg Lys Phe Ser Ala Val Val Ser Met Phe Ser Ser Val Gly Tyr Leu
            100                 105                 110

Lys Thr Val Ala Glu Leu Gly Ala Ala Val Ala Ser Phe Ala Glu His
        115                 120                 125

Leu Glu Pro Gly Gly Val Val Val Val Glu Pro Trp Trp Phe Pro Glu
    130                 135                 140

Thr Phe Ala Asp Gly Trp Val Ser Ala Asp Val Val Arg Arg Asp Gly
145                 150                 155                 160

Arg Thr Val Ala Arg Val Ser His Ser Val Arg Glu Gly Asn Ala Thr
                165                 170                 175

Arg Met Glu Val His Phe Thr Val Ala Asp Pro Gly Lys Gly Val Arg
            180                 185                 190

His Phe Ser Asp Val His Leu Ile Thr Leu Phe His Gln Arg Glu Tyr
        195                 200                 205

Glu Ala Ala Phe Met Ala Ala Gly Leu Arg Val Glu Tyr Leu Glu Gly
    210                 215                 220

Gly Pro Ser Gly Arg Gly Leu Phe Val Gly Val Pro Ala
225                 230                 235


<210>  13
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<400> 13

Met Gly Met Lys Glu Lys Phe Val Leu Ile Ile Thr His Gly Asp Phe
1 5 10 15

Gly Lys Gly Leu Leu Ser Gly Ala Glu Val Ile Ile Gly Lys Gln Glu
20 25 30

Asn Val His Thr Val Gly Leu Asn Leu Gly Asp Asn Ile Glu Lys Val
35 40 45

Ala Lys Glu Val Met Arg Ile Ile Ile Ala Lys Leu Ala Glu Asp Lys
50 55 60

Glu Ile Ile Ile Val Val Asp Leu Phe Gly Gly Ser Pro Phe Asn Ile
65 70 75 80

Ala Leu Glu Met Met Lys Thr Phe Asp Val Lys Val Ile Thr Gly Ile
85 90 95

Asn Met Pro Met Leu Val Glu Leu Leu Thr Ser Ile Asn Val Tyr Asp
100 105 110

Thr Thr Glu Leu Leu Glu Asn Ile Ser Lys Ile Gly Lys Asp Gly Ile
115 120 125

Lys Val Ile Glu Lys Ser Ser Leu Lys Met
130 135

<210> 14
<211> 154
<212> PRT
<213> Artificial Sequence

<220>
<223> I52-32B

<220>
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<222> (1)..(1)

<223> optionally absent

<400> 14

Met Lys Tyr Asp Gly Ser Lys Leu Arg Ile Gly Ile Leu His Ala Arg
1 5 10 15

Trp Asn Leu Glu Ile Ile Ala Ala Leu Val Ala Gly Ala Ile Lys Arg
20 25 30

Leu Gln Glu Phe Gly Val Lys Ala Glu Asn Ile Ile Ile Glu Thr Val
35 40 45

Pro Gly Ser Phe Glu Leu Pro Tyr Gly Ser Lys Leu Phe Val Glu Lys
50 55 60

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

Leu Ile Lys Gly Ser Thr Met His Phe Glu Tyr Ile Cys Asp Ser Thr
85 90 95

Thr His Gln Leu Met Lys Leu Asn Phe Glu Leu Gly Ile Pro Val Ile
100 105 110

Phe Gly Val Leu Thr Cys Leu Thr Asp Glu Gln Ala Glu Ala Arg Ala
115 120 125

Gly Leu Ile Glu Gly Lys Met His Asn His Gly Glu Asp Trp Gly Ala
130 135 140

Ala Ala Val Glu Met Ala Thr Lys Phe Asn
145 150

<210> 15
<211> 164
<212> PRT
<213> Artificial Sequence

<220>
<223> I52-33A

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> optionally absent

<400> 15

```
Met Ala Val Lys Gly Leu Gly Glu Val Asp Gln Lys Tyr Asp Gly Ser
1               5                  10                  15


Lys Leu Arg Ile Gly Ile Leu His Ala Arg Trp Asn Arg Lys Ile Ile
            20                  25                  30


Leu Ala Leu Val Ala Gly Ala Val Leu Arg Leu Leu Glu Phe Gly Val
        35                  40                  45


Lys Ala Glu Asn Ile Ile Ile Glu Thr Val Pro Gly Ser Phe Glu Leu
    50                  55                  60


Pro Tyr Gly Ser Lys Leu Phe Val Glu Lys Gln Lys Arg Leu Gly Lys
65                  70                  75                  80


Pro Leu Asp Ala Ile Ile Pro Ile Gly Val Leu Ile Lys Gly Ser Thr
                85                  90                  95


Met His Phe Glu Tyr Ile Cys Asp Ser Thr Thr His Gln Leu Met Lys
            100                 105                 110


Leu Asn Phe Glu Leu Gly Ile Pro Val Ile Phe Gly Val Leu Thr Cys
        115                 120                 125


Leu Thr Asp Glu Gln Ala Glu Ala Arg Ala Gly Leu Ile Glu Gly Lys
    130                 135                 140


Met His Asn His Gly Glu Asp Trp Gly Ala Ala Ala Val Glu Met Ala
145                 150                 155                 160


Thr Lys Phe Asn
```

<210> 16
<211> 175
<212> PRT
<213> Artificial Sequence

<220>
<223> I52-33B

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> optionally absent

<400> 16

```
Met Gly Ala Asn Trp Tyr Leu Asp Asn Glu Ser Ser Arg Leu Ser Phe
1               5                  10                  15

Thr Ser Thr Lys Asn Ala Asp Ile Ala Glu Val His Arg Phe Leu Val
            20                  25                  30

Leu His Gly Lys Val Asp Pro Lys Gly Leu Ala Glu Val Glu Val Glu
        35                  40                  45

Thr Glu Ser Ile Ser Thr Gly Ile Pro Leu Arg Asp Met Leu Leu Arg
    50                  55                  60

Val Leu Val Phe Gln Val Ser Lys Phe Pro Val Ala Gln Ile Asn Ala
65                  70                  75                  80

Gln Leu Asp Met Arg Pro Ile Asn Asn Leu Ala Pro Gly Ala Gln Leu
                85                  90                  95

Glu Leu Arg Leu Pro Leu Thr Val Ser Leu Arg Gly Lys Ser His Ser
            100                 105                 110

Tyr Asn Ala Glu Leu Leu Ala Thr Arg Leu Asp Glu Arg Arg Phe Gln
        115                 120                 125

Val Val Thr Leu Glu Pro Leu Val Ile His Ala Gln Asp Phe Asp Met
    130                 135                 140
```

```
Val Arg Ala Phe Asn Ala Leu Arg Leu Val Ala Gly Leu Ser Ala Val
145                 150                 155                 160


Ser Leu Ser Val Pro Val Gly Ala Val Leu Ile Phe Thr Ala Arg
                165                 170                 175


<210>  17
<211>  208
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  I32-06A


<220>
<221>  MISC_FEATURE
<222>  (1)..(1)
<223>  optionally absent

<400>  17

Met Thr Asp Tyr Ile Arg Asp Gly Ser Ala Ile Lys Ala Leu Ser Phe
1               5                   10                  15


Ala Ile Ile Leu Ala Glu Ala Asp Leu Arg His Ile Pro Gln Asp Leu
            20                  25                  30


Gln Arg Leu Ala Val Arg Val Ile His Ala Cys Gly Met Val Asp Val
        35                  40                  45


Ala Asn Asp Leu Ala Phe Ser Glu Gly Ala Gly Lys Ala Gly Arg Asn
    50                  55                  60


Ala Leu Leu Ala Gly Ala Pro Ile Leu Cys Asp Ala Arg Met Val Ala
65                  70                  75                  80


Glu Gly Ile Thr Arg Ser Arg Leu Pro Ala Asp Asn Arg Val Ile Tyr
                85                  90                  95


Thr Leu Ser Asp Pro Ser Val Pro Glu Leu Ala Lys Lys Ile Gly Asn
            100                 105                 110
```

```
Thr Arg Ser Ala Ala Ala Leu Asp Leu Trp Leu Pro His Ile Glu Gly
        115                 120                 125


Ser Ile Val Ala Ile Gly Asn Ala Pro Thr Ala Leu Phe Arg Leu Phe
    130                 135                 140


Glu Leu Leu Asp Ala Gly Ala Pro Lys Pro Ala Leu Ile Ile Gly Met
145                 150                 155                 160


Pro Val Gly Phe Val Gly Ala Ala Glu Ser Lys Asp Glu Leu Ala Ala
                165                 170                 175


Asn Ser Arg Gly Val Pro Tyr Val Ile Val Arg Gly Arg Arg Gly Gly
            180                 185                 190


Ser Ala Met Thr Ala Ala Ala Val Asn Ala Leu Ala Ser Glu Arg Glu
        195                 200                 205


<210>  18
<211>  128
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  I32-06B


<220>
<221>  MISC_FEATURE
<222>  (1)..(1)
<223>  optionally absent

<400>  18

Met Ile Thr Val Phe Gly Leu Lys Ser Lys Leu Ala Pro Arg Arg Glu
1               5                   10                  15


Lys Leu Ala Glu Val Ile Tyr Ser Ser Leu His Leu Gly Leu Asp Ile
            20                  25                  30


Pro Lys Gly Lys His Ala Ile Arg Phe Leu Cys Leu Glu Lys Glu Asp
        35                  40                  45
```

```
Phe Tyr Tyr Pro Phe Asp Arg Ser Asp Asp Tyr Thr Val Ile Glu Ile
    50                  55                  60

Asn Leu Met Ala Gly Arg Ser Glu Glu Thr Lys Met Leu Leu Ile Phe
65                  70                  75                  80

Leu Leu Phe Ile Ala Leu Glu Arg Lys Leu Gly Ile Arg Ala His Asp
                85                  90                  95

Val Glu Ile Thr Ile Lys Glu Gln Pro Ala His Cys Trp Gly Phe Arg
            100                 105                 110

Gly Arg Thr Gly Asp Ser Ala Arg Asp Leu Asp Tyr Asp Ile Tyr Val
        115                 120                 125


<210>  19
<211>  235
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  I32-19A


<220>
<221>  MISC_FEATURE
<222>  (1)..(1)
<223>  optionally absent

<400>  19

Met Gly Ser Asp Leu Gln Lys Leu Gln Arg Phe Ser Thr Cys Asp Ile
1               5                   10                  15

Ser Asp Gly Leu Leu Asn Val Tyr Asn Ile Pro Thr Gly Gly Tyr Phe
            20                  25                  30

Pro Asn Leu Thr Ala Ile Ser Pro Pro Gln Asn Ser Ser Ile Val Gly
        35                  40                  45

Thr Ala Tyr Thr Val Leu Phe Ala Pro Ile Asp Asp Pro Arg Pro Ala
    50                  55                  60
```

```
Val Asn Tyr Ile Asp Ser Val Pro Pro Asn Ser Ile Leu Val Leu Ala
65                  70                  75                  80


Leu Glu Pro His Leu Gln Ser Gln Phe His Pro Phe Ile Lys Ile Thr
                85                  90                  95


Gln Ala Met Tyr Gly Gly Leu Met Ser Thr Arg Ala Gln Tyr Leu Lys
            100                 105                 110


Ser Asn Gly Thr Val Val Phe Gly Arg Ile Arg Asp Val Asp Glu His
        115                 120                 125


Arg Thr Leu Asn His Pro Val Phe Ala Tyr Gly Val Gly Ser Cys Ala
    130                 135                 140


Pro Lys Ala Val Val Lys Ala Val Gly Thr Asn Val Gln Leu Lys Ile
145                 150                 155                 160


Leu Thr Ser Asp Gly Val Thr Gln Thr Ile Cys Pro Gly Asp Tyr Ile
                165                 170                 175


Ala Gly Asp Asn Asn Gly Ile Val Arg Ile Pro Val Gln Glu Thr Asp
            180                 185                 190


Ile Ser Lys Leu Val Thr Tyr Ile Glu Lys Ser Ile Glu Val Asp Arg
        195                 200                 205


Leu Val Ser Glu Ala Ile Lys Asn Gly Leu Pro Ala Lys Ala Ala Gln
    210                 215                 220


Thr Ala Arg Arg Met Val Leu Lys Asp Tyr Ile
225                 230                 235


<210>  20
<211>  162
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  I32-19B
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<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> optionally absent

<400> 20

```
Met Ser Gly Met Arg Val Tyr Leu Gly Ala Asp His Ala Gly Tyr Glu
1               5                  10                  15


Leu Lys Gln Ala Ile Ile Ala Phe Leu Lys Met Thr Gly His Glu Pro
            20                  25                  30


Ile Asp Cys Gly Ala Leu Arg Tyr Asp Ala Asp Asp Asp Tyr Pro Ala
        35                  40                  45


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


Gly Ile Val Leu Gly Gly Ser Gly Asn Gly Glu Gln Ile Ala Ala Asn
65                  70                  75                  80


Lys Val Pro Gly Ala Arg Cys Ala Leu Ala Trp Ser Val Gln Thr Ala
                85                  90                  95


Ala Leu Ala Arg Glu His Asn Asn Ala Gln Leu Ile Gly Ile Gly Gly
            100                 105                 110


Arg Met His Thr Leu Glu Glu Ala Leu Arg Ile Val Lys Ala Phe Val
        115                 120                 125


Thr Thr Pro Trp Ser Lys Ala Gln Arg His Gln Arg Arg Ile Asp Ile
    130                 135                 140


Leu Ala Glu Tyr Glu Arg Thr His Glu Ala Pro Pro Val Pro Gly Ala
145                 150                 155                 160


Pro Ala
```

<210> 21
<211> 157
<212> PRT
<213> Artificial Sequence

<220>
<223> I32-28A

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> optionally absent

<400> 21

Met Gly Asp Asp Ala Arg Ile Ala Ala Ile Gly Asp Val Asp Glu Leu
1 5 10 15

Asn Ser Gln Ile Gly Val Leu Leu Ala Glu Pro Leu Pro Asp Asp Val
20 25 30

Arg Ala Ala Leu Ser Ala Ile Gln His Asp Leu Phe Asp Leu Gly Gly
35 40 45

Glu Leu Cys Ile Pro Gly His Ala Ala Ile Thr Glu Asp His Leu Leu
50 55 60

Arg Leu Ala Leu Trp Leu Val His Tyr Asn Gly Gln Leu Pro Pro Leu
65 70 75 80

Glu Glu Phe Ile Leu Pro Gly Gly Ala Arg Gly Ala Ala Leu Ala His
85 90 95

Val Cys Arg Thr Val Cys Arg Arg Ala Glu Arg Ser Ile Lys Ala Leu
100 105 110

Gly Ala Ser Glu Pro Leu Asn Ile Ala Pro Ala Ala Tyr Val Asn Leu
115 120 125

Leu Ser Asp Leu Leu Phe Val Leu Ala Arg Val Leu Asn Arg Ala Ala
130 135 140

```
Gly Gly Ala Asp Val Leu Trp Asp Arg Thr Arg Ala His
145                 150                 155


<210>  22
<211>  157
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  I32-28B


<220>
<221>  MISC_FEATURE
<222>  (1)..(1)
<223>  optionally absent

<400>  22

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


Gln Ala Ala Ala Leu Ala Phe Val Arg Glu Pro Ala Ala Ala Leu Ala
            20                  25                  30


Gly Val Gln Arg Leu Arg Gly Leu Asp Ser Asp Gly Glu Gln Val Trp
        35                  40                  45


Gly Glu Leu Leu Val Arg Val Pro Leu Leu Gly Glu Val Asp Leu Pro
    50                  55                  60


Phe Arg Ser Glu Ile Val Arg Thr Pro Gln Gly Ala Glu Leu Arg Pro
65                  70                  75                  80


Leu Thr Leu Thr Gly Glu Arg Ala Trp Val Ala Val Ser Gly Gln Ala
                85                  90                  95


Thr Ala Ala Glu Gly Gly Glu Met Ala Phe Ala Phe Gln Phe Gln Ala
            100                 105                 110


His Leu Ala Thr Pro Glu Ala Glu Gly Glu Gly Gly Ala Ala Phe Glu
        115                 120                 125
```

Val Met Val Gln Ala Ala Ala Gly Val Thr Leu Leu Leu Val Ala Met
130 135 140

Ala Leu Pro Gln Gly Leu Ala Ala Gly Leu Pro Pro Ala
145 150 155

<210> 23
<211> 156
<212> PRT
<213> Artificial Sequence

<220>
<223> I53-40A.1

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> optionally absent

<400> 23

Met Thr Lys Lys Val Gly Ile Val Asp Thr Thr Phe Ala Arg Val Asp
1 5 10 15

Met Ala Ser Ala Ala Ile Leu Thr Leu Lys Met Glu Ser Pro Asn Ile
20 25 30

Lys Ile Ile Arg Lys Thr Val Pro Gly Ile Lys Asp Leu Pro Val Ala
35 40 45

Cys Lys Lys Leu Leu Glu Glu Glu Gly Cys Asp Ile Val Met Ala Leu
50 55 60

Gly Met Pro Gly Lys Lys Glu Lys Asp Lys Val Cys Ala His Glu Ala
65 70 75 80

Ser Leu Gly Leu Met Leu Ala Gln Leu Met Thr Asn Lys His Ile Ile
85 90 95

Glu Val Phe Val His Glu Asp Glu Ala Lys Asp Asp Ala Glu Leu Lys
100 105 110

Ile Leu Ala Ala Arg Arg Ala Ile Glu His Ala Leu Asn Val Tyr Tyr
115 120 125

Leu Leu Phe Lys Pro Glu Tyr Leu Thr Arg Met Ala Gly Lys Gly Leu
130 135 140

Arg Gln Gly Phe Glu Asp Ala Gly Pro Ala Arg Glu
145 150 155

<210> 24
<211> 209
<212> PRT
<213> Artificial Sequence

<220>
<223> I53-40B.1

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> optionally absent

<400> 24

Met Asp Asp Ile Asn Asn Gln Leu Lys Arg Leu Lys Val Ile Pro Val
1 5 10 15

Ile Ala Ile Asp Asn Ala Glu Asp Ile Ile Pro Leu Gly Lys Val Leu
20 25 30

Ala Glu Asn Gly Leu Pro Ala Ala Glu Ile Thr Phe Arg Ser Ser Ala
35 40 45

Ala Val Lys Ala Ile Met Leu Leu Arg Ser Ala Gln Pro Glu Met Leu
50 55 60

Ile Gly Ala Gly Thr Ile Leu Asn Gly Val Gln Ala Leu Ala Ala Lys
65 70 75 80

Glu Ala Gly Ala Asp Phe Val Val Ser Pro Gly Phe Asn Pro Asn Thr
85 90 95

Val Arg Ala Cys Gln Ile Ile Gly Ile Asp Ile Val Pro Gly Val Asn
100 105 110

Asn Pro Ser Thr Val Glu Gln Ala Leu Glu Met Gly Leu Thr Thr Leu
115 120 125

Lys Phe Phe Pro Ala Glu Ala Ser Gly Gly Ile Ser Met Val Lys Ser
130 135 140

Leu Val Gly Pro Tyr Gly Asp Ile Arg Leu Met Pro Thr Gly Gly Ile
145 150 155 160

Thr Pro Asp Asn Ile Asp Asn Tyr Leu Ala Ile Pro Gln Val Leu Ala
165 170 175

Cys Gly Gly Thr Trp Met Val Asp Lys Lys Leu Val Arg Asn Gly Glu
180 185 190

Trp Asp Glu Ile Ala Arg Leu Thr Arg Glu Ile Val Glu Gln Val Asn
195 200 205

Pro

<210> 25
<211> 114
<212> PRT
<213> Artificial Sequence

<220>
<223> I53-47A.1

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> optionally absent

<400> 25

Met Pro Ile Phe Thr Leu Asn Thr Asn Ile Lys Ala Asp Asp Val Pro
1 5 10 15

Ser Asp Phe Leu Ser Leu Thr Ser Arg Leu Val Gly Leu Ile Leu Ser
            20   25   30

Lys Pro Gly Ser Tyr Val Ala Val His Ile Asn Thr Asp Gln Gln Leu
        35   40   45

Ser Phe Gly Gly Ser Thr Asn Pro Ala Ala Phe Gly Thr Leu Met Ser
    50   55   60

Ile Gly Gly Ile Glu Pro Asp Lys Asn Arg Asp His Ser Ala Val Leu
65   70   75   80

Phe Asp His Leu Asn Ala Met Leu Gly Ile Pro Lys Asn Arg Met Tyr
                85   90   95

Ile His Phe Val Asn Leu Asn Gly Asp Asp Val Gly Trp Asn Gly Thr
            100   105   110

Thr Phe

<210> 26
<211> 114
<212> PRT
<213> Artificial Sequence

<220>
<223> I53-47A.1NegT2

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> optionally absent

<400> 26

Met Pro Ile Phe Thr Leu Asn Thr Asn Ile Lys Ala Asp Asp Val Pro
1   5   10   15

Ser Asp Phe Leu Ser Leu Thr Ser Arg Leu Val Gly Leu Ile Leu Ser
            20   25   30

```
Glu Pro Gly Ser Tyr Val Ala Val His Ile Asn Thr Asp Gln Gln Leu
        35                  40                  45


Ser Phe Gly Gly Ser Thr Asn Pro Ala Ala Phe Gly Thr Leu Met Ser
    50                  55                  60


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


Phe Asp His Leu Asn Ala Met Leu Gly Ile Pro Lys Asn Arg Met Tyr
                85                  90                  95


Ile His Phe Val Asp Leu Asp Gly Asp Asp Val Gly Trp Asn Gly Thr
            100                 105                 110


Thr Phe



<210>  27
<211>  157
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  I53-47B.1


<220>
<221>  MISC_FEATURE
<222>  (1)..(1)
<223>  optionally absent

<400>  27

Met Asn Gln His Ser His Lys Asp His Glu Thr Val Arg Ile Ala Val
1               5                   10                  15


Val Arg Ala Arg Trp His Ala Asp Ile Val Asp Ala Cys Val Glu Ala
            20                  25                  30


Phe Glu Ile Ala Met Ala Ala Ile Gly Gly Asp Arg Phe Ala Val Asp
        35                  40                  45
```

```
Val Phe Asp Val Pro Gly Ala Tyr Glu Ile Pro Leu His Ala Arg Thr
    50                  55                  60


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


Val Asn Gly Gly Ile Tyr Arg His Glu Phe Val Ala Ser Ala Val Ile
                85                  90                  95


Asp Gly Met Met Asn Val Gln Leu Asp Thr Gly Val Pro Val Leu Ser
            100                 105                 110


Ala Val Leu Thr Pro His Arg Tyr Arg Asp Ser Asp Glu His His Arg
        115                 120                 125


Phe Phe Ala Ala His Phe Ala Val Lys Gly Val Glu Ala Ala Arg Ala
    130                 135                 140


Cys Ile Glu Ile Leu Asn Ala Arg Glu Lys Ile Ala Ala
145                 150                 155


<210>  28
<211>  157
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  I53-47B.1NegT2


<220>
<221>  MISC_FEATURE
<222>  (1)..(1)
<223>  optionally absent

<400>  28

Met Asn Gln His Ser His Lys Asp His Glu Thr Val Arg Ile Ala Val
1               5                   10                  15


Val Arg Ala Arg Trp His Ala Asp Ile Val Asp Ala Cys Val Glu Ala
            20                  25                  30
```

Phe Glu Ile Ala Met Ala Ala Ile Gly Gly Asp Arg Phe Ala Val Asp
35 40 45

Val Phe Asp Val Pro Gly Ala Tyr Glu Ile Pro Leu His Ala Arg Thr
50 55 60

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

Val Asp Gly Gly Ile Tyr Asp His Glu Phe Val Ala Ser Ala Val Ile
85 90 95

Asp Gly Met Met Asn Val Gln Leu Asp Thr Gly Val Pro Val Leu Ser
100 105 110

Ala Val Leu Thr Pro His Glu Tyr Glu Asp Ser Asp Glu Asp His Glu
115 120 125

Phe Phe Ala Ala His Phe Ala Val Lys Gly Val Glu Ala Ala Arg Ala
130 135 140

Cys Ile Glu Ile Leu Asn Ala Arg Glu Lys Ile Ala Ala
145 150 155

<210> 29
<211> 205
<212> PRT
<213> Artificial Sequence

<220>
<223> I53-50A.1

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> optionally absent

<400> 29

Met Lys Met Glu Glu Leu Phe Lys Lys His Lys Ile Val Ala Val Leu
1 5 10 15

```
Arg Ala Asn Ser Val Glu Glu Ala Ile Glu Lys Ala Val Ala Val Phe
            20                  25                  30

Ala Gly Gly Val His Leu Ile Glu Ile Thr Phe Thr Val Pro Asp Ala
        35                  40                  45

Asp Thr Val Ile Lys Ala Leu Ser Val Leu Lys Glu Lys Gly Ala Ile
    50                  55                  60

Ile Gly Ala Gly Thr Val Thr Ser Val Glu Gln Cys Arg Lys Ala Val
65                  70                  75                  80

Glu Ser Gly Ala Glu Phe Ile Val Ser Pro His Leu Asp Glu Glu Ile
                85                  90                  95

Ser Gln Phe Cys Lys Glu Lys Gly Val Phe Tyr Met Pro Gly Val Met
            100                 105                 110

Thr Pro Thr Glu Leu Val Lys Ala Met Lys Leu Gly His Asp Ile Leu
        115                 120                 125

Lys Leu Phe Pro Gly Glu Val Val Gly Pro Gln Phe Val Lys Ala Met
    130                 135                 140

Lys Gly Pro Phe Pro Asn Val Lys Phe Val Pro Thr Gly Gly Val Asn
145                 150                 155                 160

Leu Asp Asn Val Cys Glu Trp Phe Lys Ala Gly Val Leu Ala Val Gly
                165                 170                 175

Val Gly Asp Ala Leu Val Lys Gly Asp Pro Asp Glu Val Arg Glu Lys
            180                 185                 190

Ala Lys Lys Phe Val Glu Lys Ile Arg Gly Cys Thr Glu
        195                 200                 205
```

<210> 30
<211> 205
<212> PRT
<213> Artificial Sequence

<220>
<223> I53-50A.1NegT2

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> optionally absent

<400> 30

Met Lys Met Glu Glu Leu Phe Lys Lys His Lys Ile Val Ala Val Leu
1   5   10   15

Arg Ala Asn Ser Val Glu Glu Ala Ile Glu Lys Ala Val Ala Val Phe
            20   25   30

Ala Gly Gly Val His Leu Ile Glu Ile Thr Phe Thr Val Pro Asp Ala
        35   40   45

Asp Thr Val Ile Lys Ala Leu Ser Val Leu Lys Glu Lys Gly Ala Ile
    50   55   60

Ile Gly Ala Gly Thr Val Thr Ser Val Glu Gln Cys Arg Lys Ala Val
65   70   75   80

Glu Ser Gly Ala Glu Phe Ile Val Ser Pro His Leu Asp Glu Glu Ile
                85   90   95

Ser Gln Phe Cys Lys Glu Lys Gly Val Phe Tyr Met Pro Gly Val Met
            100   105   110

Thr Pro Thr Glu Leu Val Lys Ala Met Lys Leu Gly His Asp Ile Leu
        115   120   125

Lys Leu Phe Pro Gly Glu Val Val Gly Pro Glu Phe Val Glu Ala Met
    130   135   140

Lys Gly Pro Phe Pro Asn Val Lys Phe Val Pro Thr Gly Gly Val Asp
145   150   155   160

```
Leu Asp Asp Val Cys Glu Trp Phe Asp Ala Gly Val Leu Ala Val Gly
                165                 170                 175


Val Gly Asp Ala Leu Val Glu Gly Asp Pro Asp Glu Val Arg Glu Asp
            180                 185                 190


Ala Lys Glu Phe Val Glu Glu Ile Arg Gly Cys Thr Glu
        195                 200                 205


<210>  31
<211>  205
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  I53-50A.1PosT1


<220>
<221>  MISC_FEATURE
<222>  (1)..(1)
<223>  optionally absent

<400>  31

Met Lys Met Glu Glu Leu Phe Lys Lys His Lys Ile Val Ala Val Leu
1               5                   10                  15


Arg Ala Asn Ser Val Glu Glu Ala Ile Glu Lys Ala Val Ala Val Phe
            20                  25                  30


Ala Gly Gly Val His Leu Ile Glu Ile Thr Phe Thr Val Pro Asp Ala
        35                  40                  45


Asp Thr Val Ile Lys Ala Leu Ser Val Leu Lys Glu Lys Gly Ala Ile
    50                  55                  60


Ile Gly Ala Gly Thr Val Thr Ser Val Glu Gln Cys Arg Lys Ala Val
65                  70                  75                  80


Glu Ser Gly Ala Glu Phe Ile Val Ser Pro His Leu Asp Glu Glu Ile
                85                  90                  95
```

```
Ser Gln Phe Cys Lys Glu Lys Gly Val Phe Tyr Met Pro Gly Val Met
            100                 105                 110


Thr Pro Thr Glu Leu Val Lys Ala Met Lys Leu Gly His Asp Ile Leu
        115                 120                 125


Lys Leu Phe Pro Gly Glu Val Val Gly Pro Gln Phe Val Lys Ala Met
    130                 135                 140


Lys Gly Pro Phe Pro Asn Val Lys Phe Val Pro Thr Gly Gly Val Asn
145                 150                 155                 160


Leu Asp Asn Val Cys Lys Trp Phe Lys Ala Gly Val Leu Ala Val Gly
                165                 170                 175


Val Gly Lys Ala Leu Val Lys Gly Lys Pro Asp Glu Val Arg Glu Lys
            180                 185                 190


Ala Lys Lys Phe Val Lys Lys Ile Arg Gly Cys Thr Glu
        195                 200                 205


<210>  32
<211>  157
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  I53-50B.1


<220>
<221>  MISC_FEATURE
<222>  (1)..(1)
<223>  optionally absent

<400>  32

Met Asn Gln His Ser His Lys Asp His Glu Thr Val Arg Ile Ala Val
1               5                   10                  15


Val Arg Ala Arg Trp His Ala Glu Ile Val Asp Ala Cys Val Ser Ala
            20                  25                  30
```

```
Phe Glu Ala Ala Met Arg Asp Ile Gly Gly Asp Arg Phe Ala Val Asp
        35                  40                  45


Val Phe Asp Val Pro Gly Ala Tyr Glu Ile Pro Leu His Ala Arg Thr
    50                  55                  60


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


Val Asn Gly Gly Ile Tyr Arg His Glu Phe Val Ala Ser Ala Val Ile
                85                  90                  95


Asp Gly Met Met Asn Val Gln Leu Asp Thr Gly Val Pro Val Leu Ser
            100                 105                 110


Ala Val Leu Thr Pro His Arg Tyr Arg Asp Ser Asp Ala His Thr Leu
        115                 120                 125


Leu Phe Leu Ala Leu Phe Ala Val Lys Gly Met Glu Ala Ala Arg Ala
    130                 135                 140


Cys Val Glu Ile Leu Ala Ala Arg Glu Lys Ile Ala Ala
145                 150                 155


<210>  33
<211>  157
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  I53-50B.1NegT2


<220>
<221>  MISC_FEATURE
<222>  (1)..(1)
<223>  optionally absent

<400>  33

Met Asn Gln His Ser His Lys Asp His Glu Thr Val Arg Ile Ala Val
1               5                   10                  15
```

```
Val Arg Ala Arg Trp His Ala Glu Ile Val Asp Ala Cys Val Ser Ala
            20                  25                  30


Phe Glu Ala Ala Met Arg Asp Ile Gly Gly Asp Arg Phe Ala Val Asp
        35                  40                  45


Val Phe Asp Val Pro Gly Ala Tyr Glu Ile Pro Leu His Ala Arg Thr
    50                  55                  60


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


Val Asp Gly Gly Ile Tyr Asp His Glu Phe Val Ala Ser Ala Val Ile
                85                  90                  95


Asp Gly Met Met Asn Val Gln Leu Asp Thr Gly Val Pro Val Leu Ser
            100                 105                 110


Ala Val Leu Thr Pro His Glu Tyr Glu Asp Ser Asp Ala Asp Thr Leu
        115                 120                 125


Leu Phe Leu Ala Leu Phe Ala Val Lys Gly Met Glu Ala Ala Arg Ala
    130                 135                 140


Cys Val Glu Ile Leu Ala Ala Arg Glu Lys Ile Ala Ala
145                 150                 155


<210>  34
<211>  157
<212>  PRT
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<220>
<223>  I53-50B.4PosT1


<220>
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<222>  (1)..(1)
<223>  optionally absent

<400>  34
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Met Asn Gln His Ser His Lys Asp His Glu Thr Val Arg Ile Ala Val
1               5                  10                  15

Val Arg Ala Arg Trp His Ala Glu Ile Val Asp Ala Cys Val Ser Ala
            20                  25                  30

Phe Glu Ala Ala Met Arg Asp Ile Gly Gly Asp Arg Phe Ala Val Asp
        35                  40                  45

Val Phe Asp Val Pro Gly Ala Tyr Glu Ile Pro Leu His Ala Arg Thr
    50                  55                  60

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

Val Asn Gly Gly Ile Tyr Arg His Glu Phe Val Ala Ser Ala Val Ile
                85                  90                  95

Asn Gly Met Met Asn Val Gln Leu Asn Thr Gly Val Pro Val Leu Ser
            100                 105                 110

Ala Val Leu Thr Pro His Asn Tyr Asp Lys Ser Lys Ala His Thr Leu
        115                 120                 125

Leu Phe Leu Ala Leu Phe Ala Val Lys Gly Met Glu Ala Ala Arg Ala
    130                 135                 140

Cys Val Glu Ile Leu Ala Ala Arg Glu Lys Ile Ala Ala
145                 150                 155
```

<210> 35
<211> 156
<212> PRT
<213> Artificial Sequence

<220>
<223> I53-40 A genus

<220>
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<222> (1)..(1)

<223> optionally absent

<220>
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<222> (70)..(70)
<223> Xaa is A or K

<400> 35

Met Thr Lys Lys Val Gly Ile Val Asp Thr Thr Phe Ala Arg Val Asp
1 5 10 15

Met Ala Ser Ala Ala Ile Leu Thr Leu Lys Met Glu Ser Pro Asn Ile
20 25 30

Lys Ile Ile Arg Lys Thr Val Pro Gly Ile Lys Asp Leu Pro Val Ala
35 40 45

Cys Lys Lys Leu Leu Glu Glu Glu Gly Cys Asp Ile Val Met Ala Leu
50 55 60

Gly Met Pro Gly Lys Xaa Glu Lys Asp Lys Val Cys Ala His Glu Ala
65 70 75 80

Ser Leu Gly Leu Met Leu Ala Gln Leu Met Thr Asn Lys His Ile Ile
85 90 95

Glu Val Phe Val His Glu Asp Glu Ala Lys Asp Asp Ala Glu Leu Lys
100 105 110

Ile Leu Ala Ala Arg Arg Ala Ile Glu His Ala Leu Asn Val Tyr Tyr
115 120 125

Leu Leu Phe Lys Pro Glu Tyr Leu Thr Arg Met Ala Gly Lys Gly Leu
130 135 140

Arg Gln Gly Phe Glu Asp Ala Gly Pro Ala Arg Glu
145 150 155

<210> 36
<211> 209
<212> PRT

<213> Artificial Sequence

<220>
<223> I53-40 B genus

<220>
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<222> (1)..(1)
<223> optionally absent

<220>
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<222> (2)..(2)
<223> Xaa is S or D

<220>
<221> MISC_FEATURE
<222> (3)..(3)
<223> Xaa is T or D

<220>
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<222> (10)..(10)
<223> Xaa is A or R

<220>
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<222> (85)..(85)
<223> Xaa is T or D

<220>
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<222> (119)..(119)
<223> Xaa is A or Q

<220>
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<222> (163)..(163)
<223> Xaa is S or D

<220>
<221> MISC_FEATURE
<222> (189)..(189)
<223> Xaa is T or R

<400> 36

Met Xaa Xaa Ile Asn Asn Gln Leu Lys Xaa Leu Lys Val Ile Pro Val
1   5   10   15

```
Ile Ala Ile Asp Asn Ala Glu Asp Ile Ile Pro Leu Gly Lys Val Leu
            20                  25                  30

Ala Glu Asn Gly Leu Pro Ala Ala Glu Ile Thr Phe Arg Ser Ser Ala
        35                  40                  45

Ala Val Lys Ala Ile Met Leu Leu Arg Ser Ala Gln Pro Glu Met Leu
    50                  55                  60

Ile Gly Ala Gly Thr Ile Leu Asn Gly Val Gln Ala Leu Ala Ala Lys
65                  70                  75                  80

Glu Ala Gly Ala Xaa Phe Val Val Ser Pro Gly Phe Asn Pro Asn Thr
                85                  90                  95

Val Arg Ala Cys Gln Ile Ile Gly Ile Asp Ile Val Pro Gly Val Asn
            100                 105                 110

Asn Pro Ser Thr Val Glu Xaa Ala Leu Glu Met Gly Leu Thr Thr Leu
        115                 120                 125

Lys Phe Phe Pro Ala Glu Ala Ser Gly Gly Ile Ser Met Val Lys Ser
    130                 135                 140

Leu Val Gly Pro Tyr Gly Asp Ile Arg Leu Met Pro Thr Gly Gly Ile
145                 150                 155                 160

Thr Pro Xaa Asn Ile Asp Asn Tyr Leu Ala Ile Pro Gln Val Leu Ala
                165                 170                 175

Cys Gly Gly Thr Trp Met Val Asp Lys Lys Leu Val Xaa Asn Gly Glu
            180                 185                 190

Trp Asp Glu Ile Ala Arg Leu Thr Arg Glu Ile Val Glu Gln Val Asn
        195                 200                 205

Pro
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<210> 37
<211> 114
<212> PRT
<213> Artificial Sequence

<220>
<223> I53-47A genus

<220>
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<222> (1)..(1)
<223> optionally absent

<220>
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<222> (13)..(13)
<223> Xaa is T or D

<220>
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<222> (33)..(33)
<223> Xaa is K or E

<220>
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<222> (71)..(71)
<223> Xaa is S or D

<220>
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<222> (74)..(74)
<223> Xaa is R or E

<220>
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<222> (101)..(101)
<223> Xaa is N or D

<220>
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<222> (103)..(103)
<223> Xaa is N or D

<400> 37

Met Pro Ile Phe Thr Leu Asn Thr Asn Ile Lys Ala Xaa Asp Val Pro
1 5 10 15

Ser Asp Phe Leu Ser Leu Thr Ser Arg Leu Val Gly Leu Ile Leu Ser
20 25 30

```
Xaa Pro Gly Ser Tyr Val Ala Val His Ile Asn Thr Asp Gln Gln Leu
        35                  40                  45


Ser Phe Gly Gly Ser Thr Asn Pro Ala Ala Phe Gly Thr Leu Met Ser
    50                  55                  60


Ile Gly Gly Ile Glu Pro Xaa Lys Asn Xaa Asp His Ser Ala Val Leu
65                  70                  75                  80


Phe Asp His Leu Asn Ala Met Leu Gly Ile Pro Lys Asn Arg Met Tyr
                85                  90                  95


Ile His Phe Val Xaa Leu Xaa Gly Asp Asp Val Gly Trp Asn Gly Thr
            100                 105                 110


Thr Phe



<210>  38
<211>  157
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  I53-47B genus


<220>
<221>  MISC_FEATURE
<222>  (1)..(1)
<223>  optionally absent

<220>
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<222>  (9)..(9)
<223>  Xaa is Y or H

<220>
<221>  MISC_FEATURE
<222>  (82)..(82)
<223>  Xaa is N or D

<220>
<221>  MISC_FEATURE
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<222> (87)..(87)
<223> Xaa is R or D

<220>
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<222> (105)..(105)
<223> Xaa is S or D

<220>
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<222> (119)..(119)
<223> Xaa is R or E

<220>
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<223> Xaa is R or E

<220>
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<222> (124)..(124)
<223> Xaa is A or D

<220>
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<222> (126)..(126)
<223> Xaa is H or D

<220>
<221> MISC_FEATURE
<222> (128)..(128)
<223> Xaa is R or E

<220>
<221> MISC_FEATURE
<222> (150)..(150)
<223> Xaa is A or N

<400> 38

Met Asn Gln His Ser His Lys Asp Xaa Glu Thr Val Arg Ile Ala Val
1 5 10 15

Val Arg Ala Arg Trp His Ala Asp Ile Val Asp Ala Cys Val Glu Ala
20 25 30

Phe Glu Ile Ala Met Ala Ala Ile Gly Gly Asp Arg Phe Ala Val Asp
35 40 45

```
Val Phe Asp Val Pro Gly Ala Tyr Glu Ile Pro Leu His Ala Arg Thr
    50                  55                  60


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


Val Xaa Gly Gly Ile Tyr Xaa His Glu Phe Val Ala Ser Ala Val Ile
                85                  90                  95


Asp Gly Met Met Asn Val Gln Leu Xaa Thr Gly Val Pro Val Leu Ser
            100                 105                 110


Ala Val Leu Thr Pro His Xaa Tyr Xaa Asp Ser Xaa Glu Xaa His Xaa
        115                 120                 125


Phe Phe Ala Ala His Phe Ala Val Lys Gly Val Glu Ala Ala Arg Ala
    130                 135                 140


Cys Ile Glu Ile Leu Xaa Ala Arg Glu Lys Ile Ala Ala
145                 150                 155


<210>  39
<211>  205
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  I53-50A genus


<220>
<221>  MISC_FEATURE
<222>  (1)..(1)
<223>  optionally absent

<220>
<221>  MISC_FEATURE
<222>  (126)..(126)
<223>  Xaa is T or D

<220>
<221>  MISC_FEATURE
<222>  (139)..(139)
<223>  Xaa is Q or E
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<220>
<221> MISC_FEATURE
<222> (142)..(142)
<223> Xaa is K or E

<220>
<221> MISC_FEATURE
<222> (160)..(160)
<223> Xaa is N or D

<220>
<221> MISC_FEATURE
<222> (163)..(163)
<223> Xaa is N or D

<220>
<221> MISC_FEATURE
<222> (166)..(166)
<223> Xaa is E or K

<220>
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<222> (169)..(169)
<223> Xaa is D or K

<220>
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<222> (179)..(179)
<223> Xaa is S, D or K

<220>
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<222> (183)..(183)
<223> Xaa is K or E

<220>
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<222> (185)..(185)
<223> Xaa is T, D, or K

<220>
<221> MISC_FEATURE
<222> (192)..(192)
<223> Xaa is D or K

<220>
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<222> (195)..(195)
<223> Xaa is A, E, or K

<220>
<221> MISC_FEATURE

<222> (198)..(198)
<223> Xaa is E or K

<220>
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<222> (199)..(199)
<223> Xaa is E or K

<400> 39

Met Lys Met Glu Glu Leu Phe Lys Lys His Lys Ile Val Ala Val Leu
1 5 10 15

Arg Ala Asn Ser Val Glu Glu Ala Ile Glu Lys Ala Val Ala Val Phe
20 25 30

Ala Gly Gly Val His Leu Ile Glu Ile Thr Phe Thr Val Pro Asp Ala
35 40 45

Asp Thr Val Ile Lys Ala Leu Ser Val Leu Lys Glu Lys Gly Ala Ile
50 55 60

Ile Gly Ala Gly Thr Val Thr Ser Val Glu Gln Cys Arg Lys Ala Val
65 70 75 80

Glu Ser Gly Ala Glu Phe Ile Val Ser Pro His Leu Asp Glu Glu Ile
85 90 95

Ser Gln Phe Cys Lys Glu Lys Gly Val Phe Tyr Met Pro Gly Val Met
100 105 110

Thr Pro Thr Glu Leu Val Lys Ala Met Lys Leu Gly His Xaa Ile Leu
115 120 125

Lys Leu Phe Pro Gly Glu Val Val Gly Pro Xaa Phe Val Xaa Ala Met
130 135 140

Lys Gly Pro Phe Pro Asn Val Lys Phe Val Pro Thr Gly Gly Val Xaa
145 150 155 160

Leu Asp Xaa Val Cys Xaa Trp Phe Xaa Ala Gly Val Leu Ala Val Gly
165 170 175

Val Gly Xaa Ala Leu Val Xaa Gly Xaa Pro Asp Glu Val Arg Glu Xaa
180 185 190

Ala Lys Xaa Phe Val Xaa Xaa Ile Arg Gly Cys Thr Glu
195 200 205

<210> 40
<211> 157
<212> PRT
<213> Artificial Sequence

<220>
<223> I53-50B genus

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> optionally absent

<220>
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<222> (9)..(9)
<223> Xaa is Y or H

<220>
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<222> (38)..(38)
<223> Xaa is A or R

<220>
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<222> (82)..(82)
<223> Xaa is N or D

<220>
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<222> (87)..(87)
<223> Xaa is R or D

<220>
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<222> (97)..(97)
<223> Xaa is N or D

<220>
<221> MISC_FEATURE
<222> (105)..(105)

<223> Xaa is S, N, or D

<220>
<221> MISC_FEATURE
<222> (119)..(119)
<223> Xaa is R, E, or N

<220>
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<223> Xaa is R, E, or D

<220>
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<223> Xaa is K or D

<220>
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<223> Xaa is K or D

<220>
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<222> (126)..(126)
<223> Xaa is H or D

<400> 40

Met Asn Gln His Ser His Lys Asp Xaa Glu Thr Val Arg Ile Ala Val
1   5   10   15

Val Arg Ala Arg Trp His Ala Glu Ile Val Asp Ala Cys Val Ser Ala
            20   25   30

Phe Glu Ala Ala Met Xaa Asp Ile Gly Gly Asp Arg Phe Ala Val Asp
        35   40   45

Val Phe Asp Val Pro Gly Ala Tyr Glu Ile Pro Leu His Ala Arg Thr
    50   55   60

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

Val Xaa Gly Gly Ile Tyr Xaa His Glu Phe Val Ala Ser Ala Val Ile
                85   90   95

Xaa Gly Met Met Asn Val Gln Leu Xaa Thr Gly Val Pro Val Leu Ser
100 105 110

Ala Val Leu Thr Pro His Xaa Tyr Xaa Xaa Ser Xaa Ala Xaa Thr Leu
115 120 125

Leu Phe Leu Ala Leu Phe Ala Val Lys Gly Met Glu Ala Ala Arg Ala
130 135 140

Cys Val Glu Ile Leu Ala Ala Arg Glu Lys Ile Ala Ala
145 150 155

<210> 41
<211> 159
<212> PRT
<213> Artificial Sequence

<220>
<223> T32-28A

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> optionally absent

<400> 41

Met Gly Glu Val Pro Ile Gly Asp Pro Lys Glu Leu Asn Gly Met Glu
1 5 10 15

Ile Ala Ala Val Tyr Leu Gln Pro Ile Glu Met Glu Pro Arg Gly Ile
20 25 30

Asp Leu Ala Ala Ser Leu Ala Asp Ile His Leu Glu Ala Asp Ile His
35 40 45

Ala Leu Lys Asn Asn Pro Asn Gly Phe Pro Glu Gly Phe Trp Met Pro
50 55 60

Tyr Leu Thr Ile Ala Tyr Ala Leu Ala Asn Ala Asp Thr Gly Ala Ile
65 70 75 80

```
Lys Thr Gly Thr Leu Met Pro Met Val Ala Asp Asp Gly Pro His Tyr
                85                  90                  95


Gly Ala Asn Ile Ala Met Glu Lys Asp Lys Lys Gly Gly Phe Gly Val
            100                 105                 110


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


Phe Gly Arg His Val Asp Glu Glu Thr Gly Val Gly Lys Trp Phe Glu
    130                 135                 140


Pro Phe Val Val Thr Tyr Phe Phe Lys Tyr Thr Gly Thr Pro Lys
145                 150                 155


<210>  42
<211>  184
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  T32-28B


<220>
<221>  MISC_FEATURE
<222>  (1)..(1)
<223>  optionally absent

<400>  42

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


Met Glu Leu Gly Asp Ala Met Leu Lys Ser Ala Asn Val Asp Leu Leu
            20                  25                  30


Val Ser Lys Thr Ile Ser Pro Gly Lys Phe Leu Leu Met Leu Gly Gly
        35                  40                  45


Asp Ile Gly Ala Ile Gln Gln Ala Ile Glu Thr Gly Thr Ser Gln Ala
    50                  55                  60
```

```
Gly Glu Met Leu Val Asp Ser Leu Val Leu Ala Asn Ile His Pro Ser
65                  70                  75                  80


Val Leu Pro Ala Ile Ser Gly Leu Asn Ser Val Asp Lys Arg Gln Ala
                85                  90                  95


Val Gly Ile Val Glu Thr Trp Ser Val Ala Ala Cys Ile Ser Ala Ala
            100                 105                 110


Asp Leu Ala Val Lys Gly Ser Asn Val Thr Leu Val Arg Val His Met
        115                 120                 125


Ala Phe Gly Ile Gly Gly Lys Cys Tyr Met Val Val Ala Gly Asp Val
    130                 135                 140


Leu Asp Val Ala Ala Ala Val Ala Thr Ala Ser Leu Ala Ala Gly Ala
145                 150                 155                 160


Lys Gly Leu Leu Val Tyr Ala Ser Ile Ile Pro Arg Pro His Glu Ala
                165                 170                 175


Met Trp Arg Gln Met Val Glu Gly
            180


<210>  43
<211>  103
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  T33-09A


<220>
<221>  MISC_FEATURE
<222>  (1)..(1)
<223>  optionally absent

<400>  43

Met Glu Glu Val Val Leu Ile Thr Val Pro Ser Ala Leu Val Ala Val
1               5                   10                  15
```

```
Lys Ile Ala His Ala Leu Val Glu Glu Arg Leu Ala Ala Cys Val Asn
            20                  25                  30


Ile Val Pro Gly Leu Thr Ser Ile Tyr Arg Trp Gln Gly Ser Val Val
        35                  40                  45


Ser Asp His Glu Leu Leu Leu Leu Val Lys Thr Thr Thr His Ala Phe
    50                  55                  60


Pro Lys Leu Lys Glu Arg Val Lys Ala Leu His Pro Tyr Thr Val Pro
65                  70                  75                  80


Glu Ile Val Ala Leu Pro Ile Ala Glu Gly Asn Arg Glu Tyr Leu Asp
                85                  90                  95


Trp Leu Arg Glu Asn Thr Gly
            100


<210>  44
<211>  122
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  T33-09B


<220>
<221>  MISC_FEATURE
<222>  (1)..(1)
<223>  optionally absent

<400>  44

Met Val Arg Gly Ile Arg Gly Ala Ile Thr Val Glu Glu Asp Thr Pro
1               5                   10                  15


Ala Ala Ile Leu Ala Ala Thr Ile Glu Leu Leu Leu Lys Met Leu Glu
            20                  25                  30


Ala Asn Gly Ile Gln Ser Tyr Glu Glu Leu Ala Ala Val Ile Phe Thr
        35                  40                  45
```

```
Val Thr Glu Asp Leu Thr Ser Ala Phe Pro Ala Glu Ala Ala Arg Leu
    50                  55                  60


Ile Gly Met His Arg Val Pro Leu Leu Ser Ala Arg Glu Val Pro Val
65                  70                  75                  80


Pro Gly Ser Leu Pro Arg Val Ile Arg Val Leu Ala Leu Trp Asn Thr
                85                  90                  95


Asp Thr Pro Gln Asp Arg Val Arg His Val Tyr Leu Asn Glu Ala Val
            100                 105                 110


Arg Leu Arg Pro Asp Leu Glu Ser Ala Gln
        115                 120


<210>  45
<211>  177
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  T33-15A


<220>
<221>  MISC_FEATURE
<222>  (1)..(1)
<223>  optionally absent

<400>  45

Met Ser Lys Ala Lys Ile Gly Ile Val Thr Val Ser Asp Arg Ala Ser
1               5                   10                  15


Ala Gly Ile Thr Ala Asp Ile Ser Gly Lys Ala Ile Ile Leu Ala Leu
            20                  25                  30


Asn Leu Tyr Leu Thr Ser Glu Trp Glu Pro Ile Tyr Gln Val Ile Pro
        35                  40                  45


Asp Glu Gln Asp Val Ile Glu Thr Thr Leu Ile Lys Met Ala Asp Glu
    50                  55                  60
```

```
Gln Asp Cys Cys Leu Ile Val Thr Thr Gly Gly Thr Gly Pro Ala Lys
65                  70                  75                  80


Arg Asp Val Thr Pro Glu Ala Thr Glu Ala Val Cys Asp Arg Met Met
                85                  90                  95


Pro Gly Phe Gly Glu Leu Met Arg Ala Glu Ser Leu Lys Glu Val Pro
            100                 105                 110


Thr Ala Ile Leu Ser Arg Gln Thr Ala Gly Leu Arg Gly Asp Ser Leu
        115                 120                 125


Ile Val Asn Leu Pro Gly Asp Pro Ala Ser Ile Ser Asp Cys Leu Leu
    130                 135                 140


Ala Val Phe Pro Ala Ile Pro Tyr Cys Ile Asp Leu Met Glu Gly Pro
145                 150                 155                 160


Tyr Leu Glu Cys Asn Glu Ala Met Ile Lys Pro Phe Arg Pro Lys Ala
                165                 170                 175


Lys
```

<210> 46
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<223> T33-15B

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> optionally absent

<400> 46

```
Met Val Arg Gly Ile Arg Gly Ala Ile Thr Val Asn Ser Asp Thr Pro
1               5                   10                  15
```

```
Thr Ser Ile Ile Ile Ala Thr Ile Leu Leu Leu Glu Lys Met Leu Glu
            20                  25                  30


Ala Asn Gly Ile Gln Ser Tyr Glu Glu Leu Ala Ala Val Ile Phe Thr
        35                  40                  45


Val Thr Glu Asp Leu Thr Ser Ala Phe Pro Ala Glu Ala Ala Arg Gln
    50                  55                  60


Ile Gly Met His Arg Val Pro Leu Leu Ser Ala Arg Glu Val Pro Val
65                  70                  75                  80


Pro Gly Ser Leu Pro Arg Val Ile Arg Val Leu Ala Leu Trp Asn Thr
                85                  90                  95


Asp Thr Pro Gln Asp Arg Val Arg His Val Tyr Leu Ser Glu Ala Val
            100                 105                 110


Arg Leu Arg Pro Asp Leu Glu Ser Ala Gln
        115                 120


<210>  47
<211>  172
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  T33-21A


<220>
<221>  MISC_FEATURE
<222>  (1)..(1)
<223>  optionally absent

<400>  47

Met Arg Ile Thr Thr Lys Val Gly Asp Lys Gly Ser Thr Arg Leu Phe
1               5                   10                  15


Gly Gly Glu Glu Val Trp Lys Asp Ser Pro Ile Ile Glu Ala Asn Gly
            20                  25                  30
```

```
Thr Leu Asp Glu Leu Thr Ser Phe Ile Gly Glu Ala Lys His Tyr Val
        35                  40                  45


Asp Glu Glu Met Lys Gly Ile Leu Glu Glu Ile Gln Asn Asp Ile Tyr
    50                  55                  60


Lys Ile Met Gly Glu Ile Gly Ser Lys Gly Lys Ile Glu Gly Ile Ser
65                  70                  75                  80


Glu Glu Arg Ile Ala Trp Leu Leu Lys Leu Ile Leu Arg Tyr Met Glu
                85                  90                  95


Met Val Asn Leu Lys Ser Phe Val Leu Pro Gly Gly Thr Leu Glu Ser
            100                 105                 110


Ala Lys Leu Asp Val Cys Arg Thr Ile Ala Arg Arg Ala Leu Arg Lys
        115                 120                 125


Val Leu Thr Val Thr Arg Glu Phe Gly Ile Gly Ala Glu Ala Ala Ala
    130                 135                 140


Tyr Leu Leu Ala Leu Ser Asp Leu Leu Phe Leu Leu Ala Arg Val Ile
145                 150                 155                 160


Glu Ile Glu Lys Asn Lys Leu Lys Glu Val Arg Ser
                165                 170


<210>  48
<211>  123
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  T33-21B


<220>
<221>  MISC_FEATURE
<222>  (1)..(1)
<223>  optionally absent

<400>  48
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```
Met Pro His Leu Val Ile Glu Ala Thr Ala Asn Leu Arg Leu Glu Thr
1               5                   10                  15


Ser Pro Gly Glu Leu Leu Glu Gln Ala Asn Lys Ala Leu Phe Ala Ser
            20                  25                  30


Gly Gln Phe Gly Glu Ala Asp Ile Lys Ser Arg Phe Val Thr Leu Glu
        35                  40                  45


Ala Tyr Arg Gln Gly Thr Ala Ala Val Glu Arg Ala Tyr Leu His Ala
    50                  55                  60


Cys Leu Ser Ile Leu Asp Gly Arg Asp Ile Ala Thr Arg Thr Leu Leu
65                  70                  75                  80


Gly Ala Ser Leu Cys Ala Val Leu Ala Glu Ala Val Ala Gly Gly Gly
                85                  90                  95


Glu Glu Gly Val Gln Val Ser Val Glu Val Arg Glu Met Glu Arg Leu
            100                 105                 110


Ser Tyr Ala Lys Arg Val Val Ala Arg Gln Arg
        115                 120


<210>  49
<211>  158
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  T33-28A


<220>
<221>  MISC_FEATURE
<222>  (1)..(1)
<223>  optionally absent

<400>  49

Met Glu Ser Val Asn Thr Ser Phe Leu Ser Pro Ser Leu Val Thr Ile
1               5                   10                  15
```

```
Arg Asp Phe Asp Asn Gly Gln Phe Ala Val Leu Arg Ile Gly Arg Thr
            20                  25                  30


Gly Phe Pro Ala Asp Lys Gly Asp Ile Asp Leu Cys Leu Asp Lys Met
        35                  40                  45


Ile Gly Val Arg Ala Ala Gln Ile Phe Leu Gly Asp Asp Thr Glu Asp
    50                  55                  60


Gly Phe Lys Gly Pro His Ile Arg Ile Arg Cys Val Asp Ile Asp Asp
65                  70                  75                  80


Lys His Thr Tyr Asn Ala Met Val Tyr Val Asp Leu Ile Val Gly Thr
                85                  90                  95


Gly Ala Ser Glu Val Glu Arg Glu Thr Ala Glu Glu Glu Ala Lys Leu
            100                 105                 110


Ala Leu Arg Val Ala Leu Gln Val Asp Ile Ala Asp Glu His Ser Cys
        115                 120                 125


Val Thr Gln Phe Glu Met Lys Leu Arg Glu Glu Leu Leu Ser Ser Asp
    130                 135                 140


Ser Phe His Pro Asp Lys Asp Glu Tyr Tyr Lys Asp Phe Leu
145                 150                 155


<210>  50
<211>  113
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  T33-28B


<220>
<221>  MISC_FEATURE
<222>  (1)..(1)
<223>  optionally absent

<400>  50
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```
Met Pro Val Ile Gln Thr Phe Val Ser Thr Pro Leu Asp His His Lys
1               5                   10                  15


Arg Leu Leu Leu Ala Ile Ile Tyr Arg Ile Val Thr Arg Val Val Leu
            20                  25                  30


Gly Lys Pro Glu Asp Leu Val Met Met Thr Phe His Asp Ser Thr Pro
        35                  40                  45


Met His Phe Phe Gly Ser Thr Asp Pro Val Ala Cys Val Arg Val Glu
    50                  55                  60


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


Val Thr Ala Ala Ile Thr Ala Val Cys Gly Ile Val Ala Asp Arg Ile
                85                  90                  95


Phe Val Leu Tyr Phe Ser Pro Leu His Cys Gly Trp Asn Gly Thr Asn
            100                 105                 110


Phe
```

<210> 51
<211> 103
<212> PRT
<213> Artificial Sequence

<220>
<223> T33-31A

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> optionally absent

<400> 51

```
Met Glu Glu Val Val Leu Ile Thr Val Pro Ser Ala Leu Val Ala Val
1               5                   10                  15
```

Lys Ile Ala His Ala Leu Val Glu Glu Arg Leu Ala Ala Cys Val Asn
            20   25   30

Ile Val Pro Gly Leu Thr Ser Ile Tyr Arg Glu Glu Gly Ser Val Val
        35   40   45

Ser Asp His Glu Leu Leu Leu Leu Val Lys Thr Thr Thr Asp Ala Phe
    50   55   60

Pro Lys Leu Lys Glu Arg Val Lys Glu Leu His Pro Tyr Glu Val Pro
65   70   75   80

Glu Ile Val Ala Leu Pro Ile Ala Glu Gly Asn Arg Glu Tyr Leu Asp
                85   90   95

Trp Leu Arg Glu Asn Thr Gly
            100

<210> 52
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic peptide

<400> 52

Gln Asn Ile Thr Glu Glu Phe
1   5

<210> 53
<211> 513
<212> PRT
<213> Artificial Sequence

<220>
<223> DS-Cav1

<220>
<221> MISC_FEATURE
<222> (1)..(25)
<223> optionally absent

<220>
<221> MISC_FEATURE
<222> (508)..(513)
<223> optionally absent

<400> 53

```
Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
1               5                   10                  15


Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
            20                  25                  30


Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
        35                  40                  45


Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
    50                  55                  60


Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65                  70                  75                  80


Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
                85                  90                  95


Met Gln Ser Thr Pro Ala Thr Asn Asn Arg Ala Arg Arg Glu Leu Pro
            100                 105                 110


Arg Phe Met Asn Tyr Thr Leu Asn Asn Ala Lys Lys Thr Asn Val Thr
        115                 120                 125


Leu Ser Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Val
    130                 135                 140


Gly Ser Ala Ile Ala Ser Gly Val Ala Val Cys Lys Val Leu His Leu
145                 150                 155                 160


Glu Gly Glu Val Asn Lys Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys
                165                 170                 175
```

```
Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Phe Lys Val
            180                 185                 190

Leu Asp Leu Lys Asn Tyr Ile Asp Lys Gln Leu Leu Pro Ile Leu Asn
        195                 200                 205

Lys Gln Ser Cys Ser Ile Ser Asn Ile Glu Thr Val Ile Glu Phe Gln
    210                 215                 220

Gln Lys Asn Asn Arg Leu Leu Glu Ile Thr Arg Glu Phe Ser Val Asn
225                 230                 235                 240

Ala Gly Val Thr Thr Pro Val Ser Thr Tyr Met Leu Thr Asn Ser Glu
                245                 250                 255

Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
            260                 265                 270

Leu Met Ser Asn Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile
        275                 280                 285

Met Cys Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro
    290                 295                 300

Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro
305                 310                 315                 320

Leu Cys Thr Thr Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg
                325                 330                 335

Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe
            340                 345                 350

Pro Gln Ala Glu Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp
        355                 360                 365

Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Val Asn Leu Cys Asn Val
    370                 375                 380
```

```
Asp Ile Phe Asn Pro Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr
385                 390                 395                 400


Asp Val Ser Ser Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys
                405                 410                 415


Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile
            420                 425                 430


Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp
        435                 440                 445


Thr Val Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly
    450                 455                 460


Lys Ser Leu Tyr Val Lys Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro
465                 470                 475                 480


Leu Val Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ser Gln Val Asn
                485                 490                 495


Glu Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Lys Ser Asp Glu Leu
            500                 505                 510


Leu



<210>  54
<211>  27
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  T4 fibritin foldon domain

<400>  54

Gly Tyr Ile Pro Glu Ala Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys
1               5                   10                  15


Asp Gly Glu Trp Val Leu Leu Ser Thr Phe Leu
            20                  25
```

<210> 55
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 55

Gly Ser Gly Gly Ser Gly Ser Gly Ser Gly Gly Ser Gly Ser Gly
1 5 10 15

<210> 56
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 56

Gly Gly Ser Gly Gly Ser Gly Ser
1 5

<210> 57
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 57

Gly Ser Gly Gly Ser Gly Ser Gly
1 5

<210> 58
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Helical extension

<400> 58

Glu Lys Ala Ala Lys Ala Glu Glu Ala Ala Arg
1 5 10

<210> 59
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> Signal peptide

<400> 59

Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
1 5 10 15

Ala Val Thr Phe Cys Phe Ala Ser Gly
20 25

<210> 60
<211> 540
<212> PRT
<213> Artificial Sequence

<220>
<223> DS-Cav1-foldon

<220>
<221> MISC_FEATURE
<222> (1)..(25)
<223> optionally absent

<400> 60

Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
1 5 10 15

Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
20 25 30

Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
35 40 45

```
Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
    50                  55                  60

Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65                  70                  75                  80

Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
                85                  90                  95

Met Gln Ser Thr Pro Ala Thr Asn Asn Arg Ala Arg Arg Glu Leu Pro
            100                 105                 110

Arg Phe Met Asn Tyr Thr Leu Asn Asn Ala Lys Lys Thr Asn Val Thr
        115                 120                 125

Leu Ser Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Val
    130                 135                 140

Gly Ser Ala Ile Ala Ser Gly Val Ala Val Cys Lys Val Leu His Leu
145                 150                 155                 160

Glu Gly Glu Val Asn Lys Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys
                165                 170                 175

Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Phe Lys Val
            180                 185                 190

Leu Asp Leu Lys Asn Tyr Ile Asp Lys Gln Leu Leu Pro Ile Leu Asn
        195                 200                 205

Lys Gln Ser Cys Ser Ile Ser Asn Ile Glu Thr Val Ile Glu Phe Gln
    210                 215                 220

Gln Lys Asn Asn Arg Leu Leu Glu Ile Thr Arg Glu Phe Ser Val Asn
225                 230                 235                 240

Ala Gly Val Thr Thr Pro Val Ser Thr Tyr Met Leu Thr Asn Ser Glu
                245                 250                 255
```

```
Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
            260                 265                 270

Leu Met Ser Asn Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile
        275                 280                 285

Met Cys Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro
    290                 295                 300

Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro
305                 310                 315                 320

Leu Cys Thr Thr Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg
                325                 330                 335

Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe
            340                 345                 350

Pro Gln Ala Glu Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp
        355                 360                 365

Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Val Asn Leu Cys Asn Val
    370                 375                 380

Asp Ile Phe Asn Pro Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr
385                 390                 395                 400

Asp Val Ser Ser Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys
                405                 410                 415

Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile
            420                 425                 430

Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp
        435                 440                 445

Thr Val Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly
    450                 455                 460
```

```
Lys Ser Leu Tyr Val Lys Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro
465                 470                 475                 480


Leu Val Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ser Gln Val Asn
                485                 490                 495


Glu Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Lys Ser Asp Glu Leu
            500                 505                 510


Leu Gly Tyr Ile Pro Glu Ala Pro Arg Asp Gly Gln Ala Tyr Val Arg
        515                 520                 525


Lys Asp Gly Glu Trp Val Leu Leu Ser Thr Phe Leu
    530                 535                 540


<210>  61
<211>  474
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  sc9-10 DS-Cav1 A149C Y458C


<220>
<221>  MISC_FEATURE
<222>  (1)..(25)
<223>  optionally absent

<220>
<221>  MISC_FEATURE
<222>  (468)..(474)
<223>  optionally absent

<400>  61

Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
1               5                   10                  15


Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
            20                  25                  30


Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
        35                  40                  45
```

```
Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
    50                  55                  60

Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65                  70                  75                  80

Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
                85                  90                  95

Met Gln Ser Thr Pro Ala Thr Gly Ser Gly Ser Ala Ile Cys Ser Gly
            100                 105                 110

Val Ala Val Cys Lys Val Leu His Leu Glu Gly Glu Val Asn Lys Ile
        115                 120                 125

Lys Ser Ala Leu Leu Ser Thr Asn Lys Ala Val Val Ser Leu Ser Asn
    130                 135                 140

Gly Val Ser Val Leu Thr Phe Lys Val Leu Asp Leu Lys Asn Tyr Ile
145                 150                 155                 160

Asp Lys Gln Leu Leu Pro Ile Leu Asn Lys Gln Ser Cys Ser Ile Ser
                165                 170                 175

Asn Ile Glu Thr Val Ile Glu Phe Gln Gln Lys Asn Asn Arg Leu Leu
            180                 185                 190

Glu Ile Thr Arg Glu Phe Ser Val Asn Ala Gly Val Thr Thr Pro Val
        195                 200                 205

Ser Thr Tyr Met Leu Thr Asn Ser Glu Leu Leu Ser Leu Ile Asn Asp
    210                 215                 220

Met Pro Ile Thr Asn Asp Gln Lys Lys Leu Met Ser Asn Asn Val Gln
225                 230                 235                 240

Ile Val Arg Gln Gln Ser Tyr Ser Ile Met Cys Ile Ile Lys Glu Glu
                245                 250                 255
```

```
Val Leu Ala Tyr Val Val Gln Leu Pro Leu Tyr Gly Val Ile Asp Thr
            260                 265                 270

Pro Cys Trp Lys Leu His Thr Ser Pro Leu Cys Thr Thr Asn Thr Lys
        275                 280                 285

Glu Gly Ser Asn Ile Cys Leu Thr Arg Thr Asp Arg Gly Trp Tyr Cys
    290                 295                 300

Asp Asn Ala Gly Ser Val Ser Phe Phe Pro Gln Ala Glu Thr Cys Lys
305                 310                 315                 320

Val Gln Ser Asn Arg Val Phe Cys Asp Thr Met Asn Ser Arg Thr Leu
                325                 330                 335

Pro Ser Glu Val Asn Leu Cys Asn Val Asp Ile Phe Asn Pro Lys Tyr
            340                 345                 350

Asp Cys Lys Ile Met Thr Ser Lys Thr Asp Val Ser Ser Ser Val Ile
        355                 360                 365

Thr Ser Leu Gly Ala Ile Val Ser Cys Tyr Gly Lys Thr Lys Cys Thr
    370                 375                 380

Ala Ser Asn Lys Asn Arg Gly Ile Ile Lys Thr Phe Ser Asn Gly Cys
385                 390                 395                 400

Asp Tyr Val Ser Asn Lys Gly Val Asp Thr Val Ser Val Gly Asn Thr
                405                 410                 415

Leu Tyr Cys Val Asn Lys Gln Glu Gly Lys Ser Leu Tyr Val Lys Gly
            420                 425                 430

Glu Pro Ile Ile Asn Phe Tyr Asp Pro Leu Val Phe Pro Ser Asp Glu
        435                 440                 445

Phe Asp Ala Ser Ile Ser Gln Val Asn Glu Lys Ile Asn Gln Ser Leu
    450                 455                 460
```

Ala Phe Ile Arg Lys Ser Asp Glu Leu Leu
465 470

<210> 62
<211> 474
<212> PRT
<213> Artificial Sequence

<220>
<223> sc9-10 DS-Cav1 A149C Y458C S46G K465Q S215P E92D

<220>
<221> MISC_FEATURE
<222> (1)..(25)
<223> optionally absent

<220>
<221> MISC_FEATURE
<222> (468)..(474)
<223> optionally absent

<400> 62

Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
1 5 10 15

Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
20 25 30

Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Gly Ala Leu
35 40 45

Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
50 55 60

Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65 70 75 80

Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Asp Leu Gln Leu Leu
85 90 95

Met Gln Ser Thr Pro Ala Thr Gly Ser Gly Ser Ala Ile Cys Ser Gly
100 105 110

```
Val Ala Val Cys Lys Val Leu His Leu Glu Gly Glu Val Asn Lys Ile
        115                 120                 125

Lys Ser Ala Leu Leu Ser Thr Asn Lys Ala Val Val Ser Leu Ser Asn
    130                 135                 140

Gly Val Ser Val Leu Thr Phe Lys Val Leu Asp Leu Lys Asn Tyr Ile
145                 150                 155                 160

Asp Lys Gln Leu Leu Pro Ile Leu Asn Lys Gln Ser Cys Ser Ile Pro
                165                 170                 175

Asn Ile Glu Thr Val Ile Glu Phe Gln Gln Lys Asn Asn Arg Leu Leu
            180                 185                 190

Glu Ile Thr Arg Glu Phe Ser Val Asn Ala Gly Val Thr Thr Pro Val
        195                 200                 205

Ser Thr Tyr Met Leu Thr Asn Ser Glu Leu Leu Ser Leu Ile Asn Asp
    210                 215                 220

Met Pro Ile Thr Asn Asp Gln Lys Lys Leu Met Ser Asn Asn Val Gln
225                 230                 235                 240

Ile Val Arg Gln Gln Ser Tyr Ser Ile Met Cys Ile Ile Lys Glu Glu
                245                 250                 255

Val Leu Ala Tyr Val Val Gln Leu Pro Leu Tyr Gly Val Ile Asp Thr
            260                 265                 270

Pro Cys Trp Lys Leu His Thr Ser Pro Leu Cys Thr Thr Asn Thr Lys
        275                 280                 285

Glu Gly Ser Asn Ile Cys Leu Thr Arg Thr Asp Arg Gly Trp Tyr Cys
    290                 295                 300

Asp Asn Ala Gly Ser Val Ser Phe Phe Pro Gln Ala Glu Thr Cys Lys
305                 310                 315                 320
```

```
Val Gln Ser Asn Arg Val Phe Cys Asp Thr Met Asn Ser Arg Thr Leu
                325                 330                 335

Pro Ser Glu Val Asn Leu Cys Asn Val Asp Ile Phe Asn Pro Lys Tyr
            340                 345                 350

Asp Cys Lys Ile Met Thr Ser Lys Thr Asp Val Ser Ser Ser Val Ile
        355                 360                 365

Thr Ser Leu Gly Ala Ile Val Ser Cys Tyr Gly Lys Thr Lys Cys Thr
    370                 375                 380

Ala Ser Asn Lys Asn Arg Gly Ile Ile Lys Thr Phe Ser Asn Gly Cys
385                 390                 395                 400

Asp Tyr Val Ser Asn Lys Gly Val Asp Thr Val Ser Val Gly Asn Thr
                405                 410                 415

Leu Tyr Cys Val Asn Lys Gln Glu Gly Gln Ser Leu Tyr Val Lys Gly
            420                 425                 430

Glu Pro Ile Ile Asn Phe Tyr Asp Pro Leu Val Phe Pro Ser Asp Glu
        435                 440                 445

Phe Asp Ala Ser Ile Ser Gln Val Asn Glu Lys Ile Asn Gln Ser Leu
    450                 455                 460

Ala Phe Ile Arg Lys Ser Asp Glu Leu Leu
465                 470


<210>  63
<211>  522
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  SC-DM (N67I, S215P)


<220>
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<221> MISC_FEATURE
<222> (1)..(25)
<223> optionally absent

<220>
<221> MISC_FEATURE
<222> (486)..(522)
<223> optionally absent

<400> 63

```
Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
1               5                  10                  15


Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
            20                  25                  30


Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
        35                  40                  45


Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
    50                  55                  60


Lys Lys Ile Lys Cys Asn Gly Thr Asp Ala Lys Ile Lys Leu Ile Lys
65                  70                  75                  80


Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
                85                  90                  95


Met Gln Ser Thr Pro Ala Thr Asn Asn Gln Ala Arg Gly Ser Gly Ser
            100                 105                 110


Gly Arg Ser Leu Gly Phe Leu Leu Gly Val Gly Ser Ala Ile Ala Ser
        115                 120                 125


Gly Val Ala Val Ser Lys Val Leu His Leu Glu Gly Glu Val Asn Lys
    130                 135                 140


Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys Ala Val Val Ser Leu Ser
145                 150                 155                 160


Asn Gly Val Ser Val Leu Thr Ser Lys Val Leu Asp Leu Lys Asn Tyr
```

```
                165                 170                 175

Ile Asp Lys Gln Leu Leu Pro Ile Val Asn Lys Gln Ser Cys Ser Ile
            180                 185                 190

Pro Asn Ile Glu Thr Val Ile Glu Phe Gln Gln Lys Asn Asn Arg Leu
        195                 200                 205

Leu Glu Ile Thr Arg Glu Phe Ser Val Asn Ala Gly Val Thr Thr Pro
    210                 215                 220

Val Ser Thr Tyr Met Leu Thr Asn Ser Glu Leu Leu Ser Leu Ile Asn
225                 230                 235                 240

Asp Met Pro Ile Thr Asn Asp Gln Lys Lys Leu Met Ser Asn Asn Val
                245                 250                 255

Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile Met Ser Ile Ile Lys Glu
            260                 265                 270

Glu Val Leu Ala Tyr Val Val Gln Leu Pro Leu Tyr Gly Val Ile Asp
        275                 280                 285

Thr Pro Cys Trp Lys Leu His Thr Ser Pro Leu Cys Thr Thr Asn Thr
    290                 295                 300

Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg Thr Asp Arg Gly Trp Tyr
305                 310                 315                 320

Cys Asp Asn Ala Gly Ser Val Ser Phe Phe Pro Gln Ala Glu Thr Cys
                325                 330                 335

Lys Val Gln Ser Asn Arg Val Phe Cys Asp Thr Met Asn Ser Leu Thr
            340                 345                 350

Leu Pro Ser Glu Val Asn Leu Cys Asn Val Asp Ile Phe Asn Pro Lys
        355                 360                 365

Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr Asp Val Ser Ser Ser Val
```

370 375 380

Ile Thr Ser Leu Gly Ala Ile Val Ser Cys Tyr Gly Lys Thr Lys Cys
385 390 395 400

Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile Lys Thr Phe Ser Asn Gly
405 410 415

Cys Asp Tyr Val Ser Asn Lys Gly Val Asp Thr Val Ser Val Gly Asn
420 425 430

Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly Lys Ser Leu Tyr Val Lys
435 440 445

Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro Leu Val Phe Pro Ser Asp
450 455 460

Glu Phe Asp Ala Ser Ile Ser Gln Val Asn Glu Lys Ile Asn Gln Ser
465 470 475 480

Leu Ala Phe Ile Arg Lys Ser Asp Glu Leu Leu Ser Ala Ile Gly Gly
485 490 495

Tyr Ile Pro Glu Ala Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp
500 505 510

Gly Glu Trp Val Leu Leu Ser Thr Phe Leu
515 520

<210> 64
<211> 522
<212> PRT
<213> Artificial Sequence

<220>
<223> SC-TM (N67I, S215P, and E487Q)

<220>
<221> MISC_FEATURE
<222> (1)..(25)
<223> optionally absent

<220>
<221> MISC_FEATURE
<222> (486)..(522)
<223> optionally absent

<400> 64

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Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
1               5                   10                  15


Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
            20                  25                  30


Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
        35                  40                  45


Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
    50                  55                  60


Lys Lys Ile Lys Cys Asn Gly Thr Asp Ala Lys Ile Lys Leu Ile Lys
65                  70                  75                  80


Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
                85                  90                  95


Met Gln Ser Thr Pro Ala Thr Asn Asn Gln Ala Arg Gly Ser Gly Ser
            100                 105                 110


Gly Arg Ser Leu Gly Phe Leu Leu Gly Val Gly Ser Ala Ile Ala Ser
        115                 120                 125


Gly Val Ala Val Ser Lys Val Leu His Leu Glu Gly Glu Val Asn Lys
    130                 135                 140


Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys Ala Val Val Ser Leu Ser
145                 150                 155                 160


Asn Gly Val Ser Val Leu Thr Ser Lys Val Leu Asp Leu Lys Asn Tyr
                165                 170                 175
```

```
Ile Asp Lys Gln Leu Leu Pro Ile Val Asn Lys Gln Ser Cys Ser Ile
            180                 185                 190

Pro Asn Ile Glu Thr Val Ile Glu Phe Gln Gln Lys Asn Asn Arg Leu
        195                 200                 205

Leu Glu Ile Thr Arg Glu Phe Ser Val Asn Ala Gly Val Thr Thr Pro
    210                 215                 220

Val Ser Thr Tyr Met Leu Thr Asn Ser Glu Leu Leu Ser Leu Ile Asn
225                 230                 235                 240

Asp Met Pro Ile Thr Asn Asp Gln Lys Lys Leu Met Ser Asn Asn Val
                245                 250                 255

Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile Met Ser Ile Ile Lys Glu
            260                 265                 270

Glu Val Leu Ala Tyr Val Val Gln Leu Pro Leu Tyr Gly Val Ile Asp
        275                 280                 285

Thr Pro Cys Trp Lys Leu His Thr Ser Pro Leu Cys Thr Thr Asn Thr
    290                 295                 300

Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg Thr Asp Arg Gly Trp Tyr
305                 310                 315                 320

Cys Asp Asn Ala Gly Ser Val Ser Phe Phe Pro Gln Ala Glu Thr Cys
                325                 330                 335

Lys Val Gln Ser Asn Arg Val Phe Cys Asp Thr Met Asn Ser Leu Thr
            340                 345                 350

Leu Pro Ser Glu Val Asn Leu Cys Asn Val Asp Ile Phe Asn Pro Lys
        355                 360                 365

Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr Asp Val Ser Ser Ser Val
    370                 375                 380
```

```
Ile Thr Ser Leu Gly Ala Ile Val Ser Cys Tyr Gly Lys Thr Lys Cys
385                 390                 395                 400


Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile Lys Thr Phe Ser Asn Gly
                405                 410                 415


Cys Asp Tyr Val Ser Asn Lys Gly Val Asp Thr Val Ser Val Gly Asn
            420                 425                 430


Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly Lys Ser Leu Tyr Val Lys
        435                 440                 445


Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro Leu Val Phe Pro Ser Asp
    450                 455                 460


Gln Phe Asp Ala Ser Ile Ser Gln Val Asn Glu Lys Ile Asn Gln Ser
465                 470                 475                 480


Leu Ala Phe Ile Arg Lys Ser Asp Glu Leu Leu Ser Ala Ile Gly Gly
                485                 490                 495


Tyr Ile Pro Glu Ala Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp
            500                 505                 510


Gly Glu Trp Val Leu Leu Ser Thr Phe Leu
        515                 520


<210>  65
<211>  490
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HMPV F protein, strain CAN97-83 (A2)


<220>
<221>  MISC_FEATURE
<222>  (1)..(18)
<223>  optionally absent

<400>  65
```

```
Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
1               5                  10                  15

His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
            20                  25                  30

Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
        35                  40                  45

Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
    50                  55                  60

Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
65                  70                  75                  80

Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
                85                  90                  95

Asn Pro Arg Gln Ser Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
            100                 105                 110

Ala Thr Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
        115                 120                 125

Arg Leu Glu Ser Glu Val Thr Ala Ile Lys Asn Ala Leu Lys Thr Thr
    130                 135                 140

Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
145                 150                 155                 160

Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
                165                 170                 175

Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser
            180                 185                 190

Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
        195                 200                 205
```

```
Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
    210                 215                 220


Ala Glu Leu Ala Arg Ala Val Ser Asn Met Pro Thr Ser Ala Gly Gln
225                 230                 235                 240


Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
                245                 250                 255


Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
            260                 265                 270


Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
        275                 280                 285


Ala Pro Ser Cys Ser Gly Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
    290                 295                 300


Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
305                 310                 315                 320


Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
                325                 330                 335


Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
            340                 345                 350


Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
        355                 360                 365


Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
    370                 375                 380


Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
385                 390                 395                 400


Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
                405                 410                 415
```

```
Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
            420                 425                 430


Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
        435                 440                 445


Ile Lys Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
    450                 455                 460


Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
465                 470                 475                 480


Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly
                485                 490


<210>  66
<211>  490
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HMPVF with A113C, A339C, T160F, I177L


<220>
<221>  MISC_FEATURE
<222>  (1)..(18)
<223>  optionally absent

<400>  66

Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
1               5                   10                  15


His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
            20                  25                  30


Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
        35                  40                  45


Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
    50                  55                  60
```

```
Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
65                  70                  75                  80


Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
                85                  90                  95


Asn Pro Arg Gln Ser Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
            100                 105                 110


Cys Thr Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
        115                 120                 125


Arg Leu Glu Ser Glu Val Thr Ala Ile Lys Asn Ala Leu Lys Thr Thr
    130                 135                 140


Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Phe
145                 150                 155                 160


Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
                165                 170                 175


Leu Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser
            180                 185                 190


Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
        195                 200                 205


Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
    210                 215                 220


Ala Glu Leu Ala Arg Ala Val Ser Asn Met Pro Thr Ser Ala Gly Gln
225                 230                 235                 240


Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
                245                 250                 255


Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
            260                 265                 270
```

```
Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
        275                 280                 285


Ala Pro Ser Cys Ser Gly Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
    290                 295                 300


Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
305                 310                 315                 320


Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
                325                 330                 335


Thr Ala Cys Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
            340                 345                 350


Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
        355                 360                 365


Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
    370                 375                 380


Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
385                 390                 395                 400


Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
                405                 410                 415


Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
            420                 425                 430


Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
        435                 440                 445


Ile Lys Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
    450                 455                 460


Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
465                 470                 475                 480
```

Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly
485 490

<210> 67
<211> 490
<212> PRT
<213> Artificial Sequence

<220>
<223> HMPV- F with A113C, A120C, A339C, T160F, I177L, and Q426C

<220>
<221> MISC_FEATURE
<222> (1)..(18)
<223> optionally absent

<400> 67

Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
1 5 10 15

His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
20 25 30

Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
35 40 45

Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
50 55 60

Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
65 70 75 80

Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
85 90 95

Asn Pro Arg Gln Ser Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
100 105 110

Cys Thr Ala Ala Ala Val Thr Cys Gly Val Ala Ile Ala Lys Thr Ile
115 120 125

```
Arg Leu Glu Ser Glu Val Thr Ala Ile Lys Asn Ala Leu Lys Thr Thr
    130                 135                 140

Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Phe
145                 150                 155                 160

Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
                165                 170                 175

Leu Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser
            180                 185                 190

Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
        195                 200                 205

Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
    210                 215                 220

Ala Glu Leu Ala Arg Ala Val Ser Asn Met Pro Thr Ser Ala Gly Gln
225                 230                 235                 240

Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
                245                 250                 255

Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
            260                 265                 270

Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
        275                 280                 285

Ala Pro Ser Cys Ser Gly Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
    290                 295                 300

Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
305                 310                 315                 320

Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
                325                 330                 335
```

```
Thr Ala Cys Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
            340                 345                 350


Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
        355                 360                 365


Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
    370                 375                 380


Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
385                 390                 395                 400


Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
                405                 410                 415


Thr Val Thr Ile Asp Asn Thr Val Tyr Cys Leu Ser Lys Val Glu Gly
            420                 425                 430


Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
        435                 440                 445


Ile Lys Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
    450                 455                 460


Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
465                 470                 475                 480


Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly
                485                 490


<210>  68
<211>  542
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  115-BV (A185P)


<220>
<221>  MISC_FEATURE
<222>  (1)..(18)
```

<223> optionally absent

<220>
<221> MISC_FEATURE
<222> (490)..(542)
<223> optionally absent

<400> 68

```
Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
1               5                   10                  15


His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
            20                  25                  30


Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
        35                  40                  45


Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ala Asp Gly Pro
    50                  55                  60


Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
65                  70                  75                  80


Leu Arg Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
                85                  90                  95


Asn Pro Arg Arg Arg Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
            100                 105                 110


Ala Thr Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
        115                 120                 125


Arg Leu Glu Ser Glu Val Thr Ala Ile Lys Asn Ala Leu Lys Lys Thr
    130                 135                 140


Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
145                 150                 155                 160


Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
                165                 170                 175
```

```
Ile Asn Lys Asn Lys Cys Asp Ile Pro Asp Leu Lys Met Ala Val Ser
            180                 185                 190

Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
        195                 200                 205

Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
    210                 215                 220

Ala Glu Leu Ala Arg Ala Val Ser Asn Met Pro Thr Ser Ala Gly Gln
225                 230                 235                 240

Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
                245                 250                 255

Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
            260                 265                 270

Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
        275                 280                 285

Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
    290                 295                 300

Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
305                 310                 315                 320

Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
                325                 330                 335

Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
            340                 345                 350

Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
        355                 360                 365

Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
    370                 375                 380
```

```
Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
385                 390                 395                 400


Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
                405                 410                 415


Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
            420                 425                 430


Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
        435                 440                 445


Val Lys Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
    450                 455                 460


Glu Ser Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
465                 470                 475                 480


Leu Ser Ser Ala Glu Lys Gly Asn Thr Ser Gly Arg Glu Asn Leu Tyr
                485                 490                 495


Phe Gln Gly Gly Gly Gly Ser Gly Tyr Ile Pro Glu Ala Pro Arg Asp
            500                 505                 510


Gly Gln Ala Tyr Val Arg Lys Asp Gly Glu Trp Val Leu Leu Ser Thr
        515                 520                 525


Phe Leu Gly Gly Ile Glu Gly Arg His His His His His His
    530                 535                 540


<210>  69
<211>  646
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  DS-Cav1-foldon-T33-31A


<220>
<221>  MISC_FEATURE
```

<222> (1)..(26)
<223> optionally absent

<400> 69

```
Met Glu Leu Leu Ile Leu Lys Ala Asn Val Ile Ala Thr Ile Leu Thr
1               5                  10                  15


Ala Val Thr Phe Cys Phe Ala Ser Ser Gln Asn Ile Thr Glu Glu Phe
            20                  25                  30


Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
        35                  40                  45


Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
    50                  55                  60


Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65                  70                  75                  80


Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
                85                  90                  95


Met Gln Ser Thr Pro Ala Thr Asn Asn Arg Ala Arg Arg Glu Leu Pro
            100                 105                 110


Arg Phe Met Asn Tyr Thr Leu Asn Asn Ala Lys Lys Thr Asn Val Thr
        115                 120                 125


Leu Ser Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Val
    130                 135                 140


Gly Ser Ala Ile Ala Ser Gly Val Ala Val Cys Lys Val Leu His Leu
145                 150                 155                 160


Glu Gly Glu Val Asn Lys Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys
                165                 170                 175


Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Phe Lys Val
            180                 185                 190
```

```
Leu Asp Leu Lys Asn Tyr Ile Asp Lys Gln Leu Leu Pro Ile Leu Asn
        195                 200                 205

Lys Gln Ser Cys Ser Ile Ser Asn Ile Glu Thr Val Ile Glu Phe Gln
    210                 215                 220

Gln Lys Asn Asn Arg Leu Leu Glu Ile Thr Arg Glu Phe Ser Val Asn
225                 230                 235                 240

Ala Gly Val Thr Thr Pro Val Ser Thr Tyr Met Leu Thr Asn Ser Glu
                245                 250                 255

Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
            260                 265                 270

Leu Met Ser Asn Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile
        275                 280                 285

Met Cys Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro
    290                 295                 300

Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro
305                 310                 315                 320

Leu Cys Thr Thr Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg
                325                 330                 335

Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe
            340                 345                 350

Pro Gln Ala Glu Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp
        355                 360                 365

Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Val Asn Leu Cys Asn Val
    370                 375                 380

Asp Ile Phe Asn Pro Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr
385                 390                 395                 400
```

```
Asp Val Ser Ser Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys
                405                 410                 415

Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile
            420                 425                 430

Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp
        435                 440                 445

Thr Val Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly
    450                 455                 460

Lys Ser Leu Tyr Val Lys Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro
465                 470                 475                 480

Leu Val Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ser Gln Val Asn
                485                 490                 495

Glu Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Lys Ser Asp Glu Leu
            500                 505                 510

Leu Gly Tyr Ile Pro Glu Ala Pro Arg Asp Gly Gln Ala Tyr Val Arg
        515                 520                 525

Lys Asp Gly Glu Trp Val Leu Leu Ser Thr Phe Leu Gly Gly Ser Met
    530                 535                 540

Glu Glu Val Val Leu Ile Thr Val Pro Ser Ala Leu Val Ala Val Lys
545                 550                 555                 560

Ile Ala His Ala Leu Val Glu Glu Arg Leu Ala Ala Cys Val Asn Ile
                565                 570                 575

Val Pro Gly Leu Thr Ser Ile Tyr Arg Glu Glu Gly Ser Val Val Ser
            580                 585                 590

Asp His Glu Leu Leu Leu Leu Val Lys Thr Thr Thr Asp Ala Phe Pro
        595                 600                 605
```

```
Lys Leu Lys Glu Arg Val Lys Glu Leu His Pro Tyr Glu Val Pro Glu
    610                 615                 620


Ile Val Ala Leu Pro Ile Ala Glu Gly Asn Arg Glu Tyr Leu Asp Trp
625                 630                 635                 640


Leu Arg Glu Asn Thr Gly
                645


<210>  70
<211>  619
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  DS-Cav1-T33-31A


<220>
<221>  MISC_FEATURE
<222>  (1)..(25)
<223>  optionally absent

<400>  70

Met Glu Leu Leu Ile Leu Lys Ala Asn Val Ile Ala Thr Ile Leu Thr
1               5                   10                  15


Ala Val Thr Phe Cys Phe Ala Ser Ser Gln Asn Ile Thr Glu Glu Phe
            20                  25                  30


Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
        35                  40                  45


Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
    50                  55                  60


Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65                  70                  75                  80


Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
                85                  90                  95
```

```
Met Gln Ser Thr Pro Ala Thr Asn Asn Arg Ala Arg Arg Glu Leu Pro
            100                 105                 110

Arg Phe Met Asn Tyr Thr Leu Asn Asn Ala Lys Lys Thr Asn Val Thr
        115                 120                 125

Leu Ser Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Val
    130                 135                 140

Gly Ser Ala Ile Ala Ser Gly Val Ala Val Cys Lys Val Leu His Leu
145                 150                 155                 160

Glu Gly Glu Val Asn Lys Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys
                165                 170                 175

Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Phe Lys Val
            180                 185                 190

Leu Asp Leu Lys Asn Tyr Ile Asp Lys Gln Leu Leu Pro Ile Leu Asn
        195                 200                 205

Lys Gln Ser Cys Ser Ile Ser Asn Ile Glu Thr Val Ile Glu Phe Gln
    210                 215                 220

Gln Lys Asn Asn Arg Leu Leu Glu Ile Thr Arg Glu Phe Ser Val Asn
225                 230                 235                 240

Ala Gly Val Thr Thr Pro Val Ser Thr Tyr Met Leu Thr Asn Ser Glu
                245                 250                 255

Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
            260                 265                 270

Leu Met Ser Asn Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile
        275                 280                 285

Met Cys Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro
    290                 295                 300
```

```
Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro
305                 310                 315                 320

Leu Cys Thr Thr Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg
                325                 330                 335

Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe
            340                 345                 350

Pro Gln Ala Glu Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp
        355                 360                 365

Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Val Asn Leu Cys Asn Val
    370                 375                 380

Asp Ile Phe Asn Pro Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr
385                 390                 395                 400

Asp Val Ser Ser Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys
                405                 410                 415

Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile
            420                 425                 430

Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp
        435                 440                 445

Thr Val Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly
    450                 455                 460

Lys Ser Leu Tyr Val Lys Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro
465                 470                 475                 480

Leu Val Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ser Gln Val Asn
                485                 490                 495

Glu Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Lys Ser Asp Glu Leu
            500                 505                 510
```

```
Leu Gly Gly Ser Met Glu Glu Val Val Leu Ile Thr Val Pro Ser Ala
        515                 520                 525


Leu Val Ala Val Lys Ile Ala His Ala Leu Val Glu Glu Arg Leu Ala
    530                 535                 540


Ala Cys Val Asn Ile Val Pro Gly Leu Thr Ser Ile Tyr Arg Glu Glu
545                 550                 555                 560


Gly Ser Val Val Ser Asp His Glu Leu Leu Leu Leu Val Lys Thr Thr
                565                 570                 575


Thr Asp Ala Phe Pro Lys Leu Lys Glu Arg Val Lys Glu Leu His Pro
            580                 585                 590


Tyr Glu Val Pro Glu Ile Val Ala Leu Pro Ile Ala Glu Gly Asn Arg
        595                 600                 605


Glu Tyr Leu Asp Trp Leu Arg Glu Asn Thr Gly
    610                 615


<210>  71
<211>  665
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  DS-Cav1-foldon-T33-15B


<220>
<221>  MISC_FEATURE
<222>  (1)..(25)
<223>  optionally absent

<400>  71

Met Glu Leu Leu Ile Leu Lys Ala Asn Val Ile Ala Thr Ile Leu Thr
1               5                   10                  15


Ala Val Thr Phe Cys Phe Ala Ser Ser Gln Asn Ile Thr Glu Glu Phe
            20                  25                  30
```

```
Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
        35                  40                  45

Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
    50                  55                  60

Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65                  70                  75                  80

Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
                85                  90                  95

Met Gln Ser Thr Pro Ala Thr Asn Asn Arg Ala Arg Arg Glu Leu Pro
            100                 105                 110

Arg Phe Met Asn Tyr Thr Leu Asn Asn Ala Lys Lys Thr Asn Val Thr
        115                 120                 125

Leu Ser Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Val
    130                 135                 140

Gly Ser Ala Ile Ala Ser Gly Val Ala Val Cys Lys Val Leu His Leu
145                 150                 155                 160

Glu Gly Glu Val Asn Lys Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys
                165                 170                 175

Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Phe Lys Val
            180                 185                 190

Leu Asp Leu Lys Asn Tyr Ile Asp Lys Gln Leu Leu Pro Ile Leu Asn
        195                 200                 205

Lys Gln Ser Cys Ser Ile Ser Asn Ile Glu Thr Val Ile Glu Phe Gln
    210                 215                 220

Gln Lys Asn Asn Arg Leu Leu Glu Ile Thr Arg Glu Phe Ser Val Asn
225                 230                 235                 240
```

```
Ala Gly Val Thr Thr Pro Val Ser Thr Tyr Met Leu Thr Asn Ser Glu
                245                 250                 255

Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
            260                 265                 270

Leu Met Ser Asn Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile
        275                 280                 285

Met Cys Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro
    290                 295                 300

Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro
305                 310                 315                 320

Leu Cys Thr Thr Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg
                325                 330                 335

Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe
            340                 345                 350

Pro Gln Ala Glu Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp
        355                 360                 365

Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Val Asn Leu Cys Asn Val
    370                 375                 380

Asp Ile Phe Asn Pro Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr
385                 390                 395                 400

Asp Val Ser Ser Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys
                405                 410                 415

Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile
            420                 425                 430

Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp
        435                 440                 445
```

```
Thr Val Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly
    450                 455                 460

Lys Ser Leu Tyr Val Lys Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro
465                 470                 475                 480

Leu Val Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ser Gln Val Asn
                485                 490                 495

Glu Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Lys Ser Asp Glu Leu
            500                 505                 510

Leu Gly Tyr Ile Pro Glu Ala Pro Arg Asp Gly Gln Ala Tyr Val Arg
        515                 520                 525

Lys Asp Gly Glu Trp Val Leu Leu Ser Thr Phe Leu Gly Gly Ser Met
    530                 535                 540

Val Arg Gly Ile Arg Gly Ala Ile Thr Val Asn Ser Asp Thr Pro Thr
545                 550                 555                 560

Ser Ile Ile Ile Ala Thr Ile Leu Leu Leu Glu Lys Met Leu Glu Ala
                565                 570                 575

Asn Gly Ile Gln Ser Tyr Glu Glu Leu Ala Ala Val Ile Phe Thr Val
            580                 585                 590

Thr Glu Asp Leu Thr Ser Ala Phe Pro Ala Glu Ala Ala Arg Gln Ile
        595                 600                 605

Gly Met His Arg Val Pro Leu Leu Ser Ala Arg Glu Val Pro Val Pro
    610                 615                 620

Gly Ser Leu Pro Arg Val Ile Arg Val Leu Ala Leu Trp Asn Thr Asp
625                 630                 635                 640

Thr Pro Gln Asp Arg Val Arg His Val Tyr Leu Ser Glu Ala Val Arg
                645                 650                 655
```

Leu Arg Pro Asp Leu Glu Ser Ala Gln
660 665

<210> 72
<211> 638
<212> PRT
<213> Artificial Sequence

<220>
<223> DS-Cav1-T33-15B

<220>
<221> MISC_FEATURE
<222> (1)..(25)
<223> optionally absent

<400> 72

Met Glu Leu Leu Ile Leu Lys Ala Asn Val Ile Ala Thr Ile Leu Thr
1 5 10 15

Ala Val Thr Phe Cys Phe Ala Ser Ser Gln Asn Ile Thr Glu Glu Phe
20 25 30

Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
35 40 45

Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
50 55 60

Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65 70 75 80

Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
85 90 95

Met Gln Ser Thr Pro Ala Thr Asn Asn Arg Ala Arg Arg Glu Leu Pro
100 105 110

Arg Phe Met Asn Tyr Thr Leu Asn Asn Ala Lys Lys Thr Asn Val Thr
115 120 125

```
Leu Ser Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Val
    130                 135                 140

Gly Ser Ala Ile Ala Ser Gly Val Ala Val Cys Lys Val Leu His Leu
145                 150                 155                 160

Glu Gly Glu Val Asn Lys Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys
                165                 170                 175

Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Phe Lys Val
            180                 185                 190

Leu Asp Leu Lys Asn Tyr Ile Asp Lys Gln Leu Leu Pro Ile Leu Asn
        195                 200                 205

Lys Gln Ser Cys Ser Ile Ser Asn Ile Glu Thr Val Ile Glu Phe Gln
    210                 215                 220

Gln Lys Asn Asn Arg Leu Leu Glu Ile Thr Arg Glu Phe Ser Val Asn
225                 230                 235                 240

Ala Gly Val Thr Thr Pro Val Ser Thr Tyr Met Leu Thr Asn Ser Glu
                245                 250                 255

Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
            260                 265                 270

Leu Met Ser Asn Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile
        275                 280                 285

Met Cys Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro
    290                 295                 300

Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro
305                 310                 315                 320

Leu Cys Thr Thr Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg
                325                 330                 335
```

```
Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe
            340                 345                 350


Pro Gln Ala Glu Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp
        355                 360                 365


Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Val Asn Leu Cys Asn Val
    370                 375                 380


Asp Ile Phe Asn Pro Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr
385                 390                 395                 400


Asp Val Ser Ser Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys
                405                 410                 415


Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile
            420                 425                 430


Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp
        435                 440                 445


Thr Val Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly
    450                 455                 460


Lys Ser Leu Tyr Val Lys Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro
465                 470                 475                 480


Leu Val Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ser Gln Val Asn
                485                 490                 495


Glu Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Lys Ser Asp Glu Leu
            500                 505                 510


Leu Gly Gly Ser Met Val Arg Gly Ile Arg Gly Ala Ile Thr Val Asn
        515                 520                 525


Ser Asp Thr Pro Thr Ser Ile Ile Ile Ala Thr Ile Leu Leu Leu Glu
    530                 535                 540
```

```
Lys Met Leu Glu Ala Asn Gly Ile Gln Ser Tyr Glu Glu Leu Ala Ala
545                 550                 555                 560


Val Ile Phe Thr Val Thr Glu Asp Leu Thr Ser Ala Phe Pro Ala Glu
                565                 570                 575


Ala Ala Arg Gln Ile Gly Met His Arg Val Pro Leu Leu Ser Ala Arg
            580                 585                 590


Glu Val Pro Val Pro Gly Ser Leu Pro Arg Val Ile Arg Val Leu Ala
        595                 600                 605


Leu Trp Asn Thr Asp Thr Pro Gln Asp Arg Val Arg His Val Tyr Leu
    610                 615                 620


Ser Glu Ala Val Arg Leu Arg Pro Asp Leu Glu Ser Ala Gln
625                 630                 635


<210>  73
<211>  769
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  DS-Cav1-foldon-I53-50A


<220>
<221>  MISC_FEATURE
<222>  (1)..(25)
<223>  optionally absent

<400>  73

Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
1               5                   10                  15


Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
            20                  25                  30


Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
        35                  40                  45
```

```
Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
    50                  55                  60

Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65                  70                  75                  80

Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
                85                  90                  95

Met Gln Ser Thr Pro Ala Thr Asn Asn Arg Ala Arg Arg Glu Leu Pro
            100                 105                 110

Arg Phe Met Asn Tyr Thr Leu Asn Asn Ala Lys Lys Thr Asn Val Thr
        115                 120                 125

Leu Ser Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Val
    130                 135                 140

Gly Ser Ala Ile Ala Ser Gly Val Ala Val Cys Lys Val Leu His Leu
145                 150                 155                 160

Glu Gly Glu Val Asn Lys Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys
                165                 170                 175

Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Phe Lys Val
            180                 185                 190

Leu Asp Leu Lys Asn Tyr Ile Asp Lys Gln Leu Leu Pro Ile Leu Asn
        195                 200                 205

Lys Gln Ser Cys Ser Ile Ser Asn Ile Glu Thr Val Ile Glu Phe Gln
    210                 215                 220

Gln Lys Asn Asn Arg Leu Leu Glu Ile Thr Arg Glu Phe Ser Val Asn
225                 230                 235                 240

Ala Gly Val Thr Thr Pro Val Ser Thr Tyr Met Leu Thr Asn Ser Glu
                245                 250                 255
```

```
Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
            260                 265                 270

Leu Met Ser Asn Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile
        275                 280                 285

Met Cys Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro
    290                 295                 300

Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro
305                 310                 315                 320

Leu Cys Thr Thr Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg
                325                 330                 335

Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe
            340                 345                 350

Pro Gln Ala Glu Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp
        355                 360                 365

Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Val Asn Leu Cys Asn Val
    370                 375                 380

Asp Ile Phe Asn Pro Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr
385                 390                 395                 400

Asp Val Ser Ser Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys
                405                 410                 415

Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile
            420                 425                 430

Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp
        435                 440                 445

Thr Val Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly
    450                 455                 460
```

```
Lys Ser Leu Tyr Val Lys Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro
465                 470                 475                 480

Leu Val Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ser Gln Val Asn
                485                 490                 495

Glu Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Gly Tyr Ile Pro Glu
            500                 505                 510

Ala Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp Gly Glu Trp Val
        515                 520                 525

Leu Leu Ser Thr Phe Leu Gly Ser Gly Ser His His His His His His
    530                 535                 540

His His Gly Gly Ser Gly Gly Ser Gly Ser Glu Lys Ala Ala Lys Ala
545                 550                 555                 560

Glu Glu Ala Ala Arg Lys Met Glu Glu Leu Phe Lys Lys His Lys Ile
                565                 570                 575

Val Ala Val Leu Arg Ala Asn Ser Val Glu Glu Ala Ile Glu Lys Ala
            580                 585                 590

Val Ala Val Phe Ala Gly Gly Val His Leu Ile Glu Ile Thr Phe Thr
        595                 600                 605

Val Pro Asp Ala Asp Thr Val Ile Lys Ala Leu Ser Val Leu Lys Glu
    610                 615                 620

Lys Gly Ala Ile Ile Gly Ala Gly Thr Val Thr Ser Val Glu Gln Cys
625                 630                 635                 640

Arg Lys Ala Val Glu Ser Gly Ala Glu Phe Ile Val Ser Pro His Leu
                645                 650                 655

Asp Glu Glu Ile Ser Gln Phe Cys Lys Glu Lys Gly Val Phe Tyr Met
            660                 665                 670
```

```
Pro Gly Val Met Thr Pro Thr Glu Leu Val Lys Ala Met Lys Leu Gly
        675                 680                 685


His Thr Ile Leu Lys Leu Phe Pro Gly Glu Val Val Gly Pro Gln Phe
    690                 695                 700


Val Lys Ala Met Lys Gly Pro Phe Pro Asn Val Lys Phe Val Pro Thr
705                 710                 715                 720


Gly Gly Val Asn Leu Asp Asn Val Cys Glu Trp Phe Lys Ala Gly Val
                725                 730                 735


Leu Ala Val Gly Val Gly Ser Ala Leu Val Lys Gly Thr Pro Asp Glu
            740                 745                 750


Val Arg Glu Lys Ala Lys Ala Phe Val Glu Lys Ile Arg Gly Cys Thr
        755                 760                 765


Glu
```

<210> 74
<211> 730
<212> PRT
<213> Artificial Sequence

<220>
<223> DS-Cav1-I53-50A

<220>
<221> MISC_FEATURE
<222> (1)..(25)
<223> optionally absent

<400> 74

```
Met Glu Leu Leu Ile Leu Lys Ala Asn Val Ile Ala Thr Ile Leu Thr
1               5                   10                  15


Ala Val Thr Phe Cys Phe Ala Ser Ser Gln Asn Ile Thr Glu Glu Phe
            20                  25                  30
```

```
Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
        35                  40                  45

Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
    50                  55                  60

Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65                  70                  75                  80

Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
                85                  90                  95

Met Gln Ser Thr Pro Ala Thr Asn Asn Arg Ala Arg Arg Glu Leu Pro
            100                 105                 110

Arg Phe Met Asn Tyr Thr Leu Asn Asn Ala Lys Lys Thr Asn Val Thr
        115                 120                 125

Leu Ser Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Val
    130                 135                 140

Gly Ser Ala Ile Ala Ser Gly Val Ala Val Cys Lys Val Leu His Leu
145                 150                 155                 160

Glu Gly Glu Val Asn Lys Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys
                165                 170                 175

Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Phe Lys Val
            180                 185                 190

Leu Asp Leu Lys Asn Tyr Ile Asp Lys Gln Leu Leu Pro Ile Leu Asn
        195                 200                 205

Lys Gln Ser Cys Ser Ile Ser Asn Ile Glu Thr Val Ile Glu Phe Gln
    210                 215                 220

Gln Lys Asn Asn Arg Leu Leu Glu Ile Thr Arg Glu Phe Ser Val Asn
225                 230                 235                 240
```

```
Ala Gly Val Thr Thr Pro Val Ser Thr Tyr Met Leu Thr Asn Ser Glu
                245                 250                 255

Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
            260                 265                 270

Leu Met Ser Asn Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile
        275                 280                 285

Met Cys Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro
    290                 295                 300

Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro
305                 310                 315                 320

Leu Cys Thr Thr Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg
                325                 330                 335

Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe
            340                 345                 350

Pro Gln Ala Glu Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp
        355                 360                 365

Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Val Asn Leu Cys Asn Val
    370                 375                 380

Asp Ile Phe Asn Pro Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr
385                 390                 395                 400

Asp Val Ser Ser Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys
                405                 410                 415

Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile
            420                 425                 430

Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp
        435                 440                 445
```

```
Thr Val Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly
    450                 455                 460

Lys Ser Leu Tyr Val Lys Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro
465                 470                 475                 480

Leu Val Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ser Gln Val Asn
                485                 490                 495

Glu Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Gly Gly Ser Gly Gly
            500                 505                 510

Ser Gly Ser Glu Lys Ala Ala Lys Ala Glu Glu Ala Ala Arg Lys Met
        515                 520                 525

Glu Glu Leu Phe Lys Lys His Lys Ile Val Ala Val Leu Arg Ala Asn
    530                 535                 540

Ser Val Glu Glu Ala Ile Glu Lys Ala Val Ala Val Phe Ala Gly Gly
545                 550                 555                 560

Val His Leu Ile Glu Ile Thr Phe Thr Val Pro Asp Ala Asp Thr Val
                565                 570                 575

Ile Lys Ala Leu Ser Val Leu Lys Glu Lys Gly Ala Ile Ile Gly Ala
            580                 585                 590

Gly Thr Val Thr Ser Val Glu Gln Cys Arg Lys Ala Val Glu Ser Gly
        595                 600                 605

Ala Glu Phe Ile Val Ser Pro His Leu Asp Glu Glu Ile Ser Gln Phe
    610                 615                 620

Cys Lys Glu Lys Gly Val Phe Tyr Met Pro Gly Val Met Thr Pro Thr
625                 630                 635                 640

Glu Leu Val Lys Ala Met Lys Leu Gly His Thr Ile Leu Lys Leu Phe
                645                 650                 655
```

```
Pro Gly Glu Val Val Gly Pro Gln Phe Val Lys Ala Met Lys Gly Pro
            660                 665                 670


Phe Pro Asn Val Lys Phe Val Pro Thr Gly Gly Val Asn Leu Asp Asn
        675                 680                 685


Val Cys Glu Trp Phe Lys Ala Gly Val Leu Ala Val Gly Val Gly Ser
    690                 695                 700


Ala Leu Val Lys Gly Thr Pro Asp Glu Val Arg Glu Lys Ala Lys Ala
705                 710                 715                 720


Phe Val Glu Lys Ile Arg Gly Cys Thr Glu
                725                 730


<210>  75
<211>  676
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  DS-Cav1-I32-28A


<220>
<221>  MISC_FEATURE
<222>  (1)..(25)
<223>  optionally absent

<400>  75

Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
1               5                   10                  15


Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
            20                  25                  30


Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
        35                  40                  45


Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
    50                  55                  60
```

```
Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65                  70                  75                  80

Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
                85                  90                  95

Met Gln Ser Thr Pro Ala Thr Asn Asn Arg Ala Arg Arg Glu Leu Pro
            100                 105                 110

Arg Phe Met Asn Tyr Thr Leu Asn Asn Ala Lys Lys Thr Asn Val Thr
        115                 120                 125

Leu Ser Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Val
    130                 135                 140

Gly Ser Ala Ile Ala Ser Gly Val Ala Val Cys Lys Val Leu His Leu
145                 150                 155                 160

Glu Gly Glu Val Asn Lys Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys
                165                 170                 175

Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Phe Lys Val
            180                 185                 190

Leu Asp Leu Lys Asn Tyr Ile Asp Lys Gln Leu Leu Pro Ile Leu Asn
        195                 200                 205

Lys Gln Ser Cys Ser Ile Ser Asn Ile Glu Thr Val Ile Glu Phe Gln
    210                 215                 220

Gln Lys Asn Asn Arg Leu Leu Glu Ile Thr Arg Glu Phe Ser Val Asn
225                 230                 235                 240

Ala Gly Val Thr Thr Pro Val Ser Thr Tyr Met Leu Thr Asn Ser Glu
                245                 250                 255

Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
            260                 265                 270
```

```
Leu Met Ser Asn Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile
        275                 280                 285


Met Cys Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro
    290                 295                 300


Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro
305                 310                 315                 320


Leu Cys Thr Thr Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg
                325                 330                 335


Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe
            340                 345                 350


Pro Gln Ala Glu Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp
        355                 360                 365


Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Val Asn Leu Cys Asn Val
    370                 375                 380


Asp Ile Phe Asn Pro Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr
385                 390                 395                 400


Asp Val Ser Ser Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys
                405                 410                 415


Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile
            420                 425                 430


Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp
        435                 440                 445


Thr Val Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly
    450                 455                 460


Lys Ser Leu Tyr Val Lys Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro
465                 470                 475                 480
```

```
Leu Val Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ser Gln Val Asn
                485                 490                 495

Glu Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Lys Ser Asp Glu Leu
            500                 505                 510

Leu Gly Gly Ser Gly Gly Ser Gly Ser Asp Asp Ala Arg Ile Ala Ala
        515                 520                 525

Ile Gly Asp Val Asp Glu Leu Asn Ser Gln Ile Gly Val Leu Leu Ala
    530                 535                 540

Glu Pro Leu Pro Asp Asp Val Arg Ala Ala Leu Ser Ala Ile Gln His
545                 550                 555                 560

Asp Leu Phe Asp Leu Gly Gly Glu Leu Cys Ile Pro Gly His Ala Ala
                565                 570                 575

Ile Thr Glu Asp His Leu Leu Arg Leu Ala Leu Trp Leu Val His Tyr
            580                 585                 590

Asn Gly Gln Leu Pro Pro Leu Glu Glu Phe Ile Leu Pro Gly Gly Ala
        595                 600                 605

Arg Gly Ala Ala Leu Ala His Val Cys Arg Thr Val Cys Arg Arg Ala
    610                 615                 620

Glu Arg Ser Ile Lys Ala Leu Gly Ala Ser Glu Pro Leu Asn Ile Ala
625                 630                 635                 640

Pro Ala Ala Tyr Val Asn Leu Leu Ser Asp Leu Leu Phe Val Leu Ala
                645                 650                 655

Arg Val Leu Asn Arg Ala Ala Gly Gly Ala Asp Val Leu Trp Asp Arg
            660                 665                 670

Thr Arg Ala His
        675
```

<210> 76
<211> 730
<212> PRT
<213> Artificial Sequence

<220>
<223> DS-Cav1-8GS-HelExt-I53-50A (F10)

<220>
<221> MISC_FEATURE
<222> (1)..(25)
<223> optionally absent

<400> 76

```
Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
1               5                  10                  15

Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
            20                  25                  30

Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
        35                  40                  45

Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
    50                  55                  60

Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65                  70                  75                  80

Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
                85                  90                  95

Met Gln Ser Thr Pro Ala Thr Asn Asn Arg Ala Arg Arg Glu Leu Pro
            100                 105                 110

Arg Phe Met Asn Tyr Thr Leu Asn Asn Ala Lys Lys Thr Asn Val Thr
        115                 120                 125

Leu Ser Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Val
    130                 135                 140
```

```
Gly Ser Ala Ile Ala Ser Gly Val Ala Val Cys Lys Val Leu His Leu
145                 150                 155                 160

Glu Gly Glu Val Asn Lys Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys
                165                 170                 175

Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Phe Lys Val
            180                 185                 190

Leu Asp Leu Lys Asn Tyr Ile Asp Lys Gln Leu Leu Pro Ile Leu Asn
        195                 200                 205

Lys Gln Ser Cys Ser Ile Ser Asn Ile Glu Thr Val Ile Glu Phe Gln
    210                 215                 220

Gln Lys Asn Asn Arg Leu Leu Glu Ile Thr Arg Glu Phe Ser Val Asn
225                 230                 235                 240

Ala Gly Val Thr Thr Pro Val Ser Thr Tyr Met Leu Thr Asn Ser Glu
                245                 250                 255

Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
            260                 265                 270

Leu Met Ser Asn Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile
        275                 280                 285

Met Cys Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro
    290                 295                 300

Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro
305                 310                 315                 320

Leu Cys Thr Thr Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg
                325                 330                 335

Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe
            340                 345                 350
```

```
Pro Gln Ala Glu Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp
        355                 360                 365

Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Val Asn Leu Cys Asn Val
    370                 375                 380

Asp Ile Phe Asn Pro Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr
385                 390                 395                 400

Asp Val Ser Ser Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys
                405                 410                 415

Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile
            420                 425                 430

Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp
        435                 440                 445

Thr Val Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly
    450                 455                 460

Lys Ser Leu Tyr Val Lys Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro
465                 470                 475                 480

Leu Val Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ser Gln Val Asn
                485                 490                 495

Glu Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Gly Ser Gly Gly Ser
            500                 505                 510

Gly Ser Gly Glu Lys Ala Ala Lys Ala Glu Glu Ala Ala Arg Lys Met
        515                 520                 525

Glu Glu Leu Phe Lys Lys His Lys Ile Val Ala Val Leu Arg Ala Asn
    530                 535                 540

Ser Val Glu Glu Ala Ile Glu Lys Ala Val Ala Val Phe Ala Gly Gly
545                 550                 555                 560
```

```
Val His Leu Ile Glu Ile Thr Phe Thr Val Pro Asp Ala Asp Thr Val
                565                 570                 575


Ile Lys Ala Leu Ser Val Leu Lys Glu Lys Gly Ala Ile Ile Gly Ala
            580                 585                 590


Gly Thr Val Thr Ser Val Glu Gln Cys Arg Lys Ala Val Glu Ser Gly
        595                 600                 605


Ala Glu Phe Ile Val Ser Pro His Leu Asp Glu Glu Ile Ser Gln Phe
    610                 615                 620


Cys Lys Glu Lys Gly Val Phe Tyr Met Pro Gly Val Met Thr Pro Thr
625                 630                 635                 640


Glu Leu Val Lys Ala Met Lys Leu Gly His Thr Ile Leu Lys Leu Phe
                645                 650                 655


Pro Gly Glu Val Val Gly Pro Gln Phe Val Lys Ala Met Lys Gly Pro
            660                 665                 670


Phe Pro Asn Val Lys Phe Val Pro Thr Gly Gly Val Asn Leu Asp Asn
        675                 680                 685


Val Cys Glu Trp Phe Lys Ala Gly Val Leu Ala Val Gly Val Gly Ser
    690                 695                 700


Ala Leu Val Lys Gly Thr Pro Asp Glu Val Arg Glu Lys Ala Lys Ala
705                 710                 715                 720


Phe Val Glu Lys Ile Arg Gly Cys Thr Glu
                725                 730
```

<210> 77
<211> 764
<212> PRT
<213> Artificial Sequence

<220>
<223> DS-Cav1-foldon-15GS-HelExt-I53-50A (F14)

<220>
<221> MISC_FEATURE
<222> (1)..(25)
<223> optionally absent

<400> 77

```
Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
1               5                   10                  15


Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
            20                  25                  30


Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
        35                  40                  45


Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
    50                  55                  60


Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65                  70                  75                  80


Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
                85                  90                  95


Met Gln Ser Thr Pro Ala Thr Asn Asn Arg Ala Arg Arg Glu Leu Pro
            100                 105                 110


Arg Phe Met Asn Tyr Thr Leu Asn Asn Ala Lys Lys Thr Asn Val Thr
        115                 120                 125


Leu Ser Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Val
    130                 135                 140


Gly Ser Ala Ile Ala Ser Gly Val Ala Val Cys Lys Val Leu His Leu
145                 150                 155                 160


Glu Gly Glu Val Asn Lys Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys
                165                 170                 175
```

```
Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Phe Lys Val
            180                 185                 190

Leu Asp Leu Lys Asn Tyr Ile Asp Lys Gln Leu Leu Pro Ile Leu Asn
        195                 200                 205

Lys Gln Ser Cys Ser Ile Ser Asn Ile Glu Thr Val Ile Glu Phe Gln
    210                 215                 220

Gln Lys Asn Asn Arg Leu Leu Glu Ile Thr Arg Glu Phe Ser Val Asn
225                 230                 235                 240

Ala Gly Val Thr Thr Pro Val Ser Thr Tyr Met Leu Thr Asn Ser Glu
                245                 250                 255

Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
            260                 265                 270

Leu Met Ser Asn Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile
        275                 280                 285

Met Cys Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro
    290                 295                 300

Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro
305                 310                 315                 320

Leu Cys Thr Thr Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg
                325                 330                 335

Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe
            340                 345                 350

Pro Gln Ala Glu Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp
        355                 360                 365

Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Val Asn Leu Cys Asn Val
    370                 375                 380
```

```
Asp Ile Phe Asn Pro Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr
385                 390                 395                 400

Asp Val Ser Ser Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys
                405                 410                 415

Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile
            420                 425                 430

Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp
        435                 440                 445

Thr Val Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly
    450                 455                 460

Lys Ser Leu Tyr Val Lys Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro
465                 470                 475                 480

Leu Val Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ser Gln Val Asn
                485                 490                 495

Glu Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Gly Tyr Ile Pro Glu
            500                 505                 510

Ala Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp Gly Glu Trp Val
        515                 520                 525

Leu Leu Ser Thr Phe Leu Gly Ser Gly Gly Ser Gly Ser Gly Ser Gly
    530                 535                 540

Gly Ser Gly Ser Gly Glu Lys Ala Ala Lys Ala Glu Glu Ala Ala Arg
545                 550                 555                 560

Lys Met Glu Glu Leu Phe Lys Lys His Lys Ile Val Ala Val Leu Arg
                565                 570                 575

Ala Asn Ser Val Glu Glu Ala Ile Glu Lys Ala Val Ala Val Phe Ala
            580                 585                 590
```

```
Gly Gly Val His Leu Ile Glu Ile Thr Phe Thr Val Pro Asp Ala Asp
        595                 600                 605


Thr Val Ile Lys Ala Leu Ser Val Leu Lys Glu Lys Gly Ala Ile Ile
    610                 615                 620


Gly Ala Gly Thr Val Thr Ser Val Glu Gln Cys Arg Lys Ala Val Glu
625                 630                 635                 640


Ser Gly Ala Glu Phe Ile Val Ser Pro His Leu Asp Glu Glu Ile Ser
                645                 650                 655


Gln Phe Cys Lys Glu Lys Gly Val Phe Tyr Met Pro Gly Val Met Thr
            660                 665                 670


Pro Thr Glu Leu Val Lys Ala Met Lys Leu Gly His Thr Ile Leu Lys
        675                 680                 685


Leu Phe Pro Gly Glu Val Val Gly Pro Gln Phe Val Lys Ala Met Lys
    690                 695                 700


Gly Pro Phe Pro Asn Val Lys Phe Val Pro Thr Gly Gly Val Asn Leu
705                 710                 715                 720


Asp Asn Val Cys Glu Trp Phe Lys Ala Gly Val Leu Ala Val Gly Val
                725                 730                 735


Gly Ser Ala Leu Val Lys Gly Thr Pro Asp Glu Val Arg Glu Lys Ala
            740                 745                 750


Lys Ala Phe Val Glu Lys Ile Arg Gly Cys Thr Glu
        755                 760


<210>  78
<211>  774
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HMPV F wt_CAN97-83 strain-I53-50A
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<220>
<221> MISC_FEATURE
<222> (1)..(18)
<223> optionally absent

<400> 78

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Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
1               5                   10                  15


His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
            20                  25                  30


Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
        35                  40                  45


Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
    50                  55                  60


Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
65                  70                  75                  80


Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
                85                  90                  95


Asn Pro Arg Gln Ser Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
            100                 105                 110


Ala Thr Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
        115                 120                 125


Arg Leu Glu Ser Glu Val Thr Ala Ile Lys Asn Ala Leu Lys Thr Thr
    130                 135                 140


Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
145                 150                 155                 160


Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
                165                 170                 175
```

```
Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser
            180                 185                 190

Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
        195                 200                 205

Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
    210                 215                 220

Ala Glu Leu Ala Arg Ala Val Ser Asn Met Pro Thr Ser Ala Gly Gln
225                 230                 235                 240

Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
                245                 250                 255

Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
            260                 265                 270

Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
        275                 280                 285

Ala Pro Ser Cys Ser Gly Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
    290                 295                 300

Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
305                 310                 315                 320

Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
                325                 330                 335

Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
            340                 345                 350

Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
        355                 360                 365

Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
    370                 375                 380
```

```
Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
385                 390                 395                 400


Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
                405                 410                 415


Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
            420                 425                 430


Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
        435                 440                 445


Ile Lys Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
    450                 455                 460


Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
465                 470                 475                 480


Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile
                485                 490                 495


Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile
            500                 505                 510


Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser
        515                 520                 525


Gly Val Thr Asn Asn Gly Phe Ile Pro His Ser Gly Ser Gly Ser His
    530                 535                 540


His His His His His His His Gly Gly Ser Gly Gly Ser Gly Ser Glu
545                 550                 555                 560


Lys Ala Ala Lys Ala Glu Glu Ala Ala Arg Lys Met Glu Glu Leu Phe
                565                 570                 575


Lys Lys His Lys Ile Val Ala Val Leu Arg Ala Asn Ser Val Glu Glu
            580                 585                 590
```

```
Ala Ile Glu Lys Ala Val Ala Val Phe Ala Gly Gly Val His Leu Ile
        595                 600                 605


Glu Ile Thr Phe Thr Val Pro Asp Ala Asp Thr Val Ile Lys Ala Leu
    610                 615                 620


Ser Val Leu Lys Glu Lys Gly Ala Ile Ile Gly Ala Gly Thr Val Thr
625                 630                 635                 640


Ser Val Glu Gln Cys Arg Lys Ala Val Glu Ser Gly Ala Glu Phe Ile
                645                 650                 655


Val Ser Pro His Leu Asp Glu Glu Ile Ser Gln Phe Cys Lys Glu Lys
            660                 665                 670


Gly Val Phe Tyr Met Pro Gly Val Met Thr Pro Thr Glu Leu Val Lys
        675                 680                 685


Ala Met Lys Leu Gly His Thr Ile Leu Lys Leu Phe Pro Gly Glu Val
    690                 695                 700


Val Gly Pro Gln Phe Val Lys Ala Met Lys Gly Pro Phe Pro Asn Val
705                 710                 715                 720


Lys Phe Val Pro Thr Gly Gly Val Asn Leu Asp Asn Val Cys Glu Trp
                725                 730                 735


Phe Lys Ala Gly Val Leu Ala Val Gly Val Gly Ser Ala Leu Val Lys
            740                 745                 750


Gly Thr Pro Asp Glu Val Arg Glu Lys Ala Lys Ala Phe Val Glu Lys
        755                 760                 765


Ile Arg Gly Cys Thr Glu
    770
```

<210> 79
<211> 725
<212> PRT

<213> Artificial Sequence

<220>
<223> HMPV F A113C_A339C_T160F_I177L-I53-50A

<220>
<221> MISC_FEATURE
<222> (1)..(18)
<223> optionally absent

<400> 79

```
Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
1               5                  10                  15

His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
            20                  25                  30

Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
        35                  40                  45

Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
    50                  55                  60

Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
65                  70                  75                  80

Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
                85                  90                  95

Asn Pro Arg Gln Ser Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
            100                 105                 110

Cys Thr Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
        115                 120                 125

Arg Leu Glu Ser Glu Val Thr Ala Ile Lys Asn Ala Leu Lys Thr Thr
    130                 135                 140

Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Phe
145                 150                 155                 160
```

```
Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
                165                 170                 175

Leu Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser
            180                 185                 190

Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
        195                 200                 205

Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
    210                 215                 220

Ala Glu Leu Ala Arg Ala Val Ser Asn Met Pro Thr Ser Ala Gly Gln
225                 230                 235                 240

Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
                245                 250                 255

Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
            260                 265                 270

Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
        275                 280                 285

Ala Pro Ser Cys Ser Gly Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
    290                 295                 300

Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
305                 310                 315                 320

Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
                325                 330                 335

Thr Ala Cys Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
            340                 345                 350

Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
        355                 360                 365
```

```
Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
    370                 375                 380

Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
385                 390                 395                 400

Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
                405                 410                 415

Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
            420                 425                 430

Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
        435                 440                 445

Ile Lys Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
    450                 455                 460

Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
465                 470                 475                 480

Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Gly Ser Gly Ser His His
                485                 490                 495

His His His His His His Gly Gly Ser Gly Gly Ser Gly Ser Glu Lys
            500                 505                 510

Ala Ala Lys Ala Glu Glu Ala Ala Arg Lys Met Glu Glu Leu Phe Lys
        515                 520                 525

Lys His Lys Ile Val Ala Val Leu Arg Ala Asn Ser Val Glu Glu Ala
    530                 535                 540

Ile Glu Lys Ala Val Ala Val Phe Ala Gly Gly Val His Leu Ile Glu
545                 550                 555                 560

Ile Thr Phe Thr Val Pro Asp Ala Asp Thr Val Ile Lys Ala Leu Ser
                565                 570                 575
```

```
Val Leu Lys Glu Lys Gly Ala Ile Ile Gly Ala Gly Thr Val Thr Ser
            580                 585                 590


Val Glu Gln Cys Arg Lys Ala Val Glu Ser Gly Ala Glu Phe Ile Val
        595                 600                 605


Ser Pro His Leu Asp Glu Glu Ile Ser Gln Phe Cys Lys Glu Lys Gly
    610                 615                 620


Val Phe Tyr Met Pro Gly Val Met Thr Pro Thr Glu Leu Val Lys Ala
625                 630                 635                 640


Met Lys Leu Gly His Thr Ile Leu Lys Leu Phe Pro Gly Glu Val Val
                645                 650                 655


Gly Pro Gln Phe Val Lys Ala Met Lys Gly Pro Phe Pro Asn Val Lys
            660                 665                 670


Phe Val Pro Thr Gly Gly Val Asn Leu Asp Asn Val Cys Glu Trp Phe
        675                 680                 685


Lys Ala Gly Val Leu Ala Val Gly Val Gly Ser Ala Leu Val Lys Gly
    690                 695                 700


Thr Pro Asp Glu Val Arg Glu Lys Ala Lys Ala Phe Val Glu Lys Ile
705                 710                 715                 720


Arg Gly Cys Thr Glu
                725


<210>  80
<211>  725
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HMPV F A113C_A339C_T160F_I177L_A120C, Q426C - I53-50A


<220>
<221>  MISC_FEATURE
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<222> (1)..(18)
<223> optionally absent

<400> 80

```
Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
1               5                  10                  15


His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
            20                  25                  30


Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
        35                  40                  45


Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
    50                  55                  60


Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
65                  70                  75                  80


Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
                85                  90                  95


Asn Pro Arg Gln Ser Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
            100                 105                 110


Cys Thr Ala Ala Ala Val Thr Cys Gly Val Ala Ile Ala Lys Thr Ile
        115                 120                 125


Arg Leu Glu Ser Glu Val Thr Ala Ile Lys Asn Ala Leu Lys Thr Thr
    130                 135                 140


Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Phe
145                 150                 155                 160


Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
                165                 170                 175


Leu Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser
            180                 185                 190
```

```
Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
        195                 200                 205

Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
    210                 215                 220

Ala Glu Leu Ala Arg Ala Val Ser Asn Met Pro Thr Ser Ala Gly Gln
225                 230                 235                 240

Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
                245                 250                 255

Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
            260                 265                 270

Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
        275                 280                 285

Ala Pro Ser Cys Ser Gly Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
    290                 295                 300

Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
305                 310                 315                 320

Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
                325                 330                 335

Thr Ala Cys Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
            340                 345                 350

Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
        355                 360                 365

Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
    370                 375                 380

Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
385                 390                 395                 400
```

```
Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
                405                 410                 415

Thr Val Thr Ile Asp Asn Thr Val Tyr Cys Leu Ser Lys Val Glu Gly
            420                 425                 430

Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
        435                 440                 445

Ile Lys Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
    450                 455                 460

Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
465                 470                 475                 480

Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Gly Ser Gly Ser His His
                485                 490                 495

His His His His His His Gly Gly Ser Gly Gly Ser Gly Ser Glu Lys
            500                 505                 510

Ala Ala Lys Ala Glu Glu Ala Ala Arg Lys Met Glu Glu Leu Phe Lys
        515                 520                 525

Lys His Lys Ile Val Ala Val Leu Arg Ala Asn Ser Val Glu Glu Ala
    530                 535                 540

Ile Glu Lys Ala Val Ala Val Phe Ala Gly Gly Val His Leu Ile Glu
545                 550                 555                 560

Ile Thr Phe Thr Val Pro Asp Ala Asp Thr Val Ile Lys Ala Leu Ser
                565                 570                 575

Val Leu Lys Glu Lys Gly Ala Ile Ile Gly Ala Gly Thr Val Thr Ser
            580                 585                 590

Val Glu Gln Cys Arg Lys Ala Val Glu Ser Gly Ala Glu Phe Ile Val
        595                 600                 605
```

```
Ser Pro His Leu Asp Glu Glu Ile Ser Gln Phe Cys Lys Glu Lys Gly
    610                 615                 620


Val Phe Tyr Met Pro Gly Val Met Thr Pro Thr Glu Leu Val Lys Ala
625                 630                 635                 640


Met Lys Leu Gly His Thr Ile Leu Lys Leu Phe Pro Gly Glu Val Val
                645                 650                 655


Gly Pro Gln Phe Val Lys Ala Met Lys Gly Pro Phe Pro Asn Val Lys
            660                 665                 670


Phe Val Pro Thr Gly Gly Val Asn Leu Asp Asn Val Cys Glu Trp Phe
        675                 680                 685


Lys Ala Gly Val Leu Ala Val Gly Val Gly Ser Ala Leu Val Lys Gly
    690                 695                 700


Thr Pro Asp Glu Val Arg Glu Lys Ala Lys Ala Phe Val Glu Lys Ile
705                 710                 715                 720


Arg Gly Cys Thr Glu
                725


<210>  81
<211>  703
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  sc-DS2-I53-50A


<220>
<221>  MISC_FEATURE
<222>  (1)..(25)
<223>  optionally absent

<400>  81

Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
1               5                   10                  15
```

```
Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
            20                  25                  30

Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
        35                  40                  45

Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
    50                  55                  60

Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65                  70                  75                  80

Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
                85                  90                  95

Met Gln Ser Thr Pro Ala Thr Gly Ser Gly Ser Cys Ile Ala Ser Gly
            100                 105                 110

Val Ala Val Cys Lys Val Leu His Leu Glu Gly Glu Val Asn Lys Ile
        115                 120                 125

Lys Ser Ala Leu Leu Ser Thr Asn Lys Ala Val Val Ser Leu Ser Asn
    130                 135                 140

Gly Val Ser Val Leu Thr Phe Lys Val Leu Asp Leu Lys Asn Tyr Ile
145                 150                 155                 160

Asp Lys Gln Leu Leu Pro Ile Leu Asn Lys Gln Ser Cys Ser Ile Ser
                165                 170                 175

Asn Ile Glu Thr Val Ile Glu Phe Gln Gln Lys Asn Asn Arg Leu Leu
            180                 185                 190

Glu Ile Thr Arg Glu Phe Ser Val Asn Ala Gly Val Thr Thr Pro Val
        195                 200                 205

Ser Thr Tyr Met Leu Thr Asn Ser Glu Leu Leu Ser Leu Ile Asn Asp
    210                 215                 220
```

```
Met Pro Ile Thr Asn Asp Gln Lys Lys Leu Met Ser Asn Asn Val Gln
225                 230                 235                 240

Ile Val Arg Gln Gln Ser Tyr Ser Ile Met Cys Ile Ile Lys Glu Glu
                245                 250                 255

Val Leu Ala Tyr Val Val Gln Leu Pro Leu Tyr Gly Val Ile Asp Thr
            260                 265                 270

Pro Cys Trp Lys Leu His Thr Ser Pro Leu Cys Thr Thr Asn Thr Lys
        275                 280                 285

Glu Gly Ser Asn Ile Cys Leu Thr Arg Thr Asp Arg Gly Trp Tyr Cys
    290                 295                 300

Asp Asn Ala Gly Ser Val Ser Phe Phe Pro Gln Ala Glu Thr Cys Lys
305                 310                 315                 320

Val Gln Ser Asn Arg Val Phe Cys Asp Thr Met Asn Ser Leu Thr Leu
                325                 330                 335

Pro Ser Glu Val Asn Leu Cys Asn Val Asp Ile Phe Asn Pro Lys Tyr
            340                 345                 350

Asp Cys Lys Ile Met Thr Ser Lys Thr Asp Val Ser Ser Ser Val Ile
        355                 360                 365

Thr Ser Leu Gly Ala Ile Val Ser Cys Tyr Gly Lys Thr Lys Cys Thr
    370                 375                 380

Ala Ser Asn Lys Asn Arg Gly Ile Ile Lys Thr Phe Ser Asn Gly Cys
385                 390                 395                 400

Asp Tyr Val Ser Asn Lys Gly Val Asp Thr Val Ser Val Gly Asn Thr
                405                 410                 415

Leu Tyr Cys Val Asn Lys Gln Glu Gly Lys Ser Leu Tyr Val Lys Gly
            420                 425                 430
```

```
Glu Pro Ile Ile Asn Phe Tyr Asp Pro Leu Val Phe Pro Ser Asp Glu
        435                 440                 445

Phe Asp Ala Ser Ile Ser Gln Val Asn Glu Lys Ile Asn Gln Ser Leu
    450                 455                 460

Ala Phe Ile Arg Gly Ser Gly Ser His His His His His His His His
465                 470                 475                 480

Gly Gly Ser Gly Gly Ser Gly Ser Glu Lys Ala Ala Lys Ala Glu Glu
                485                 490                 495

Ala Ala Arg Lys Met Glu Glu Leu Phe Lys Lys His Lys Ile Val Ala
            500                 505                 510

Val Leu Arg Ala Asn Ser Val Glu Glu Ala Ile Glu Lys Ala Val Ala
        515                 520                 525

Val Phe Ala Gly Gly Val His Leu Ile Glu Ile Thr Phe Thr Val Pro
    530                 535                 540

Asp Ala Asp Thr Val Ile Lys Ala Leu Ser Val Leu Lys Glu Lys Gly
545                 550                 555                 560

Ala Ile Ile Gly Ala Gly Thr Val Thr Ser Val Glu Gln Cys Arg Lys
                565                 570                 575

Ala Val Glu Ser Gly Ala Glu Phe Ile Val Ser Pro His Leu Asp Glu
            580                 585                 590

Glu Ile Ser Gln Phe Cys Lys Glu Lys Gly Val Phe Tyr Met Pro Gly
        595                 600                 605

Val Met Thr Pro Thr Glu Leu Val Lys Ala Met Lys Leu Gly His Thr
    610                 615                 620

Ile Leu Lys Leu Phe Pro Gly Glu Val Val Gly Pro Gln Phe Val Lys
625                 630                 635                 640
```

```
Ala Met Lys Gly Pro Phe Pro Asn Val Lys Phe Val Pro Thr Gly Gly
                645                 650                 655


Val Asn Leu Asp Asn Val Cys Glu Trp Phe Lys Ala Gly Val Leu Ala
            660                 665                 670


Val Gly Val Gly Ser Ala Leu Val Lys Gly Thr Pro Asp Glu Val Arg
        675                 680                 685


Glu Lys Ala Lys Ala Phe Val Glu Lys Ile Arg Gly Cys Thr Glu
    690                 695                 700


<210>  82
<211>  742
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  tc-DS2-I53-50A


<220>
<221>  MISC_FEATURE
<222>  (1)..(25)
<223>  optionally absent

<400>  82

Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
1               5                   10                  15


Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
            20                  25                  30


Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
        35                  40                  45


Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
    50                  55                  60


Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65                  70                  75                  80
```

```
Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
                85                  90                  95

Met Gln Ser Thr Pro Ala Thr Asn Asn Arg Ala Arg Arg Glu Leu Pro
            100                 105                 110

Arg Phe Met Asn Tyr Thr Leu Asn Asn Ala Lys Lys Thr Asn Val Thr
        115                 120                 125

Leu Ser Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Val
    130                 135                 140

Gly Ser Cys Ile Ala Ser Gly Val Ala Val Cys Lys Val Leu His Leu
145                 150                 155                 160

Glu Gly Glu Val Asn Lys Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys
                165                 170                 175

Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Phe Lys Val
            180                 185                 190

Leu Asp Leu Lys Asn Tyr Ile Asp Lys Gln Leu Leu Pro Ile Leu Asn
        195                 200                 205

Lys Gln Ser Cys Ser Ile Ser Asn Ile Glu Thr Val Ile Glu Phe Gln
    210                 215                 220

Gln Lys Asn Asn Arg Leu Leu Glu Ile Thr Arg Glu Phe Ser Val Asn
225                 230                 235                 240

Ala Gly Val Thr Thr Pro Val Ser Thr Tyr Met Leu Thr Asn Ser Glu
                245                 250                 255

Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
            260                 265                 270

Leu Met Ser Asn Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile
        275                 280                 285
```

```
Met Cys Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro
    290                 295                 300

Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro
305                 310                 315                 320

Leu Cys Thr Thr Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg
                325                 330                 335

Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe
            340                 345                 350

Pro Gln Ala Glu Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp
        355                 360                 365

Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Val Asn Leu Cys Asn Val
    370                 375                 380

Asp Ile Phe Asn Pro Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr
385                 390                 395                 400

Asp Val Ser Ser Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys
                405                 410                 415

Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile
            420                 425                 430

Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp
        435                 440                 445

Thr Val Ser Val Gly Asn Thr Leu Tyr Cys Val Asn Lys Gln Glu Gly
    450                 455                 460

Lys Ser Leu Tyr Val Lys Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro
465                 470                 475                 480

Leu Val Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ser Gln Val Asn
                485                 490                 495
```

```
Glu Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Gly Ser Gly Ser His
            500                 505                 510

His His His His His His His Gly Gly Ser Gly Gly Ser Gly Ser Glu
        515                 520                 525

Lys Ala Ala Lys Ala Glu Glu Ala Ala Arg Lys Met Glu Glu Leu Phe
    530                 535                 540

Lys Lys His Lys Ile Val Ala Val Leu Arg Ala Asn Ser Val Glu Glu
545                 550                 555                 560

Ala Ile Glu Lys Ala Val Ala Val Phe Ala Gly Gly Val His Leu Ile
                565                 570                 575

Glu Ile Thr Phe Thr Val Pro Asp Ala Asp Thr Val Ile Lys Ala Leu
            580                 585                 590

Ser Val Leu Lys Glu Lys Gly Ala Ile Ile Gly Ala Gly Thr Val Thr
        595                 600                 605

Ser Val Glu Gln Cys Arg Lys Ala Val Glu Ser Gly Ala Glu Phe Ile
    610                 615                 620

Val Ser Pro His Leu Asp Glu Glu Ile Ser Gln Phe Cys Lys Glu Lys
625                 630                 635                 640

Gly Val Phe Tyr Met Pro Gly Val Met Thr Pro Thr Glu Leu Val Lys
                645                 650                 655

Ala Met Lys Leu Gly His Thr Ile Leu Lys Leu Phe Pro Gly Glu Val
            660                 665                 670

Val Gly Pro Gln Phe Val Lys Ala Met Lys Gly Pro Phe Pro Asn Val
        675                 680                 685

Lys Phe Val Pro Thr Gly Gly Val Asn Leu Asp Asn Val Cys Glu Trp
    690                 695                 700
```

```
Phe Lys Ala Gly Val Leu Ala Val Gly Val Gly Ser Ala Leu Val Lys
705                 710                 715                 720


Gly Thr Pro Asp Glu Val Arg Glu Lys Ala Lys Ala Phe Val Glu Lys
                725                 730                 735


Ile Arg Gly Cys Thr Glu
            740


<210>  83
<211>  734
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  DS-Cav1-12GS-HelExt-I53-50A (F11)


<220>
<221>  MISC_FEATURE
<222>  (1)..(25)
<223>  optionally absent

<400>  83

Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
1               5                   10                  15


Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
            20                  25                  30


Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
        35                  40                  45


Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
    50                  55                  60


Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65                  70                  75                  80


Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
                85                  90                  95
```

```
Met Gln Ser Thr Pro Ala Thr Asn Asn Arg Ala Arg Arg Glu Leu Pro
            100                 105                 110

Arg Phe Met Asn Tyr Thr Leu Asn Asn Ala Lys Lys Thr Asn Val Thr
        115                 120                 125

Leu Ser Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Val
    130                 135                 140

Gly Ser Ala Ile Ala Ser Gly Val Ala Val Cys Lys Val Leu His Leu
145                 150                 155                 160

Glu Gly Glu Val Asn Lys Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys
                165                 170                 175

Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Phe Lys Val
            180                 185                 190

Leu Asp Leu Lys Asn Tyr Ile Asp Lys Gln Leu Leu Pro Ile Leu Asn
        195                 200                 205

Lys Gln Ser Cys Ser Ile Ser Asn Ile Glu Thr Val Ile Glu Phe Gln
    210                 215                 220

Gln Lys Asn Asn Arg Leu Leu Glu Ile Thr Arg Glu Phe Ser Val Asn
225                 230                 235                 240

Ala Gly Val Thr Thr Pro Val Ser Thr Tyr Met Leu Thr Asn Ser Glu
                245                 250                 255

Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
            260                 265                 270

Leu Met Ser Asn Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile
        275                 280                 285

Met Cys Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro
    290                 295                 300
```

```
Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro
305                 310                 315                 320

Leu Cys Thr Thr Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg
                325                 330                 335

Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe
            340                 345                 350

Pro Gln Ala Glu Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp
        355                 360                 365

Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Val Asn Leu Cys Asn Val
    370                 375                 380

Asp Ile Phe Asn Pro Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr
385                 390                 395                 400

Asp Val Ser Ser Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys
                405                 410                 415

Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile
            420                 425                 430

Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp
        435                 440                 445

Thr Val Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly
    450                 455                 460

Lys Ser Leu Tyr Val Lys Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro
465                 470                 475                 480

Leu Val Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ser Gln Val Asn
                485                 490                 495

Glu Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Gly Ser Gly Gly Ser
            500                 505                 510
```

```
Gly Ser Gly Ser Gly Gly Ser Glu Lys Ala Ala Lys Ala Glu Glu Ala
        515                 520                 525

Ala Arg Lys Met Glu Glu Leu Phe Lys Lys His Lys Ile Val Ala Val
    530                 535                 540

Leu Arg Ala Asn Ser Val Glu Glu Ala Ile Glu Lys Ala Val Ala Val
545                 550                 555                 560

Phe Ala Gly Gly Val His Leu Ile Glu Ile Thr Phe Thr Val Pro Asp
                565                 570                 575

Ala Asp Thr Val Ile Lys Ala Leu Ser Val Leu Lys Glu Lys Gly Ala
            580                 585                 590

Ile Ile Gly Ala Gly Thr Val Thr Ser Val Glu Gln Cys Arg Lys Ala
        595                 600                 605

Val Glu Ser Gly Ala Glu Phe Ile Val Ser Pro His Leu Asp Glu Glu
    610                 615                 620

Ile Ser Gln Phe Cys Lys Glu Lys Gly Val Phe Tyr Met Pro Gly Val
625                 630                 635                 640

Met Thr Pro Thr Glu Leu Val Lys Ala Met Lys Leu Gly His Thr Ile
                645                 650                 655

Leu Lys Leu Phe Pro Gly Glu Val Val Gly Pro Gln Phe Val Lys Ala
            660                 665                 670

Met Lys Gly Pro Phe Pro Asn Val Lys Phe Val Pro Thr Gly Gly Val
        675                 680                 685

Asn Leu Asp Asn Val Cys Glu Trp Phe Lys Ala Gly Val Leu Ala Val
    690                 695                 700

Gly Val Gly Ser Ala Leu Val Lys Gly Thr Pro Asp Glu Val Arg Glu
705                 710                 715                 720
```

Lys Ala Lys Ala Phe Val Glu Lys Ile Arg Gly Cys Thr Glu
725 730

<210> 84
<211> 738
<212> PRT
<213> Artificial Sequence

<220>
<223> DS-Cav1-16GS-HelExt-I53-50A (F12)

<220>
<221> MISC_FEATURE
<222> (1)..(25)
<223> optionally absent

<400> 84

Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
1 5 10 15

Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
20 25 30

Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
35 40 45

Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
50 55 60

Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65 70 75 80

Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
85 90 95

Met Gln Ser Thr Pro Ala Thr Asn Asn Arg Ala Arg Arg Glu Leu Pro
100 105 110

Arg Phe Met Asn Tyr Thr Leu Asn Asn Ala Lys Lys Thr Asn Val Thr
115 120 125

```
Leu Ser Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Val
    130                 135                 140

Gly Ser Ala Ile Ala Ser Gly Val Ala Val Cys Lys Val Leu His Leu
145                 150                 155                 160

Glu Gly Glu Val Asn Lys Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys
                165                 170                 175

Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Phe Lys Val
            180                 185                 190

Leu Asp Leu Lys Asn Tyr Ile Asp Lys Gln Leu Leu Pro Ile Leu Asn
        195                 200                 205

Lys Gln Ser Cys Ser Ile Ser Asn Ile Glu Thr Val Ile Glu Phe Gln
    210                 215                 220

Gln Lys Asn Asn Arg Leu Leu Glu Ile Thr Arg Glu Phe Ser Val Asn
225                 230                 235                 240

Ala Gly Val Thr Thr Pro Val Ser Thr Tyr Met Leu Thr Asn Ser Glu
                245                 250                 255

Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
            260                 265                 270

Leu Met Ser Asn Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile
        275                 280                 285

Met Cys Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro
    290                 295                 300

Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro
305                 310                 315                 320

Leu Cys Thr Thr Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg
                325                 330                 335
```

```
Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe
            340                 345                 350


Pro Gln Ala Glu Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp
        355                 360                 365


Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Val Asn Leu Cys Asn Val
    370                 375                 380


Asp Ile Phe Asn Pro Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr
385                 390                 395                 400


Asp Val Ser Ser Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys
                405                 410                 415


Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile
            420                 425                 430


Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp
        435                 440                 445


Thr Val Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly
    450                 455                 460


Lys Ser Leu Tyr Val Lys Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro
465                 470                 475                 480


Leu Val Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ser Gln Val Asn
                485                 490                 495


Glu Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Gly Ser Gly Gly Ser
            500                 505                 510


Gly Ser Gly Ser Gly Gly Ser Gly Ser Gly Gly Glu Lys Ala Ala Lys
        515                 520                 525


Ala Glu Glu Ala Ala Arg Lys Met Glu Glu Leu Phe Lys Lys His Lys
    530                 535                 540
```

```
Ile Val Ala Val Leu Arg Ala Asn Ser Val Glu Glu Ala Ile Glu Lys
545                 550                 555                 560

Ala Val Ala Val Phe Ala Gly Gly Val His Leu Ile Glu Ile Thr Phe
                565                 570                 575

Thr Val Pro Asp Ala Asp Thr Val Ile Lys Ala Leu Ser Val Leu Lys
            580                 585                 590

Glu Lys Gly Ala Ile Ile Gly Ala Gly Thr Val Thr Ser Val Glu Gln
        595                 600                 605

Cys Arg Lys Ala Val Glu Ser Gly Ala Glu Phe Ile Val Ser Pro His
    610                 615                 620

Leu Asp Glu Glu Ile Ser Gln Phe Cys Lys Glu Lys Gly Val Phe Tyr
625                 630                 635                 640

Met Pro Gly Val Met Thr Pro Thr Glu Leu Val Lys Ala Met Lys Leu
                645                 650                 655

Gly His Thr Ile Leu Lys Leu Phe Pro Gly Glu Val Val Gly Pro Gln
            660                 665                 670

Phe Val Lys Ala Met Lys Gly Pro Phe Pro Asn Val Lys Phe Val Pro
        675                 680                 685

Thr Gly Gly Val Asn Leu Asp Asn Val Cys Glu Trp Phe Lys Ala Gly
    690                 695                 700

Val Leu Ala Val Gly Val Gly Ser Ala Leu Val Lys Gly Thr Pro Asp
705                 710                 715                 720

Glu Val Arg Glu Lys Ala Lys Ala Phe Val Glu Lys Ile Arg Gly Cys
                725                 730                 735

Thr Glu
```

<210> 85
<211> 759
<212> PRT
<213> Artificial Sequence

<220>
<223> DS-Cav1-foldon-10GS-HelExt-I53-50A (F13)

<220>
<221> MISC_FEATURE
<222> (1)..(25)
<223> optionally absent

<400> 85

```
Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
1               5                  10                  15

Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
            20                  25                  30

Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
        35                  40                  45

Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
    50                  55                  60

Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65                  70                  75                  80

Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
                85                  90                  95

Met Gln Ser Thr Pro Ala Thr Asn Asn Arg Ala Arg Arg Glu Leu Pro
            100                 105                 110

Arg Phe Met Asn Tyr Thr Leu Asn Asn Ala Lys Lys Thr Asn Val Thr
        115                 120                 125

Leu Ser Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Val
    130                 135                 140
```

```
Gly Ser Ala Ile Ala Ser Gly Val Ala Val Cys Lys Val Leu His Leu
145                 150                 155                 160

Glu Gly Glu Val Asn Lys Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys
                165                 170                 175

Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Phe Lys Val
            180                 185                 190

Leu Asp Leu Lys Asn Tyr Ile Asp Lys Gln Leu Leu Pro Ile Leu Asn
        195                 200                 205

Lys Gln Ser Cys Ser Ile Ser Asn Ile Glu Thr Val Ile Glu Phe Gln
    210                 215                 220

Gln Lys Asn Asn Arg Leu Leu Glu Ile Thr Arg Glu Phe Ser Val Asn
225                 230                 235                 240

Ala Gly Val Thr Thr Pro Val Ser Thr Tyr Met Leu Thr Asn Ser Glu
                245                 250                 255

Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
            260                 265                 270

Leu Met Ser Asn Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile
        275                 280                 285

Met Cys Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro
    290                 295                 300

Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro
305                 310                 315                 320

Leu Cys Thr Thr Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg
                325                 330                 335

Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe
            340                 345                 350
```

```
Pro Gln Ala Glu Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp
        355                 360                 365

Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Val Asn Leu Cys Asn Val
    370                 375                 380

Asp Ile Phe Asn Pro Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr
385                 390                 395                 400

Asp Val Ser Ser Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys
                405                 410                 415

Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile
            420                 425                 430

Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp
        435                 440                 445

Thr Val Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly
    450                 455                 460

Lys Ser Leu Tyr Val Lys Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro
465                 470                 475                 480

Leu Val Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ser Gln Val Asn
                485                 490                 495

Glu Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Gly Tyr Ile Pro Glu
            500                 505                 510

Ala Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp Gly Glu Trp Val
        515                 520                 525

Leu Leu Ser Thr Phe Leu Gly Ser Gly Gly Ser Gly Ser Gly Ser Gly
    530                 535                 540

Glu Lys Ala Ala Lys Ala Glu Glu Ala Ala Arg Lys Met Glu Glu Leu
545                 550                 555                 560
```

```
Phe Lys Lys His Lys Ile Val Ala Val Leu Arg Ala Asn Ser Val Glu
                565                 570                 575

Glu Ala Ile Glu Lys Ala Val Ala Val Phe Ala Gly Gly Val His Leu
            580                 585                 590

Ile Glu Ile Thr Phe Thr Val Pro Asp Ala Asp Thr Val Ile Lys Ala
        595                 600                 605

Leu Ser Val Leu Lys Glu Lys Gly Ala Ile Ile Gly Ala Gly Thr Val
    610                 615                 620

Thr Ser Val Glu Gln Cys Arg Lys Ala Val Glu Ser Gly Ala Glu Phe
625                 630                 635                 640

Ile Val Ser Pro His Leu Asp Glu Glu Ile Ser Gln Phe Cys Lys Glu
                645                 650                 655

Lys Gly Val Phe Tyr Met Pro Gly Val Met Thr Pro Thr Glu Leu Val
            660                 665                 670

Lys Ala Met Lys Leu Gly His Thr Ile Leu Lys Leu Phe Pro Gly Glu
        675                 680                 685

Val Val Gly Pro Gln Phe Val Lys Ala Met Lys Gly Pro Phe Pro Asn
    690                 695                 700

Val Lys Phe Val Pro Thr Gly Gly Val Asn Leu Asp Asn Val Cys Glu
705                 710                 715                 720

Trp Phe Lys Ala Gly Val Leu Ala Val Gly Val Gly Ser Ala Leu Val
                725                 730                 735

Lys Gly Thr Pro Asp Glu Val Arg Glu Lys Ala Lys Ala Phe Val Glu
            740                 745                 750

Lys Ile Arg Gly Cys Thr Glu
        755
```

<210> 86
<211> 769
<212> PRT
<213> Artificial Sequence

<220>
<223> DS-Cav1-foldon-20GS-HelExt-I53-50A (F15)

<220>
<221> MISC_FEATURE
<222> (1)..(25)
<223> optionally absent

<400> 86

Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
1 5 10 15

Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
20 25 30

Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
35 40 45

Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
50 55 60

Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65 70 75 80

Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
85 90 95

Met Gln Ser Thr Pro Ala Thr Asn Asn Arg Ala Arg Arg Glu Leu Pro
100 105 110

Arg Phe Met Asn Tyr Thr Leu Asn Asn Ala Lys Lys Thr Asn Val Thr
115 120 125

Leu Ser Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Val
130 135 140

```
Gly Ser Ala Ile Ala Ser Gly Val Ala Val Cys Lys Val Leu His Leu
145                 150                 155                 160

Glu Gly Glu Val Asn Lys Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys
                165                 170                 175

Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Phe Lys Val
            180                 185                 190

Leu Asp Leu Lys Asn Tyr Ile Asp Lys Gln Leu Leu Pro Ile Leu Asn
        195                 200                 205

Lys Gln Ser Cys Ser Ile Ser Asn Ile Glu Thr Val Ile Glu Phe Gln
    210                 215                 220

Gln Lys Asn Asn Arg Leu Leu Glu Ile Thr Arg Glu Phe Ser Val Asn
225                 230                 235                 240

Ala Gly Val Thr Thr Pro Val Ser Thr Tyr Met Leu Thr Asn Ser Glu
                245                 250                 255

Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
            260                 265                 270

Leu Met Ser Asn Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile
        275                 280                 285

Met Cys Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro
    290                 295                 300

Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro
305                 310                 315                 320

Leu Cys Thr Thr Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg
                325                 330                 335

Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe
            340                 345                 350
```

```
Pro Gln Ala Glu Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp
        355                 360                 365

Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Val Asn Leu Cys Asn Val
    370                 375                 380

Asp Ile Phe Asn Pro Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr
385                 390                 395                 400

Asp Val Ser Ser Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys
                405                 410                 415

Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile
            420                 425                 430

Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp
        435                 440                 445

Thr Val Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly
    450                 455                 460

Lys Ser Leu Tyr Val Lys Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro
465                 470                 475                 480

Leu Val Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ser Gln Val Asn
                485                 490                 495

Glu Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Gly Tyr Ile Pro Glu
            500                 505                 510

Ala Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp Gly Glu Trp Val
        515                 520                 525

Leu Leu Ser Thr Phe Leu Gly Ser Gly Gly Ser Gly Ser Gly Ser Gly
    530                 535                 540

Gly Ser Gly Ser Gly Gly Ser Ser Gly Ser Glu Lys Ala Ala Lys Ala
545                 550                 555                 560
```

```
Glu Glu Ala Ala Arg Lys Met Glu Glu Leu Phe Lys Lys His Lys Ile
                565                 570                 575

Val Ala Val Leu Arg Ala Asn Ser Val Glu Glu Ala Ile Glu Lys Ala
            580                 585                 590

Val Ala Val Phe Ala Gly Gly Val His Leu Ile Glu Ile Thr Phe Thr
        595                 600                 605

Val Pro Asp Ala Asp Thr Val Ile Lys Ala Leu Ser Val Leu Lys Glu
    610                 615                 620

Lys Gly Ala Ile Ile Gly Ala Gly Thr Val Thr Ser Val Glu Gln Cys
625                 630                 635                 640

Arg Lys Ala Val Glu Ser Gly Ala Glu Phe Ile Val Ser Pro His Leu
                645                 650                 655

Asp Glu Glu Ile Ser Gln Phe Cys Lys Glu Lys Gly Val Phe Tyr Met
            660                 665                 670

Pro Gly Val Met Thr Pro Thr Glu Leu Val Lys Ala Met Lys Leu Gly
        675                 680                 685

His Thr Ile Leu Lys Leu Phe Pro Gly Glu Val Val Gly Pro Gln Phe
    690                 695                 700

Val Lys Ala Met Lys Gly Pro Phe Pro Asn Val Lys Phe Val Pro Thr
705                 710                 715                 720

Gly Gly Val Asn Leu Asp Asn Val Cys Glu Trp Phe Lys Ala Gly Val
                725                 730                 735

Leu Ala Val Gly Val Gly Ser Ala Leu Val Lys Gly Thr Pro Asp Glu
            740                 745                 750

Val Arg Glu Lys Ala Lys Ala Phe Val Glu Lys Ile Arg Gly Cys Thr
        755                 760                 765
```

Glu

<210> 87
<211> 736
<212> PRT
<213> Artificial Sequence

<220>
<223> sc9-10 DS-Cav1 A149C Y458C-foldon-I53-50A embodiment

<220>
<221> MISC_FEATURE
<222> (1)..(25)
<223> optionally absent

<220>
<221> MISC_FEATURE
<222> (469)..(474)
<223> optionally absent

<400> 87

Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
1 5 10 15

Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
20 25 30

Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
35 40 45

Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
50 55 60

Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65 70 75 80

Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
85 90 95

Met Gln Ser Thr Pro Ala Thr Gly Ser Gly Ser Ala Ile Cys Ser Gly
100 105 110

```
Val Ala Val Cys Lys Val Leu His Leu Glu Gly Glu Val Asn Lys Ile
        115                 120                 125

Lys Ser Ala Leu Leu Ser Thr Asn Lys Ala Val Val Ser Leu Ser Asn
    130                 135                 140

Gly Val Ser Val Leu Thr Phe Lys Val Leu Asp Leu Lys Asn Tyr Ile
145                 150                 155                 160

Asp Lys Gln Leu Leu Pro Ile Leu Asn Lys Gln Ser Cys Ser Ile Ser
                165                 170                 175

Asn Ile Glu Thr Val Ile Glu Phe Gln Gln Lys Asn Asn Arg Leu Leu
            180                 185                 190

Glu Ile Thr Arg Glu Phe Ser Val Asn Ala Gly Val Thr Thr Pro Val
        195                 200                 205

Ser Thr Tyr Met Leu Thr Asn Ser Glu Leu Leu Ser Leu Ile Asn Asp
    210                 215                 220

Met Pro Ile Thr Asn Asp Gln Lys Lys Leu Met Ser Asn Asn Val Gln
225                 230                 235                 240

Ile Val Arg Gln Gln Ser Tyr Ser Ile Met Cys Ile Ile Lys Glu Glu
                245                 250                 255

Val Leu Ala Tyr Val Val Gln Leu Pro Leu Tyr Gly Val Ile Asp Thr
            260                 265                 270

Pro Cys Trp Lys Leu His Thr Ser Pro Leu Cys Thr Thr Asn Thr Lys
        275                 280                 285

Glu Gly Ser Asn Ile Cys Leu Thr Arg Thr Asp Arg Gly Trp Tyr Cys
    290                 295                 300

Asp Asn Ala Gly Ser Val Ser Phe Phe Pro Gln Ala Glu Thr Cys Lys
305                 310                 315                 320
```

```
Val Gln Ser Asn Arg Val Phe Cys Asp Thr Met Asn Ser Arg Thr Leu
                325                 330                 335

Pro Ser Glu Val Asn Leu Cys Asn Val Asp Ile Phe Asn Pro Lys Tyr
            340                 345                 350

Asp Cys Lys Ile Met Thr Ser Lys Thr Asp Val Ser Ser Ser Val Ile
        355                 360                 365

Thr Ser Leu Gly Ala Ile Val Ser Cys Tyr Gly Lys Thr Lys Cys Thr
    370                 375                 380

Ala Ser Asn Lys Asn Arg Gly Ile Ile Lys Thr Phe Ser Asn Gly Cys
385                 390                 395                 400

Asp Tyr Val Ser Asn Lys Gly Val Asp Thr Val Ser Val Gly Asn Thr
                405                 410                 415

Leu Tyr Cys Val Asn Lys Gln Glu Gly Lys Ser Leu Tyr Val Lys Gly
            420                 425                 430

Glu Pro Ile Ile Asn Phe Tyr Asp Pro Leu Val Phe Pro Ser Asp Glu
        435                 440                 445

Phe Asp Ala Ser Ile Ser Gln Val Asn Glu Lys Ile Asn Gln Ser Leu
    450                 455                 460

Ala Phe Ile Arg Lys Ser Asp Glu Leu Leu Gly Tyr Ile Pro Glu Ala
465                 470                 475                 480

Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp Gly Glu Trp Val Leu
                485                 490                 495

Leu Ser Thr Phe Leu Gly Ser Gly Ser His His His His His His His
            500                 505                 510

His Gly Gly Ser Gly Gly Ser Gly Ser Glu Lys Ala Ala Lys Ala Glu
        515                 520                 525
```

```
Glu Ala Ala Arg Lys Met Glu Glu Leu Phe Lys Lys His Lys Ile Val
    530                 535                 540

Ala Val Leu Arg Ala Asn Ser Val Glu Glu Ala Ile Glu Lys Ala Val
545                 550                 555                 560

Ala Val Phe Ala Gly Gly Val His Leu Ile Glu Ile Thr Phe Thr Val
                565                 570                 575

Pro Asp Ala Asp Thr Val Ile Lys Ala Leu Ser Val Leu Lys Glu Lys
            580                 585                 590

Gly Ala Ile Ile Gly Ala Gly Thr Val Thr Ser Val Glu Gln Cys Arg
        595                 600                 605

Lys Ala Val Glu Ser Gly Ala Glu Phe Ile Val Ser Pro His Leu Asp
    610                 615                 620

Glu Glu Ile Ser Gln Phe Cys Lys Glu Lys Gly Val Phe Tyr Met Pro
625                 630                 635                 640

Gly Val Met Thr Pro Thr Glu Leu Val Lys Ala Met Lys Leu Gly His
                645                 650                 655

Thr Ile Leu Lys Leu Phe Pro Gly Glu Val Val Gly Pro Gln Phe Val
            660                 665                 670

Lys Ala Met Lys Gly Pro Phe Pro Asn Val Lys Phe Val Pro Thr Gly
        675                 680                 685

Gly Val Asn Leu Asp Asn Val Cys Glu Trp Phe Lys Ala Gly Val Leu
    690                 695                 700

Ala Val Gly Val Gly Ser Ala Leu Val Lys Gly Thr Pro Asp Glu Val
705                 710                 715                 720

Arg Glu Lys Ala Lys Ala Phe Val Glu Lys Ile Arg Gly Cys Thr Glu
                725                 730                 735
```

<210> 88
<211> 697
<212> PRT
<213> Artificial Sequence

<220>
<223> sc9-10 DS-Cav1 A149C Y458C - F10 embodiment

<220>
<221> MISC_FEATURE
<222> (1)..(25)
<223> optionally absent

<220>
<221> MISC_FEATURE
<222> (469)..(474)
<223> optionally absent

<400> 88

Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
1 5 10 15

Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
20 25 30

Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
35 40 45

Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
50 55 60

Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65 70 75 80

Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
85 90 95

Met Gln Ser Thr Pro Ala Thr Gly Ser Gly Ser Ala Ile Cys Ser Gly
100 105 110

Val Ala Val Cys Lys Val Leu His Leu Glu Gly Glu Val Asn Lys Ile

115 120 125

Lys Ser Ala Leu Leu Ser Thr Asn Lys Ala Val Val Ser Leu Ser Asn
130 135 140

Gly Val Ser Val Leu Thr Phe Lys Val Leu Asp Leu Lys Asn Tyr Ile
145 150 155 160

Asp Lys Gln Leu Leu Pro Ile Leu Asn Lys Gln Ser Cys Ser Ile Ser
165 170 175

Asn Ile Glu Thr Val Ile Glu Phe Gln Gln Lys Asn Asn Arg Leu Leu
180 185 190

Glu Ile Thr Arg Glu Phe Ser Val Asn Ala Gly Val Thr Thr Pro Val
195 200 205

Ser Thr Tyr Met Leu Thr Asn Ser Glu Leu Leu Ser Leu Ile Asn Asp
210 215 220

Met Pro Ile Thr Asn Asp Gln Lys Lys Leu Met Ser Asn Asn Val Gln
225 230 235 240

Ile Val Arg Gln Gln Ser Tyr Ser Ile Met Cys Ile Ile Lys Glu Glu
245 250 255

Val Leu Ala Tyr Val Val Gln Leu Pro Leu Tyr Gly Val Ile Asp Thr
260 265 270

Pro Cys Trp Lys Leu His Thr Ser Pro Leu Cys Thr Thr Asn Thr Lys
275 280 285

Glu Gly Ser Asn Ile Cys Leu Thr Arg Thr Asp Arg Gly Trp Tyr Cys
290 295 300

Asp Asn Ala Gly Ser Val Ser Phe Phe Pro Gln Ala Glu Thr Cys Lys
305 310 315 320

Val Gln Ser Asn Arg Val Phe Cys Asp Thr Met Asn Ser Arg Thr Leu

```
                325                 330                 335

Pro Ser Glu Val Asn Leu Cys Asn Val Asp Ile Phe Asn Pro Lys Tyr
            340                 345                 350

Asp Cys Lys Ile Met Thr Ser Lys Thr Asp Val Ser Ser Ser Val Ile
        355                 360                 365

Thr Ser Leu Gly Ala Ile Val Ser Cys Tyr Gly Lys Thr Lys Cys Thr
    370                 375                 380

Ala Ser Asn Lys Asn Arg Gly Ile Ile Lys Thr Phe Ser Asn Gly Cys
385                 390                 395                 400

Asp Tyr Val Ser Asn Lys Gly Val Asp Thr Val Ser Val Gly Asn Thr
                405                 410                 415

Leu Tyr Cys Val Asn Lys Gln Glu Gly Lys Ser Leu Tyr Val Lys Gly
            420                 425                 430

Glu Pro Ile Ile Asn Phe Tyr Asp Pro Leu Val Phe Pro Ser Asp Glu
        435                 440                 445

Phe Asp Ala Ser Ile Ser Gln Val Asn Glu Lys Ile Asn Gln Ser Leu
    450                 455                 460

Ala Phe Ile Arg Lys Ser Asp Glu Leu Leu Gly Ser Gly Gly Ser Gly
465                 470                 475                 480

Ser Gly Glu Lys Ala Ala Lys Ala Glu Glu Ala Ala Arg Lys Met Glu
                485                 490                 495

Glu Leu Phe Lys Lys His Lys Ile Val Ala Val Leu Arg Ala Asn Ser
            500                 505                 510

Val Glu Glu Ala Ile Glu Lys Ala Val Ala Val Phe Ala Gly Gly Val
        515                 520                 525

His Leu Ile Glu Ile Thr Phe Thr Val Pro Asp Ala Asp Thr Val Ile
```

530 535 540

Lys Ala Leu Ser Val Leu Lys Glu Lys Gly Ala Ile Ile Gly Ala Gly
545 550 555 560

Thr Val Thr Ser Val Glu Gln Cys Arg Lys Ala Val Glu Ser Gly Ala
565 570 575

Glu Phe Ile Val Ser Pro His Leu Asp Glu Glu Ile Ser Gln Phe Cys
580 585 590

Lys Glu Lys Gly Val Phe Tyr Met Pro Gly Val Met Thr Pro Thr Glu
595 600 605

Leu Val Lys Ala Met Lys Leu Gly His Thr Ile Leu Lys Leu Phe Pro
610 615 620

Gly Glu Val Val Gly Pro Gln Phe Val Lys Ala Met Lys Gly Pro Phe
625 630 635 640

Pro Asn Val Lys Phe Val Pro Thr Gly Gly Val Asn Leu Asp Asn Val
645 650 655

Cys Glu Trp Phe Lys Ala Gly Val Leu Ala Val Gly Val Gly Ser Ala
660 665 670

Leu Val Lys Gly Thr Pro Asp Glu Val Arg Glu Lys Ala Lys Ala Phe
675 680 685

Val Glu Lys Ile Arg Gly Cys Thr Glu
690 695

<210> 89
<211> 736
<212> PRT
<213> Artificial Sequence

<220>
<223> sc9-10 DS-Cav1 A149C Y458C S46G K465Q S215P E92D -foldon-I53-50A embodiment

<220>
<221> MISC_FEATURE
<222> (1)..(25)
<223> optionally absent

<220>
<221> MISC_FEATURE
<222> (469)..(474)
<223> optionally absent

<400> 89

```
Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
1               5                  10                  15


Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
            20                  25                  30


Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Gly Ala Leu
        35                  40                  45


Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
    50                  55                  60


Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65                  70                  75                  80


Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Asp Leu Gln Leu Leu
                85                  90                  95


Met Gln Ser Thr Pro Ala Thr Gly Ser Gly Ser Ala Ile Cys Ser Gly
            100                 105                 110


Val Ala Val Cys Lys Val Leu His Leu Glu Gly Glu Val Asn Lys Ile
        115                 120                 125


Lys Ser Ala Leu Leu Ser Thr Asn Lys Ala Val Val Ser Leu Ser Asn
    130                 135                 140


Gly Val Ser Val Leu Thr Phe Lys Val Leu Asp Leu Lys Asn Tyr Ile
145                 150                 155                 160
```

```
Asp Lys Gln Leu Leu Pro Ile Leu Asn Lys Gln Ser Cys Ser Ile Pro
                165                 170                 175

Asn Ile Glu Thr Val Ile Glu Phe Gln Gln Lys Asn Asn Arg Leu Leu
            180                 185                 190

Glu Ile Thr Arg Glu Phe Ser Val Asn Ala Gly Val Thr Thr Pro Val
        195                 200                 205

Ser Thr Tyr Met Leu Thr Asn Ser Glu Leu Leu Ser Leu Ile Asn Asp
    210                 215                 220

Met Pro Ile Thr Asn Asp Gln Lys Lys Leu Met Ser Asn Asn Val Gln
225                 230                 235                 240

Ile Val Arg Gln Gln Ser Tyr Ser Ile Met Cys Ile Ile Lys Glu Glu
                245                 250                 255

Val Leu Ala Tyr Val Val Gln Leu Pro Leu Tyr Gly Val Ile Asp Thr
            260                 265                 270

Pro Cys Trp Lys Leu His Thr Ser Pro Leu Cys Thr Thr Asn Thr Lys
        275                 280                 285

Glu Gly Ser Asn Ile Cys Leu Thr Arg Thr Asp Arg Gly Trp Tyr Cys
    290                 295                 300

Asp Asn Ala Gly Ser Val Ser Phe Phe Pro Gln Ala Glu Thr Cys Lys
305                 310                 315                 320

Val Gln Ser Asn Arg Val Phe Cys Asp Thr Met Asn Ser Arg Thr Leu
                325                 330                 335

Pro Ser Glu Val Asn Leu Cys Asn Val Asp Ile Phe Asn Pro Lys Tyr
            340                 345                 350

Asp Cys Lys Ile Met Thr Ser Lys Thr Asp Val Ser Ser Ser Val Ile
        355                 360                 365
```

```
Thr Ser Leu Gly Ala Ile Val Ser Cys Tyr Gly Lys Thr Lys Cys Thr
    370                 375                 380

Ala Ser Asn Lys Asn Arg Gly Ile Ile Lys Thr Phe Ser Asn Gly Cys
385                 390                 395                 400

Asp Tyr Val Ser Asn Lys Gly Val Asp Thr Val Ser Val Gly Asn Thr
                405                 410                 415

Leu Tyr Cys Val Asn Lys Gln Glu Gly Gln Ser Leu Tyr Val Lys Gly
            420                 425                 430

Glu Pro Ile Ile Asn Phe Tyr Asp Pro Leu Val Phe Pro Ser Asp Glu
        435                 440                 445

Phe Asp Ala Ser Ile Ser Gln Val Asn Glu Lys Ile Asn Gln Ser Leu
    450                 455                 460

Ala Phe Ile Arg Lys Ser Asp Glu Leu Leu Gly Tyr Ile Pro Glu Ala
465                 470                 475                 480

Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp Gly Glu Trp Val Leu
                485                 490                 495

Leu Ser Thr Phe Leu Gly Ser Gly Ser His His His His His His His
            500                 505                 510

His Gly Gly Ser Gly Gly Ser Gly Ser Glu Lys Ala Ala Lys Ala Glu
        515                 520                 525

Glu Ala Ala Arg Lys Met Glu Glu Leu Phe Lys Lys His Lys Ile Val
    530                 535                 540

Ala Val Leu Arg Ala Asn Ser Val Glu Glu Ala Ile Glu Lys Ala Val
545                 550                 555                 560

Ala Val Phe Ala Gly Gly Val His Leu Ile Glu Ile Thr Phe Thr Val
                565                 570                 575
```

```
Pro Asp Ala Asp Thr Val Ile Lys Ala Leu Ser Val Leu Lys Glu Lys
            580                 585                 590

Gly Ala Ile Ile Gly Ala Gly Thr Val Thr Ser Val Glu Gln Cys Arg
        595                 600                 605

Lys Ala Val Glu Ser Gly Ala Glu Phe Ile Val Ser Pro His Leu Asp
    610                 615                 620

Glu Glu Ile Ser Gln Phe Cys Lys Glu Lys Gly Val Phe Tyr Met Pro
625                 630                 635                 640

Gly Val Met Thr Pro Thr Glu Leu Val Lys Ala Met Lys Leu Gly His
                645                 650                 655

Thr Ile Leu Lys Leu Phe Pro Gly Glu Val Val Gly Pro Gln Phe Val
            660                 665                 670

Lys Ala Met Lys Gly Pro Phe Pro Asn Val Lys Phe Val Pro Thr Gly
        675                 680                 685

Gly Val Asn Leu Asp Asn Val Cys Glu Trp Phe Lys Ala Gly Val Leu
    690                 695                 700

Ala Val Gly Val Gly Ser Ala Leu Val Lys Gly Thr Pro Asp Glu Val
705                 710                 715                 720

Arg Glu Lys Ala Lys Ala Phe Val Glu Lys Ile Arg Gly Cys Thr Glu
                725                 730                 735


<210>  90
<211>  697
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  sc9-10 DS-Cav1 A149C Y458C S46G K465Q S215P E92D - F10 embodiment


<220>
<221>  MISC_FEATURE
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<222> (1)..(25)
<223> optionally absent

<220>
<221> MISC_FEATURE
<222> (469)..(474)
<223> optionally absent

<400> 90

Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
1 5 10 15

Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
20 25 30

Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Gly Ala Leu
35 40 45

Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
50 55 60

Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65 70 75 80

Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Asp Leu Gln Leu Leu
85 90 95

Met Gln Ser Thr Pro Ala Thr Gly Ser Gly Ser Ala Ile Cys Ser Gly
100 105 110

Val Ala Val Cys Lys Val Leu His Leu Glu Gly Glu Val Asn Lys Ile
115 120 125

Lys Ser Ala Leu Leu Ser Thr Asn Lys Ala Val Val Ser Leu Ser Asn
130 135 140

Gly Val Ser Val Leu Thr Phe Lys Val Leu Asp Leu Lys Asn Tyr Ile
145 150 155 160

Asp Lys Gln Leu Leu Pro Ile Leu Asn Lys Gln Ser Cys Ser Ile Pro
165 170 175

```
Asn Ile Glu Thr Val Ile Glu Phe Gln Gln Lys Asn Asn Arg Leu Leu
            180                 185                 190

Glu Ile Thr Arg Glu Phe Ser Val Asn Ala Gly Val Thr Thr Pro Val
        195                 200                 205

Ser Thr Tyr Met Leu Thr Asn Ser Glu Leu Leu Ser Leu Ile Asn Asp
    210                 215                 220

Met Pro Ile Thr Asn Asp Gln Lys Lys Leu Met Ser Asn Asn Val Gln
225                 230                 235                 240

Ile Val Arg Gln Gln Ser Tyr Ser Ile Met Cys Ile Ile Lys Glu Glu
                245                 250                 255

Val Leu Ala Tyr Val Val Gln Leu Pro Leu Tyr Gly Val Ile Asp Thr
            260                 265                 270

Pro Cys Trp Lys Leu His Thr Ser Pro Leu Cys Thr Thr Asn Thr Lys
        275                 280                 285

Glu Gly Ser Asn Ile Cys Leu Thr Arg Thr Asp Arg Gly Trp Tyr Cys
    290                 295                 300

Asp Asn Ala Gly Ser Val Ser Phe Phe Pro Gln Ala Glu Thr Cys Lys
305                 310                 315                 320

Val Gln Ser Asn Arg Val Phe Cys Asp Thr Met Asn Ser Arg Thr Leu
                325                 330                 335

Pro Ser Glu Val Asn Leu Cys Asn Val Asp Ile Phe Asn Pro Lys Tyr
            340                 345                 350

Asp Cys Lys Ile Met Thr Ser Lys Thr Asp Val Ser Ser Ser Val Ile
        355                 360                 365

Thr Ser Leu Gly Ala Ile Val Ser Cys Tyr Gly Lys Thr Lys Cys Thr
    370                 375                 380
```

```
Ala Ser Asn Lys Asn Arg Gly Ile Ile Lys Thr Phe Ser Asn Gly Cys
385                 390                 395                 400

Asp Tyr Val Ser Asn Lys Gly Val Asp Thr Val Ser Val Gly Asn Thr
                405                 410                 415

Leu Tyr Cys Val Asn Lys Gln Glu Gly Gln Ser Leu Tyr Val Lys Gly
            420                 425                 430

Glu Pro Ile Ile Asn Phe Tyr Asp Pro Leu Val Phe Pro Ser Asp Glu
        435                 440                 445

Phe Asp Ala Ser Ile Ser Gln Val Asn Glu Lys Ile Asn Gln Ser Leu
    450                 455                 460

Ala Phe Ile Arg Lys Ser Asp Glu Leu Leu Gly Ser Gly Gly Ser Gly
465                 470                 475                 480

Ser Gly Glu Lys Ala Ala Lys Ala Glu Glu Ala Ala Arg Lys Met Glu
                485                 490                 495

Glu Leu Phe Lys Lys His Lys Ile Val Ala Val Leu Arg Ala Asn Ser
            500                 505                 510

Val Glu Glu Ala Ile Glu Lys Ala Val Ala Val Phe Ala Gly Gly Val
        515                 520                 525

His Leu Ile Glu Ile Thr Phe Thr Val Pro Asp Ala Asp Thr Val Ile
    530                 535                 540

Lys Ala Leu Ser Val Leu Lys Glu Lys Gly Ala Ile Ile Gly Ala Gly
545                 550                 555                 560

Thr Val Thr Ser Val Glu Gln Cys Arg Lys Ala Val Glu Ser Gly Ala
                565                 570                 575

Glu Phe Ile Val Ser Pro His Leu Asp Glu Glu Ile Ser Gln Phe Cys
            580                 585                 590
```

```
Lys Glu Lys Gly Val Phe Tyr Met Pro Gly Val Met Thr Pro Thr Glu
        595                 600                 605


Leu Val Lys Ala Met Lys Leu Gly His Thr Ile Leu Lys Leu Phe Pro
    610                 615                 620


Gly Glu Val Val Gly Pro Gln Phe Val Lys Ala Met Lys Gly Pro Phe
625                 630                 635                 640


Pro Asn Val Lys Phe Val Pro Thr Gly Gly Val Asn Leu Asp Asn Val
                645                 650                 655


Cys Glu Trp Phe Lys Ala Gly Val Leu Ala Val Gly Val Gly Ser Ala
            660                 665                 670


Leu Val Lys Gly Thr Pro Asp Glu Val Arg Glu Lys Ala Lys Ala Phe
        675                 680                 685


Val Glu Lys Ile Arg Gly Cys Thr Glu
    690                 695


<210>  91
<211>  753
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  SC-DM (N67I, S215P) - foldon-I53-50A embodiment


<220>
<221>  MISC_FEATURE
<222>  (1)..(25)
<223>  optionally absent

<220>
<221>  MISC_FEATURE
<222>  (486)..(491)
<223>  optionally absent

<400>  91

Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
```

```
1               5                   10                  15

Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
            20                  25                  30

Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
        35                  40                  45

Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
    50                  55                  60

Lys Lys Ile Lys Cys Asn Gly Thr Asp Ala Lys Ile Lys Leu Ile Lys
65                  70                  75                  80

Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
                85                  90                  95

Met Gln Ser Thr Pro Ala Thr Asn Asn Gln Ala Arg Gly Ser Gly Ser
            100                 105                 110

Gly Arg Ser Leu Gly Phe Leu Leu Gly Val Gly Ser Ala Ile Ala Ser
        115                 120                 125

Gly Val Ala Val Ser Lys Val Leu His Leu Glu Gly Glu Val Asn Lys
    130                 135                 140

Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys Ala Val Val Ser Leu Ser
145                 150                 155                 160

Asn Gly Val Ser Val Leu Thr Ser Lys Val Leu Asp Leu Lys Asn Tyr
                165                 170                 175

Ile Asp Lys Gln Leu Leu Pro Ile Val Asn Lys Gln Ser Cys Ser Ile
            180                 185                 190

Pro Asn Ile Glu Thr Val Ile Glu Phe Gln Gln Lys Asn Asn Arg Leu
        195                 200                 205

Leu Glu Ile Thr Arg Glu Phe Ser Val Asn Ala Gly Val Thr Thr Pro
```

```
    210                 215                 220

Val Ser Thr Tyr Met Leu Thr Asn Ser Glu Leu Leu Ser Leu Ile Asn
225                 230                 235                 240

Asp Met Pro Ile Thr Asn Asp Gln Lys Lys Leu Met Ser Asn Asn Val
                245                 250                 255

Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile Met Ser Ile Ile Lys Glu
            260                 265                 270

Glu Val Leu Ala Tyr Val Val Gln Leu Pro Leu Tyr Gly Val Ile Asp
        275                 280                 285

Thr Pro Cys Trp Lys Leu His Thr Ser Pro Leu Cys Thr Thr Asn Thr
    290                 295                 300

Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg Thr Asp Arg Gly Trp Tyr
305                 310                 315                 320

Cys Asp Asn Ala Gly Ser Val Ser Phe Phe Pro Gln Ala Glu Thr Cys
                325                 330                 335

Lys Val Gln Ser Asn Arg Val Phe Cys Asp Thr Met Asn Ser Leu Thr
            340                 345                 350

Leu Pro Ser Glu Val Asn Leu Cys Asn Val Asp Ile Phe Asn Pro Lys
        355                 360                 365

Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr Asp Val Ser Ser Ser Val
    370                 375                 380

Ile Thr Ser Leu Gly Ala Ile Val Ser Cys Tyr Gly Lys Thr Lys Cys
385                 390                 395                 400

Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile Lys Thr Phe Ser Asn Gly
                405                 410                 415

Cys Asp Tyr Val Ser Asn Lys Gly Val Asp Thr Val Ser Val Gly Asn
```

```
            420                 425                 430

Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly Lys Ser Leu Tyr Val Lys
        435                 440                 445

Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro Leu Val Phe Pro Ser Asp
    450                 455                 460

Glu Phe Asp Ala Ser Ile Ser Gln Val Asn Glu Lys Ile Asn Gln Ser
465                 470                 475                 480

Leu Ala Phe Ile Arg Lys Ser Asp Glu Leu Leu Gly Tyr Ile Pro Glu
                485                 490                 495

Ala Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp Gly Glu Trp Val
            500                 505                 510

Leu Leu Ser Thr Phe Leu Gly Ser Gly Ser His His His His His His
        515                 520                 525

His His Gly Gly Ser Gly Gly Ser Gly Ser Glu Lys Ala Ala Lys Ala
    530                 535                 540

Glu Glu Ala Ala Arg Lys Met Glu Glu Leu Phe Lys Lys His Lys Ile
545                 550                 555                 560

Val Ala Val Leu Arg Ala Asn Ser Val Glu Glu Ala Ile Glu Lys Ala
                565                 570                 575

Val Ala Val Phe Ala Gly Gly Val His Leu Ile Glu Ile Thr Phe Thr
            580                 585                 590

Val Pro Asp Ala Asp Thr Val Ile Lys Ala Leu Ser Val Leu Lys Glu
        595                 600                 605

Lys Gly Ala Ile Ile Gly Ala Gly Thr Val Thr Ser Val Glu Gln Cys
    610                 615                 620

Arg Lys Ala Val Glu Ser Gly Ala Glu Phe Ile Val Ser Pro His Leu
```

625 630 635 640

Asp Glu Glu Ile Ser Gln Phe Cys Lys Glu Lys Gly Val Phe Tyr Met
645 650 655

Pro Gly Val Met Thr Pro Thr Glu Leu Val Lys Ala Met Lys Leu Gly
660 665 670

His Thr Ile Leu Lys Leu Phe Pro Gly Glu Val Val Gly Pro Gln Phe
675 680 685

Val Lys Ala Met Lys Gly Pro Phe Pro Asn Val Lys Phe Val Pro Thr
690 695 700

Gly Gly Val Asn Leu Asp Asn Val Cys Glu Trp Phe Lys Ala Gly Val
705 710 715 720

Leu Ala Val Gly Val Gly Ser Ala Leu Val Lys Gly Thr Pro Asp Glu
725 730 735

Val Arg Glu Lys Ala Lys Ala Phe Val Glu Lys Ile Arg Gly Cys Thr
740 745 750

Glu

<210> 92
<211> 714
<212> PRT
<213> Artificial Sequence

<220>
<223> SC-DM (N67I, S215P) - F10 embodiment

<220>
<221> MISC_FEATURE
<222> (1)..(25)
<223> optionally absent

<220>
<221> MISC_FEATURE
<222> (486)..(491)

<223> optionally absent

<400> 92

```
Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
1               5                  10                  15


Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
            20                  25                  30


Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
        35                  40                  45


Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
    50                  55                  60


Lys Lys Ile Lys Cys Asn Gly Thr Asp Ala Lys Ile Lys Leu Ile Lys
65                  70                  75                  80


Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
                85                  90                  95


Met Gln Ser Thr Pro Ala Thr Asn Asn Gln Ala Arg Gly Ser Gly Ser
            100                 105                 110


Gly Arg Ser Leu Gly Phe Leu Leu Gly Val Gly Ser Ala Ile Ala Ser
        115                 120                 125


Gly Val Ala Val Ser Lys Val Leu His Leu Glu Gly Glu Val Asn Lys
    130                 135                 140


Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys Ala Val Val Ser Leu Ser
145                 150                 155                 160


Asn Gly Val Ser Val Leu Thr Ser Lys Val Leu Asp Leu Lys Asn Tyr
                165                 170                 175


Ile Asp Lys Gln Leu Leu Pro Ile Val Asn Lys Gln Ser Cys Ser Ile
            180                 185                 190
```

```
Pro Asn Ile Glu Thr Val Ile Glu Phe Gln Gln Lys Asn Asn Arg Leu
        195                 200                 205

Leu Glu Ile Thr Arg Glu Phe Ser Val Asn Ala Gly Val Thr Thr Pro
    210                 215                 220

Val Ser Thr Tyr Met Leu Thr Asn Ser Glu Leu Leu Ser Leu Ile Asn
225                 230                 235                 240

Asp Met Pro Ile Thr Asn Asp Gln Lys Lys Leu Met Ser Asn Asn Val
                245                 250                 255

Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile Met Ser Ile Ile Lys Glu
            260                 265                 270

Glu Val Leu Ala Tyr Val Val Gln Leu Pro Leu Tyr Gly Val Ile Asp
        275                 280                 285

Thr Pro Cys Trp Lys Leu His Thr Ser Pro Leu Cys Thr Thr Asn Thr
    290                 295                 300

Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg Thr Asp Arg Gly Trp Tyr
305                 310                 315                 320

Cys Asp Asn Ala Gly Ser Val Ser Phe Phe Pro Gln Ala Glu Thr Cys
                325                 330                 335

Lys Val Gln Ser Asn Arg Val Phe Cys Asp Thr Met Asn Ser Leu Thr
            340                 345                 350

Leu Pro Ser Glu Val Asn Leu Cys Asn Val Asp Ile Phe Asn Pro Lys
        355                 360                 365

Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr Asp Val Ser Ser Ser Val
    370                 375                 380

Ile Thr Ser Leu Gly Ala Ile Val Ser Cys Tyr Gly Lys Thr Lys Cys
385                 390                 395                 400
```

```
Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile Lys Thr Phe Ser Asn Gly
                405                 410                 415

Cys Asp Tyr Val Ser Asn Lys Gly Val Asp Thr Val Ser Val Gly Asn
            420                 425                 430

Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly Lys Ser Leu Tyr Val Lys
        435                 440                 445

Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro Leu Val Phe Pro Ser Asp
    450                 455                 460

Glu Phe Asp Ala Ser Ile Ser Gln Val Asn Glu Lys Ile Asn Gln Ser
465                 470                 475                 480

Leu Ala Phe Ile Arg Lys Ser Asp Glu Leu Leu Gly Ser Gly Gly Ser
                485                 490                 495

Gly Ser Gly Glu Lys Ala Ala Lys Ala Glu Glu Ala Ala Arg Lys Met
            500                 505                 510

Glu Glu Leu Phe Lys Lys His Lys Ile Val Ala Val Leu Arg Ala Asn
        515                 520                 525

Ser Val Glu Glu Ala Ile Glu Lys Ala Val Ala Val Phe Ala Gly Gly
    530                 535                 540

Val His Leu Ile Glu Ile Thr Phe Thr Val Pro Asp Ala Asp Thr Val
545                 550                 555                 560

Ile Lys Ala Leu Ser Val Leu Lys Glu Lys Gly Ala Ile Ile Gly Ala
                565                 570                 575

Gly Thr Val Thr Ser Val Glu Gln Cys Arg Lys Ala Val Glu Ser Gly
            580                 585                 590

Ala Glu Phe Ile Val Ser Pro His Leu Asp Glu Glu Ile Ser Gln Phe
        595                 600                 605
```

```
Cys Lys Glu Lys Gly Val Phe Tyr Met Pro Gly Val Met Thr Pro Thr
    610                 615                 620


Glu Leu Val Lys Ala Met Lys Leu Gly His Thr Ile Leu Lys Leu Phe
625                 630                 635                 640


Pro Gly Glu Val Val Gly Pro Gln Phe Val Lys Ala Met Lys Gly Pro
                645                 650                 655


Phe Pro Asn Val Lys Phe Val Pro Thr Gly Gly Val Asn Leu Asp Asn
            660                 665                 670


Val Cys Glu Trp Phe Lys Ala Gly Val Leu Ala Val Gly Val Gly Ser
        675                 680                 685


Ala Leu Val Lys Gly Thr Pro Asp Glu Val Arg Glu Lys Ala Lys Ala
    690                 695                 700


Phe Val Glu Lys Ile Arg Gly Cys Thr Glu
705                 710


<210>  93
<211>  753
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  SC-TM (N67I, S215P, and E487Q) - foldon-I53-50A embodiment


<220>
<221>  MISC_FEATURE
<222>  (1)..(25)
<223>  optionally absent

<220>
<221>  MISC_FEATURE
<222>  (486)..(491)
<223>  optionally absent

<400>  93

Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
1               5                   10                  15
```

```
Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
            20                  25                  30

Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
        35                  40                  45

Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
    50                  55                  60

Lys Lys Ile Lys Cys Asn Gly Thr Asp Ala Lys Ile Lys Leu Ile Lys
65                  70                  75                  80

Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
                85                  90                  95

Met Gln Ser Thr Pro Ala Thr Asn Asn Gln Ala Arg Gly Ser Gly Ser
            100                 105                 110

Gly Arg Ser Leu Gly Phe Leu Leu Gly Val Gly Ser Ala Ile Ala Ser
        115                 120                 125

Gly Val Ala Val Ser Lys Val Leu His Leu Glu Gly Glu Val Asn Lys
    130                 135                 140

Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys Ala Val Val Ser Leu Ser
145                 150                 155                 160

Asn Gly Val Ser Val Leu Thr Ser Lys Val Leu Asp Leu Lys Asn Tyr
                165                 170                 175

Ile Asp Lys Gln Leu Leu Pro Ile Val Asn Lys Gln Ser Cys Ser Ile
            180                 185                 190

Pro Asn Ile Glu Thr Val Ile Glu Phe Gln Gln Lys Asn Asn Arg Leu
        195                 200                 205

Leu Glu Ile Thr Arg Glu Phe Ser Val Asn Ala Gly Val Thr Thr Pro
    210                 215                 220
```

```
Val Ser Thr Tyr Met Leu Thr Asn Ser Glu Leu Leu Ser Leu Ile Asn
225                 230                 235                 240

Asp Met Pro Ile Thr Asn Asp Gln Lys Lys Leu Met Ser Asn Asn Val
                245                 250                 255

Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile Met Ser Ile Ile Lys Glu
            260                 265                 270

Glu Val Leu Ala Tyr Val Val Gln Leu Pro Leu Tyr Gly Val Ile Asp
        275                 280                 285

Thr Pro Cys Trp Lys Leu His Thr Ser Pro Leu Cys Thr Thr Asn Thr
    290                 295                 300

Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg Thr Asp Arg Gly Trp Tyr
305                 310                 315                 320

Cys Asp Asn Ala Gly Ser Val Ser Phe Phe Pro Gln Ala Glu Thr Cys
                325                 330                 335

Lys Val Gln Ser Asn Arg Val Phe Cys Asp Thr Met Asn Ser Leu Thr
            340                 345                 350

Leu Pro Ser Glu Val Asn Leu Cys Asn Val Asp Ile Phe Asn Pro Lys
        355                 360                 365

Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr Asp Val Ser Ser Ser Val
    370                 375                 380

Ile Thr Ser Leu Gly Ala Ile Val Ser Cys Tyr Gly Lys Thr Lys Cys
385                 390                 395                 400

Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile Lys Thr Phe Ser Asn Gly
                405                 410                 415

Cys Asp Tyr Val Ser Asn Lys Gly Val Asp Thr Val Ser Val Gly Asn
            420                 425                 430
```

```
Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly Lys Ser Leu Tyr Val Lys
        435                 440                 445


Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro Leu Val Phe Pro Ser Asp
    450                 455                 460


Gln Phe Asp Ala Ser Ile Ser Gln Val Asn Glu Lys Ile Asn Gln Ser
465                 470                 475                 480


Leu Ala Phe Ile Arg Lys Ser Asp Glu Leu Leu Gly Tyr Ile Pro Glu
                485                 490                 495


Ala Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp Gly Glu Trp Val
            500                 505                 510


Leu Leu Ser Thr Phe Leu Gly Ser Gly Ser His His His His His His
        515                 520                 525


His His Gly Gly Ser Gly Gly Ser Gly Ser Glu Lys Ala Ala Lys Ala
    530                 535                 540


Glu Glu Ala Ala Arg Lys Met Glu Glu Leu Phe Lys Lys His Lys Ile
545                 550                 555                 560


Val Ala Val Leu Arg Ala Asn Ser Val Glu Glu Ala Ile Glu Lys Ala
                565                 570                 575


Val Ala Val Phe Ala Gly Gly Val His Leu Ile Glu Ile Thr Phe Thr
            580                 585                 590


Val Pro Asp Ala Asp Thr Val Ile Lys Ala Leu Ser Val Leu Lys Glu
        595                 600                 605


Lys Gly Ala Ile Ile Gly Ala Gly Thr Val Thr Ser Val Glu Gln Cys
    610                 615                 620


Arg Lys Ala Val Glu Ser Gly Ala Glu Phe Ile Val Ser Pro His Leu
625                 630                 635                 640
```

```
Asp Glu Glu Ile Ser Gln Phe Cys Lys Glu Lys Gly Val Phe Tyr Met
                645                 650                 655


Pro Gly Val Met Thr Pro Thr Glu Leu Val Lys Ala Met Lys Leu Gly
            660                 665                 670


His Thr Ile Leu Lys Leu Phe Pro Gly Glu Val Val Gly Pro Gln Phe
        675                 680                 685


Val Lys Ala Met Lys Gly Pro Phe Pro Asn Val Lys Phe Val Pro Thr
    690                 695                 700


Gly Gly Val Asn Leu Asp Asn Val Cys Glu Trp Phe Lys Ala Gly Val
705                 710                 715                 720


Leu Ala Val Gly Val Gly Ser Ala Leu Val Lys Gly Thr Pro Asp Glu
                725                 730                 735


Val Arg Glu Lys Ala Lys Ala Phe Val Glu Lys Ile Arg Gly Cys Thr
            740                 745                 750


Glu
```

<210> 94
<211> 714
<212> PRT
<213> Artificial Sequence

<220>
<223> SC-TM (N67I, S215P, and E487Q)-I53-50A - F10 embodiment

<220>
<221> MISC_FEATURE
<222> (1)..(25)
<223> optionally absent

<220>
<221> MISC_FEATURE
<222> (486)..(491)
<223> optionally absent

<400> 94

```
Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
1               5                  10                  15

Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
            20                  25                  30

Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
        35                  40                  45

Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
    50                  55                  60

Lys Lys Ile Lys Cys Asn Gly Thr Asp Ala Lys Ile Lys Leu Ile Lys
65                  70                  75                  80

Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
                85                  90                  95

Met Gln Ser Thr Pro Ala Thr Asn Asn Gln Ala Arg Gly Ser Gly Ser
            100                 105                 110

Gly Arg Ser Leu Gly Phe Leu Leu Gly Val Gly Ser Ala Ile Ala Ser
        115                 120                 125

Gly Val Ala Val Ser Lys Val Leu His Leu Glu Gly Glu Val Asn Lys
    130                 135                 140

Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys Ala Val Val Ser Leu Ser
145                 150                 155                 160

Asn Gly Val Ser Val Leu Thr Ser Lys Val Leu Asp Leu Lys Asn Tyr
                165                 170                 175

Ile Asp Lys Gln Leu Leu Pro Ile Val Asn Lys Gln Ser Cys Ser Ile
            180                 185                 190

Pro Asn Ile Glu Thr Val Ile Glu Phe Gln Gln Lys Asn Asn Arg Leu
        195                 200                 205
```

```
Leu Glu Ile Thr Arg Glu Phe Ser Val Asn Ala Gly Val Thr Thr Pro
    210                 215                 220

Val Ser Thr Tyr Met Leu Thr Asn Ser Glu Leu Leu Ser Leu Ile Asn
225                 230                 235                 240

Asp Met Pro Ile Thr Asn Asp Gln Lys Lys Leu Met Ser Asn Asn Val
                245                 250                 255

Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile Met Ser Ile Ile Lys Glu
            260                 265                 270

Glu Val Leu Ala Tyr Val Val Gln Leu Pro Leu Tyr Gly Val Ile Asp
        275                 280                 285

Thr Pro Cys Trp Lys Leu His Thr Ser Pro Leu Cys Thr Thr Asn Thr
    290                 295                 300

Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg Thr Asp Arg Gly Trp Tyr
305                 310                 315                 320

Cys Asp Asn Ala Gly Ser Val Ser Phe Phe Pro Gln Ala Glu Thr Cys
                325                 330                 335

Lys Val Gln Ser Asn Arg Val Phe Cys Asp Thr Met Asn Ser Leu Thr
            340                 345                 350

Leu Pro Ser Glu Val Asn Leu Cys Asn Val Asp Ile Phe Asn Pro Lys
        355                 360                 365

Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr Asp Val Ser Ser Ser Val
    370                 375                 380

Ile Thr Ser Leu Gly Ala Ile Val Ser Cys Tyr Gly Lys Thr Lys Cys
385                 390                 395                 400

Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile Lys Thr Phe Ser Asn Gly
                405                 410                 415
```

```
Cys Asp Tyr Val Ser Asn Lys Gly Val Asp Thr Val Ser Val Gly Asn
            420                 425                 430

Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly Lys Ser Leu Tyr Val Lys
        435                 440                 445

Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro Leu Val Phe Pro Ser Asp
    450                 455                 460

Gln Phe Asp Ala Ser Ile Ser Gln Val Asn Glu Lys Ile Asn Gln Ser
465                 470                 475                 480

Leu Ala Phe Ile Arg Lys Ser Asp Glu Leu Leu Gly Ser Gly Gly Ser
                485                 490                 495

Gly Ser Gly Glu Lys Ala Ala Lys Ala Glu Glu Ala Ala Arg Lys Met
            500                 505                 510

Glu Glu Leu Phe Lys Lys His Lys Ile Val Ala Val Leu Arg Ala Asn
        515                 520                 525

Ser Val Glu Glu Ala Ile Glu Lys Ala Val Ala Val Phe Ala Gly Gly
    530                 535                 540

Val His Leu Ile Glu Ile Thr Phe Thr Val Pro Asp Ala Asp Thr Val
545                 550                 555                 560

Ile Lys Ala Leu Ser Val Leu Lys Glu Lys Gly Ala Ile Ile Gly Ala
                565                 570                 575

Gly Thr Val Thr Ser Val Glu Gln Cys Arg Lys Ala Val Glu Ser Gly
            580                 585                 590

Ala Glu Phe Ile Val Ser Pro His Leu Asp Glu Glu Ile Ser Gln Phe
        595                 600                 605

Cys Lys Glu Lys Gly Val Phe Tyr Met Pro Gly Val Met Thr Pro Thr
    610                 615                 620
```

```
Glu Leu Val Lys Ala Met Lys Leu Gly His Thr Ile Leu Lys Leu Phe
625                 630                 635                 640


Pro Gly Glu Val Val Gly Pro Gln Phe Val Lys Ala Met Lys Gly Pro
                645                 650                 655


Phe Pro Asn Val Lys Phe Val Pro Thr Gly Gly Val Asn Leu Asp Asn
            660                 665                 670


Val Cys Glu Trp Phe Lys Ala Gly Val Leu Ala Val Gly Val Gly Ser
        675                 680                 685


Ala Leu Val Lys Gly Thr Pro Asp Glu Val Arg Glu Lys Ala Lys Ala
    690                 695                 700


Phe Val Glu Lys Ile Arg Gly Cys Thr Glu
705                 710


<210>  95
<211>  752
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HMPV-F with A113C, A339C, T160F, I177L - foldon-I53-50A
       embodiment


<220>
<221>  MISC_FEATURE
<222>  (1)..(18)
<223>  optionally absent

<400>  95

Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
1               5                   10                  15


His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
            20                  25                  30


Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
```

```
        35                  40                  45

Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
    50                  55                  60

Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
65                  70                  75                  80

Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
                85                  90                  95

Asn Pro Arg Gln Ser Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
            100                 105                 110

Cys Thr Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
        115                 120                 125

Arg Leu Glu Ser Glu Val Thr Ala Ile Lys Asn Ala Leu Lys Thr Thr
    130                 135                 140

Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Phe
145                 150                 155                 160

Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
                165                 170                 175

Leu Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser
            180                 185                 190

Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
        195                 200                 205

Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
    210                 215                 220

Ala Glu Leu Ala Arg Ala Val Ser Asn Met Pro Thr Ser Ala Gly Gln
225                 230                 235                 240

Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
```

```
                245                 250                 255

Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
            260                 265                 270

Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
        275                 280                 285

Ala Pro Ser Cys Ser Gly Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
    290                 295                 300

Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
305                 310                 315                 320

Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
                325                 330                 335

Thr Ala Cys Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
            340                 345                 350

Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
        355                 360                 365

Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
    370                 375                 380

Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
385                 390                 395                 400

Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
                405                 410                 415

Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
            420                 425                 430

Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
        435                 440                 445

Ile Lys Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
```

```
    450                 455                 460

Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
465                 470                 475                 480

Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Gly Tyr Ile Pro Glu Ala
                485                 490                 495

Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp Gly Glu Trp Val Leu
            500                 505                 510

Leu Ser Thr Phe Leu Gly Ser Gly Ser His His His His His His His
        515                 520                 525

His Gly Gly Ser Gly Gly Ser Gly Ser Glu Lys Ala Ala Lys Ala Glu
    530                 535                 540

Glu Ala Ala Arg Lys Met Glu Glu Leu Phe Lys Lys His Lys Ile Val
545                 550                 555                 560

Ala Val Leu Arg Ala Asn Ser Val Glu Glu Ala Ile Glu Lys Ala Val
                565                 570                 575

Ala Val Phe Ala Gly Gly Val His Leu Ile Glu Ile Thr Phe Thr Val
            580                 585                 590

Pro Asp Ala Asp Thr Val Ile Lys Ala Leu Ser Val Leu Lys Glu Lys
        595                 600                 605

Gly Ala Ile Ile Gly Ala Gly Thr Val Thr Ser Val Glu Gln Cys Arg
    610                 615                 620

Lys Ala Val Glu Ser Gly Ala Glu Phe Ile Val Ser Pro His Leu Asp
625                 630                 635                 640

Glu Glu Ile Ser Gln Phe Cys Lys Glu Lys Gly Val Phe Tyr Met Pro
                645                 650                 655

Gly Val Met Thr Pro Thr Glu Leu Val Lys Ala Met Lys Leu Gly His
```

660 665 670

Thr Ile Leu Lys Leu Phe Pro Gly Glu Val Val Gly Pro Gln Phe Val
675 680 685

Lys Ala Met Lys Gly Pro Phe Pro Asn Val Lys Phe Val Pro Thr Gly
690 695 700

Gly Val Asn Leu Asp Asn Val Cys Glu Trp Phe Lys Ala Gly Val Leu
705 710 715 720

Ala Val Gly Val Gly Ser Ala Leu Val Lys Gly Thr Pro Asp Glu Val
725 730 735

Arg Glu Lys Ala Lys Ala Phe Val Glu Lys Ile Arg Gly Cys Thr Glu
740 745 750

<210> 96
<211> 713
<212> PRT
<213> Artificial Sequence

<220>
<223> HMPV-F with A113C, A339C, T160F, I177L-I53-50A F10 embodiment

<220>
<221> MISC_FEATURE
<222> (1)..(18)
<223> optionally absent

<400> 96

Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
1 5 10 15

His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
20 25 30

Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
35 40 45

Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro

```
    50                  55                  60

Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
65                  70                  75                  80

Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
                85                  90                  95

Asn Pro Arg Gln Ser Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
            100                 105                 110

Cys Thr Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
        115                 120                 125

Arg Leu Glu Ser Glu Val Thr Ala Ile Lys Asn Ala Leu Lys Thr Thr
    130                 135                 140

Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Phe
145                 150                 155                 160

Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
                165                 170                 175

Leu Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser
            180                 185                 190

Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
        195                 200                 205

Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
    210                 215                 220

Ala Glu Leu Ala Arg Ala Val Ser Asn Met Pro Thr Ser Ala Gly Gln
225                 230                 235                 240

Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
                245                 250                 255

Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
```

```
            260                 265                 270

Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
        275                 280                 285

Ala Pro Ser Cys Ser Gly Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
    290                 295                 300

Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
305                 310                 315                 320

Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
                325                 330                 335

Thr Ala Cys Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
            340                 345                 350

Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
        355                 360                 365

Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
    370                 375                 380

Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
385                 390                 395                 400

Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
                405                 410                 415

Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
            420                 425                 430

Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
        435                 440                 445

Ile Lys Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
    450                 455                 460

Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
```

465 470 475 480

Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Gly Ser Gly Gly Ser Gly
485 490 495

Ser Gly Glu Lys Ala Ala Lys Ala Glu Glu Ala Ala Arg Lys Met Glu
500 505 510

Glu Leu Phe Lys Lys His Lys Ile Val Ala Val Leu Arg Ala Asn Ser
515 520 525

Val Glu Glu Ala Ile Glu Lys Ala Val Ala Val Phe Ala Gly Gly Val
530 535 540

His Leu Ile Glu Ile Thr Phe Thr Val Pro Asp Ala Asp Thr Val Ile
545 550 555 560

Lys Ala Leu Ser Val Leu Lys Glu Lys Gly Ala Ile Ile Gly Ala Gly
565 570 575

Thr Val Thr Ser Val Glu Gln Cys Arg Lys Ala Val Glu Ser Gly Ala
580 585 590

Glu Phe Ile Val Ser Pro His Leu Asp Glu Glu Ile Ser Gln Phe Cys
595 600 605

Lys Glu Lys Gly Val Phe Tyr Met Pro Gly Val Met Thr Pro Thr Glu
610 615 620

Leu Val Lys Ala Met Lys Leu Gly His Thr Ile Leu Lys Leu Phe Pro
625 630 635 640

Gly Glu Val Val Gly Pro Gln Phe Val Lys Ala Met Lys Gly Pro Phe
645 650 655

Pro Asn Val Lys Phe Val Pro Thr Gly Gly Val Asn Leu Asp Asn Val
660 665 670

Cys Glu Trp Phe Lys Ala Gly Val Leu Ala Val Gly Val Gly Ser Ala

675 680 685

Leu Val Lys Gly Thr Pro Asp Glu Val Arg Glu Lys Ala Lys Ala Phe
690 695 700

Val Glu Lys Ile Arg Gly Cys Thr Glu
705 710

<210> 97
<211> 752
<212> PRT
<213> Artificial Sequence

<220>
<223> HMPV-F with A113C, A120C, A339C, T160F, I177L, and Q426C - foldon-I53-50A embodiment

<220>
<221> MISC_FEATURE
<222> (1)..(18)
<223> optionally absent

<400> 97

Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
1 5 10 15

His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
20 25 30

Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
35 40 45

Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
50 55 60

Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
65 70 75 80

Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
85 90 95

```
Asn Pro Arg Gln Ser Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
            100                 105                 110


Cys Thr Ala Ala Ala Val Thr Cys Gly Val Ala Ile Ala Lys Thr Ile
        115                 120                 125


Arg Leu Glu Ser Glu Val Thr Ala Ile Lys Asn Ala Leu Lys Thr Thr
    130                 135                 140


Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Phe
145                 150                 155                 160


Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
                165                 170                 175


Leu Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser
            180                 185                 190


Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
        195                 200                 205


Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
    210                 215                 220


Ala Glu Leu Ala Arg Ala Val Ser Asn Met Pro Thr Ser Ala Gly Gln
225                 230                 235                 240


Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
                245                 250                 255


Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
            260                 265                 270


Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
        275                 280                 285


Ala Pro Ser Cys Ser Gly Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
    290                 295                 300
```

```
Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
305                 310                 315                 320


Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
                325                 330                 335


Thr Ala Cys Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
            340                 345                 350


Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
        355                 360                 365


Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
    370                 375                 380


Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
385                 390                 395                 400


Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
                405                 410                 415


Thr Val Thr Ile Asp Asn Thr Val Tyr Cys Leu Ser Lys Val Glu Gly
            420                 425                 430


Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
        435                 440                 445


Ile Lys Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
    450                 455                 460


Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
465                 470                 475                 480


Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Gly Tyr Ile Pro Glu Ala
                485                 490                 495


Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp Gly Glu Trp Val Leu
            500                 505                 510
```

```
Leu Ser Thr Phe Leu Gly Ser Gly Ser His His His His His His His
        515                 520                 525

His Gly Gly Ser Gly Gly Ser Gly Ser Glu Lys Ala Ala Lys Ala Glu
    530                 535                 540

Glu Ala Ala Arg Lys Met Glu Glu Leu Phe Lys Lys His Lys Ile Val
545                 550                 555                 560

Ala Val Leu Arg Ala Asn Ser Val Glu Glu Ala Ile Glu Lys Ala Val
                565                 570                 575

Ala Val Phe Ala Gly Gly Val His Leu Ile Glu Ile Thr Phe Thr Val
            580                 585                 590

Pro Asp Ala Asp Thr Val Ile Lys Ala Leu Ser Val Leu Lys Glu Lys
        595                 600                 605

Gly Ala Ile Ile Gly Ala Gly Thr Val Thr Ser Val Glu Gln Cys Arg
    610                 615                 620

Lys Ala Val Glu Ser Gly Ala Glu Phe Ile Val Ser Pro His Leu Asp
625                 630                 635                 640

Glu Glu Ile Ser Gln Phe Cys Lys Glu Lys Gly Val Phe Tyr Met Pro
                645                 650                 655

Gly Val Met Thr Pro Thr Glu Leu Val Lys Ala Met Lys Leu Gly His
            660                 665                 670

Thr Ile Leu Lys Leu Phe Pro Gly Glu Val Val Gly Pro Gln Phe Val
        675                 680                 685

Lys Ala Met Lys Gly Pro Phe Pro Asn Val Lys Phe Val Pro Thr Gly
    690                 695                 700

Gly Val Asn Leu Asp Asn Val Cys Glu Trp Phe Lys Ala Gly Val Leu
705                 710                 715                 720
```

Ala Val Gly Val Gly Ser Ala Leu Val Lys Gly Thr Pro Asp Glu Val
725 730 735

Arg Glu Lys Ala Lys Ala Phe Val Glu Lys Ile Arg Gly Cys Thr Glu
740 745 750

<210> 98
<211> 713
<212> PRT
<213> Artificial Sequence

<220>
<223> HMPV-F with A113C, A120C, A339C, T160F, I177L, and Q426C - F10 embodiment

<220>
<221> MISC_FEATURE
<222> (1)..(18)
<223> optionally absent

<400> 98

Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
1 5 10 15

His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
20 25 30

Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
35 40 45

Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro
50 55 60

Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
65 70 75 80

Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
85 90 95

Asn Pro Arg Gln Ser Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
100 105 110

```
Cys Thr Ala Ala Ala Val Thr Cys Gly Val Ala Ile Ala Lys Thr Ile
        115                 120                 125


Arg Leu Glu Ser Glu Val Thr Ala Ile Lys Asn Ala Leu Lys Thr Thr
    130                 135                 140


Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Phe
145                 150                 155                 160


Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
                165                 170                 175


Leu Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser
            180                 185                 190


Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
        195                 200                 205


Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
    210                 215                 220


Ala Glu Leu Ala Arg Ala Val Ser Asn Met Pro Thr Ser Ala Gly Gln
225                 230                 235                 240


Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
                245                 250                 255


Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
            260                 265                 270


Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
        275                 280                 285


Ala Pro Ser Cys Ser Gly Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
    290                 295                 300


Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
305                 310                 315                 320
```

```
Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
                325                 330                 335

Thr Ala Cys Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
            340                 345                 350

Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
        355                 360                 365

Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
    370                 375                 380

Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
385                 390                 395                 400

Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
                405                 410                 415

Thr Val Thr Ile Asp Asn Thr Val Tyr Cys Leu Ser Lys Val Glu Gly
            420                 425                 430

Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
        435                 440                 445

Ile Lys Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
    450                 455                 460

Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
465                 470                 475                 480

Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Gly Ser Gly Gly Ser Gly
                485                 490                 495

Ser Gly Glu Lys Ala Ala Lys Ala Glu Glu Ala Ala Arg Lys Met Glu
            500                 505                 510

Glu Leu Phe Lys Lys His Lys Ile Val Ala Val Leu Arg Ala Asn Ser
        515                 520                 525
```

```
Val Glu Glu Ala Ile Glu Lys Ala Val Ala Val Phe Ala Gly Gly Val
    530                 535                 540

His Leu Ile Glu Ile Thr Phe Thr Val Pro Asp Ala Asp Thr Val Ile
545                 550                 555                 560

Lys Ala Leu Ser Val Leu Lys Glu Lys Gly Ala Ile Ile Gly Ala Gly
                565                 570                 575

Thr Val Thr Ser Val Glu Gln Cys Arg Lys Ala Val Glu Ser Gly Ala
            580                 585                 590

Glu Phe Ile Val Ser Pro His Leu Asp Glu Glu Ile Ser Gln Phe Cys
        595                 600                 605

Lys Glu Lys Gly Val Phe Tyr Met Pro Gly Val Met Thr Pro Thr Glu
    610                 615                 620

Leu Val Lys Ala Met Lys Leu Gly His Thr Ile Leu Lys Leu Phe Pro
625                 630                 635                 640

Gly Glu Val Val Gly Pro Gln Phe Val Lys Ala Met Lys Gly Pro Phe
                645                 650                 655

Pro Asn Val Lys Phe Val Pro Thr Gly Gly Val Asn Leu Asp Asn Val
            660                 665                 670

Cys Glu Trp Phe Lys Ala Gly Val Leu Ala Val Gly Val Gly Ser Ala
        675                 680                 685

Leu Val Lys Gly Thr Pro Asp Glu Val Arg Glu Lys Ala Lys Ala Phe
    690                 695                 700

Val Glu Lys Ile Arg Gly Cys Thr Glu
705                 710
```

<210> 99
<211> 751
<212> PRT

<213> Artificial Sequence

<220>
<223> HMPV-F 115-BV (A185P) -foldon-I53-50A embodiment

<220>
<221> MISC_FEATURE
<222> (1)..(18)
<223> optionally absent

<400> 99

```
Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
1               5                  10                  15


His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
            20                  25                  30


Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
        35                  40                  45


Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ala Asp Gly Pro
    50                  55                  60


Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
65                  70                  75                  80


Leu Arg Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
                85                  90                  95


Asn Pro Arg Arg Arg Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
            100                 105                 110


Ala Thr Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
        115                 120                 125


Arg Leu Glu Ser Glu Val Thr Ala Ile Lys Asn Ala Leu Lys Lys Thr
    130                 135                 140


Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
145                 150                 155                 160
```

```
Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
                165                 170                 175

Ile Asn Lys Asn Lys Cys Asp Ile Pro Asp Leu Lys Met Ala Val Ser
            180                 185                 190

Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
        195                 200                 205

Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
    210                 215                 220

Ala Glu Leu Ala Arg Ala Val Ser Asn Met Pro Thr Ser Ala Gly Gln
225                 230                 235                 240

Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
                245                 250                 255

Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
            260                 265                 270

Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
        275                 280                 285

Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
    290                 295                 300

Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
305                 310                 315                 320

Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
                325                 330                 335

Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
            340                 345                 350

Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
        355                 360                 365
```

```
Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
    370                 375                 380

Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
385                 390                 395                 400

Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
                405                 410                 415

Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
            420                 425                 430

Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
        435                 440                 445

Val Lys Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
    450                 455                 460

Glu Ser Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
465                 470                 475                 480

Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Tyr Ile Pro Glu Ala Pro
                485                 490                 495

Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp Gly Glu Trp Val Leu Leu
            500                 505                 510

Ser Thr Phe Leu Gly Ser Gly Ser His His His His His His His His
        515                 520                 525

Gly Gly Ser Gly Gly Ser Gly Ser Glu Lys Ala Ala Lys Ala Glu Glu
    530                 535                 540

Ala Ala Arg Lys Met Glu Glu Leu Phe Lys Lys His Lys Ile Val Ala
545                 550                 555                 560

Val Leu Arg Ala Asn Ser Val Glu Glu Ala Ile Glu Lys Ala Val Ala
                565                 570                 575
```

```
Val Phe Ala Gly Gly Val His Leu Ile Glu Ile Thr Phe Thr Val Pro
            580                 585                 590

Asp Ala Asp Thr Val Ile Lys Ala Leu Ser Val Leu Lys Glu Lys Gly
        595                 600                 605

Ala Ile Ile Gly Ala Gly Thr Val Thr Ser Val Glu Gln Cys Arg Lys
    610                 615                 620

Ala Val Glu Ser Gly Ala Glu Phe Ile Val Ser Pro His Leu Asp Glu
625                 630                 635                 640

Glu Ile Ser Gln Phe Cys Lys Glu Lys Gly Val Phe Tyr Met Pro Gly
                645                 650                 655

Val Met Thr Pro Thr Glu Leu Val Lys Ala Met Lys Leu Gly His Thr
            660                 665                 670

Ile Leu Lys Leu Phe Pro Gly Glu Val Val Gly Pro Gln Phe Val Lys
        675                 680                 685

Ala Met Lys Gly Pro Phe Pro Asn Val Lys Phe Val Pro Thr Gly Gly
    690                 695                 700

Val Asn Leu Asp Asn Val Cys Glu Trp Phe Lys Ala Gly Val Leu Ala
705                 710                 715                 720

Val Gly Val Gly Ser Ala Leu Val Lys Gly Thr Pro Asp Glu Val Arg
                725                 730                 735

Glu Lys Ala Lys Ala Phe Val Glu Lys Ile Arg Gly Cys Thr Glu
            740                 745                 750
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<210> 100
<211> 712
<212> PRT
<213> Artificial Sequence

<220>
<223> HMPV-F 115-BV (A185P)-I53-50A - F10 embodiment

<220>
<221> MISC_FEATURE
<222> (1)..(18)
<223> optionally absent

<400> 100

```
Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
1               5                   10                  15


His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
            20                  25                  30


Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
        35                  40                  45


Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ala Asp Gly Pro
    50                  55                  60


Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
65                  70                  75                  80


Leu Arg Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
                85                  90                  95


Asn Pro Arg Arg Arg Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
            100                 105                 110


Ala Thr Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
        115                 120                 125


Arg Leu Glu Ser Glu Val Thr Ala Ile Lys Asn Ala Leu Lys Lys Thr
    130                 135                 140


Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
145                 150                 155                 160


Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
                165                 170                 175
```

```
Ile Asn Lys Asn Lys Cys Asp Ile Pro Asp Leu Lys Met Ala Val Ser
            180                 185                 190

Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
        195                 200                 205

Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
    210                 215                 220

Ala Glu Leu Ala Arg Ala Val Ser Asn Met Pro Thr Ser Ala Gly Gln
225                 230                 235                 240

Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
                245                 250                 255

Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
            260                 265                 270

Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
        275                 280                 285

Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
    290                 295                 300

Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
305                 310                 315                 320

Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
                325                 330                 335

Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
            340                 345                 350

Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
        355                 360                 365

Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
    370                 375                 380
```

```
Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
385                 390                 395                 400

Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
                405                 410                 415

Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
            420                 425                 430

Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
        435                 440                 445

Val Lys Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
    450                 455                 460

Glu Ser Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
465                 470                 475                 480

Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Ser Gly Gly Ser Gly Ser
                485                 490                 495

Gly Glu Lys Ala Ala Lys Ala Glu Glu Ala Ala Arg Lys Met Glu Glu
            500                 505                 510

Leu Phe Lys Lys His Lys Ile Val Ala Val Leu Arg Ala Asn Ser Val
        515                 520                 525

Glu Glu Ala Ile Glu Lys Ala Val Ala Val Phe Ala Gly Gly Val His
    530                 535                 540

Leu Ile Glu Ile Thr Phe Thr Val Pro Asp Ala Asp Thr Val Ile Lys
545                 550                 555                 560

Ala Leu Ser Val Leu Lys Glu Lys Gly Ala Ile Ile Gly Ala Gly Thr
                565                 570                 575

Val Thr Ser Val Glu Gln Cys Arg Lys Ala Val Glu Ser Gly Ala Glu
            580                 585                 590
```

```
Phe Ile Val Ser Pro His Leu Asp Glu Glu Ile Ser Gln Phe Cys Lys
        595                 600                 605


Glu Lys Gly Val Phe Tyr Met Pro Gly Val Met Thr Pro Thr Glu Leu
    610                 615                 620


Val Lys Ala Met Lys Leu Gly His Thr Ile Leu Lys Leu Phe Pro Gly
625                 630                 635                 640


Glu Val Val Gly Pro Gln Phe Val Lys Ala Met Lys Gly Pro Phe Pro
                645                 650                 655


Asn Val Lys Phe Val Pro Thr Gly Gly Val Asn Leu Asp Asn Val Cys
            660                 665                 670


Glu Trp Phe Lys Ala Gly Val Leu Ala Val Gly Val Gly Ser Ala Leu
        675                 680                 685


Val Lys Gly Thr Pro Asp Glu Val Arg Glu Lys Ala Lys Ala Phe Val
    690                 695                 700


Glu Lys Ile Arg Gly Cys Thr Glu
705                 710


<210>  101
<211>  490
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  HMPV F >AAK62968.2 fusion protein [Human metapneumovirus]


<220>
<221>  MISC_FEATURE
<222>  (1)..(18)
<223>  optionally absent

<400>  101

Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln
1               5                   10                  15
```

```
His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr
            20                  25                  30

Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe
        35                  40                  45

Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ala Asp Gly Pro
    50                  55                  60

Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu
65                  70                  75                  80

Leu Arg Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu
                85                  90                  95

Asn Pro Arg Gln Ser Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val
            100                 105                 110

Ala Thr Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile
        115                 120                 125

Arg Leu Glu Ser Glu Val Thr Ala Ile Lys Asn Ala Leu Lys Lys Thr
    130                 135                 140

Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr
145                 150                 155                 160

Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala
                165                 170                 175

Ile Asn Lys Asn Lys Cys Asp Ile Ala Asp Leu Lys Met Ala Val Ser
            180                 185                 190

Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser
        195                 200                 205

Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp
    210                 215                 220
```

```
Ala Glu Leu Ala Arg Ala Val Ser Asn Met Pro Thr Ser Ala Gly Gln
225                 230                 235                 240

Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe
                245                 250                 255

Gly Phe Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln
            260                 265                 270

Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala
        275                 280                 285

Ala Pro Ser Cys Ser Gly Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg
    290                 295                 300

Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr
305                 310                 315                 320

Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp
                325                 330                 335

Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile
            340                 345                 350

Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His
        355                 360                 365

Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys
    370                 375                 380

Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile
385                 390                 395                 400

Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp
                405                 410                 415

Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly
            420                 425                 430
```

```
Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro
        435                 440                 445


Val Lys Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe
    450                 455                 460


Glu Ser Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile
465                 470                 475                 480


Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly
                485                 490
```