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(71) Applicant(s)
INSTITUTE FOR RESEARCH IN BIOMEDICINE

(72) Inventor(s)
Lanzavecchia, Antonio

(74) Agent / Attorney
E F WELLINGTON & CO, 312 St. Kilda Road Southbank, Melbourne, VIC, 3006

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(71) Applicant *(for all designated States except US)*: **INSTITUTE FOR RESEARCH IN BIOMEDICINE** [CH/CH]; Via Vela 6, CH-5400 Bellinzona (CH).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: **LANZAVECCHIA, Antonio** [CH/CH]; Institute For Research In Biomedicine, Via Vela 6, CH-5400 Bellinzona (CH).

(74) Agent: **SMAGGASGALE, Gillian, Helen**; W.P. Thompson & Co., 55 Drury Lane, London WC2B 5SQ (GB).

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(54) Title: DENGUE VIRUS NEUTRALIZING ANTIBODIES AND USES THEREOF

(57) Abstract: The invention relates to antibodies and antigen binding fragments thereof and to cocktails of antibodies and antigen binding fragments that neutralize dengue virus infection without contributing to antibody-dependent enhancement of dengue virus infection. The invention also relates to immortalized B cells that produce, and to epitopes that bind to, such antibodies and antigen binding fragments. In addition, the invention relates to the use of the antibodies, antigen binding fragments, and epitopes in screening methods as well as in the diagnosis and therapy of dengue virus infection.

DENGUE VIRUS NEUTRALIZING ANTIBODIES AND USES THEREOF

This application claims priority to U.S. Provisional Application Serial No. 61/104,911, entitled "Dengue Virus Neutralizing Antibodies and Use Thereof," filed October 13, 2008, which is incorporated herein by reference in its entirety.

BACKGROUND

Dengue viruses (DENV) are human pathogens with a significant threat to world health. These viruses are estimated to cause several hundred thousand cases of dengue fever, dengue hemorrhagic fever and dengue shock syndrome annually. There are four closely related serotypes of dengue viruses, DENV-1, DENV-2, DENV-3 and DENV-4, of the genus *Flavivirus*. The four viruses are spread from human to human through the bite of *Aedes aegypti*, a highly urbanized mosquito species that has successfully resisted all attempts at eradication and control. Vaccination is considered to be the only efficient method of control of dengue. To this end, several tetravalent dengue candidate vaccines are in late stages of development.

A first infection with one Dengue virus serotype induces a life-long protective immunity to the homologous serotype. However, there is no cross-protection against infection by a different serotype. Indeed, pre-existing immunity against one serotype is associated with increased risk for dengue infection and dengue hemorrhagic fever caused by a different serotype due to antibody-dependent enhancement (ADE) of infection. In ADE, antibodies raised by prior dengue infection or passively transferred from mother form infectious immune complexes that attach to Fc-receptor-bearing cells in the mononuclear phagocyte lineage resulting in efficient infection.

Accordingly, there is a need for materials and methods for preventing dengue virus infection without increasing the risk of antibody-dependent enhancement of infection.

SUMMARY

The invention is based, in part, on the discovery of antibodies and cocktails of antibodies that neutralize dengue virus infection without contributing to antibody-dependent enhancement of dengue virus infection. Accordingly, in one aspect of the invention, the invention comprises a human antibody, an antibody variant, or an antigen binding fragment thereof, that neutralize a dengue virus, wherein the antibody, antibody variant, or antigen binding fragment does not contribute to antibody-dependent enhancement of dengue virus infection. In one embodiment,

the invention comprises a human antibody, an antibody variant, or an antigen binding fragment thereof, that neutralize a dengue virus, wherein the antibody, antibody variant, or antigen binding fragment comprises a mutation in the Fc region, and wherein the mutation reduces binding of the antibody to an Fc receptor.

In another embodiment of the invention, the invention comprises a pharmaceutical composition comprising two or more human antibodies, or antigen binding fragments thereof. The antibodies or antigen binding fragments neutralize dengue virus serotypes DENV-1, DENV-2, DENV-3, and DENV-4 by binding at least two distinct epitopes on each dengue virus serotype. The antibodies of the pharmaceutical composition do not contribute to antibody-dependent enhancement of dengue virus infection.

In yet another embodiment, the invention comprises an antibody, or an antigen binding fragment thereof, comprising at least one complementarity determining region (CDR) sequence having the sequence of any one of SEQ ID NOs: 1-6, 17-22, 33-38, 49-54, 67-72, 83-88, 99, 100, 105-110, 121-123, 124, 125, 135-139, 149, 153-158, 169-174, 185-188, or 189, wherein the antibody neutralizes dengue virus infection.

In yet another embodiment, the invention comprises an antibody, or an antigen binding fragment thereof, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 13 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 14; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 29 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 30; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 45 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 46; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 61 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 62; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 65 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 62; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 79 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 80; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 95 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 96; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 95 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 103; or a heavy chain variable region comprising the amino acid

sequence of SEQ ID NO: 117 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 118; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 131 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 132; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 145 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 146; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 151 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 146; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 165 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 166; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 181 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 182; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 195 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 196, wherein the antibody neutralizes dengue virus infection.

In a further embodiment, the invention comprises a recombinant antibody, antibody variant, or antigen binding fragment thereof, that can neutralize a dengue virus. The recombinant antibody, antibody variant, or antigen binding fragment does not contribute to antibody-dependent enhancement of dengue virus infection.

In another aspect, the invention comprises a nucleic acid molecule comprising a polynucleotide encoding an antibody or antibody fragment of the invention that neutralizes dengue virus infection. In yet another aspect, the invention comprises a cell expressing an antibody of the invention. In still another aspect, the invention comprises an isolated or purified immunogenic polypeptide comprising an epitope that binds to an antibody of the invention.

The invention also comprises a pharmaceutical composition comprising an antibody, an antibody variant or an antigen binding fragment of the invention, a nucleic acid of the invention, or an immunogenic polypeptide of the invention and a pharmaceutically acceptable diluent or carrier and, optionally, an agent useful for extending the half life of the antibody or antigen binding fragment thereof.

In another aspect of the invention, the invention provides a method of inhibiting or preventing dengue virus infection or a dengue virus-related disease or a method of treating dengue virus infection or a dengue virus-related disease. The method comprises administering to a subject in need thereof, a therapeutically effective amount of at least one antibody, antibody variant, antigen binding fragment, or a pharmaceutical composition of the invention.

In yet another aspect of the invention, the invention comprises a method of screening for polypeptides that can induce or reveal an immune response against dengue virus, comprising screening polypeptide libraries using an antibody, an antibody fragment or variant of the invention.

In yet another aspect of the invention, the invention comprises a method of monitoring the quality of anti-dengue virus vaccines. The method comprises using an antibody, an antibody variant, or an antigen binding fragment thereof of the invention to check that the antigen of the vaccine contains the specific epitope in the correct conformation.

In a further aspect of the invention, the invention comprises a vaccine comprising an epitope which specifically binds to an antibody, an antibody fragment or variant of the invention.

Use of an antibody of the invention, or an antigen binding fragment thereof, a nucleic acid of the invention, an immunogenic polypeptide of the invention, or a pharmaceutical composition of the invention (i) in the manufacture of a medicament for the treatment of dengue virus infection, (ii) in a vaccine, or (iii) in diagnosis of dengue virus infection is also contemplated to be within the scope of the invention. Further, use of an antibody of the invention, or an antigen binding fragment thereof, for monitoring the quality of anti-DENV vaccines by checking that the antigen of said vaccine contains the specific epitope in the correct conformation is also contemplated to be within the scope of the invention.

In a further aspect, the invention comprises an epitope which specifically binds to an antibody of any one of the invention, or an antigen binding fragment thereof, for use (i) in therapy, (ii) in the manufacture of a medicament for treating dengue virus infection, (iii) as a vaccine, or (iv) in screening for ligands able to neutralise dengue virus infection.

BRIEF DESCRIPTION OF FIGURES

Figure 1. VERO cells and K562 cells were used in virus neutralization and enhancement assays with each serotype of dengue virus using wild-type anti-dengue virus antibodies. Antibodies to dengue virus inhibit infection of the target virus on VERO cells in a dose-dependent manner. On K562 cells, the antibodies lead to a dose dependent antibody-dependent enhancement (ADE) of infection.

Figure 2. Anti-dengue virus antibodies that have a CH2 L4A and L5A substitution (LALA variants) in the heavy chain neutralize target virus infection on VERO cells as did the unmodified antibodies. However, the LALA variants completely abolished the antibody-dependent enhancement of infection by the target virus on K562 cells.

DETAILED DESCRIPTION OF THE INVENTION

The invention is based on the discovery of antibodies and cocktails of antibodies that neutralize dengue virus (DENV) infection without contributing to antibody-dependent enhancement (ADE) of dengue virus infection. In one aspect of the invention, the invention comprises a human antibody, a variant antibody, or an antigen binding fragment thereof, that neutralizes a dengue virus without contributing to antibody-dependent enhancement of dengue virus infection. The antibodies or antibody fragments can neutralize more than one dengue virus serotype, for example, 2, 3 or all 4 dengue virus serotypes DENV-1, DENV-2, DENV-3, and DENV-4.

The invention also comprises a pharmaceutical composition comprising, for example, an antibody cocktail that comprises two or more human antibodies, antibody variants or antigen binding fragments thereof. The pharmaceutical compositions of the invention comprising a cocktail of human antibodies, antibody fragments or variants neutralize all four dengue virus serotypes, *i.e.*, DENV-1, DENV-2, DENV-3, and DENV-4. In one embodiment, the cocktail of antibodies, antibody fragments or variants neutralize dengue virus by binding at least two distinct epitopes on each dengue virus serotype. It is noted that the antibodies, variants and fragments of the pharmaceutical composition do not contribute to antibody-dependent enhancement of dengue virus infection. In one embodiment, the cocktail comprises two antibodies, fragments or variants thereof. In another embodiment, the cocktail comprises three antibodies, fragments or variants thereof. In yet another embodiment, the cocktail comprises more than 3 antibodies, *e.g.*, 4, 5, 6, 7 or 8 antibodies.

As used herein, the terms "fragment," "antibody fragment," and "antigen binding fragment" are used interchangeably to refer to any fragment of an antibody of the invention that retains the antigen-binding activity of the antibody. Exemplary antibody fragments include, but are not limited to, Fab, Fab', $F(ab')_2$, Fv, and scFv fragments.

The terms "mutation," and "substitution" are used interchangeably to refer to a change in one or more nucleic acid or amino acid residues.

As used herein, the terms "variant," and "antibody variant" are used interchangeably to refer to any variant of an antibody of the invention that retains the antigen-binding activity of the antibodies. The term variant includes antibodies that comprise mutations and/or substitutions. Exemplary antibody variants include, but are not limited to, those that have an L to A substitution at position CH2 4, 5, or both.

Antibodies of the invention

The invention provides antibodies that neutralize dengue virus, but do not contribute to ADE of dengue virus infection. A "neutralizing antibody" is one that can neutralize the ability of a pathogen to initiate and/or perpetuate an infection in a host. The antibodies of the invention are able to neutralize one or more dengue virus serotypes DENV-1, DENV-2, DENV-3, and DENV-4. In one embodiment, the antibody of the invention neutralizes more than one, *e.g.*, 2, 3, or all 4 dengue virus serotypes. In another embodiment, a pharmaceutical composition comprising two or more antibodies, antibody fragments or variants can neutralize all 4 dengue virus serotypes. In yet another embodiment, the pharmaceutical composition comprising two or more antibodies, antibody fragments or variants neutralizes dengue virus infection by targeting two distinct epitopes on each dengue virus serotype. These antibodies, antigen binding fragment and variants can be used as prophylactic or therapeutic agents upon appropriate formulation, or as a diagnostic tool, as described herein.

The antibodies of the invention may be monoclonal, for example, human monoclonal antibodies, or recombinant antibodies. The invention also provides fragments of the antibodies of the invention, particularly fragments that retain the antigen-binding activity of the antibodies. Although the specification, including the claims, may, in some places, refer explicitly to antibody fragment(s), variant(s) and/or derivative(s) of antibodies, it is understood that the term "antibody" or "antibody of the invention" includes all categories of antibodies, namely, antibody fragment(s), variant(s) and derivative(s) of antibodies.

Without being bound to any theory, it is believed that antibody-dependent enhancement of dengue virus infection is brought about by the binding of the Fc region of the antibody, in particular, the Fc region of the heavy chain of an IgG molecule, to an Fc receptor, *e.g.*, an Fcγ receptor on a host cell. The invention, on the other hand, provides antibodies, including IgG molecules, that have reduced binding to the Fc receptors (FcR). In one embodiment, the antibody of the invention comprises one or more mutations in the Fc region. The mutation(s) may be any mutation that reduces binding of the antibody to an Fc receptor. In one embodiment, the Fc region of an antibody of the invention comprises a substitution at positions CH2 4, 5, or both. In general, the amino acid at positions 4 and 5 of CH2 of the wild-type IgG1 and IgG3 is a leucine ("L"). In one embodiment, the antibodies of the invention comprise an amino acid at position CH2 4, 5, or both, that is not an L. In another embodiment, the antibodies of the invention comprise an alanine ("A") at position CH2 4, or 5, or both. An antibody comprising a CH2 L4A and an L5A substitution is referred to herein as a "LALA" variant.

Alternatively, the invention provides antibody fragments that do not comprise an Fc region and thus do not bind to an FcR. Exemplary antibody fragments include, but are not limited to, Fab, Fab', $F(ab')_2$, Fv and scFv.

The sequences of the heavy chains and light chains of several exemplary antibodies of the invention, each comprising three CDRs on the heavy chain and three CDRs on the light chain have been determined. The position of the CDR amino acids are defined according to the IMGT numbering system [1, 2, 3]. The sequences of the CDRs, heavy chains, light chains as well as the sequences of the nucleic acid molecules encoding the CDRs, heavy chains, light chains of many exemplary antibodies of the invention are disclosed in the sequence listing. Table 1 provides the SEQ ID NOs for the amino acid sequences of the six CDRs, the variable region of the heavy and light chains, respectively, of exemplary antibodies of the invention. Table 2 provides the SEQ ID NOs for the sequences of the nucleic acid molecules encoding the CDRs, heavy chains and light chains of exemplary antibodies of the invention.

Table 1. Amino Acid SEQ IDs for Antibody CDRs, Heavy and Light Chains

Antibody	CDRs	Heavy Chain Variable Region	Light Chain Variable Region
HMB-DV-1	1-6	13	14
HMB-DV-2	17-22	29	30
HMB-DV-3	33-38	45	46
HMB-DV-4	49-54	61, 65	62
HMB-DV-5	67-72	79	80
HMB-DV-6	83-88	95	96
HMB-DV-7	83-85, 99, 53, 100	95	103
HMB-DV-8	105-110	117	118
HMB-DV-9	121-123, 70 124, 125	131	132
HMB-DV-10	135-139, 109	145	146
HMB-DV-11	149, 136-139, 109	151	146
HMB-DV-12	153-158	165	166
HMB-DV-13	169-174	181	182
HMB-DV-14	185-188, 37, 189	195	196

Table 2. Nucleic Acid SEQ IDs for Antibody CDRs, Heavy and Light Chains

Antibody	CDRs	Heavy Chain Variable Region	Light Chain Variable Region
HMB-DV-1	7-12	15	16
HMB-DV-2	23-28	31	32
HMB-DV-3	39-44	47	48
HMB-DV-4	55-60	63, 66	64
HMB-DV-5	73-78	81	82
HMB-DV-6	89-94	97	98
HMB-DV-7	89-91, 101, 59, 102	97	104
HMB-DV-8	111-116	119	120

HMB-DV-9	126-128, 76, 129, 130	133	134
HMB-DV-10	140-143, 115, 144	147	148
HMB-DV-11	150, 141-143, 115, 144	152	148
HMB-DV-12	159-164	167	168
HMB-DV-13	175-180	183	184
HMB-DV-14	190-193, 43, 194	197	198

In one embodiment, the antibodies or antigen-binding fragments of the invention comprise one or more heavy or light chain CDRs of the exemplary antibodies of the invention. In an exemplary embodiment, the antibodies or antigen-binding fragments of the invention neutralize dengue virus infection and comprise at least one CDR sequence having the sequence of any one of SEQ ID NOs: 1-6, 17-22, 33-38, 49-54, 67-72, 83-88, 99, 100, 105-110, 121-123, 124, 125, 135-139, 149, 153-158, 169-174, 185-188, or 189.

In another embodiment, the antibodies, antibody variants or antigen binding fragments of the invention comprise a heavy chain comprising an amino acid sequence of one or more of SEQ ID NOs: 1-3, 17-19, 33-35, 49-51, 67-69, 83-85, 105-107, 121-123, 135-137, 149, 153-155, 169-171, or 185-187. In yet another embodiment, the antibodies, antibody variants or antigen binding fragments of the invention comprise a heavy chain CDR1 selected from the group consisting of SEQ ID NOs: 1, 17, 33, 49, 67, 83, 105, 121, 135, 149, 153, 169, and 185; a heavy chain CDR2 selected from the group consisting of SEQ ID NOs: 2, 18, 34, 50, 68, 84, 106, 122, 136, 154, 170, and 186; and a heavy chain CDR3 selected from the group consisting of SEQ ID NOs: 3, 19, 35, 51, 69, 85, 107, 123, 137, 155, 171, and 187.

For example, the antibodies of the invention comprise a heavy chain comprising SEQ ID NO: 1 for CDRH1, SEQ ID NO: 2 for CDRH2, SEQ ID NO: 3 for CDRH3; SEQ ID NO: 17 for CDRH1, SEQ ID NO: 18 for CDRH2 and SEQ ID NO: 19 for CDRH3; SEQ ID NO: 33 for CDRH1, SEQ ID NO: 34 for CDRH2 and SEQ ID NO: 35 for CDRH3; SEQ ID NO: 49 for CDRH1, SEQ ID NO: 50 for CDRH2 and SEQ ID NO: 51 for CDRH3; SEQ ID NO: 67 for CDRH1, SEQ ID NO: 68 for CDRH2 and SEQ ID NO: 69 for CDRH3; SEQ ID NO: 83 for CDRH1, SEQ ID NO: 84 for CDRH2 and SEQ ID NO: 85 for CDRH3; SEQ ID NO: 105 for CDRH1, SEQ ID NO: 106 for CDRH2 and SEQ ID NO: 107 for CDRH3; SEQ ID NO: 121 for CDRH1, SEQ ID NO: 122 for CDRH2 and SEQ ID NO: 123 for CDRH3; SEQ ID NO: 135 for CDRH1, SEQ ID NO: 136 for CDRH2 and SEQ ID NO: 137 for CDRH3; SEQ ID NO: 149 for CDRH1, SEQ ID NO: 136 for CDRH2 and SEQ ID NO: 137 for CDRH3; SEQ ID NO: 153 for CDRH1, SEQ ID NO: 154 for CDRH2 and SEQ ID NO: 155 for CDRH3; SEQ ID NO: 169 for CDRH1, SEQ ID NO: 170 for CDRH2 and SEQ ID NO: 171 for CDRH3; and SEQ ID NO: 185 for CDRH1, SEQ ID NO: 186 for CDRH2 and SEQ ID NO: 187 for CDRH3.

In yet another embodiment, the antibodies, antibody variants or antibody fragments of the invention comprise a light chain comprising an amino acid sequence of one or more of SEQ ID NOs: 4-6, 20-22, 36-38, 52-54, 70-72, 86-88, 99, 100, 108-110, 124, 125, 138, 139, 156-158, 172-174, 188, or 189. In a further embodiment, the antibodies, antibody variants or antibody fragments of the invention comprise a light chain CDR1 selected from the group consisting of SEQ ID NOs: 4, 20, 36, 52, 70, 86, 99, 108, 138, 156, 172, and 188; a light chain CDR2 selected from the group consisting of SEQ ID NOs: 5, 21, 37, 53, 71, 87, 109, 124, 157, and 173; and a light chain CDR3 selected from the group consisting of SEQ ID NOs: 6, 22, 38, 54, 72, 88, 100, 110, 125, 139, 158, 174, and 189.

For example, the antibodies of the invention comprise a light chain comprising SEQ ID NO: 4 for CDRL1, SEQ ID NO: 5 for CDRL2; SEQ ID NO: 6 for CDRL3; SEQ ID NO: 20 for CDRL1, SEQ ID NO: 21 for CDRL2; SEQ ID NO: 22 for CDRL3; SEQ ID NO: 36 for CDRL1, SEQ ID NO: 37 for CDRL2; SEQ ID NO: 38 for CDRL3; SEQ ID NO: 52 for CDRL1, SEQ ID NO: 53 for CDRL2; SEQ ID NO: 54 for CDRL3; SEQ ID NO: 70 for CDRL1, SEQ ID NO: 71 for CDRL2; SEQ ID NO: 72 for CDRL3; SEQ ID NO: 86 for CDRL1, SEQ ID NO: 87 for CDRL2; SEQ ID NO: 88 for CDRL3; SEQ ID NO: 99 for CDRL1, SEQ ID NO: 53 for CDRL2; SEQ ID NO: 100 for CDRL3; SEQ ID NO: 108 for CDRL1, SEQ ID NO: 109 for CDRL2; SEQ ID NO: 110 for CDRL3; SEQ ID NO: 70 for CDRL1, SEQ ID NO: 124 for CDRL2; SEQ ID NO: 125 for CDRL3; SEQ ID NO: 138 for CDRL1, SEQ ID NO: 109 for CDRL2; SEQ ID NO: 139 for CDRL3; SEQ ID NO: 156 for CDRL1, SEQ ID NO: 157 for CDRL2; SEQ ID NO: 158 for CDRL3; SEQ ID NO: 172 for CDRL1, SEQ ID NO: 173 for CDRL2; SEQ ID NO: 174 for CDRL3; and SEQ ID NO: 188 for CDRL1, SEQ ID NO: 37 for CDRL2; SEQ ID NO: 189 for CDRL3.

In one embodiment, an antibody of the invention, or antigen binding fragment thereof, comprises all of the CDRs of antibody HMB-DV-1 as listed in Table 1, and neutralizes dengue virus infection in a human host. In another embodiment, an antibody of the invention, or antigen binding fragment thereof, comprises all of the CDRs of antibody HMB-DV-2 as listed in Table 1, and neutralizes dengue virus infection in a human host. In another embodiment, an antibody of the invention, or antigen binding fragment thereof, comprises all of the CDRs of antibody HMB-DV-3 as listed in Table 1, and neutralizes dengue virus infection in a human host. In yet another embodiment, an antibody of the invention, or antigen binding fragment thereof, comprises all of the CDRs of antibody HMB-DV-4 as listed in Table 1, and neutralizes dengue virus infection in a human host. In yet another embodiment, an antibody of the invention, or antigen binding fragment thereof, comprises all of the CDRs of antibody HMB-DV-5 as listed in Table 1, and

neutralizes dengue virus infection in a human host. In yet another embodiment, an antibody of the invention, or antigen binding fragment thereof, comprises all of the CDRs of antibody HMB-DV-6 as listed in Table 1, and neutralizes dengue virus infection in a human host. In yet another embodiment, an antibody of the invention, or antigen binding fragment thereof, comprises all of the CDRs of antibody HMB-DV-7 as listed in Table 1, and neutralizes dengue virus infection in a human host.

In a further embodiment, an antibody of the invention, or antigen binding fragment thereof, comprises all of the CDRs of antibody HMB-DV-8 as listed in Table 1, and neutralizes dengue virus infection in a human host. In another embodiment, an antibody of the invention, or antigen binding fragment thereof, comprises all of the CDRs of antibody HMB-DV-9 as listed in Table 1, and neutralizes dengue virus infection in a human host. In still another embodiment, an antibody of the invention, or antigen binding fragment thereof, comprises all of the CDRs of antibody HMB-DV-10 as listed in Table 1, and neutralizes dengue virus infection in a human host. In yet another embodiment, an antibody of the invention, or antigen binding fragment thereof, comprises all of the CDRs of antibody HMB-DV-11 as listed in Table 1, and neutralizes dengue virus infection in a human host. In yet another embodiment, an antibody of the invention, or antigen binding fragment thereof, comprises all of the CDRs of antibody HMB-DV-12 as listed in Table 1, and neutralizes dengue virus infection in a human host. In yet another embodiment, an antibody of the invention, or antigen binding fragment thereof, comprises all of the CDRs of antibody HMB-DV-13 as listed in Table 1, and neutralizes dengue virus infection in a human host. In yet another embodiment, an antibody of the invention, or antigen binding fragment thereof, comprises all of the CDRs of antibody HMB-DV-14 as listed in Table 1, and neutralizes dengue virus infection in a human host.

In still another embodiment, the antibodies of the invention comprise a heavy chain with an amino acid sequence that is at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% identical to those of SEQ ID NOs: 13, 29, 45, 61, 65, 79, 95, 117, 131, 145, 151, 165, 181, or 195. In yet another embodiment, the antibodies of the invention comprise a light chain with an amino acid sequence that is at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% identical to those of SEQ ID NOs: 14, 30, 46, 62, 80, 96, 103, 118, 132, 146, 166, 182, or 196.

In a further embodiment, the antibodies, antibody variants or antibody fragments of the invention comprise a heavy chain variable region comprising the amino acid sequence of any one of SEQ ID NOs: 13, 29, 45, 61, 65, 79, 95, 117, 131, 145, 151, 165, 181, or 195, and a light chain

variable region comprising the amino acid sequence of any one of SEQ ID NOs: 14, 30, 46, 62, 80, 96, 103, 118, 132, 146, 166, 182, or 196.

In yet another embodiment, the antibodies, antibody variants or antibody fragments of the invention neutralize dengue virus infection and comprise a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 13 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 14; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 29 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 30; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 45 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 46; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 61 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 62; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 65 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 62; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 79 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 80; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 95 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 96; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 95 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 103; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 117 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 118; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 131 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 132; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 145 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 146; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 151 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 146; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 165 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 166; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 181 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 182; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 195 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 196.

Methods for chain replacement and for CDR grafting are well known in the art. Originally these methods were developed to humanize non-human antibodies (generally mouse antibodies) or to select human antibody counterparts having equivalent bioactivity to the non-

human antibodies. These methods include replacement techniques where only one of the CDRs, for example, the CDR3s, of the non-human antibody are retained and the remainder of the V-region, including the framework and the other two CDRs, for example, the CDRs 1 and 2, are individually replaced in steps performed sequentially (e.g. U.S. Patent Application No. 20030166871; Rader, et al., *Proc Natl Acad Sci USA* 95:8910-15, 1998; Steinberg, et al., *J Biol Chem* 275:36073-78, 2000; Rader, et al., *J Biol Chem* 275:13668-76, 2000).

In addition, methods of creating antibodies with the binding specificities of a reference antibody for a target antigen are described in Patent Application No. WO05/069,970. The methods include transferring, from the reference antibody to a recipient antibody or antibody fragment, the minimal essential binding specificity of the reference antibody. Examples of regions that can be transferred include, but are not limited to, the transfer of a single CDR segment, for example a CDR3 segment, from the heavy and/or from the light chain, or a D segment, or a CDR3-FR4 segment, or any CDR3-FR4 segment that comprises the minimal essential binding specificity determinant. Antibodies created using these methods retain the binding specificity, and often affinity, of the reference antibody.

The antibodies, antibody variants or antibody fragments of the invention include antibodies that comprise, *inter alia*, one or more CDRs, a heavy chain or a light chain of an exemplary antibody of the invention and retain their specificity and ability to neutralize dengue virus infection.

Exemplary antibodies of the invention include, but are not limited to, HMB-DV1, HMB-DV2, HMB-DV3, HMB-DV4, HMB-DV5, HMB-DV6, HMB-DV7, HMB-DV8, HMB-DV9, HMB-DV10, HMB-DV11, HMB-DV12, HMB-DV13, and HMB-DV14.

Variants of HMB-DV4 consist of a heavy chain variants having amino acid sequence recited in SEQ ID NO: 61 and SEQ ID NO: 65, and a light chain having the amino acid sequence recited in SEQ ID NO: 62. The nucleic acid sequences encoding the heavy chain variants are recited in SEQ ID NO: 63 and SEQ ID NO: 66. The nucleic acid encoding the light chain is recited in SEQ ID NO: 64. Thus, antibodies comprising the HMB-DV4 variant heavy chains (SEQ ID NOs: 61, 65) and light chain (SEQ ID NO: 62) are included within the scope of the invention.

As used herein, the term "HMB-DV4" is used to refer to any and/or all variants of HMB-DV4, for example, those with heavy chains corresponding to SEQ ID NOs: 61and 65 and light chain corresponding to SEQ ID NO: 62.

In one embodiment, an antibody cocktail of the invention comprises two or more antibodies selected from the group consisting of HMB-DV1, HMB-DV2, HMB-DV3, HMB-DV4, HMB-DV5, HMB-DV6, HMB-DV7, HMB-DV8, HMB-DV9, HMB-DV10, HMB-DV11, HMB-DV12, HMB-DV13, and HMB-DV14. In another embodiment, a cocktail of the invention comprises three antibodies selected from the group consisting of HMB-DV1, HMB-DV2, HMB-DV3, HMB-DV4, HMB-DV5, HMB-DV6, HMB-DV7, HMB-DV8, HMB-DV9, HMB-DV10, HMB-DV11, HMB-DV12, HMB-DV13, and HMB-DV14. In yet another embodiment, an antibody cocktail of the invention comprises more than three, for example, 4, 5, 6, 7, or 8 antibodies selected from the group consisting of HMB-DV1, HMB-DV2, HMB-DV3, HMB-DV4, HMB-DV5, HMB-DV6, HMB-DV7, HMB-DV8, HMB-DV9, HMB-DV10, HMB-DV11, HMB-DV12, HMB-DV13, and HMB-DV14. In an exemplary embodiment, a cocktail of the invention comprises HMB-DV5, HMB-DV6, and HMB-DV8.

The invention further comprises an antibody, or fragment thereof, that binds to an epitope capable of binding to an antibody of the invention. The invention also comprises an antibody or an antibody fragment that competes with an antibody of the invention.

In another aspect, the invention also includes nucleic acid sequences encoding part or all of the light and heavy chains and CDRs of the antibodies of the present invention. In one embodiment, nucleic acid sequences according to the invention include nucleic acid sequences having at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% identity to the nucleic acid encoding a heavy or light chain of an antibody of the invention. In another embodiment, a nucleic acid sequence of the invention has the sequence of a nucleic acid encoding a heavy or light chain CDR of an antibody of the invention. For example, a nucleic acid sequence according to the invention comprises a sequence that is at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% identical to the nucleic acid sequences of SEQ ID NOs: 7-12, 23-28, 39-44, 55-60, 73-78, 89-94, 101, 102, 111-116, 126-128, 129, 130, 140-144, 150, 159-164, 175-180, and 190-194.

Due to the redundancy of the genetic code, variants of these sequences will exist that encode the same amino acid sequences. These variants are included within the scope of the invention.

Variant antibodies are also included within the scope of the invention. Thus, variants of the sequences recited in the application are also included within the scope of the invention. Such variants include natural variants generated by somatic mutation *in vivo* during the immune response or *in vitro* upon culture of immortalized B cell clones. Alternatively, variants may arise

due to the degeneracy of the genetic code, as mentioned above or may be produced due to errors in transcription or translation. Variants may also be introduced to modify the antibody effector function, for instance in the Fc region to reduce the binding of the antibody to an Fc receptor.

Further variants of the antibody sequences having improved affinity and/or potency may be obtained using methods known in the art and are included within the scope of the invention. For example, amino acid substitutions may be used to obtain antibodies with further improved affinity. Alternatively, codon optimisation of the nucleotide sequence may be used to improve the efficiency of translation in expression systems for the production of the antibody. Further, polynucleotides comprising a sequence optimized for antibody specificity or neutralizing activity by the application of a directed evolution method to any of the nucleic acid sequences of the invention are also within the scope of the invention.

In one embodiment variant antibody sequences may share 70% or more (*i.e.* 75%, 80%, 85%, 90%, 95%, 97%, 98%, 99% or more) amino acid sequence identity with the sequences recited in the application. In some embodiments such sequence identity is calculated with regard to the full length of the reference sequence (*i.e.* the sequence recited in the application). In some further embodiments, percentage identity, as referred to herein, is as determined using BLAST version 2.1.3 using the default parameters specified by the NCBI (the National Center for Biotechnology Information; http://www.ncbi.nlm.nih.gov/) [Blosum 62 matrix; gap open penalty=11 and gap extension penalty=1].

Further included within the scope of the invention are vectors, for example expression vectors, comprising a nucleic acid sequence according to the invention. Cells transformed with such vectors are also included within the scope of the invention. Examples of such cells include but are not limited to, eukaryotic cells, *e.g.* yeast cells, animal cells or plant cells. In one embodiment the cells are mammalian, *e.g.* human, CHO, HEK293T, PER.C6, NS0, myeloma or hybridoma cells.

The invention also relates to monoclonal antibodies that bind to an epitope capable of binding an antibody of the invention. In one embodiment, the invention includes a monoclonal antibody that binds to an epitope capable of binding a monoclonal antibody selected from the group consisting of HMB-DV1, HMB-DV2, HMB-DV3, HMB-DV4, HMB-DV5, HMB-DV6, HMB-DV7, HMB-DV8, HMB-DV9, HMB-DV10, HMB-DV11, HMB-DV12, HMB-DV13, and HMB-DV14.

Monoclonal and recombinant antibodies are particularly useful in identification and purification of the individual polypeptides or other antigens against which they are directed. The

antibodies of the invention have additional utility in that they may be employed as reagents in immunoassays, radioimmunoassays (RIA) or enzyme-linked immunosorbent assays (ELISA). In these applications, the antibodies can be labelled with an analytically-detectable reagent such as a radioisotope, a fluorescent molecule or an enzyme. The antibodies may also be used for the molecular identification and characterisation (epitope mapping) of antigens.

Antibodies of the invention will typically be glycosylated. N-linked glycans attached to the C_H2 domain of a heavy chain, for instance, can influence C1q and FcR binding, with aglycosylated antibodies having lower affinity for these receptors. The glycan structure can also affect activity *e.g.* differences in complement-mediated cell death may be seen depending on the number of galactose sugars (0, 1 or 2) at the terminus of a glycan's biantennary chain. An antibody's glycans preferably do not lead to a human immunogenic response after administration.

Antibodies of the invention can be coupled to a drug for delivery to a treatment site or coupled to a detectable label to facilitate imaging of a site comprising cells of interest, such as cells infected with dengue virus. Methods for coupling antibodies to drugs and detectable labels are well known in the art, as are methods for imaging using detectable labels. Labelled antibodies may be employed in a wide variety of assays, employing a wide variety of labels. Detection of the formation of an antibody-antigen complex between an antibody of the invention and an epitope of interest (a DENV epitope) can be facilitated by attaching a detectable substance to the antibody. Suitable detection means include the use of labels such as radionuclides, enzymes, coenzymes, fluorescers, chemiluminescers, chromogens, enzyme substrates or co-factors, enzyme inhibitors, prosthetic group complexes, free radicals, particles, dyes, and the like. Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, β-galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material is luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin; and examples of suitable radioactive material include ^{125}I, ^{131}I, ^{35}S, or ^{3}H. Such labeled reagents may be used in a variety of well-known assays, such as radioimmunoassays, enzyme immunoassays, *e.g.*, ELISA, fluorescent immunoassays, and the like.

An antibody according to the invention may be conjugated to a therapeutic moiety such as a cytotoxin, a therapeutic agent, or a radioactive metal ion or radioisotope. Examples of radioisotopes include, but are not limited to, I-131, I-123, I-125, Y-90, Re-188, Re-186, At-211, Cu-67, Bi-212, Bi-213, Pd-109, Tc-99, In-111, and the like. Such antibody conjugates can be used for modifying a given biological response; the drug moiety is not to be construed as limited to classical chemical therapeutic agents. For example, the drug moiety may be a protein or polypeptide possessing a desired biological activity. Such proteins may include, for example, a toxin such as abrin, ricin A, pseudomonas exotoxin, calicheamicin bacterial toxin, or diphtheria toxin.

Techniques for conjugating such therapeutic moiety to antibodies are well known. See, for example, Arnon *et al.* (1985) "Monoclonal Antibodies for Immunotargeting of Drugs in Cancer Therapy," in *Monoclonal Antibodies and Cancer Therapy*, ed. Reisfeld *et al.* (Alan R. Liss, Inc.), pp. 243-256; ed. Hellstrom *et al.* (1987) "Antibodies for Drug Delivery," in *Controlled Drug Delivery*, ed. Robinson *et al.* (2d ed; Marcel Dekker, Inc.), pp. 623-653; Thorpe (1985) "Antibody Carriers of Cytotoxic Agents in Cancer Therapy: A Review," in *Monoclonal Antibodies '84: Biological and Clinical Applications*, ed. Pinchera *et al.* pp. 475-506 (Editrice Kurtis, Milano, Italy, 1985); "Analysis, Results, and Future Prospective of the Therapeutic Use of Radiolabeled Antibody in Cancer Therapy," in *Monoclonal Antibodies for Cancer Detection and Therapy*, ed. Baldwin *et al.* (Academic Press, New York, 1985), pp. 303-316; and Thorpe *et al.* (1982) *Immunol. Rev.* 62:119-158.

Alternatively, an antibody can be conjugated to a second antibody to form an antibody heteroconjugate as described in reference 4. In addition, linkers may be used between the labels and the antibodies of the invention [5]. Antibodies or, antigen-binding fragments thereof may be directly labelled with radioactive iodine, indium, yttrium, or other radioactive particle known in the art [6]. Treatment may consist of a combination of treatment with conjugated and non-conjugated antibodies administered simultaneously or subsequently [7, 8].

Antibodies of the invention may also be attached to a solid support.

Additionally, antibodies of the invention, or functional antibody fragments thereof, can be chemically modified by covalent conjugation to a polymer to, for example, increase their circulating half-life, for example. Examples of polymers, and methods to attach them to peptides, are shown in references 9-12. In some embodiments the polymers may be selected from polyoxyethylated polyols and polyethylene glycol (PEG). PEG is soluble in water at room temperature and has the general formula: $R(O--CH_2--CH_2)_n O--R$ where R can be hydrogen, or a

protective group such as an alkyl or alkanol group. In one embodiment the protective group may have between 1 and 8 carbons. In a further embodiment the protective group is methyl. The symbol n is a positive integer. In one embodiment n is between 1 and 1,000. In another embodiment n is between 2 and 500. In one embodiment the PEG has an average molecular weight between 1,000 and 40,000. In a further embodiment the PEG has a molecular weight between 2,000 and 20,000. In yet a further embodiment the PEG has a molecular weight of between 3,000 and 12,000. In one embodiment PEG has at least one hydroxy group. In another embodiment the PEG has a terminal hydroxy group. In yet another embodiment it is the terminal hydroxy group which is activated to react with a free amino group on the inhibitor. However, it will be understood that the type and amount of the reactive groups may be varied to achieve a covalently conjugated PEG/antibody of the present invention.

Antibodies of the invention can be modified by introducing random amino acid mutations into particular region of the CH2 or CH3 domain of the heavy chain in order to alter their binding affinity for FcRn and/or their serum half-life in comparison to the unmodified antibodies. Examples of such modifications include, but are not limited to, substitutions of at least one amino acid from the heavy chain constant region selected from the group consisting of amino acid residues 250, 314, and 428.

Water-soluble polyoxyethylated polyols are also useful in the present invention. They include polyoxyethylated sorbitol, polyoxyethylated glucose, polyoxyethylated glycerol (POG), and the like. In one embodiment, POG is used. Without being bound by any theory, because the glycerol backbone of polyoxyethylated glycerol is the same backbone occurring naturally in, for example, animals and humans in mono-, di-, triglycerides, this branching would not necessarily be seen as a foreign agent in the body. In some embodiments POG has a molecular weight in the same range as PEG. The structure for POG is shown in reference 13, and a discussion of POG/IL-2 conjugates is found in reference 9.

Another drug delivery system that can be used for increasing circulatory half-life is the liposome. Methods of preparing liposome delivery systems are discussed in references 14, 15 and 16. Other drug delivery systems are known in the art and are described in, for example, references 17 and 18.

Antibodies of the invention may be provided in purified form. Typically, the antibody will be present in a composition that is substantially free of other polypeptides *e.g.* where less than 90% (by weight), usually less than 60% and more usually less than 50% of the composition is made up of other polypeptides.

Antibodies of the invention may be immunogenic in non-human (or heterologous) hosts *e.g.* in mice. In particular, the antibodies may have an idiotope that is immunogenic in non-human hosts, but not in a human host. Antibodies of the invention for human use include those that cannot be easily isolated from hosts such as mice, goats, rabbits, rats, non-primate mammals, *etc.* and cannot generally be obtained by humanisation or from xeno-mice.

Antibodies of the invention can be of any isotype (*e.g.* IgA, IgG, IgM *i.e.* an α, γ or μ heavy chain), but will generally be IgG. Within the IgG isotype, antibodies may be IgG1, IgG2, IgG3 or IgG4 subclass. In one embodiment, the antibody is IgG1. Antibodies of the invention may have a κ or a λ light chain.

Included within the scope of the invention are DENV-neutralizing recombinant or engineered bispecific antibody molecules or antigen binding fragments thereof. Such antibodies and fragments may comprise a first binding site for an epitope on a first Dengue virus serotype and a second binding site for a second epitope on the same dengue virus serotype or on a different, for example, a second, third or fourth, dengue virus serotype. The variable domains of the respective binding sites can be formed as immunoglobulin isotypes of the invention or as heterodimeric Fab, Fab', $F(ab')_2$, ScFv or diabodies that can be linked together via one or more peptide linkers.

Production of antibodies

Monoclonal antibodies according to the invention can be made by any method known in the art. The general methodology for making monoclonal antibodies using hybridoma technology is well known [19, 20]. Preferably, the alternative EBV immortalisation method described in reference 21 is used.

Using the method described in reference 21, B cells producing the antibody of the invention can be transformed with EBV in the presence of a polyclonal B cell activator. Transformation with EBV is a standard technique and can easily be adapted to include polyclonal B cell activators.

Additional stimulants of cellular growth and differentiation may optionally be added during the transformation step to further enhance the efficiency. These stimulants may be cytokines such as IL-2 and IL-15. In one aspect, IL-2 is added during the immortalisation step to further improve the efficiency of immortalisation, but its use is not essential.

The immortalised B cells produced using these methods can then be cultured using methods known in the art and antibodies isolated therefrom.

The antibodies of the invention can also be made by culturing single plasma cells in microwell culture plates using the method described in UK Patent Application 0819376.5. Further, from single plasma cell cultures, RNA can be extracted and single cell PCR can be performed using methods known in the art. The VH and VL regions of the antibodies can be amplified by RT-PCR, sequenced and cloned into an expression vector that is then transfected into HEK293T cells or other host cells. The cloning of nucleic acid in expression vectors, the transfection of host cells, the culture of the transfected host cells and the isolation of the produced antibody can be done using any methods known to one of skill in the art.

Monoclonal antibodies may be further purified, if desired, using filtration, centrifugation and various chromatographic methods such as HPLC or affinity chromatography. Techniques for purification of monoclonal antibodies, including techniques for producing pharmaceutical-grade antibodies, are well known in the art.

Fragments of the monoclonal antibodies of the invention can be obtained from the monoclonal antibodies by methods that include digestion with enzymes, such as pepsin or papain, and/or by cleavage of disulfide bonds by chemical reduction. Alternatively, fragments of the monoclonal antibodies can be obtained by cloning and expression of part of the sequences of the heavy or light chains. Antibody "fragments" may include Fab, Fab', $F(ab')_2$ and Fv fragments. The invention also encompasses single-chain Fv fragments (scFv) derived from the heavy and light chains of a monoclonal antibody of the invention *e.g.* the invention includes a scFv comprising the CDRs from an antibody of the invention. Also included are heavy or light chain monomers and dimers as well as single chain antibodies, *e.g.* single chain Fv in which the heavy and light chain variable domains are joined by a peptide linker.

Standard techniques of molecular biology may be used to prepare DNA sequences coding for the antibodies or fragments or variants of the antibodies of the present invention. Desired DNA sequences may be synthesised completely or in part using oligonucleotide synthesis techniques. Site-directed mutagenesis and polymerase chain reaction (PCR) techniques may be used as appropriate.

Any suitable host cell/vector system may be used for expression of the DNA sequences encoding the antibody molecules of the present invention or fragments thereof. Bacterial, for example *E. coli*, and other microbial systems may be used, in part, for expression of antibody fragments such as Fab and $F(ab')_2$ fragments, and especially Fv fragments and single chain antibody fragments, for example, single chain Fvs. Eukaryotic, *e.g.* mammalian, host cell expression systems may be used for production of larger antibody molecules, including complete

antibody molecules. Suitable mammalian host cells include CHO, HEK293T, PER.C6, NS0, myeloma or hybridoma cells.

The present invention also provides a process for the production of an antibody of the invention comprising culturing a host cell comprising a vector of the present invention under conditions suitable for leading to expression of protein from DNA encoding the antibody of the present invention, and isolating the antibody molecule.

The antibody molecule may comprise only a heavy or light chain polypeptide, in which case only a heavy chain or light chain polypeptide coding sequence needs to be used to transfect the host cells. For production of products comprising both heavy and light chains, the cell line may be transfected with two vectors, a first vector encoding a light chain polypeptide and a second vector encoding a heavy chain polypeptide. Alternatively, a single vector may be used, the vector including sequences encoding light chain and heavy chain polypeptides.

Alternatively, antibodies according to the invention may be produced by i) expressing a nucleic acid sequence according to the invention in a cell, and ii) isolating the expressed antibody product. Additionally, the method may include iii) purifying the antibody.

Screening and isolation of B cells

Transformed B cells may be screened for those producing antibodies of the desired antigen specificity, and individual B cell clones may then be produced from the positive cells.

The screening step may be carried out by ELISA, by staining of tissues or cells (including infected or transfected cells), a neutralisation assay or one of a number of other methods known in the art for identifying desired antigen specificity. The assay may select on the basis of simple antigen recognition, or may select on the additional basis of a desired function *e.g.* to select neutralizing antibodies rather than just antigen-binding antibodies, to select antibodies that can change characteristics of targeted cells, such as their signalling cascades, their shape, their growth rate, their capability of influencing other cells, their response to the influence by other cells or by other reagents or by a change in conditions, their differentiation status, *etc.*

The cloning step for separating individual clones from the mixture of positive cells may be carried out using limiting dilution, micromanipulation, single cell deposition by cell sorting or another method known in the art.

The immortalised B cell clones of the invention can be used in various ways *e.g.* as a source of monoclonal antibodies, as a source of nucleic acid (DNA or mRNA) encoding a monoclonal antibody of interest, for research, *etc.*

The invention provides a composition comprising immortalised B memory cells, wherein the cells produce antibodies that neutralize one or more dengue virus serotypes, and wherein the antibodies are produced at ≥5pg per cell per day. The invention also provides a composition comprising clones of an immortalised B memory cell, wherein the clones produce a monoclonal antibody that neutralizes one or more dengue virus serotypes, and wherein the antibody is produced at ≥5pg per cell per day.

Exemplary immortalised B cell clone according to the invention include, but are not limited to, HMB-DV1, HMB-DV2, HMB-DV3, HMB-DV4, HMB-DV5, HMB-DV6, HMB-DV7, HMB-DV8, HMB-DV9, HMB-DV10, HMB-DV11, HMB-DV12, HMB-DV13, and HMB-DV14.

Epitopes

As mentioned above, the antibodies of the invention can be used to map the epitopes to which they bind. The epitopes recognised by the antibodies of the present invention may have a number of uses. The epitope and mimotopes thereof in purified or synthetic form can be used to raise immune responses (*i.e.* as a vaccine, or for the production of antibodies for other uses) or for screening patient serum for antibodies that immunoreact with the epitope or mimotopes thereof. In one embodiment such an epitope or mimotope, or antigen comprising such an epitope or mimotope may be used as a vaccine for raising an immune response. The antibodies and antigen binding fragments of the invention can also be used in a method of monitoring the quality of vaccines. In particular the antibodies can be used to check that the antigen in a vaccine contains the specific epitope in the correct conformation.

The epitope may also be useful in screening for ligands that bind to said epitope. Such ligands, include but are not limited to antibodies, including those from camels, sharks and other species, fragments of antibodies, peptides, phage display technology products, aptamers, adnectins, synthetic compounds, or fragments of other viral or cellular proteins, that may block the epitope and so prevent infection. Such ligands are encompassed within the scope of the invention.

Recombinant expression

The immortalised B memory cells of the invention may also be used as a source of nucleic acid for the cloning of antibody genes for subsequent recombinant expression. Expression from recombinant sources is more common for pharmaceutical purposes than

expression from B cells or hybridomas *e.g.* for reasons of stability, reproducibility, culture ease, *etc.*

Thus the invention provides a method for preparing a recombinant cell, comprising the steps of: (i) obtaining one or more nucleic acids (*e.g.* heavy and/or light chain genes) from the B cell clone that encodes the antibody of interest; and (ii) inserting the nucleic acid into an expression host in order to permit expression of the antibody of interest in that host.

Similarly, the invention provides a method for preparing a recombinant cell, comprising the steps of: (i) sequencing nucleic acid(s) from the B cell clone that encodes the antibody of interest; and (ii) using the sequence information from step (i) to prepare nucleic acid(s) for insertion into an expression host in order to permit expression of the antibody of interest in that host. The nucleic acid may, but need not, be manipulated between steps (i) and (ii) to introduce restriction sites, to change codon usage, to optimise transcription and/or translation regulatory sequences, and/or to modify effector function.

The invention also provides a method of preparing a recombinant cell, comprising the step of transforming a host cell with one or more nucleic acids that encode a monoclonal antibody of interest, wherein the nucleic acids are nucleic acids that were derived from an immortalised B cell clone of the invention. Thus the procedures for first preparing the nucleic acid(s) and then using it to transform a host cell can be performed at different times by different people in different places (*e.g.*, in different countries).

These recombinant cells of the invention can then be used for expression and culture purposes. They are particularly useful for expression of antibodies for large-scale pharmaceutical production. They can also be used as the active ingredient of a pharmaceutical composition. Any suitable culture techniques can be used, including but not limited to static culture, roller bottle culture, ascites fluid, hollow-fiber type bioreactor cartridge, modular minifermenter, stirred tank, microcarrier culture, ceramic core perfusion, *etc.*

Methods for obtaining and sequencing immunoglobulin genes from B cells are well known in the art (*e.g.*, see reference 22).

The expression host is preferably a eukaryotic cell, including yeast and animal cells, particularly mammalian cells (*e.g.* CHO cells, NS0 cells, human cells such as PER.C6 [Crucell; reference 23] or HKB-11 [Bayer; references 24 & 25] cells, myeloma cells [26 & 27], *etc.*), as well as plant cells. Preferred expression hosts can glycosylate the antibody of the invention, particularly with carbohydrate structures that are not themselves immunogenic in humans. In one embodiment the expression host may be able to grow in serum-free media. In a further

embodiment the expression host may be able to grow in culture without the presence of animal-derived products.

The expression host may be cultured to give a cell line.

The invention provides a method for preparing one or more nucleic acid molecules (*e.g.* heavy and light chain genes) that encode an antibody of interest, comprising the steps of: (i) preparing an immortalised B cell clone according to the invention; (ii) obtaining from the B cell clone nucleic acid that encodes the antibody of interest. The invention also provides a method for obtaining a nucleic acid sequence that encodes an antibody of interest, comprising the steps of: (i) preparing an immortalised B cell clone according to the invention; (ii) sequencing nucleic acid from the B cell clone that encodes the antibody of interest.

The invention also provides a method of preparing nucleic acid molecule(s) that encodes an antibody of interest, comprising the step of obtaining the nucleic acid from a B cell clone that was obtained from a transformed B cell of the invention. Thus the procedures for first obtaining the B cell clone and then preparing nucleic acid(s) from it can be performed at very different times by different people in different places (*e.g.* in different countries).

The invention provides a method for preparing an antibody (*e.g.* for pharmaceutical use), comprising the steps of: (i) obtaining and/or sequencing one or more nucleic acids (*e.g.* heavy and light chain genes); (ii) using the sequence information from step (i) to prepare nucleic acid(s) for insertion into an expression host in order to permit expression of the antibody of interest in that host; (iii) culturing or sub-culturing the expression host under conditions where the antibody of interest is expressed; and, optionally, (iv) purifying the antibody of the interest. The nucleic acid can, but need not be, obtained and/or sequenced from a B cell clone expressing the antibody of interest. In one embodiment, the nucleic acid from step (i) may, optionally be modified so as to introduce desired substitutions in the amino acid sequence of the antibody.

The invention also provides a method of preparing an antibody comprising the steps of: culturing or sub-culturing an expression host cell population under conditions where the antibody of interest is expressed and, optionally, purifying the antibody of the interest, wherein said expression host cell population has been prepared by (i) providing nucleic acid(s) encoding an antibody of interest; (ii) inserting the nucleic acid(s) into an expression host that can express the antibody of interest, and (iii) culturing or sub-culturing expression hosts comprising said inserted nucleic acids to produce said expression host cell population.

Pharmaceutical compositions

The invention provides a pharmaceutical composition containing the antibodies and/or antibody fragments of the invention and/or nucleic acid encoding such antibodies and/or immortalised B cells that express such antibodies and/or the epitopes recognised by the antibodies of the invention. A pharmaceutical composition may also contain a pharmaceutically acceptable carrier to allow administration. The carrier should not itself induce the production of antibodies harmful to the individual receiving the composition and should not be toxic. Suitable carriers may be large, slowly metabolised macromolecules such as proteins, polypeptides, liposomes, polysaccharides, polylactic acids, polyglycolic acids, polymeric amino acids, amino acid copolymers and inactive virus particles.

Pharmaceutically acceptable salts can be used, for example mineral acid salts, such as hydrochlorides, hydrobromides, phosphates and sulphates, or salts of organic acids, such as acetates, propionates, malonates and benzoates.

Pharmaceutically acceptable carriers in therapeutic compositions may additionally contain liquids such as water, saline, glycerol and ethanol. Additionally, auxiliary substances, such as wetting or emulsifying agents or pH buffering substances, may be present in such compositions. Such carriers enable the pharmaceutical compositions to be formulated as tablets, pills, dragees, capsules, liquids, gels, syrups, slurries and suspensions, for ingestion by the patient.

Within the scope of the invention, forms of administration may include those forms suitable for parenteral administration, *e.g.* by injection or infusion, for example by bolus injection or continuous infusion. Where the product is for injection or infusion, it may take the form of a suspension, solution or emulsion in an oily or aqueous vehicle and it may contain formulatory agents, such as suspending, preservative, stabilising and/or dispersing agents. Alternatively, the antibody molecule may be in dry form, for reconstitution before use with an appropriate sterile liquid.

Once formulated, the compositions of the invention can be administered directly to the subject. In one embodiment the compositions are adapted for administration to human subjects.

The pharmaceutical compositions of this invention may be administered by any number of routes including, but not limited to, oral, intravenous, intramuscular, intra-arterial, intramedullary, intraperitoneal, intrathecal, intraventricular, transdermal, transcutaneous, topical, subcutaneous, intranasal, enteral, sublingual, intravaginal or rectal routes. Hyposprays may also be used to administer the pharmaceutical compositions of the invention. Typically, the

therapeutic compositions may be prepared as injectables, either as liquid solutions or suspensions. Solid forms suitable for solution in, or suspension in, liquid vehicles prior to injection may also be prepared.

Direct delivery of the compositions will generally be accomplished by injection, subcutaneously, intraperitoneally, intravenously or intramuscularly, or delivered to the interstitial space of a tissue. Dosage treatment may be a single dose schedule or a multiple dose schedule. Known antibody-based pharmaceuticals provide guidance relating to frequency of administration *e.g.* whether a pharmaceutical should be delivered daily, weekly, monthly, *etc*. Frequency and dosage may also depend on the severity of symptoms.

Compositions of the invention may be prepared in various forms. For example, the compositions may be prepared as injectables, either as liquid solutions or suspensions. Solid forms suitable for solution, or suspension, in liquid vehicles prior to injection can also be prepared (*e.g.* a lyophilised composition, like Synagis™ and Herceptin™, for reconstitution with sterile water containing a preservative). The composition may be prepared for topical administration *e.g.* as an ointment, cream or powder. The composition may be prepared for oral administration *e.g.* as a tablet or capsule, as a spray, or as a syrup (optionally flavoured). The composition may be prepared for pulmonary administration *e.g.* as an inhaler, using a fine powder or a spray. The composition may be prepared as a suppository or pessary. The composition may be prepared for nasal, aural or ocular administration *e.g.* as drops. The composition may be in kit form, designed such that a combined composition is reconstituted just prior to administration to a patient. For example, a lyophilised antibody can be provided in kit form with sterile water or a sterile buffer.

It will be appreciated that the active ingredient in the composition will be an antibody molecule, an antibody fragment or variants and derivatives thereof. As such, it will be susceptible to degradation in the gastrointestinal tract. Thus, if the composition is to be administered by a route using the gastrointestinal tract, the composition will need to contain agents which protect the antibody from degradation but which release the antibody once it has been absorbed from the gastrointestinal tract.

A thorough discussion of pharmaceutically acceptable carriers is available in Gennaro (2000) *Remington: The Science and Practice of Pharmacy,* 20th edition, ISBN: 0683306472.

Pharmaceutical compositions of the invention generally have a pH between 5.5 and 8.5, in some embodiments this may be between 6 and 8, and in further embodiments about 7. The pH may be maintained by the use of a buffer. The composition may be sterile and/or pyrogen free.

The composition may be isotonic with respect to humans. In one embodiment pharmaceutical compositions of the invention are supplied in hermetically-sealed containers.

Pharmaceutical compositions will include a therapeutically effective amount of one or more antibodies of the invention and/or a polypeptide comprising an epitope that binds an antibody of the invention *i.e.* an amount that is sufficient to treat, ameliorate, or prevent a desired disease or condition, or to exhibit a detectable therapeutic effect. Therapeutic effects also include reduction in physical symptoms. The precise effective amount for any particular subject will depend upon their size and health, the nature and extent of the condition, and the therapeutics or combination of therapeutics selected for administration. The effective amount for a given situation is determined by routine experimentation and is within the judgment of a clinician. For purposes of the present invention, an effective dose will generally be from about 0.01mg/kg to about 50mg/kg, or about 0.05 mg/kg to about 10 mg/kg of the compositions of the present invention in the individual to which it is administered. Known antibody-based pharmaceuticals provide guidance in this respect *e.g.*, Herceptin™ is administered by intravenous infusion of a 21 mg/ml solution, with an initial loading dose of 4mg/kg body weight and a weekly maintenance dose of 2mg/kg body weight; Rituxan™ is administered weekly at 375mg/m^2; *etc.*

In one embodiment pharmaceutical compositions can include more than one (*e.g.* 2, 3, 4, 5, 6, 7, 8, *etc.*) antibody of the invention. In another embodiment the composition comprises two or more (*e.g.* 2, 3, 4, 5, *etc.*) antibodies, wherein the first antibody is specific for a first DENV epitope, and the second antibody is specific for a second DENV epitope. In yet another embodiment, the pharmaceutical composition comprises three antibodies of the invention. In another embodiment, the composition comprises two or more (*e.g.* 2, 3, 4, 5, *etc.*) antibodies, that together neutralise more than one dengue virus serotype. In yet another embodiment, the two or more antibodies of the invention together neutralise all four dengue virus serotypes, DENV-1, DENV-2, DENV-3 and DENV-4. In a further embodiment two or more antibodies of the invention together neutralise all four dengue virus serotypes by binding at least two distinct epitopes on each dengue virus serotype.

Exemplary antibodies of the invention for use in a pharmaceutical composition that neutralize a dengue virus without contributing to antibody-dependent enhancement of dengue virus infection include, but are not limited to, HMB-DV1, HMB-DV2, HMB-DV3, HMB-DV4, HMB-DV5, HMB-DV6, HMB-DV7, HMB-DV8, HMB-DV9, HMB-DV10, HMB-DV11, HMB-DV12, HMB-DV13, and HMB-DV14.

In one embodiment, a pharmaceutical composition includes two exemplary antibodies of the invention, for example, HMB-DV3 and HMB-DV7; HMB-DV3 and HMB-DV9; HMB-DV3 and HMB-DV12; HMB-DV3 and HMB-DV14; HMB-DV6 and HMB-DV7; HMB-DV6 and HMB-DV8. In another embodiment, a pharmaceutical composition includes three exemplary antibodies of the invention, for example, HMB-DV2, HMB-DV3 and HMB-DV6; HMB-DV2, HMB-DV6 and HMB-DV8; HMB-DV2, HMB-DV8 and HMB-DV9; HMB-DV2, HMB-DV8 and HMB-DV12; HMB-DV2, HMB-DV8 and HMB-DV14; HMB-DV5, HMB-DV6 and HMB-DV8. Based on the teachings herein, one of skill in the art can determine other combinations of antibodies for use in a pharmaceutical composition.

In one embodiment, the invention provides a pharmaceutical composition comprising the antibody HMB-DV1 or an antigen binding fragment thereof, and a pharmaceutically acceptable diluent or carrier. In another embodiment, the invention provides a pharmaceutical composition comprising the antibody HMB-DV2 or an antigen binding fragment thereof, and a pharmaceutically acceptable diluent or carrier. In another embodiment, the invention provides a pharmaceutical composition comprising the antibody HMB-DV3 or an antigen binding fragment thereof, and a pharmaceutically acceptable diluent or carrier. In another embodiment, the invention provides a pharmaceutical composition comprising the antibody HMB-DV4 or an antigen binding fragment thereof, and a pharmaceutically acceptable diluent or carrier. In yet another embodiment, the invention provides a pharmaceutical composition comprising the antibody HMB-DV5 or an antigen binding fragment thereof, and a pharmaceutically acceptable diluent or carrier. In another embodiment, the invention provides a pharmaceutical composition comprising the antibody HMB-DV6 or an antigen binding fragment thereof, and a pharmaceutically acceptable diluent or carrier. In another embodiment, the invention provides a pharmaceutical composition comprising the antibody HMB-DV7 or an antigen binding fragment thereof, and a pharmaceutically acceptable diluent or carrier.

In yet another embodiment, the invention provides a pharmaceutical composition comprising the antibody HMB-DV8 or an antigen binding fragment thereof, and a pharmaceutically acceptable diluent or carrier. In another embodiment, the invention provides a pharmaceutical composition comprising the antibody HMB-DV9 or an antigen binding fragment thereof, and a pharmaceutically acceptable diluent or carrier. In another embodiment, the invention provides a pharmaceutical composition comprising the antibody HMB-DV10 or an antigen binding fragment thereof, and a pharmaceutically acceptable diluent or carrier. In yet another embodiment, the invention provides a pharmaceutical composition comprising the antibody HMB-DV11 or an antigen binding fragment thereof, and a pharmaceutically acceptable

diluent or carrier. In another embodiment, the invention provides a pharmaceutical composition comprising the antibody HMB-DV12 or an antigen binding fragment thereof, and a pharmaceutically acceptable diluent or carrier. In another embodiment, the invention provides a pharmaceutical composition comprising the antibody HMB-DV13 or an antigen binding fragment thereof, and a pharmaceutically acceptable diluent or carrier. In yet another embodiment, the invention provides a pharmaceutical composition comprising the antibody HMB-DV14 or an antigen binding fragment thereof, and a pharmaceutically acceptable diluent or carrier.

Antibodies of the invention may be administered (either combined or separately) with other therapeutics *e.g.* with chemotherapeutic compounds, with radiotherapy, *etc.* Preferred therapeutic compounds include anti-viral compounds. Such combination therapy provides an additive or synergistic improvement in therapeutic efficacy relative to the individual therapeutic agents when administered alone. The term "synergy" is used to describe a combined effect of two or more active agents that is greater than the sum of the individual effects of each respective active agent. Thus, where the combined effect of two or more agents results in "synergistic inhibition" of an activity or process, it is intended that the inhibition of the activity or process is greater than the sum of the inhibitory effects of each respective active agent. The term "synergistic therapeutic effect" refers to a therapeutic effect observed with a combination of two or more therapies wherein the therapeutic effect (as measured by any of a number of parameters) is greater than the sum of the individual therapeutic effects observed with the respective individual therapies.

In compositions of the invention that include antibodies of the invention, the antibodies may make up at least 50% by weight (*e.g.* 60%, 70%, 75%, 80%, 85%, 90%, 95%, 97%, 98%, 99% or more) of the total protein in the composition. The antibodies are thus in purified form.

The invention provides a method of preparing a pharmaceutical, comprising the steps of: (i) preparing an antibody of the invention; and (ii) admixing the purified antibody with one or more pharmaceutically-acceptable carriers.

The invention also provides a method of preparing a pharmaceutical, comprising the step of admixing an antibody with one or more pharmaceutically-acceptable carriers, wherein the antibody is a monoclonal antibody that was obtained from a transformed B cell of the invention. Thus the procedures for first obtaining the monoclonal antibody and then preparing the pharmaceutical can be performed at very different times by different people in different places (*e.g.* in different countries).

As an alternative to delivering antibodies for therapeutic purposes, it is possible to deliver nucleic acid (typically DNA) that encodes the monoclonal antibody (or active fragment thereof) of interest to a subject, such that the nucleic acid can be expressed in the subject *in situ* to provide a desired therapeutic effect. Suitable gene therapy and nucleic acid delivery vectors are known in the art.

Compositions of the invention may be immunogenic compositions, and in some embodiments may be vaccine compositions comprising an antigen comprising a DENV epitope. Vaccines according to the invention may either be prophylactic (*i.e.* to prevent infection) or therapeutic (*i.e.* to treat infection).

Compositions may include an antimicrobial, particularly if packaged in a multiple dose format. Compositions may comprise detergent *e.g.* a Tween (polysorbate), such as Tween 80. Detergents are generally present at low levels *e.g.* <0.01%. Compositions may include sodium salts (*e.g.* sodium chloride) to give tonicity. A concentration of 10±2mg/ml NaCl is typical.

Compositions may comprise a sugar alcohol (*e.g.* mannitol) or a disaccharide (*e.g.* sucrose or trehalose) *e.g.* at around 15-30mg/ml (*e.g.* 25 mg/ml), particularly if they are to be lyophilised or if they include material which has been reconstituted from lyophilised material. The pH of a composition for lyophilisation may be adjusted to around 6.1 prior to lyophilisation.

The compositions of the invention may also comprise one or more immunoregulatory agents. In one embodiment, one or more of the immunoregulatory agents include(s) an adjuvant.

Medical treatments and uses

The antibodies, antigen binding fragments, derivatives and variants thereof, or the cocktails and pharmaceutical compositions of the invention can be used for the treatment of DENV infection, for the prevention of DENV infection or for the diagnosis of DENV infection.

Methods of diagnosis may include contacting an antibody or an antibody fragment with a sample. Such samples may be tissue samples taken from, for example, salivary glands, lung, liver, pancreas, kidney, ear, eye, placenta, alimentary tract, heart, ovaries, pituitary, adrenals, thyroid, brain or skin. The methods of diagnosis may also include the detection of an antigen/antibody complex.

The invention therefore provides (i) an antibody, an antibody fragment, or variants and derivatives thereof according to the invention, (ii) an immortalised B cell clone according to the invention, (iii) an epitope capable of binding an antibody of the invention or (iv) a ligand,

preferably an antibody, capable of binding an epitope that binds an antibody of the invention for use in therapy.

Also provided is a method of treating a subject comprising administering to that subject (i) an antibody, an antibody fragment, variants and derivatives thereof, or a pharmaceutical composition according to the invention, or, a ligand, preferably an antibody, capable of binding an epitope that binds an antibody of the invention.

The invention also provides the use of (i) an antibody, an antibody fragment, or variants and derivatives thereof according to the invention, (ii) an immortalised B cell clone according to the invention, (iii) an epitope capable of binding an antibody of the invention, or (iv) a ligand, preferably an antibody, that binds to an epitope capable of binding an antibody of the invention, in the manufacture of a medicament for the prevention or treatment of DENV infection.

The invention provides a pharmaceutical composition for use as a medicament for the prevention or treatment of DENV infection. It also provides the use of an antibody of the invention and/or a protein comprising an epitope to which such an antibody binds in the manufacture of a medicament for treatment of a patient and/or diagnosis in a patient. It also provides a method for treating a subject, *e.g.*, a human subject. The method comprises the step of administering to the subject a therapeutically effective dose of a composition of the invention. One way of checking efficacy of therapeutic treatment involves monitoring disease symptoms after administration of the composition of the invention. Treatment can be a single dose schedule or a multiple dose schedule.

In one embodiment, an antibody, antibody fragment, antibody variant, epitope or pharmaceutical composition according to the invention is administered to a subject in need of such treatment. Such a subject includes, but is not limited to, one who is particularly at risk of or susceptible to DENV infection.

Antibodies of the invention can be used in passive immunisation. Antibodies and fragments or variants thereof, or a nucleic acid encoding an antibody or an antibody fragment or variant as described in the present invention may also be used in a kit for the diagnosis of dengue virus infection.

Epitopes capable of binding an antibody of the invention, *e.g.*, the monoclonal antibodies HMB-DV1, HMB-DV2, HMB-DV3, HMB-DV4, HMB-DV5, HMB-DV6, HMB-DV7, HMB-DV8, HMB-DV9, HMB-DV10, HMB-DV11, HMB-DV12, HMB-DV13, and HMB-DV14, may be used in a kit for monitoring the efficacy of vaccination procedures by detecting the presence of protective anti-DENV antibodies.

Antibodies, antibody fragments, or variants and derivatives thereof, as described in the present invention may also be used in a kit for monitoring vaccine manufacture with the desired immunogenicity.

The invention also provides a method of preparing a pharmaceutical composition, comprising the step of admixing a monoclonal antibody with one or more pharmaceutically-acceptable carriers, wherein the monoclonal antibody is a monoclonal antibody that was obtained from an expression host of the invention. Thus the procedures for first obtaining the monoclonal antibody (*e.g.* expressing it and/or purifying it) and then admixing it with the pharmaceutical carrier(s) can be performed at very different times by different people in different places (*e.*g. in different countries).

Starting with a transformed B cell of the invention, various steps of culturing, sub-culturing, cloning, sub-cloning, sequencing, nucleic acid preparation *etc.* can be performed in order to perpetuate the antibody expressed by the transformed B cell, with optional optimisation at each step. In a preferred embodiment, the above methods further comprise techniques of optimisation (*e.g.* affinity maturation or optimisation) applied to the nucleic acids encoding the antibody. The invention encompasses all cells, nucleic acids, vectors, sequences, antibodies *etc.* used and prepared during such steps.

In all these methods, the nucleic acid used in the expression host may be manipulated to insert, delete or amend certain nucleic acid sequences. Changes from such manipulation include, but are not limited to, changes to introduce restriction sites, to amend codon usage, to add or optimise transcription and/or translation regulatory sequences, *etc*. It is also possible to change the nucleic acid to alter the encoded amino acids. For example, it may be useful to introduce one or more (*e.g.* 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, *etc.*) amino acid substitutions, deletions and/or insertions into the antibody's amino acid sequence. Such point mutations can modify effector functions, antigen-binding affinity, post-translational modifications, immunogenicity, *etc.*, can introduce amino acids for the attachment of covalent groups (*e.g.* labels) or can introduce tags (*e.g.* for purification purposes). Mutations can be introduced in specific sites or can be introduced at random, followed by selection (*e.g.* molecular evolution). For instance, one or more nucleic acids encoding any of the CDR regions, heavy chain variable regions or light chain variable regions of antibodies of the invention can be randomly or directionally mutated to introduce different properties in the encoded amino acids. Such changes can be the result of an iterative process wherein initial changes are retained and new changes at other nucleotide positions are introduced. Moreover, changes achieved in independent steps may be combined. Different

properties introduced into the encoded amino acids may include, but are not limited to, enhanced affinity.

General

The term "comprising" encompasses "including" as well as "consisting" *e.g.* a composition "comprising" X may consist exclusively of X or may include something additional *e.g.* X + Y.

The word "substantially" does not exclude "completely" *e.g.* a composition which is "substantially free" from Y may be completely free from Y. Where necessary, the word "substantially" may be omitted from the definition of the invention.

The term "about" in relation to a numerical value *x* means, for example, $x \pm 10\%$.

The term "disease" as used herein is intended to be generally synonymous, and is used interchangeably with, the terms "disorder" and "condition" (as in medical condition), in that all reflect an abnormal condition of the human or animal body or of one of its parts that impairs normal functioning, is typically manifested by distinguishing signs and symptoms, and causes the human or animal to have a reduced duration or quality of life.

As used herein, reference to "treatment" of a patient is intended to include prevention and prophylaxis as well as therapy. The term "patient" means all mammals including humans. Generally, the patient is a human.

EXAMPLES

Exemplary embodiments of the present invention are provided in the following examples. The following examples are presented only by way of illustration and to assist one of ordinary skill in using the invention. The examples are not intended in any way to limit the scope of the invention.

Example 1. Cloning of B cells and screening for identification of Dengue virus specific Abs.

Memory B cells were isolated from the blood of DENV immune donors and immortalized using EBV and CpG as described in reference. Briefly, IgG^+ memory B cells were isolated using CD22 beads, followed by removal of IgM^+, IgD^+ IgA^+ B cells using specific antibodies and cell sorting. The sorted cells (IgG^+) were immortalized with EBV in the presence of CpG 2006 and irradiated allogeneic mononuclear cells. Replicate cultures each containing 30-50 memory B cells were set up in several 96 well U-bottom plates. After two weeks the culture supernatants were collected and tested for their capacity to stain C6/36 cells infected with DENV

of serotypes 1, 2, 3 or 4 by immunofluorescence analysis and/or to bind to recombinant DENV1-4 E2 proteins by ELISA. Supernatants were tested for their capacity to neutralize DENV infection of either VERO cells or DC-SIGN-transfected Raji cells and to enhance infection of K562 cells. B cell clones were isolated from positive polyclonal cultures as described previously [28]. IgG concentrations in the supernatants of selected clones were determined using an IgG-specific ELISA.

Example 2. Human mAbs from immortalized B cells recognize Dengue virus proteins and neutralize infection.

For the viral neutralization and viral enhancement assay, titrated amounts of attenuated DENV of serotypes 1, 2, 3 or 4 were mixed with an equal volume of culture supernatants. Viruses and multiplicity of infection (MOI) used were: rDEN1Δ30 (03JB186-1A+V2) MOI 0.04; rDEN2/4Δ30 (04JBV351-1A-V2) MOI 0.04; rDEN3/4Δ30 (DEN3#107C) MOI 0.02; rDEN4Δ30 (06JBV591-V3+1A1+v2) MOI 0.04. After 1-hour incubation at room temperature the mixture was added to target cells (e.g. VERO cells, DC-SIGN-Raji cells or K562 cells) in 96 well flat bottom plates and incubated at 37°C for 72-96 hours. The cells were then stained with a mouse monoclonal antibody to Dengue virus 1-4 E proteins (clone 4G2), followed by a fluorescein-labeled goat anti mouse Ig and analyzed by FACS. The neutralizing titer is indicated as the concentration of antibody (μg/ml) that gives a 50% reduction of DENV infection.

For identification of the target antigens recognized by the monoclonal antibodies yeasts displaying Dengue virus E protein domains III or domain I-II were stained with the monoclonal antibodies followed by Cy5-labeled goat anti human IgG antibodies and analyzed by FACS. Western blotting experiments were performed using lysates of DENV-infected cells.

Table 3 shows that three different types of antibodies have been identified. They include those that are specific for domain III (DIII) of E protein, those that are specific for domains I-II (DI-II) of E protein and those specific for prM. The antibodies show different degrees of cross-reactivity with the 4 different DENV serotypes and neutralize those serotypes to which they bind.

Table 3. Target Antigen Specificity of Neutralizing anti-Dengue Virus Antibodies

Antibody	Target Antigen	Dengue Virus Serotypes Neutralized
HMB-DV-1	E, DIII	1,2,3
HMB-DV-2	E, DIII	1,3
HMB-DV-3	prM	1,2,3,4
HMB-DV-4	E, DI-II	1,2,3,4
HMB-DV-5	E, DI-II	1,2,3,4
HMB-DV-6	E, DIII	1,2,3
HMB-DV-7	E, DIII	1,2,3
HMB-DV- 8	E	4
HMB-DV- 9	E, DIII	2
HMB-DV-10	E, DIII	1,2,3,4
HMB-DV-11	E, DIII	1,2,3,4
HMB-DV-12	E, DI-DII	2
HMB-DV-13	E, DIII	1,2,3,4
HMB-DV-14	E, DIII	2

Table 4 shows the results of virus neutralization assays on VERO cells and DC-SIGN-transfected Raji cells.

Table 4. Neutralization of Dengue Virus (serotypes DENV1-DENV4) by Antibodies

Antibody	Cell type	Neutralization EC_{50} values (µg/ml)			
		DENV1	**DENV2**	**DENV3**	**DENV4**
HMB-DV-1	VERO	0.013	0.577	0.014	> 20
	DC-SIGN-Raji	0.032	5.340	0.055	> 20
HMB-DV-2	VERO	0.006	> 20	0.006	> 20
	DC-SIGN-Raji	0.014	> 20	0.013	> 20
HMB-DV-3	VERO	0.912	1.615	0.120	0.070
	DC-SIGN-Raji	ND	ND	ND	ND
HMB-DV-4	VERO	0.591	0.251	0.809	0.367
	DC-SIGN-Raji	2.250	1.370	0.613	> 20
HMB-DV-5	VERO	0.066	0.034	0.118	0.200
	DC-SIGN-Raji	2.390	0.504	0.348	> 20
HMB-DV-6	VERO	0.008	0.002	0.011	> 20
	DC-SIGN-Raji	0.027	0.440	0.332	> 20
HMB-DV-7	VERO	0.016	0.004	0.020	> 20
	DC-SIGN-Raji	ND	ND	ND	ND
HMB-DV-8	VERO	> 20	> 20	> 20	0.006
	DC-SIGN-Raji	ND	ND	ND	ND

HMB-DV-9	VERO	> 20	0.002	> 20	> 20
	DC-SIGN-Raji	ND	ND	ND	ND
HMB-DV-10	VERO	> 20	0.084	> 20	0.466
	DC-SIGN-Raji	ND	ND	ND	ND
HMB-DV-11	VERO	> 20	0.048	> 20	0.520
	DC-SIGN-Raji	ND	ND	ND	ND
HMB-DV-12	VERO	ND	0.003	ND	ND
	DC-SIGN-Raji	ND	ND	ND	ND
HMB-DV-13	VERO	0.993	3.326	1.513	> 20
	DC-SIGN-Raji	ND	ND	ND	ND
HMB-DV-14	VERO	> 20	0.002	> 20	> 20
	DC-SIGN-Raji	ND	ND	ND	ND

ND: not determined

Example 3. Neutralizing recombinant anti-Dengue virus antibodies with mutations in the Fc region do not cause enhancement of virus infection on K562 cells.

Antibody-dependent enhancement (ADE) of dengue virus infection has been described in the literature. This property could limit the therapeutic effectiveness of anti-dengue virus antibodies for use in clinical situations. Therefore, mRNAs from the immortalized B cell lines expressing antibodies HMB-DV-5, HMB-DV-6 and HMB-DV-8 were isolated, cDNA was synthesized using oligo-dT specific primers, variable regions of heavy and light chain were sequenced and cloned into an expression vector using specific primers. Vectors were transfected into host cells for recombinant expression. In addition to recombinant production of the wild-type IgG1 antibodies, each of the heavy chains was mutated at amino acids 4 and 5 of CH2 domain by substituting an alanine in place of the natural leucine using site-directed mutagenesis thereby creating the LALA variant of each antibody. Both recombinant wild type and mutated antibodies were harvested from the expression cell lines and purified. Both wild-type IgG1 anti-dengue virus antibody and the LALA variant bound to the target protein in comparable manner (data not shown).

Virus neutralization and enhancement was determined as above on VERO cells and K562 cells. Each of the three antibodies has a defined molecular target as well as serotype target (see Table 3). Figure 1 shows that the unmodified recombinant antibodies neutralize target virus infection of VERO cells in a dose-dependent manner (DOTTED LINES). On K562 cells, a cell line that is not efficiently infected by Dengue viruses, the unmodified antibodies show an enhancement of viral infection at concentrations that are generally higher that those required for neutralization (SOLID LINES). The experiment was repeated using the LALA variants of each antibody. Figure 2 shows that each of the LALA variants of the recombinant anti-dengue virus antibodies also neutralized the target virus on VERO cells (DOTTED LINES) in a dose-dependent manner. However, each of the LALA antibodies did not show evidence of antibody-dependent enhancement of infection on K562

cells (SOLID LINES). Note, the dose-response is flat on the K562 cells at the concentrations of antibodies used in this experiment and the line appears very close to the X-axis.

All patents and publications referred to herein are expressly incorporated by reference in their entirety. A reference herein to a patent document or other matter which is given as prior art is not taken as an admission that that document or prior art was part of common general knowledge at the priority date of any of the claims.

With reference to the use of the word(s) "comprise" or "comprises" or "comprising" in the foregoing description and/or in the following claims, unless the context requires otherwise, those words are used on the basis and clear understanding that they are to be interpreted inclusively, rather than exclusively, and that each of those words is to be so interpreted in construing the foregoing description and/or the following claims.

It should be noted that there are alternative ways of implementing the present invention and that various modifications can be made without departing from the scope and spirit of the invention. Accordingly, the present embodiments are to be considered as illustrative and not restrictive, and the invention is not to be limited to the details given herein, but may be modified within the scope and equivalents of the appended claims.

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CLAIMS

1. A pharmaceutical composition comprising one, two or three human antibodies, or antigen-binding fragments thereof, wherein said antibody, antibodies, or antigen-binding fragments thereof, bind to, and neutralize dengue virus, and wherein said antibody, antibodies or antigen-binding fragments thereof, comprise the heavy chain CDR1, CDR2 and CDR3 and the light chain CDR1, CDR2 and CDR3 sequences as set forth in: (i) SEQ ID NOs: 1-6, respectively; (ii) SEQ ID NOs: 17-22, respectively; (iii) SEQ ID NOs: 33-38, respectively; (iv) SEQ ID NOs: 49-54, respectively; (v) SEQ ID NOs: 67-72, respectively; (vi) SEQ ID NOs: 83-88, respectively; (vii) SEQ ID NOs: 83-85, 99, 53 and 100, respectively; (viii) SEQ ID NOs: 105-110, respectively; (ix) SEQ ID NOs: 121-123, 70, 124 and 125, respectively; (x) SEQ ID NOs: 135-137, 138, 109 and 139, respectively; (xi) SEQ ID NOs: 149, 136-138, 109 and 139, respectively; (xii) SEQ ID NOs: 153-158, respectively; (xiii) SEQ ID NOs: 169-174, respectively; or (xiv) SEQ ID NOs: 185-188, 37 and 189, respectively.

2. The pharmaceutical composition of claim 1, wherein the composition neutralizes dengue virus serotypes DENV-1, DENV-2, DENV-3, and DENV-4.

3. The pharmaceutical composition of claim 2, wherein the composition neutralizes dengue virus serotypes DENV-1, DENV-2, DENV-3, and DENV-4 by binding at least two distinct epitopes on each dengue virus serotype.

4. The pharmaceutical composition of any one of claims 1 to 3, wherein the Fc region of said antibodies, or antigen-binding fragments thereof, comprises a CH2 L4A mutation, a CH2 L5A mutation, or both.

5. The pharmaceutical composition of any one of claims 1 to 4 wherein said antibodies or said antigen-binding fragments thereof, neutralizes more than one dengue virus of two, three or four different dengue virus serotypes.

6. The pharmaceutical composition of any one of the previous claims, wherein at least one of said antibodies, or antigen-binding fragments thereof, comprise: (i) a heavy chain variable region having at least 70% sequence identity to any one of SEQ ID NOs: 13, 29, 45, 61, 65, 79, 95, 117, 131, 145, 151, 165, 181, or 195; or (ii) a light chain variable region having at least 70% sequence identity to any one of SEQ ID NOs: 14, 30, 46, 62, 80, 96, 103, 118, 132, 146, 166, 182, or 196.

7. The pharmaceutical composition of any one of the previous claims, wherein at least one of said antibodies, or antigen-binding fragments thereof, comprise: (i) a heavy chain variable region comprising the amino acid sequence of any one of SEQ ID NOs: 13, 29, 45, 61, 65, 79, 95, 117, 131, 145, 151, 165, 181, or 195; or (ii) a light chain variable region comprising the amino acid sequence of any one of SEQ ID NOs: 14, 30, 46, 62, 80, 96, 103, 118, 132, 146, 166, 182, or 196.

8. The pharmaceutical composition of any one of the preceding claims, wherein at least one of said antibodies or antigen-binding fragments thereof, comprise: a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 13 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 14; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 29 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 30; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 45 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 46; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 61 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 62; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 65 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 62; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 79 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 80; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 95 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 96; or a heavy chain variable region comprising the amino acid

sequence of SEQ ID NO: 95 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 103; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 117 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 118; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 131 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 132; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 145 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 146; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 151 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 146; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 165 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 166; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 181 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 182; or a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 195 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 196.

9. The pharmaceutical composition of any one of claims 1-8, comprising an antibody, antibodies or antigen-binding fragments thereof, comprising the heavy chain CDR1, CDR2 and CDR3 and the light chain CDR1, CDR2 and CDR3 sequences as set forth in: (v) SEQ ID NOs: 67-72, respectively; (vi) SEQ ID NOs: 83-88, respectively; or (viii) SEQ ID NOs: 105-110, respectively, or a combination thereof.

10. The pharmaceutical composition of any one of claims 1-9, wherein the pharmaceutical composition comprises a pharmaceutically acceptable diluent or carrier and, optionally, an agent useful for extending the half life of the antibody or antigen binding fragment thereof.

11. A pharmaceutical composition comprising one or more nucleic acid molecules comprising a polynucleotide encoding an antibody, antibodies, or antigen-binding

fragments thereof, binding to, and neutralizing dengue virus, wherein said antibody, antibodies or antigen-binding fragments thereof, comprise the heavy chain CDR1, CDR2 and CDR3 and the light chain CDR1, CDR2 and CDR3 sequences that is at least 95%, preferably at least 98%, more preferably at least 99% and most preferably 100% identical to the nucleic acid sequences of: (i) SEQ ID NOs: 7-12, respectively; (ii) SEQ ID NOs: 23-28, respectively; (iii) SEQ ID NOs: 39-44, respectively; (iv) SEQ ID NOs: 55-60, respectively; (v) SEQ ID NOs: 73-78, respectively; (vi) SEQ ID NOs: 89-94, respectively; (vii) SEQ ID NOs: 89-91, 101, 59, 102, respectively; (viii) SEQ ID NOs: 111-116, respectively; (ix) SEQ ID NOs: 126-128, 76, 129, 130, respectively; (x) SEQ ID NOs: 140-143, 115, 144, respectively; (xi) SEQ ID NOs: 150, 141-143, 115, 144, respectively; (xii) SEQ ID NOs: 159-164, respectively; (xiii) SEQ ID NOs: 175-180, respectively; or (xiv) SEQ ID NOs: 190-193, 43, 194, respectively.

12. The pharmaceutical composition of claim 11, wherein the polynucleotide encoding the heavy chain CDR1, CDR2 and CDR3 and the light chain CDR1, CDR2 and CDR3 has the nucleic acid sequence of : (i) SEQ ID NOs: 7-12, respectively; (ii) SEQ ID NOs: 23-28, respectively; (iii) SEQ ID NOs: 39-44, respectively; (iv) SEQ ID NOs: 55-60, respectively; (v) SEQ ID NOs: 73-78, respectively; (vi) SEQ ID NOs: 89-94, respectively; (vii) SEQ ID NOs: 89-91, 101, 59, 102, respectively; (viii) SEQ ID NOs: 111-116, respectively; (ix) SEQ ID NOs: 126-128, 76, 129, 130, respectively, (x) SEQ ID NOs: 140-143, 115, 144, respectively; (xi) SEQ ID NOs: 150, 141-143, 115, 144, respectively; (xii) SEQ ID NOs: 159-164, respectively; (xiii) SEQ ID NOs: 175-180, respectively; or (xiv) SEQ ID NOs: 190-193, 43, 194, respectively.

13. The pharmaceutical composition of claim 11 or 12, wherein the pharmaceutical composition comprises a pharmaceutically acceptable diluent or carrier.

14. A cell expressing the antibody, antibodies, or an antigen-binding fragment thereof, of the pharmaceutical composition of any one of claims 1-9, or a cell expressing a

vector comprising one or more nucleic acid molecules of the pharmaceutical composition of claim 11 or 12.

15. A method of inhibiting or preventing, or a method of treating, a dengue virus infection or a dengue virus-related disease comprising the steps of: administering to a subject in need thereof, a therapeutically or prophylactically effective amount of the pharmaceutical composition of any one of claims 1-13.

16. The method of claim 15, additionally comprising the administration of a second therapeutic agent.

17. The method of claim 16, wherein said second therapeutic agent is an anti-viral agent.

18. The pharmaceutical composition of any one of claims 1-13, for use in a method of inhibiting or preventing, or a method of treating, a dengue virus infection or a dengue virus-related disease comprising the steps of: administering to a subject in need thereof, a therapeutically or prophylactically effective amount of the pharmaceutical composition of any one of claims 1-13.

19. Use of the pharmaceutical composition of any one of claims 1-13 (i) in the manufacture of a medicament for the treatment of dengue virus infection, (ii) in a vaccine, or (iii) in diagnosis of dengue virus infection.

20. Use of the pharmaceutical composition of any one of claims 1-13, for monitoring the quality of anti-dengue virus vaccines by checking that the antigen of said vaccine contains the specific epitope in the correct conformation.

Figure 1. Neutralization and antibody-dependent enhancement of wild-type mAbs

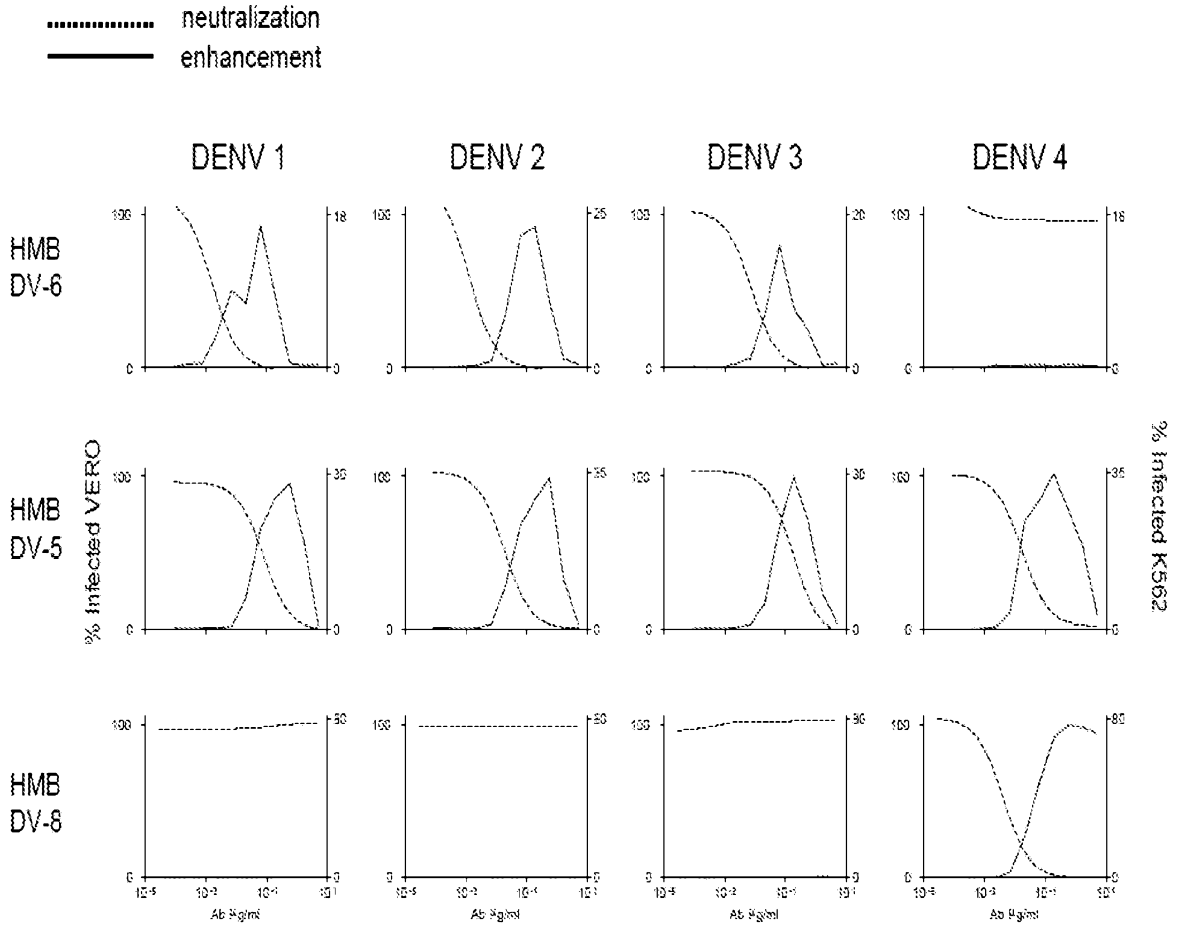
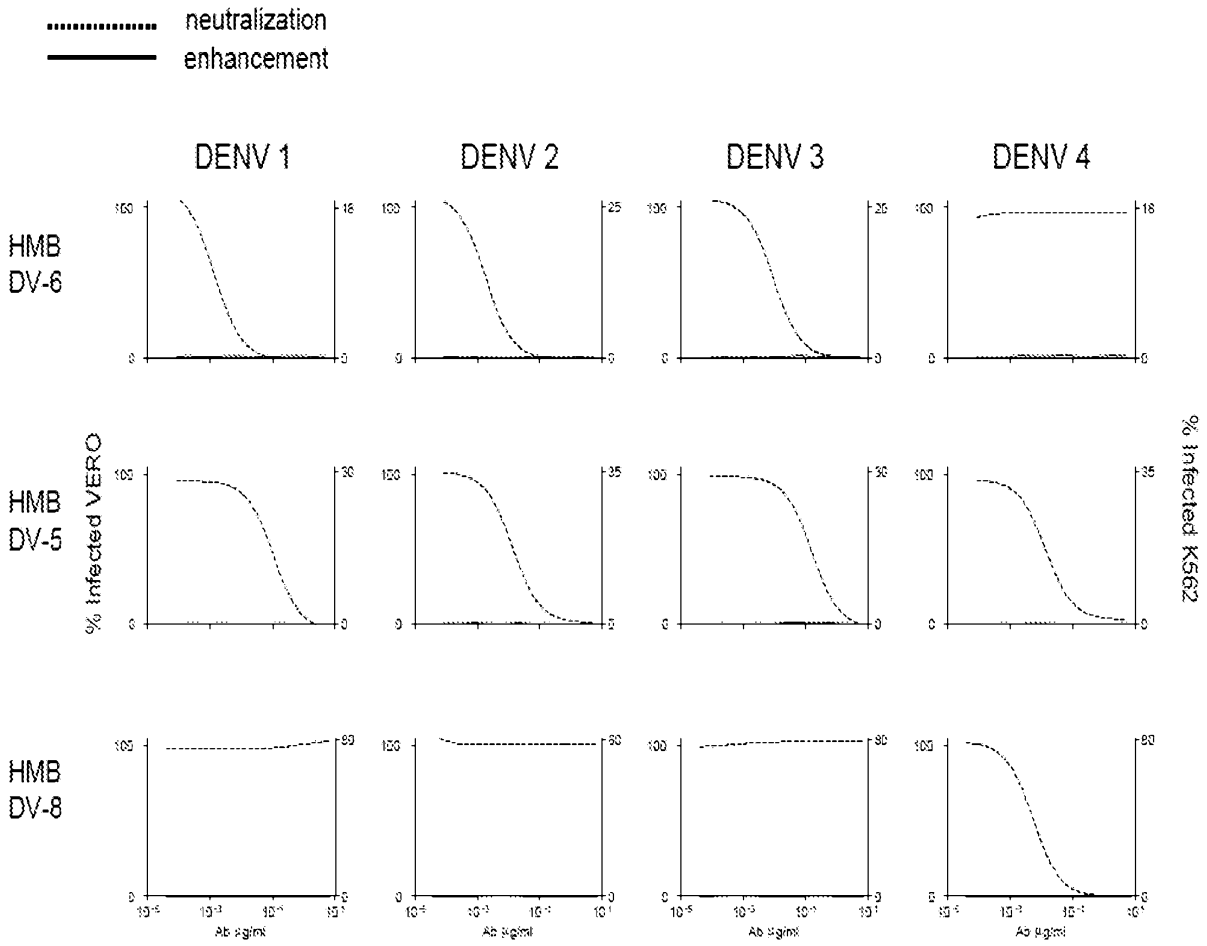


Figure 2. Neutralization and antibody-dependent enhancement of LALA-variant mAbs



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Pro Glu Tyr Ser Gln Pro Leu Cys Thr Ala Ile Gln Ile Ala Leu Val

1 5 10 15

Glu Leu Leu Glu Ser Phe Gly Val Val Pro Lys Ala Val Val Gly His
20 25 30

Ser Ser Gly Glu Ile Ala Ala
35

<210> 37
<211> 36
<212> PRT
<213> Penicillium coprobium PF1169

<400> 37

Ile Ser Gln Pro Ala Cys Thr Ala Leu Gln Ile Ala Leu Val Asp Leu
1 5 10 15

Leu Ala Glu Trp Ser Ile Thr Pro Ser Val Val Val Gly His Ser Ser
20 25 30

Gly Glu Ile Ala
35

<210> 38
<211> 39
<212> PRT
<213> Penicillium coprobium PF1169

<400> 38

Pro Glu Tyr Ser Gln Pro Leu Cys Thr Ala Ile Gln Ile Ala Leu Val
1 5 10 15

Glu Leu Leu Glu Ser Phe Gly Val Val Pro Lys Ala Val Val Gly His
20 25 30

Ser Ser Gly Glu Ile Ala Ala
35

<210> 39
<211> 76
<212> PRT
<213> Penicillium coprobium PF1169

<400> 39

Glu Glu Phe Trp Asp Leu Cys Ser Arg Gly Arg Gly Ala Trp Ser Pro

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1 5 10 15

Val Pro Lys Asp Arg Phe Asn Ala Gly Ser Phe Tyr His Pro Asn Ala
20 25 30

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

Asp Ile Gly Leu Phe Asp Ala Pro Phe Phe Asn Ile Thr Leu Gln Glu
50 55 60

Ala Gln Thr Met Asp Pro Gln Gln Arg Ile Phe Leu
65 70 75

<210> 40
<211> 77
<212> PRT
<213> Penicillium coprobium PF1169

<400> 40

Ile Asn Glu Pro Arg Asp Arg Pro Gln Phe Phe His Ala His Gly Thr
1 5 10 15

Gly Thr Gln Ala Gly Asp Pro Gln Glu Ala Glu Ala Val Ser Thr Ala
20 25 30

Leu Phe Pro Asp Gly Ser Asn Ile Glu Thr Lys Leu Phe Val Gly Ser
35 40 45

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

Leu Ile Gly Ser Ser Leu Ala Met Lys His Gly Val Ile
65 70 75

<210> 41
<211> 43
<212> PRT
<213> Penicillium coprobium PF1169

<400> 41

Lys Leu Ala Phe Val Phe Thr Gly Gln Gly Gly Gln Trp Ala Gly Met
1 5 10 15

Gly Arg Glu Leu Leu Ser Ile Ser Thr Phe Arg Glu Ser Met Ala Arg
20 25 30

Ser Gln Glu Ile Leu Ala Ser Leu Gly Cys Pro
35 40

<210> 42
<211> 71
<212> PRT
<213> Penicillium coprobium PF1169

<400> 42

Lys Ser Phe Leu Asp Asp Leu Ala Phe Thr Val Asn Glu Arg Arg Ser
1 5 10 15

Ile Phe Pro Trp Lys Ala Ala Val Val Gly Asp Thr Met Glu Gly Leu
20 25 30

Ala Ala Ser Leu Ala Gln Asn Ile Lys Pro Arg Ser Val Leu Arg Met
35 40 45

Pro Thr Leu Gly Phe Val Phe Thr Gly Gln Gly Ala Gln Trp Pro Gly
50 55 60

Met Gly Lys Glu Leu Leu Gln
65 70

<210> 43
<211> 55
<212> PRT
<213> Penicillium coprobium PF1169

<400> 43

Ser Val Ala Cys Ile Asn Ser Pro Phe Asn Cys Thr Leu Ser Gly Pro
1 5 10 15

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

Phe Ala Gln Lys Leu Lys Thr Gly Val Ala Tyr His Ser Thr Ala Met
35 40 45

Ser Ala Ile Ala Asn Asp Tyr
50 55

<210> 44
<211> 68
<212> PRT
<213> Penicillium coprobium PF1169

<400> 44

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

Ala Met Arg Gly Asn Lys Ala Val Ile Ala Cys Val Asn Ser Glu Ser
20 25 30

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

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

Ala Tyr His Ser
65

<210> 45
<211> 38
<212> PRT
<213> Penicillium coprobium PF1169

<400> 45

Gly Asn Gly Ser Ala Met Ile Ser Asn Arg Ile Ser Trp Phe Phe Asp
1 5 10 15

Leu Lys Gly Pro Ser Leu Ser Leu Asp Thr Ala Cys Ser Ser Ser Leu
20 25 30

Val Ala Leu His Leu Ala
35

<210> 46
<211> 77
<212> PRT
<213> Penicillium coprobium PF1169

<400> 46

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

Leu His Gln Ala Val Gln Ser Leu Arg Ser Gly Glu Thr Asp Val Ala
20 25 30

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

Glu Ser Lys Leu Lys Met Leu Ser Pro Asn Gly Arg Ser Arg Met Trp
50 55 60

Asp Lys Asp Ala Asp Gly Tyr Ala Arg Gly Asp Gly Ile
65 70 75

<210> 47
<211> 61
<212> PRT
<213> Penicillium coprobium PF1169

<400> 47

Ile Gly Ser Ile Lys Pro Asn Ile Gly His Leu Glu Ala Gly Ala Gly
1 5 10 15

Val Met Gly Phe Ile Lys Ala Ile Leu Ser Ile Gln Lys Gly Val Leu
20 25 30

Ala Pro Gln Ala Asn Leu Thr Lys Leu Asn Ser Arg Ile Asp Trp Lys
35 40 45

Thr Ala Gly Val Lys Val Val Gln Glu Ala Thr Pro Trp
50 55 60

<210> 48
<211> 37
<212> PRT
<213> Penicillium coprobium PF1169

<400> 48

Gly Leu Phe Asp Ala Pro Phe Phe Asn Ile Thr Leu Gln Glu Ala Gln
1 5 10 15

Thr Met Asp Pro Gln Gln Arg Ile Phe Leu Glu Cys Val Tyr Glu Ala
20 25 30

Leu Glu Asn Gly Gly
35

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<210> 49
<211> 70
<212> PRT
<213> Penicillium coprobium PF1169

<400> 49

Gly Arg Phe Leu Ser Ser Asp Gly Arg Cys His Thr Phe Asp Glu Lys
1 5 10 15

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

Pro Leu Ala Lys Ala Leu His Asp Gln Asn Lys Ile Arg Ala Val Ile
35 40 45

Arg Gly Thr Gly Ser Asn Gln Asp Gly Arg Thr Ala Gly Ile Thr Val
50 55 60

Pro Asn Gly Ala Ala Gln
65 70

<210> 50
<211> 37
<212> PRT
<213> Penicillium coprobium PF1169

<400> 50

Ser Phe Asp Ser Arg Ala Glu Gly Tyr Ala Arg Gly Glu Gly Val Gly
1 5 10 15

Thr Val Val Val Lys Pro Leu Ser Thr Ala Ile Arg Asp Gly Asp Thr
20 25 30

Ile Arg Ala Val Ile
35

<210> 51
<211> 83
<212> PRT
<213> Penicillium coprobium PF1169

<400> 51

Trp Pro Arg Leu Pro Glu Arg Arg Arg Ile Ala Val Val Asn Asn Phe
1 5 10 15

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

Arg Thr Arg Ser Gly Ser Asp Pro Arg Ser Leu His Pro Ile Ala Ile
35 40 45

Ser Ala Lys Ser Lys Val Ser Leu Arg Gly Asn Leu Glu Asn Leu Leu
50 55 60

Ala Tyr Leu Asp Thr His Pro Asp Val Ser Leu Ser Asp Leu Ser Tyr
65 70 75 80

Thr Thr Thr

<210> 52
<211> 59
<212> PRT
<213> Penicillium coprobium PF1169

<400> 52

Val Tyr Ser Gly Ser Met Thr Asn Asp Tyr Glu Leu Leu Ser Thr Arg
1 5 10 15

Asp Ile Tyr Asp Met Pro His Asn Ser Ala Thr Gly Asn Gly Arg Thr
20 25 30

Met Leu Ala Asn Arg Leu Ser Trp Phe Phe Asp Leu Gln Gly Pro Ser
35 40 45

Ile Met Met Asp Thr Ala Cys Ser Ser Ser Leu
50 55

<210> 53
<211> 67
<212> PRT
<213> Penicillium coprobium PF1169

<400> 53

Leu Ser Pro Gln Asn Asn Pro Glu Asp Arg Cys Gln Tyr Phe Glu Ala
1 5 10 15

His Gly Thr Gly Thr Gln Ala Gly Asp Pro Gln Glu Ala Ala Ala Ile

20 25 30

Asn Ser Ser Phe Phe Gly Pro Glu Ser Val Pro Asp Ser Thr Asp Arg
35 40 45

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

Ala Gly Leu
65

<210> 54
<211> 83
<212> PRT
<213> Penicillium coprobium PF1169

<400> 54

Asp Gly Tyr Gly Arg Gly Glu Gly Val Ala Ser Val Val Leu Lys Arg
1 5 10 15

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

Ala Ser Gly Ala Asn Ser Asp Gly Arg Thr Met Gly Ile Thr Met Pro
35 40 45

Asn Pro Lys Ala Gln Gln Ser Leu Ile Leu Ala Thr Tyr Ala Arg Ala
50 55 60

Gly Leu Ser Pro Gln Asn Asn Pro Glu Asp Arg Cys Gln Tyr Phe Glu
65 70 75 80

Ala His Gly

<210> 55
<211> 38
<212> PRT
<213> Penicillium coprobium PF1169

<400> 55

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

Ala Met Arg Gly Asn Lys Ala Val Ile Ala Cys Val Asn Ser Glu Ser
20 25 30

Ser Val Thr Leu Ser Gly
35

<210> 56
<211> 29
<212> PRT
<213> Penicillium coprobium PF1169

<400> 56

Ser Gly Cys Tyr Arg Glu Leu Ala Asp Cys Pro Gly Gln Arg Gly Ile
1 5 10 15

Phe Thr Arg Lys Leu Lys Val Asp Val Ala Tyr His Ser
20 25

<210> 57
<211> 38
<212> PRT
<213> Penicillium coprobium PF1169

<400> 57

Gly Asn Gly Ser Ala Met Ile Ser Asn Arg Ile Ser Trp Phe Phe Asp
1 5 10 15

Leu Lys Gly Pro Ser Leu Ser Leu Asp Thr Ala Cys Ser Ser Ser Leu
20 25 30

Val Ala Leu His Leu Ala
35

<210> 58
<211> 59
<212> PRT
<213> Penicillium coprobium PF1169

<400> 58

Ile Ser Glu Cys Val Thr Val Tyr Trp Lys Ala Ile Lys Ser Ala Gln
1 5 10 15

Pro Asp Gly Pro Tyr Ala Leu Ala Gly Tyr Ser Tyr Gly Ser Met Leu
20 25 30

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

Phe Leu Gly Cys Phe Asn Leu Pro Pro His Ile
50 55

<210> 59
<211> 72
<212> PRT
<213> Penicillium coprobium PF1169

<400> 59

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

Ala Met Met Ala Val Gly Ala Asn Ala Ser Thr Val Gln Pro Leu Leu
20 25 30

Asp Ala Met Lys Asp Lys His Ala Val Val Ala Cys Ile Asn Ser Asp
35 40 45

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

Ser Val Leu Lys Arg Gln Asp Ile
65 70

<210> 60
<211> 79
<212> PRT
<213> Penicillium coprobium PF1169

<400> 60

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

Thr Cys Val Gln Met Ala Leu Thr Lys Tyr Trp Thr Ser Leu Gly Val
20 25 30

Thr Pro Ser Phe Val Met Gly His Ser Leu Gly Glu Phe Ala Ala Leu
35 40 45

Asn Ala Ala Gly Val Leu Thr Ile Ser Asp Thr Ile Tyr Leu Ala Gly
50 55 60

Arg Arg Ala Gln Leu Leu Thr Glu Gln Ile Lys Val Gly Thr His
65 70 75

<210> 61
<211> 67
<212> PRT
<213> Penicillium coprobium PF1169

<400> 61

Phe Ile Glu Asp Ser Ile Ser Lys Glu His Lys Pro Thr Arg Val Pro
1 5 10 15

Ile His Gly Pro Tyr His Ala Ser His Leu Tyr Asn Asp Arg Asp Ile
20 25 30

Asp Arg Ile Met Glu Ser Trp Pro Thr Glu Gln Leu Trp Ala Tyr Val
35 40 45

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

Asp Ser Leu
65

<210> 62
<211> 76
<212> PRT
<213> Penicillium coprobium PF1169

<400> 62

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

Leu His Gln Ala Val Gln Ser Leu Arg Ser Gly Glu Thr Asp Val Ala
20 25 30

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

Glu Ser Lys Leu Lys Met Leu Ser Pro Asn Gly Arg Ser Arg Met Trp
50 55 60

Asp Lys Asp Ala Asp Gly Tyr Ala Arg Gly Asp Gly
65 70 75

<210> 63
<211> 31
<212> PRT
<213> Penicillium coprobium PF1169

<400> 63

Leu Phe Leu Phe Pro Asp Gly Ser Gly Ser Ala Thr Ser Tyr Ala Thr
1 5 10 15

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

<210> 64
<211> 26
<212> PRT
<213> Penicillium coprobium PF1169

<400> 64

Ala Lys His Pro Pro Ala Thr Ser Ile Leu Leu Gln Gly Asn Pro Lys
1 5 10 15

Thr Ala Thr Gln Ser Phe Ile Phe Val Pro
20 25

<210> 65
<211> 46
<212> PRT
<213> Penicillium coprobium PF1169

<400> 65

Tyr Gln Ala Thr Gly Cys Ala Ala Ser Leu Gln Ser Asn Arg Ile Ser
1 5 10 15

Tyr Phe Phe Asp Leu Arg Gly Pro Ser Ile Thr Ile Asp Thr Ala Cys
20 25 30

Ser Ser Ser Leu Val Ala Leu His Tyr Ala Val Gln Ser Leu
35 40 45

<210> 66
<211> 66
<212> PRT
<213> Penicillium coprobium PF1169

<400> 66

Tyr Ser Ala Thr Gly Ser Gly Leu Thr Val Leu Ala Asn Arg Ile Thr
1 5 10 15

His Cys Phe Asp Leu Arg Gly Pro Ser His Val Val Asp Thr Ala Cys
20 25 30

Ser Ser Ser Leu Tyr Ala Leu His Ser Ala Cys Leu Ala Leu Asp Ser
35 40 45

Arg Asp Cys Asp Gly Ala Val Val Ala Ala Ala Asn Leu Ile Gln Ser
50 55 60

Pro Glu
65

<210> 67
<211> 76
<212> PRT
<213> Penicillium coprobium PF1169

<400> 67

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

Thr Cys Val Gln Met Ala Leu Thr Lys Tyr Trp Thr Ser Leu Gly Val
20 25 30

Thr Pro Ser Phe Val Met Gly His Ser Leu Gly Glu Phe Ala Ala Leu
35 40 45

Asn Ala Ala Gly Val Leu Thr Ile Ser Asp Thr Ile Tyr Leu Ala Gly
50 55 60

Arg Arg Ala Gln Leu Leu Thr Glu Gln Ile Lys Val
65 70 75

<210> 68
<211> 71
<212> PRT
<213> Penicillium coprobium PF1169

<400> 68

His Leu Asn Leu Met Gly Pro Ser Thr Ala Val Asp Ala Ala Cys Ala
1 5 10 15

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

Glu Ser Arg Val Ala Ile Val Gly Gly Val Asn Ala Leu Cys Gly Pro
35 40 45

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

Ser Cys Lys Ser Phe Asp Asp
65 70

<210> 69
<211> 84
<212> PRT
<213> Penicillium coprobium PF1169

<400> 69

Ser Phe Arg Arg Gln Glu Asp Thr Trp Lys Val Leu Ser Asn Ala Thr
1 5 10 15

Ser Thr Leu Tyr Leu Ala Gly Ile Glu Ile Lys Trp Lys Glu Tyr His
20 25 30

Gln Asp Phe Asn Ala Ala His Arg Val Leu Pro Leu Pro Ser Tyr Lys
35 40 45

Trp Asp Leu Lys Asn Tyr Trp Ile Pro Tyr Thr Asn Asn Phe Cys Leu
50 55 60

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

Val Phe Leu Ser

<210> 70
<211> 78
<212> PRT
<213> Penicillium coprobium PF1169

<400> 70

Lys Thr Ser Cys Phe Val Gly Ser Phe Ser Ala Asp Tyr Thr Asp Leu

1 5 10 15

Leu Leu Arg Asp Pro Glu Cys Val Pro Met Tyr Gln Cys Thr Asn Ala
20 25 30

Gly Gln Ser Arg Ala Met Thr Ala Asn Arg Leu Ser Tyr Phe Phe Asp
35 40 45

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

Val Ala Leu His Leu Ala Cys Gln Ser Leu Arg Thr Gly Asp
65 70 75

<210> 71
<211> 67
<212> PRT
<213> Penicillium coprobium PF1169

<400> 71

Tyr Ser Ala Thr Gly Ser Gly Leu Thr Val Leu Ala Asn Arg Ile Thr
1 5 10 15

His Cys Phe Asp Leu Arg Gly Pro Ser His Val Val Asp Thr Ala Cys
20 25 30

Ser Ser Ser Leu Tyr Ala Leu His Ser Ala Cys Phe Gly Pro Leu Asn
35 40 45

Ser Arg Asp Cys Asp Gly Ala Val Val Ala Ala Ala Asn Leu Ile Gln
50 55 60

Ser Pro Glu
65

<210> 72
<211> 79
<212> PRT
<213> Penicillium coprobium PF1169

<400> 72

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

Thr Cys Val Gln Met Ala Leu Thr Lys Tyr Trp Thr Ser Leu Gly Val
20 25 30

Thr Pro Ser Phe Val Met Gly His Ser Leu Gly Glu Phe Ala Ala Leu
35 40 45

Asn Ala Ala Gly Val Leu Thr Ile Ser Asp Thr Ile Tyr Leu Ala Gly
50 55 60

Arg Arg Ala Gln Leu Leu Thr Glu Gln Ile Glu Gly Gly Thr His
65 70 75

<210> 73
<211> 40
<212> PRT
<213> Penicillium coprobium PF1169

<400> 73

Glu Ala Asn Leu His Val Pro Leu Glu Pro Thr Pro Trp Pro Ala Gly
1 5 10 15

Arg Pro Glu Arg Ile Ser Val Asn Ser Phe Gly Ile Gly Gly Ser Asn
20 25 30

Ala His Ala Ile Leu Glu Ser Ala
35 40

<210> 74
<211> 70
<212> PRT
<213> Penicillium coprobium PF1169

<220>
<221> misc_feature
<222> (5)..(5)
<223> Xaa can be any naturally occurring amino acid

<400> 74

Ile Gly His Thr Xaa Gly Ser Ala Gly Leu Ala Ser Leu Ile Gly Ser
1 5 10 15

Ser Leu Ala Met Lys His Gly Val Ile Pro Pro Asn Leu His Phe Gly
20 25 30

Gln Leu Ser Glu Lys Val Ala Pro Phe Tyr Thr His Leu Asn Ile Pro

35 40 45

Thr Glu Pro Val Pro Trp Pro Asn Ser Thr Ser Ser Gln Val Lys Arg
50 55 60

Ala Ser Ile Asn Ser Phe
65 70

<210> 75
<211> 45
<212> PRT
<213> Penicillium coprobium PF1169

<400> 75

Pro Val Cys Ser Gly Met Val Lys Ala Thr Phe Gly Pro Gln Ala Thr
1 5 10 15

Thr Val Ala Ser Phe Arg Arg Gln Glu Asp Thr Trp Lys Val Leu Ser
20 25 30

Asn Ala Thr Ser Thr Leu Tyr Leu Ala Gly Ile Glu Ile
35 40 45

<210> 76
<211> 19
<212> PRT
<213> Penicillium coprobium PF1169

<220>
<221> misc_feature
<222> (13)..(13)
<223> Xaa can be any naturally occurring amino acid

<400> 76

Leu Leu Gly Leu Arg Leu Lys Trp Lys Glu Tyr His Xaa Asp Phe Asn
1 5 10 15

Ala Ala His

<210> 77
<211> 69
<212> PRT
<213> Penicillium coprobium PF1169

<400> 77

Val Tyr Ser Gly Ser Met Thr Asn Asp Tyr Glu Leu Leu Ser Thr Arg
1 5 10 15

Asp Ile Tyr Asp Met Pro His Asn Ser Ala Thr Gly Asn Gly Arg Thr
20 25 30

Met Leu Ala Asn Arg Leu Ser Trp Phe Phe Asp Leu Gln Gly Pro Ser
35 40 45

Ile Met Met Asp Thr Ala Cys Ser Ser Ser Leu Thr Ala Val His Leu
50 55 60

Ala Ala Gln Ser Leu
65

<210> 78
<211> 85
<212> PRT
<213> Penicillium coprobium PF1169

<400> 78

Asp Ala Gln Phe Phe Gly Thr Lys Pro Val Glu Ala Asn Ser Ile Asp
1 5 10 15

Pro Gln Gln Arg Leu Leu Leu Glu Thr Val Tyr Glu Gly Leu Glu Thr
20 25 30

Ser Gly Ile Pro Met Glu Arg Leu Gln Gly Ser Asn Thr Ala Val Tyr
35 40 45

Val Gly Leu Met Thr Asn Asp Tyr Ala Asp Met Leu Gly Arg Asp Met
50 55 60

Gln Asn Phe Pro Thr Tyr Phe Ala Ser Gly Thr Ala Arg Ser Ile Leu
65 70 75 80

Ser Asn Arg Val Ser
85

<210> 79
<211> 28
<212> PRT
<213> Penicillium coprobium PF1169

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<400> 79

Asp Pro Ala Tyr Phe Asp Ser Ser Phe Phe Asn Ile Thr Lys Thr Glu
1 5 10 15

Leu Leu Thr Leu Asp Pro Gln Gln Arg Leu Val Leu
20 25

<210> 80
<211> 51
<212> PRT
<213> Penicillium coprobium PF1169

<400> 80

Val Ala Cys Val Asn Ser Pro Ala Ser Thr Thr Leu Ser Gly Asp Val
1 5 10 15

Asp Tyr Ile Asn Gln Leu Glu Ala Arg Leu Gln Gln Asp Gly His Phe
20 25 30

Ala Arg Lys Leu Arg Ile Asp Thr Ala Tyr His Ser Pro His Met Glu
35 40 45

Glu Leu Val
50

<210> 81
<211> 24
<212> PRT
<213> Penicillium coprobium PF1169

<400> 81

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

Gln Met Ala Leu Thr Lys Tyr Trp
20

<210> 82
<211> 59
<212> PRT
<213> Penicillium coprobium PF1169

<400> 82

Gly Cys Phe Tyr Gly Met Thr Ser Asp Asp Tyr Arg Glu Val Asn Ser
1 5 10 15

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Gly Gln Asp Ile Asp Thr Tyr Phe Ile Pro Gly Gly Asn Arg Ala Phe
20 25 30

Thr Pro Gly Arg Ile Asn Tyr Tyr Phe Lys Phe Ser Gly Pro Ser Val
35 40 45

Ser Val Asp Thr Ala Cys Ser Ser Ser Leu Ala
50 55

<210> 83
<211> 16
<212> PRT
<213> Penicillium coprobium PF1169

<400> 83

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

<210> 84
<211> 53
<212> PRT
<213> Penicillium coprobium PF1169

<400> 84

Ala Ile Val Gly Gly Val Asn Ala Leu Cys Gly Pro Gly Leu Thr Arg
1 5 10 15

Val Leu Asp Lys Ala Gly Ala Ile Ser Ser Asp Gly Ser Cys Lys Ser
20 25 30

Phe Asp Asp Asp Ala His Gly Tyr Ala Arg Gly Glu Gly Ala Gly Ala
35 40 45

Leu Val Thr Lys Lys
50

<210> 85
<211> 60
<212> PRT
<213> Penicillium coprobium PF1169

<400> 85

Ile Ala Ile Val Gly Ile Gly Gly Arg Phe Pro Gly Glu Ala Thr Asn
1 5 10 15

Pro Asn Arg Leu Trp Asp Met Val Ser Asn Gly Arg Ser Ala Leu Thr
20 25 30

Glu Val Pro Lys Asp Arg Phe Asn Ile Asp Ala Phe Tyr His Pro His
35 40 45

Ala Glu Arg Gln Gly Thr Met Asn Val Arg Arg Gly
50 55 60

<210> 86
<211> 53
<212> PRT
<213> Penicillium coprobium PF1169

<400> 86

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

Thr Cys Val Gln Met Ala Leu Thr Lys Tyr Trp Thr Ser Leu Gly Val
20 25 30

Thr Pro Ser Phe Val Met Gly His Ser Leu Gly Glu Phe Ala Ala Leu
35 40 45

Asn Ala Ala Gly Val
50

<210> 87
<211> 18
<212> PRT
<213> Penicillium coprobium PF1169

<400> 87

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

Thr Cys

<210> 88
<211> 62
<212> PRT
<213> Penicillium coprobium PF1169

<400> 88

Phe Leu Asp Asp Leu Ala Phe Thr Val Asn Glu Arg Arg Ser Ile Phe
1 5 10 15

Pro Trp Lys Ala Ala Val Val Gly Asp Thr Met Glu Gly Leu Ala Ala
20 25 30

Ser Leu Ala Gln Asn Ile Lys Pro Arg Ser Val Leu Arg Met Pro Thr
35 40 45

Leu Gly Phe Val Phe Thr Gly Gln Gly Ala Gln Trp Pro Gly
50 55 60

<210> 89
<211> 51
<212> PRT
<213> Penicillium coprobium PF1169

<400> 89

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

Gln Gly Gly Thr Gly Gln Val Val Met Glu Ser Asp Leu Met Gln Thr
20 25 30

Glu Phe Leu Glu Ala Ala Asn Gly His Arg Met Asn Asp Cys Gly Val
35 40 45

Val Thr Ser
50

<210> 90
<211> 77
<212> PRT
<213> Penicillium coprobium PF1169

<400> 90

Glu Cys Gly Phe Val Glu Met His Gly Thr Gly Thr Lys Ala Gly Asp
1 5 10 15

Pro Val Glu Ala Ala Ala Val His Ala Ala Leu Gly Lys Asn Arg Thr
20 25 30

Leu Arg Asn Pro Leu Tyr Ile Gly Ser Val Lys Ser Asn Ile Gly His

35 40 45

Leu Glu Gly Ala Ser Gly Ile Val Ala Val Ile Lys Ala Ala Met Met
50 55 60

Leu Asp Arg Asp Leu Met Leu Pro Asn Ala Glu Phe Lys
65 70 75

<210> 91
<211> 78
<212> PRT
<213> Penicillium coprobium PF1169

<220>
<221> misc_feature
<222> (4)..(4)
<223> Xaa can be any naturally occurring amino acid

<400> 91

Phe Phe Lys Xaa Ser Gly Pro Ser Phe Ser Ile Asp Thr Ala Cys Ser
1 5 10 15

Ser Ser Leu Ala Thr Ile Gln Val Cys Thr His Leu Phe His Val His
20 25 30

Leu Asn Arg Gln Leu Thr Ile Ala Ala Cys Thr Ser Leu Trp Asn Gly
35 40 45

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

Asp Ala Phe Ala Gly Leu Ser His Gly His Phe Leu Thr Lys
65 70 75

<210> 92
<211> 79
<212> PRT
<213> Penicillium coprobium PF1169

<400> 92

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

Thr Cys Val Gln Met Ala Leu Thr Lys Tyr Trp Thr Ser Leu Gly Val
20 25 30

Thr Pro Ser Phe Val Met Gly His Ser Leu Gly Glu Phe Ala Ala Leu
35 40 45

Asn Ala Ala Gly Val Leu Thr Ile Ser Asp Thr Ile Tyr Leu Ala Gly
50 55 60

Arg Arg Ala Gln Leu Leu Thr Glu Gln Ile Glu Gly Gly Thr His
65 70 75

<210> 93
<211> 68
<212> PRT
<213> Penicillium coprobium PF1169

<400> 93

Leu Ser Ser Asp Gly Arg Cys His Thr Phe Asp Glu Lys Ala Asn Gly
1 5 10 15

Tyr Ala Arg Gly Glu Ala Val Gly Cys Leu Ile Leu Lys Pro Leu Ala
20 25 30

Lys Ala Leu His Asp Gln Asn Lys Ile Arg Ala Val Ile Arg Gly Thr
35 40 45

Gly Ser Asn Gln Asp Gly Arg Thr Ala Gly Ile Thr Val Pro Asn Gly
50 55 60

Ala Ala Gln Glu
65

<210> 94
<211> 80
<212> PRT
<213> Penicillium coprobium PF1169

<400> 94

Ser Pro Leu Phe Gly Leu Ala Arg Ile Ile Ala Ser Glu His Pro Asp
1 5 10 15

Leu Gly Ser Leu Ile Asp Ile Glu Glu Pro Ile Ile Pro Leu Ser Thr
20 25 30

Met Arg Tyr Ile Gln Gly Ala Asp Ile Val Arg Ile Ser Asp Gly Ile

35 40 45

Ala Arg Thr Ser Arg Phe Arg Ser Leu Pro Arg Thr Lys Leu Arg Pro
50 55 60

Val Ser Asp Gly Pro Arg Leu Leu Pro Arg Pro Glu Gly Thr Tyr Leu
65 70 75 80

<210> 95
<211> 75
<212> PRT
<213> Penicillium coprobium PF1169

<400> 95

Asn Arg Ile Ser Tyr Tyr Phe Asp Trp Gln Gly Pro Ser Met Ala Val
1 5 10 15

Asp Thr Gly Cys Ser Ser Ser Leu Leu Ala Val His Leu Gly Val Glu
20 25 30

Ala Leu Gln Asn Asp Asp Cys Ser Met Ala Val Ala Val Gly Ser Asn
35 40 45

Leu Ile Leu Ser Pro Asn Ala Tyr Ile Ala Asp Ser Lys Thr Arg Met
50 55 60

Leu Ser Pro Thr Gly Arg Ser Arg Met Trp Asp
65 70 75

<210> 96
<211> 81
<212> PRT
<213> Penicillium coprobium PF1169

<400> 96

Val Asp Val Asn Pro Ala Val Leu Lys Asp Ala Pro Leu Pro Trp Asp
1 5 10 15

Pro Ser Ser Trp Ala Pro Ile Leu Asp Ala Ala Thr Ser Val Gly Ser
20 25 30

Thr Ile Phe Gln Thr Ala Ala Leu Arg Met Pro Ala Gln Ile Glu Arg
35 40 45

Val Glu Ile Phe Thr Ser Glu Asn Pro Pro Lys Thr Ser Trp Leu Tyr
50 55 60

Val Gln Glu Ala Ser Asp Ala Val Pro Thr Ser His Val Ser Val Val
65 70 75 80

Ser

<210> 97
<211> 37
<212> PRT
<213> Penicillium coprobium PF1169

<400> 97

Pro Leu Phe Gly Leu Ala Arg Ile Ile Ala Ser Glu His Pro Asp Leu
1 5 10 15

Gly Ser Leu Ile Asp Ile Glu Glu Pro Ile Ile Pro Leu Ser Thr Met
20 25 30

Arg Tyr Ile Arg Gly
35

<210> 98
<211> 84
<212> PRT
<213> Penicillium coprobium PF1169

<400> 98

Ala Val Ile Arg Gly Thr Gly Ser Asn Gln Asp Gly Arg Thr Ala Gly
1 5 10 15

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

Tyr Ala Gln Ala Asp Leu Asp Pro Ser Glu Thr Asp Phe Val Glu Ala
35 40 45

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

Ala Arg Val Phe Gly Thr Asp Arg Pro Pro Gly Asp Pro Val Arg Ile
65 70 75 80

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Gly Ser Ile Lys

<210> 99
<211> 69
<212> PRT
<213> Penicillium coprobium PF1169

<400> 99

Leu Glu Val Val Trp Glu Cys Leu Glu Asn Ser Gly Glu Thr Gln Trp
1 5 10 15

Arg Gly Lys Glu Ile Gly Cys Phe Val Gly Val Phe Gly Glu Asp Trp
20 25 30

Leu Glu Met Ser His Lys Asp Pro Gln His Leu Asn Gln Met Phe Pro
35 40 45

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

Asp Leu Thr Gly Pro
65

<210> 100
<211> 79
<212> PRT
<213> Penicillium coprobium PF1169

<400> 100

Gly Gly Ala Thr Asp Thr Glu Lys Phe Trp Asp Leu Leu Ala Ser Gly
1 5 10 15

Val Asp Val His Arg Lys Ile Pro Ala Asp Arg Phe Asp Val Glu Thr
20 25 30

His Tyr Asp Pro Asn Gly Lys Arg Met Asn Ala Ser His Thr Pro Tyr
35 40 45

Gly Cys Phe Ile Asp Glu Pro Gly Leu Phe Asp Ala Ala Phe Phe Asn
50 55 60

Met Ser Pro Arg Glu Ala Gln Gln Thr Asp Pro Met Gln Arg Leu
65 70 75

<210> 101
<211> 52
<212> PRT
<213> Penicillium coprobium PF1169

<400> 101

Glu Leu Arg His Gly Lys Asn Ile Asp Lys Pro Glu Tyr Ser Gln Pro
1 5 10 15

Leu Cys Thr Ala Ile Gln Ile Ala Leu Val Glu Leu Leu Glu Ser Phe
20 25 30

Gly Val Val Pro Lys Ala Val Val Gly His Ser Ser Gly Glu Ile Ala
35 40 45

Ala Ala Tyr Val
50

<210> 102
<211> 34
<212> PRT
<213> Penicillium coprobium PF1169

<400> 102

Val Gly Phe Val Phe Thr Gly Gln Gly Ala Gln Trp His Gly Met Gly
1 5 10 15

Lys Glu Leu Leu Ser Thr Tyr Pro Ile Phe Arg Gln Thr Met Gln Asp
20 25 30

Val Asp

<210> 103
<211> 63
<212> PRT
<213> Penicillium coprobium PF1169

<400> 103

Phe Asp Ala Ala Phe Phe Asn Met Ser Pro Arg Glu Ala Gln Gln Thr
1 5 10 15

Asp Pro Met Gln Arg Leu Ala Ile Val Thr Ala Tyr Glu Ala Leu Glu
20 25 30

Arg Ala Gly Tyr Val Ala Asn Arg Thr Ala Ala Thr Asn Leu His Arg
35 40 45

Ile Gly Thr Phe Tyr Gly Gln Ala Ser Asp Asp Tyr Arg Glu Val
50 55 60

<210> 104
<211> 43
<212> PRT
<213> Penicillium coprobium PF1169

<400> 104

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

Gly Met Ser His His Gly Leu Leu Gly Pro Gln Gly Arg Ser Phe Ser
20 25 30

Phe Asp Ser Arg Ala Glu Gly Tyr Ala Arg Gly
35 40

<210> 105
<211> 71
<212> PRT
<213> Penicillium coprobium PF1169

<400> 105

Lys Ala Ser Leu Ser Leu Gln His Gly Met Ile Ala Pro Asn Leu Leu
1 5 10 15

Met Gln His Leu Asn Pro Lys Ile Lys Pro Phe Ala Ala Lys Leu Ser
20 25 30

Val Pro Thr Glu Cys Ile Pro Trp Pro Ala Val Pro Asp Gly Cys Pro
35 40 45

Arg Arg Ala Ser Val Asn Ser Phe Gly Phe Gly Gly Ala Asn Val His
50 55 60

Val Val Leu Glu Ser Tyr Thr
65 70

<210> 106

<211> 28
<212> PRT
<213> Penicillium coprobium PF1169

<400> 106

Pro Trp Pro Thr Thr Gly Leu Arg Arg Ala Ser Val Asn Ser Phe Gly
1 5 10 15

Tyr Gly Gly Thr Asn Ala His Cys Val Leu Asp Asp
20 25

<210> 107
<211> 71
<212> PRT
<213> Penicillium coprobium PF1169

<400> 107

Lys Ala Ser Leu Ser Leu Gln His Gly Met Ile Ala Pro Asn Leu Leu
1 5 10 15

Met Gln His Leu Asn Pro Lys Ile Lys Pro Phe Ala Ala Lys Leu Ser
20 25 30

Val Pro Thr Glu Cys Ile Pro Trp Pro Ala Val Pro Asp Gly Cys Pro
35 40 45

Arg Arg Ala Ser Val Asn Ser Phe Gly Phe Gly Gly Ala Asn Val His
50 55 60

Val Val Leu Glu Ser Tyr Thr
65 70

<210> 108
<211> 50
<212> PRT
<213> Penicillium coprobium PF1169

<400> 108

Asp Arg Leu Phe Leu Gln Met Ser His Glu Glu Trp Glu Ala Ala Leu
1 5 10 15

Ala Pro Lys Val Thr Gly Thr Trp Asn Leu His His Ala Thr Ala Gln
20 25 30

His Ser Leu Asp Phe Phe Val Val Phe Gly Ser Ile Ala Gly Val Cys

35 40 45

Gly Asn
50

<210> 109
<211> 82
<212> PRT
<213> Penicillium coprobium PF1169

<400> 109

Thr Phe Leu Lys Gly Thr Gly Gly Gln Met Leu Gln Asn Val Val Leu
1 5 10 15

Arg Val Pro Val Ala Ile Asn Ala Pro Arg Ser Val Gln Val Val Val
20 25 30

Gln Gln Asp Gln Val Lys Val Val Ser Arg Leu Ile Pro Ser Glu Ala
35 40 45

Ser Val Leu Asp Asp Asp Ala Ser Trp Val Thr His Thr Thr Ala Tyr
50 55 60

Trp Asp Arg Arg Val Leu Gly Ser Glu Asp Arg Ile Asp Leu Ala Ala
65 70 75 80

Val Lys

<210> 110
<211> 30
<212> PRT
<213> Penicillium coprobium PF1169

<400> 110

Asp Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His Tyr Ala Val Gln
1 5 10 15

Ser Leu Arg Asn Gly Glu Ser Thr Glu Ala Leu Ile Ala Gly
20 25 30

<210> 111
<211> 38
<212> PRT
<213> Penicillium coprobium PF1169

<400> 111

Gly Thr Gly Asn Gly Ser Ala Met Ile Ser Asn Arg Ile Ser Trp Phe
1 5 10 15

Phe Asp Leu Lys Gly Pro Ser Leu Ser Leu Asp Thr Ala Cys Ser Ser
20 25 30

Ser Leu Val Ala Leu His
35

<210> 112
<211> 72
<212> PRT
<213> Penicillium coprobium PF1169

<400> 112

Thr Ser Thr Gln Leu Asn Asp Leu Asn Glu Thr Asn Ala Ile Lys Lys
1 5 10 15

Val Phe Gly Lys Gln Ala Tyr Asn Ile Pro Ile Ser Ser Thr Lys Ser
20 25 30

Tyr Thr Gly His Leu Ile Gly Ala Ala Gly Thr Met Glu Thr Ile Phe
35 40 45

Cys Ile Lys Thr Met Gln Glu Lys Ile Ala Pro Ala Thr Thr Asn Leu
50 55 60

Lys Glu Arg Asp Ser Asn Cys Asp
65 70

<210> 113
<211> 50
<212> PRT
<213> Penicillium coprobium PF1169

<400> 113

Val Ile Val Gly Ser Ala Ala Asn Gln Asn Leu Asn Leu Ser His Ile
1 5 10 15

Thr Val Pro His Ser Gly Ser Gln Val Lys Leu Tyr Gln Asn Val Met
20 25 30

Ser Gln Ala Gly Val His Pro His Ser Val Thr Tyr Val Glu Ala His
35 40 45

Gly Thr
50

<210> 114
<211> 48
<212> PRT
<213> Penicillium coprobium PF1169

<400> 114

Leu Pro Thr Ala Ile Gln Pro Leu Phe Arg Ala Asn Val Ser Tyr Leu
1 5 10 15

Leu Val Gly Gly Leu Gly Gly Ile Gly Lys Glu Val Ala Leu Trp Met
20 25 30

Val Gln Asn Gly Ala Lys Ser Leu Ile Phe Val Asn Arg Ser Gly Leu
35 40 45

<210> 115
<211> 53
<212> PRT
<213> Penicillium coprobium PF1169

<400> 115

Val Ala Ile Val Gly Gly Val Asn Ala Leu Cys Gly Pro Gly Leu Thr
1 5 10 15

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

Ser Phe Asp Asp Asp Ala His Gly Tyr Ala Arg Gly Glu Gly Ala Gly
35 40 45

Ala Leu Val Leu Lys
50

<210> 116
<211> 28
<212> PRT
<213> Penicillium coprobium PF1169

<400> 116

Pro Trp Glu Ser Pro Gly Ala Arg Arg Val Ser Val Asn Ser Phe Gly
1 5 10 15

Tyr Gly Gly Ser Asn Ala His Val Ile Ile Glu Asp
20 25

<210> 117
<211> 72
<212> PRT
<213> Penicillium coprobium PF1169

<400> 117

Lys Thr Leu Arg Glu Trp Met Thr Ala Glu Gly Lys Asp His Asn Leu
1 5 10 15

Ser Asp Ile Leu Thr Thr Leu Ala Thr Arg Arg Asp His His Asp Tyr
20 25 30

Arg Ala Ala Leu Val Val Asp Asp Asn Arg Asp Ala Glu Leu Ala Leu
35 40 45

Gln Ala Leu Glu His Gly Val Asp Gln Thr Phe Thr Thr Gln Ser Arg
50 55 60

Val Phe Gly Ala Asp Ile Ser Lys
65 70

<210> 118
<211> 80
<212> PRT
<213> Penicillium coprobium PF1169

<400> 118

Ser Asp Asp Tyr Arg Glu Val Asn Ser Gly Gln Asp Ile Asp Thr Tyr
1 5 10 15

Phe Ile Pro Gly Gly Asn Arg Ala Phe Thr Pro Gly Arg Ile Asn Tyr
20 25 30

Tyr Phe Lys Phe Ser Gly Pro Ser Val Ser Val Asp Thr Ala Cys Ser
35 40 45

Ser Ser Leu Ala Ala Ile His Val Ala Cys Asn Ser Leu Trp Arg Asn
50 55 60

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

<210> 119
<211> 56
<212> PRT
<213> Penicillium coprobium PF1169

<400> 119

Leu Ser Ser Asp Gly Arg Cys His Thr Phe Asp Glu Lys Ala Asn Gly
1 5 10 15

Tyr Ala Arg Gly Glu Ala Val Gly Cys Leu Ile Leu Lys Pro Leu Ala
20 25 30

Lys Ala Leu His Asp Gln Asn Lys Ile Arg Ala Val Ile Arg Gly Thr
35 40 45

Gly Ser Asn Gln Gly Arg Ala Asn
50 55

<210> 120
<211> 63
<212> PRT
<213> Penicillium coprobium PF1169

<400> 120

Asp Thr Ala Cys Ser Ser Ser Leu Tyr Ala Leu His Ser Ala Cys Leu
1 5 10 15

Ala Leu Asp Ser Arg Asp Cys Asp Gly Ala Val Val Ala Ala Ala Asn
20 25 30

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

Leu Ser Pro Asp Ser Met Cys His Thr Phe Asp Glu Ser Ala Asn
50 55 60

<210> 121
<211> 28
<212> PRT
<213> Penicillium coprobium PF1169

<400> 121

Pro Trp Pro Thr Thr Gly Leu Arg Arg Ala Ser Val Asn Ser Phe Gly
1 5 10 15

Tyr Gly Gly Thr Asn Ala His Cys Val Leu Asp Asp
20 25

<210> 122
<211> 62
<212> PRT
<213> Penicillium coprobium PF1169

<400> 122

Ala Gly Ile Pro Leu Ala Asn Ile Met Gly Thr Lys Thr Ser Cys Phe
1 5 10 15

Val Gly Ser Phe Ser Ala Asp Tyr Thr Asp Leu Leu Leu Arg Asp Pro
20 25 30

Glu Cys Val Pro Met Tyr Gln Cys Thr Asn Ala Gly Gln Ser Arg Ala
35 40 45

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

<210> 123
<211> 80
<212> PRT
<213> Penicillium coprobium PF1169

<400> 123

Arg Trp Glu Pro Tyr Tyr Arg Arg Asp Pro Arg Asn Glu Lys Phe Leu
1 5 10 15

Lys Gln Thr Thr Ser Arg Gly Tyr Phe Leu Asp His Leu Glu Asp Phe
20 25 30

Asp Cys Gln Phe Phe Gly Ile Ser Pro Lys Glu Ala Glu Gln Met Asp
35 40 45

Pro Gln Gln Arg Val Ser Leu Glu Val Ala Ser Glu Ala Leu Glu Asp
50 55 60

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

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<210> 124
<211> 28
<212> PRT
<213> Penicillium coprobium PF1169

<400> 124

Pro Gly Arg Ile Asn Tyr Phe Phe Lys Phe Ser Gly Pro Ser Phe Ser
1 5 10 15

Ile Asp Thr Ala Cys Ser Ser Ser Leu Ala Thr Ile
20 25

<210> 125
<211> 64
<212> PRT
<213> Penicillium coprobium PF1169

<400> 125

Ala Gly Ile Pro Leu Ala Asn Ile Met Gly Thr Lys Thr Ser Cys Phe
1 5 10 15

Val Gly Ser Phe Ser Ala Asp Tyr Thr Asp Leu Leu Leu Arg Asp Pro
20 25 30

Glu Cys Val Pro Met Tyr Gln Cys Thr Asn Ala Gly Gln Ser Arg Ala
35 40 45

Met Thr Ala Asn Arg Leu Ser Tyr Phe Phe Asp Leu Lys Gly Pro Ser
50 55 60

<210> 126
<211> 52
<212> PRT
<213> Penicillium coprobium PF1169

<400> 126

Glu Leu Arg His Gly Lys Asn Ile Asp Lys Pro Glu Tyr Ser Gln Pro
1 5 10 15

Leu Cys Thr Ala Ile Gln Ile Ala Leu Val Glu Leu Leu Glu Ser Phe
20 25 30

Gly Val Val Pro Lys Ala Val Val Gly His Ser Ser Gly Glu Ile Ala
35 40 45

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Ala Ala Tyr Val
50

<210> 127
<211> 38
<212> PRT
<213> Penicillium coprobium PF1169

<400> 127

Gln Pro Leu Cys Thr Ala Ile Gln Ile Ala Leu Val Glu Leu Leu Glu
1 5 10 15

Ser Phe Gly Val Val Pro Lys Ala Val Val Gly His Ser Ser Gly Glu
20 25 30

Ile Ala Ala Ala Tyr Val
35

<210> 128
<211> 86
<212> PRT
<213> Penicillium coprobium PF1169

<400> 128

Arg Leu Pro Gly Asp Val Ser Thr Pro Glu Glu Phe Trp Asp Leu Cys
1 5 10 15

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

Ala Gly Ser Phe Tyr His Pro Asn Ala Asp Arg Pro Gly Ser Phe Asn
35 40 45

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

Pro Phe Phe Asn Ile Thr Leu Gln Glu Ala Gln Thr Met Asp Pro Gln
65 70 75 80

Gln Arg Ile Phe Leu Glu
85

<210> 129

<211> 69
<212> PRT
<213> Penicillium coprobium PF1169

<400> 129

Gln Phe Phe His Ala His Gly Thr Gly Thr Gln Ala Gly Asp Pro Gln
1 5 10 15

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

Glu Thr Lys Leu Phe Val Gly Ser Ile Lys Thr Val Ile Gly His Thr
35 40 45

Glu Gly Ser Ala Gly Leu Ala Ser Leu Ile Gly Ser Ser Leu Ala Met
50 55 60

Lys His Gly Val Ile
65

<210> 130
<211> 64
<212> PRT
<213> Penicillium coprobium PF1169

<400> 130

Ala Gly Ile Pro Leu Ala Asn Ile Met Gly Thr Lys Thr Ser Cys Phe
1 5 10 15

Val Gly Ser Phe Ser Ala Asp Tyr Thr Asp Leu Leu Leu Arg Asp Pro
20 25 30

Glu Cys Val Pro Met Tyr Gln Cys Thr Asn Ala Gly Gln Ser Arg Ala
35 40 45

Met Thr Ala Asn Arg Leu Ser Tyr Phe Phe Asp Leu Lys Gly Pro Ser
50 55 60

<210> 131
<211> 67
<212> PRT
<213> Penicillium coprobium PF1169

<400> 131

Leu Asp Asp Leu Ala Phe Thr Val Asn Glu Arg Arg Ser Ile Phe Pro

1 5 10 15

Trp Lys Ala Ala Val Val Gly Asp Thr Met Glu Gly Leu Ala Ala Ser
20 25 30

Leu Ala Gln Asn Ile Lys Pro Arg Ser Val Leu Arg Met Pro Thr Leu
35 40 45

Gly Phe Val Phe Thr Gly Gln Gly Ala Gln Trp Pro Gly Met Gly Lys
50 55 60

Glu Leu Leu
65

<210> 132
<211> 21
<212> PRT
<213> Penicillium coprobium PF1169

<400> 132

Ala His Gly Thr Gly Thr Lys Val Gly Asp Pro Met Glu Val Glu Ala
1 5 10 15

Ile Ala Asp Val Phe
20

<210> 133
<211> 71
<212> PRT
<213> Penicillium coprobium PF1169

<400> 133

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

Ile Leu Asp Ala Met Arg Gly Asn Lys Ala Val Ile Ala Cys Val Asn
20 25 30

Ser Glu Ser Ser Val Thr Leu Ser Gly Asp Leu Asp Val Ile Ala Asn
35 40 45

Leu Gln Thr Ala Leu Asp Lys Glu Gly Ile Phe Thr Arg Lys Leu Lys
50 55 60

Val Asp Val Ala Tyr His Ser
65 70

<210> 134
<211> 75
<212> PRT
<213> Penicillium coprobium PF1169

<400> 134

Leu Glu Asn Leu Glu Thr Ala Leu Ala Arg Asn Ala Pro Ile Tyr Ala
1 5 10 15

Glu Val Thr Gly Tyr Ala Asn Tyr Ser Asp Ala Tyr Asp Ile Thr Ala
20 25 30

Pro Ala Asp Asp Leu Met Gly Arg Tyr Met Ser Ile Thr Lys Ala Ile
35 40 45

Glu Gln Ala Gln Leu Asn Ile Asn Glu Ile Asp Tyr Ile Asn Ala His
50 55 60

Gly Thr Ser Thr Gln Leu Asn Asp Leu Asn Glu
65 70 75

<210> 135
<211> 53
<212> PRT
<213> Penicillium coprobium PF1169

<400> 135

Met Ala Met Lys Lys Ala Leu Lys Gln Ala Gln Leu Arg Pro Ser Ala
1 5 10 15

Val Asp Tyr Val Asn Ala His Ala Thr Ser Thr Ile Val Gly Asp Ala
20 25 30

Ala Glu Asn Ala Ala Ile Lys Ala Leu Leu Leu Gly Ala Asp Gly Lys
35 40 45

Asp Lys Ala Ala Asp
50

<210> 136
<211> 38
<212> PRT

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<213> Penicillium coprobium PF1169

<400> 136

Gly Thr Gly Asn Gly Ser Ala Met Ile Ser Asn Arg Ile Ser Trp Phe
1 5 10 15

Phe Asp Leu Lys Gly Pro Ser Leu Ser Leu Asp Thr Ala Cys Ser Ser
20 25 30

Ser Leu Val Ala Leu His
35

<210> 137
<211> 76
<212> PRT
<213> Penicillium coprobium PF1169

<400> 137

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

Leu His Gln Ala Val Gln Ser Leu Arg Ser Gly Glu Thr Asp Val Ala
20 25 30

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

Glu Ser Lys Leu Lys Met Leu Ser Pro Asn Gly Arg Ser Arg Met Trp
50 55 60

Asp Lys Asp Ala Asp Gly Tyr Ala Arg Gly Asp Gly
65 70 75

<210> 138
<211> 85
<212> PRT
<213> Penicillium coprobium PF1169

<400> 138

Ile Gly Ser Ile Lys Pro Asn Ile Gly His Leu Glu Ala Gly Ala Gly
1 5 10 15

Val Met Gly Phe Ile Lys Ala Ile Leu Ser Ile Gln Lys Gly Val Leu
20 25 30

Ala Pro Gln Ala Asn Leu Thr Lys Leu Asn Ser Arg Ile Asp Trp Lys
35 40 45

Thr Ala Gly Val Lys Val Val Gln Glu Ala Thr Pro Trp Pro Ser Ser
50 55 60

Asp Ser Ile Arg Arg Ala Gly Val Cys Ser Tyr Gly Tyr Gly Gly Thr
65 70 75 80

Val Ser His Ala Val
85

<210> 139
<211> 57
<212> PRT
<213> Penicillium coprobium PF1169

<400> 139

Asn Ala Ala Gly Ala His Phe Leu Thr Glu Asp Ile Gly Leu Phe Asp
1 5 10 15

Ala Pro Phe Phe Asn Ile Thr Leu Gln Glu Ala Gln Thr Met Asp Pro
20 25 30

Gln Gln Arg Ile Phe Leu Glu Cys Val Tyr Glu Ala Leu Glu Asn Gly
35 40 45

Gly Ile Pro Thr His Glu Ile Thr Gly
50 55

<210> 140
<211> 68
<212> PRT
<213> Penicillium coprobium PF1169

<400> 140

Leu Ser Ser Asp Gly Arg Cys His Thr Phe Asp Glu Lys Ala Asn Gly
1 5 10 15

Tyr Ala Arg Gly Glu Ala Val Gly Cys Leu Ile Leu Lys Pro Leu Ala
20 25 30

Lys Ala Leu His Asp Gln Asn Lys Ile Arg Ala Val Ile Arg Gly Thr
35 40 45

Gly Ser Asn Gln Asp Gly Arg Thr Ala Gly Ile Thr Val Pro Asn Gly
50 55 60

Ala Ala Gln Glu
65

<210> 141
<211> 37
<212> PRT
<213> Penicillium coprobium PF1169

<400> 141

Ser Phe Asp Ser Arg Ala Glu Gly Tyr Ala Arg Gly Glu Gly Val Gly
1 5 10 15

Thr Val Val Val Lys Pro Leu Ser Thr Ala Ile Arg Asp Gly Asp Thr
20 25 30

Ile Arg Ala Val Ile
35

<210> 142
<211> 72
<212> PRT
<213> Penicillium coprobium PF1169

<400> 142

Gly Ile Pro Ile Asp Thr Leu Pro Gly Ser Asn Thr Ala Val Tyr Ser
1 5 10 15

Gly Ser Met Thr Asn Asp Tyr Glu Leu Leu Ser Thr Arg Asp Ile Tyr
20 25 30

Asp Met Pro His Asn Ser Ala Thr Gly Asn Gly Arg Thr Met Leu Ala
35 40 45

Asn Arg Leu Ser Trp Phe Phe Asp Leu Gln Gly Pro Ser Ile Met Met
50 55 60

Asp Thr Ala Cys Ser Ser Ser Leu
65 70

<210> 143

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<211> 83
<212> PRT
<213> Penicillium coprobium PF1169

<400> 143

Ala Gln Gln Ser Leu Ile Leu Ala Thr Tyr Ala Arg Ala Gly Leu Ser
1 5 10 15

Pro Gln Asn Asn Pro Glu Asp Arg Cys Gln Tyr Phe Glu Ala His Gly
20 25 30

Thr Gly Thr Gln Ala Gly Asp Pro Gln Glu Ala Ala Ala Ile Asn Ser
35 40 45

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

Val Gly Ser Ile Lys Thr Ile Ile Gly His Thr Glu Ala Thr Ala Gly
65 70 75 80

Leu Ala Gly

<210> 144
<211> 69
<212> PRT
<213> Penicillium coprobium PF1169

<400> 144

Pro Leu Trp Arg Lys Ile Glu Thr Ala Pro Leu Asn Thr Gly Leu Thr
1 5 10 15

His Asp Val Glu Lys His Thr Leu Leu Gly Gln Arg Ile Pro Val Ala
20 25 30

Gly Thr Asp Thr Phe Val Tyr Thr Thr Arg Leu Asp Asn Glu Thr Lys
35 40 45

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

Ala Gly Leu Ile Asn
65

<210> 145
<211> 64
<212> PRT
<213> Penicillium coprobium PF1169

<400> 145

Ala Gly Ile Pro Leu Ala Asn Ile Met Gly Thr Lys Thr Ser Cys Phe
1 5 10 15

Val Gly Ser Phe Ser Ala Asp Tyr Thr Asp Leu Leu Leu Arg Asp Pro
20 25 30

Glu Cys Val Pro Met Tyr Gln Cys Thr Asn Ala Gly Gln Ser Arg Ala
35 40 45

Met Thr Ala Asn Arg Leu Ser Tyr Phe Phe Asp Leu Lys Gly Pro Ser
50 55 60

<210> 146
<211> 81
<212> PRT
<213> Penicillium coprobium PF1169

<400> 146

Gly Tyr Gly Arg Gly Glu Gly Val Ala Ser Val Val Leu Lys Arg Leu
1 5 10 15

Gln Asp Ala Ile Asn Asp Gly Asp Pro Ile Glu Cys Val Ile Arg Ala
20 25 30

Ser Gly Ala Asn Ser Asp Gly Arg Thr Met Gly Ile Thr Met Pro Asn
35 40 45

Pro Lys Ala Gln Gln Ser Leu Ile Leu Ala Thr Tyr Ala Arg Ala Gly
50 55 60

Leu Ser Pro Gln Asn Asn Pro Glu Asp Arg Cys Gln Tyr Phe Glu Ala
65 70 75 80

His

<210> 147
<211> 38
<212> PRT

<213> Penicillium coprobium PF1169

<400> 147

Gly Thr Gly Asn Gly Ser Ala Met Ile Ser Asn Arg Ile Ser Trp Phe
1 5 10 15

Phe Asp Leu Lys Gly Pro Ser Leu Ser Leu Asp Thr Ala Cys Ser Ser
20 25 30

Ser Leu Val Ala Leu His
35

<210> 148
<211> 53
<212> PRT
<213> Penicillium coprobium PF1169

<400> 148

Glu Ala Thr Ser Met Asp Ala Gln Gln Arg Lys Leu Leu Glu Val Thr
1 5 10 15

Tyr Glu Ala Leu Glu Asn Ala Gly Val Pro Leu Glu Thr Ile Gln Gly
20 25 30

Ser Asn Thr Gly Val Tyr Val Gly Asn Phe Thr Asn Asp Phe Leu Asn
35 40 45

Met Gln Tyr Lys Asp
50

<210> 149
<211> 82
<212> PRT
<213> Penicillium coprobium PF1169

<400> 149

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

Arg Tyr Ile Gln Gly Ala Asp Ile Val Arg Ile Ser Asp Gly Ile Ala
20 25 30

Arg Thr Ser Arg Phe Arg Ser Leu Pro Arg Thr Lys Leu Arg Pro Val
35 40 45

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

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

Glu Lys

<210> 150
<211> 65
<212> PRT
<213> Penicillium coprobium PF1169

<400> 150

Gln Leu Gly Thr Thr Cys Val Gln Met Ala Leu Thr Lys Tyr Trp Thr
1 5 10 15

Ser Leu Gly Val Thr Pro Ser Phe Val Met Gly His Ser Leu Gly Glu
20 25 30

Phe Ala Ala Leu Asn Ala Ala Gly Val Leu Thr Ile Ser Asp Thr Ile
35 40 45

Tyr Leu Ala Gly Arg Arg Ala Gln Leu Leu Thr Glu Gln Ile Lys Val
50 55 60

Gly
65

<210> 151
<211> 78
<212> PRT
<213> Penicillium coprobium PF1169

<220>
<221> misc_feature
<222> (45)..(45)
<223> Xaa can be any naturally occurring amino acid

<400> 151

Gly Pro Arg Leu Leu Pro Arg Pro Glu Gly Thr Tyr Leu Ile Thr Gly
1 5 10 15

Gly Leu Gly Ile Leu Gly Leu Glu Val Ala Asp Phe Leu Val Glu Lys
20 25 30

Gly Ala Arg Arg Val Leu Leu Ile Ser Arg Arg Ala Xaa Pro Pro Arg
35 40 45

Arg Thr Trp Asp Gln Val Ala Thr Glu Phe Gln Pro Ala Ile Thr Lys
50 55 60

Ile Arg Leu Leu Glu Ser Arg Gly Ala Ser Val Tyr Val Leu
65 70 75

<210> 152
<211> 76
<212> PRT
<213> Penicillium coprobium PF1169

<400> 152

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

Leu His Gln Ala Val Gln Ser Leu Arg Ser Gly Glu Thr Asp Val Ala
20 25 30

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

Glu Ser Lys Leu Lys Met Leu Ser Pro Asn Gly Arg Ser Arg Met Trp
50 55 60

Asp Lys Asp Ala Asp Gly Tyr Ala Arg Gly Asp Gly
65 70 75

<210> 153
<211> 38
<212> PRT
<213> Penicillium coprobium PF1169

<400> 153

Asn Arg Ile Ser Tyr Phe Phe Asp Leu Arg Gly Pro Ser Ile Thr Ile
1 5 10 15

Asp Thr Ala Cys Ser Ser Ser Leu Val Ala Leu His Tyr Ala Val Gln
20 25 30

Ser Leu Arg Asn Gly Glu
35

<210> 154
<211> 74
<212> PRT
<213> Penicillium coprobium PF1169

<400> 154

Gly Ser Gly Leu Thr Val Leu Ala Asn Arg Ile Thr His Cys Phe Asp
1 5 10 15

Leu Arg Gly Pro Ser His Val Val Asp Thr Ala Cys Ser Ser Ser Leu
20 25 30

Tyr Ala Leu His Ser Ala Cys Leu Ala Leu Asp Ser Arg Asp Cys Asp
35 40 45

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

Met Ile Ala Val Lys Ala Gly Ile Leu Ser
65 70

<210> 155
<211> 57
<212> PRT
<213> Penicillium coprobium PF1169

<400> 155

Gln Leu Gly Thr Thr Cys Val Gln Met Ala Leu Thr Lys Tyr Trp Thr
1 5 10 15

Ser Leu Gly Val Thr Pro Ser Phe Val Met Gly His Ser Leu Gly Glu
20 25 30

Phe Ala Ala Leu Asn Ala Ala Gly Val Leu Thr Ile Ser Asp Thr Ile
35 40 45

Tyr Leu Ala Gly Arg Arg Ala Gln Leu
50 55

<210> 156
<211> 72

<212> PRT
<213> Penicillium coprobium PF1169

<400> 156

His Leu Asn Leu Met Gly Pro Ser Thr Ala Val Asp Ala Ala Cys Ala
1 5 10 15

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

Glu Ser Arg Val Ala Ile Val Gly Gly Val Asn Ala Leu Cys Gly Pro
35 40 45

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

Ser Cys Lys Ser Phe Asp Asp Asp
65 70

<210> 157
<211> 81
<212> PRT
<213> Penicillium coprobium PF1169

<400> 157

Leu Lys Gly Thr Gly Gly Gln Met Leu Gln Asn Val Val Leu Arg Val
1 5 10 15

Pro Val Ala Ile Asn Ala Pro Arg Ser Val Gln Val Val Val Gln Gln
20 25 30

Asp Gln Val Lys Val Val Ser Arg Leu Ile Pro Ser Glu Ala Ser Val
35 40 45

Leu Asp Asp Asp Ala Ser Trp Val Thr His Thr Thr Ala Tyr Trp Asp
50 55 60

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

Ser

<210> 158

<211> 82
<212> PRT
<213> Penicillium coprobium PF1169

<400> 158

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

Tyr Thr Asp Leu Leu Leu Arg Asp Pro Glu Cys Val Pro Met Tyr Gln
20 25 30

Cys Thr Asn Ala Gly Gln Ser Arg Ala Met Thr Ala Asn Arg Leu Ser
35 40 45

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

Ser Gly Ser Leu Val Ala Leu His Leu Ala Cys Gln Ser Leu Arg Thr
65 70 75 80

Gly Asp

<210> 159
<211> 75
<212> PRT
<213> Penicillium coprobium PF1169

<400> 159

Gly Ser Gly Leu Thr Val Leu Ala Asn Arg Ile Thr His Cys Phe Asp
1 5 10 15

Leu Arg Gly Pro Ser His Val Val Asp Thr Ala Cys Ser Ser Ser Leu
20 25 30

Tyr Ala Leu His Ser Ala Cys Phe Gly Pro Leu Asn Ser Arg Asp Cys
35 40 45

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

Gln Met Ile Ala Val Lys Arg Asp Ser Ile Ala
65 70 75

<210> 160
<211> 28
<212> PRT
<213> Penicillium coprobium PF1169

<400> 160

Pro Trp Pro Thr Thr Gly Leu Arg Arg Ala Ser Val Asn Ser Phe Gly
1 5 10 15

Tyr Gly Gly Thr Asn Ala His Cys Val Leu Asp Asp
20 25

<210> 161
<211> 64
<212> PRT
<213> Penicillium coprobium PF1169

<400> 161

Gln Leu Gly Thr Thr Cys Val Gln Met Ala Leu Thr Lys Tyr Trp Thr
1 5 10 15

Ser Leu Gly Val Thr Pro Ser Phe Val Met Gly His Ser Leu Gly Glu
20 25 30

Phe Ala Ala Leu Asn Ala Ala Gly Val Leu Thr Ile Ser Asp Thr Ile
35 40 45

Tyr Leu Ala Gly Arg Arg Ala Gln Leu Leu Thr Glu Gln Ile Glu Gly
50 55 60

<210> 162
<211> 60
<212> PRT
<213> Penicillium coprobium PF1169

<400> 162

Ile Ala Pro Asn Ile His Phe Lys Met Pro Asn Pro Gln Ile Pro Phe
1 5 10 15

Asn Glu Ala Asn Leu His Val Pro Leu Glu Pro Thr Pro Trp Pro Ala
20 25 30

Gly Arg Pro Glu Arg Ile Ser Val Asn Ser Phe Gly Ile Gly Gly Ser
35 40 45

Asn Ala His Ala Ile Leu Glu Ser Ala Ser Thr Val
50 55 60

<210> 163
<211> 34
<212> PRT
<213> Penicillium coprobium PF1169

<400> 163

Gly Leu Val Asn Ile Leu Arg Ser Trp Gly Ile Glu Pro Ser Thr Val
1 5 10 15

Val Gly His Ser Ser Gly Glu Ile Val Ala Ala Tyr Thr Ala Arg Ala
20 25 30

Ile Ser

<210> 164
<211> 51
<212> PRT
<213> Penicillium coprobium PF1169

<400> 164

Pro Trp Pro Ser Glu Gly Leu Arg Arg Ile Ser Val Asn Ser Phe Gly
1 5 10 15

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

Met Gln Gln Arg Gly Leu Thr Gly Asn His Cys Thr Ala Arg Leu Pro
35 40 45

Gly Ile Leu
50

<210> 165
<211> 71
<212> PRT
<213> Penicillium coprobium PF1169

<220>
<221> misc_feature
<222> (5)..(5)
<223> Xaa can be any naturally occurring amino acid

<400> 165

Ile Gly His Thr Xaa Gly Ser Ala Gly Leu Ala Ser Leu Ile Gly Ser
1 5 10 15

Ser Leu Ala Met Lys His Gly Val Ile Pro Pro Asn Leu His Phe Gly
20 25 30

Gln Leu Ser Glu Lys Val Ala Pro Phe Tyr Thr His Leu Asn Ile Pro
35 40 45

Thr Glu Pro Val Pro Trp Pro Asn Ser Thr Ser Ser Gln Val Lys Arg
50 55 60

Ala Ser Ile Asn Ser Phe Gly
65 70

<210> 166
<211> 74
<212> PRT
<213> Penicillium coprobium PF1169

<400> 166

Gly Ser Asn Thr Ala Val Tyr Ser Gly Ser Met Thr Asn Asp Tyr Glu
1 5 10 15

Leu Leu Ser Thr Arg Asp Ile Tyr Asp Met Pro His Asn Ser Ala Thr
20 25 30

Gly Asn Gly Arg Thr Met Leu Ala Asn Arg Leu Ser Trp Phe Phe Asp
35 40 45

Leu Gln Gly Pro Ser Ile Met Met Asp Thr Ala Cys Ser Ser Ser Leu
50 55 60

Thr Ala Val His Leu Ala Ala Gln Ser Leu
65 70

<210> 167
<211> 85
<212> PRT
<213> Penicillium coprobium PF1169

<400> 167

Asp Ala Gln Phe Phe Gly Thr Lys Pro Val Glu Ala Asn Ser Ile Asp

1 5 10 15

Pro Gln Gln Arg Leu Leu Leu Glu Thr Val Tyr Glu Gly Leu Glu Thr
20 25 30

Ser Gly Ile Pro Met Glu Arg Leu Gln Gly Ser Asn Thr Ala Val Tyr
35 40 45

Val Gly Leu Met Thr Asn Asp Tyr Ala Asp Met Leu Gly Arg Asp Met
50 55 60

Gln Asn Phe Pro Thr Tyr Phe Ala Ser Gly Thr Ala Arg Ser Ile Leu
65 70 75 80

Ser Asn Arg Val Ser
85

<210> 168
<211> 60
<212> PRT
<213> Penicillium coprobium PF1169

<400> 168

Val Val Ala Cys Val Asn Ser Pro Ala Ser Thr Thr Leu Ser Gly Asp
1 5 10 15

Val Asp Tyr Ile Asn Gln Leu Glu Ala Arg Leu Gln Gln Asp Gly His
20 25 30

Phe Ala Arg Lys Leu Arg Ile Asp Thr Ala Tyr His Ser Pro His Met
35 40 45

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

<210> 169
<211> 56
<212> PRT
<213> Penicillium coprobium PF1169

<400> 169

Phe Tyr Gly Met Thr Ser Asp Asp Tyr Arg Glu Val Asn Ser Gly Gln
1 5 10 15

Asp Ile Asp Thr Tyr Phe Ile Pro Gly Gly Asn Arg Ala Phe Thr Pro
20 25 30

Gly Arg Ile Asn Tyr Tyr Phe Lys Phe Ser Gly Pro Ser Val Ser Val
35 40 45

Asp Thr Ala Cys Ser Ser Ser Leu
50 55

<210> 170
<211> 53
<212> PRT
<213> Penicillium coprobium PF1169

<400> 170

Val Ala Ile Val Gly Gly Val Asn Ala Leu Cys Gly Pro Gly Leu Thr
1 5 10 15

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

Ser Phe Asp Asp Asp Ala His Gly Tyr Ala Arg Gly Glu Gly Ala Gly
35 40 45

Ala Leu Val Thr Lys
50

<210> 171
<211> 40
<212> PRT
<213> Penicillium coprobium PF1169

<400> 171

Gln Leu Gly Thr Thr Cys Val Gln Met Ala Leu Thr Lys Tyr Trp Thr
1 5 10 15

Ser Leu Gly Val Thr Pro Ser Phe Val Met Gly His Ser Leu Gly Glu
20 25 30

Phe Ala Ala Leu Asn Ala Ala Gly
35 40

<210> 172
<211> 69
<212> PRT

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<213> Penicillium coprobium PF1169

<400> 172

Arg Glu Trp Met Thr Ala Glu Gly Lys Asp His Asn Leu Ser Asp Ile
1 5 10 15

Leu Thr Thr Leu Ala Thr Arg Arg Asp His His Asp Tyr Arg Ala Ala
20 25 30

Leu Val Val Asp Asp Asn Arg Asp Ala Glu Leu Ala Leu Gln Ala Leu
35 40 45

Glu His Gly Val Asp Gln Thr Phe Thr Thr Gln Ser Arg Val Phe Gly
50 55 60

Ala Asp Ile Ser Lys
65

<210> 173
<211> 51
<212> PRT
<213> Penicillium coprobium PF1169

<400> 173

Pro Trp Pro Ser Glu Gly Leu Arg Arg Ile Ser Val Asn Ser Phe Gly
1 5 10 15

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

Met Gln Gln Arg Gly Leu Thr Gly Asn His Cys Thr Ala Arg Leu Pro
35 40 45

Gly Ile Leu
50

<210> 174
<211> 71
<212> PRT
<213> Penicillium coprobium PF1169

<400> 174

Phe Val Glu Met His Gly Thr Gly Thr Lys Ala Gly Asp Pro Val Glu
1 5 10 15

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

Pro Leu Tyr Ile Gly Ser Val Lys Ser Asn Ile Gly His Leu Glu Gly
35 40 45

Ala Ser Gly Ile Val Ala Val Ile Lys Ala Ala Met Met Leu Asp Arg
50 55 60

Asp Leu Met Leu Pro Asn Ala
65 70

<210> 175
<211> 41
<212> PRT
<213> Penicillium coprobium PF1169

<400> 175

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

Pro Gln Glu Leu Trp Glu Leu Cys Ser Arg Gly Arg Ser Ala Trp Ser
20 25 30

Glu Ile Pro Pro Glu Arg Phe Asn Pro
35 40

<210> 176
<211> 64
<212> PRT
<213> Penicillium coprobium PF1169

<400> 176

Gln Leu Gly Thr Thr Cys Val Gln Met Ala Leu Thr Lys Tyr Trp Thr
1 5 10 15

Ser Leu Gly Val Thr Pro Ser Phe Val Met Gly His Ser Leu Gly Glu
20 25 30

Phe Ala Ala Leu Asn Ala Ala Gly Val Leu Thr Ile Ser Asp Thr Ile
35 40 45

Tyr Leu Ala Gly Arg Arg Ala Gln Leu Leu Thr Glu Gln Ile Glu Gly
50 55 60

<210> 177
<211> 74
<212> PRT
<213> Penicillium coprobium PF1169

<400> 177

Gly Ala Ser Val Tyr Val Leu Ala Leu Asp Ile Thr Lys Pro Asp Ala
1 5 10 15

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

Gln Gly Val Val His Ala Ala Gly Val Leu Asp Asn Glu Leu Val Met
35 40 45

Gln Thr Thr Gln Glu Ala Phe Asn Arg Val Leu Ala Pro Lys Ile Ala
50 55 60

Gly Ala Leu Ala Leu His Glu Pro Phe Pro
65 70

<210> 178
<211> 72
<212> PRT
<213> Penicillium coprobium PF1169

<400> 178

Gly Leu Val Asn Ile Leu Arg Ser Trp Gly Ile Glu Pro Ser Thr Val
1 5 10 15

Val Gly His Ser Ser Gly Glu Ile Val Ala Ala Tyr Thr Ala Arg Ala
20 25 30

Ile Ser Met Arg Thr Ala Ile Ile Leu Ala Tyr Tyr Arg Gly Lys Val
35 40 45

Ala Gln Pro Leu Glu Gly Leu Gly Ala Met Val Ala Val Gly Leu Ser
50 55 60

Pro Asp Glu Val Ala Gln Tyr Met
65 70

<210> 179

<211> 70
<212> PRT
<213> Penicillium coprobium PF1169

<400> 179

Gly Arg Phe Leu Ser Ser Asp Gly Arg Cys His Thr Phe Asp Glu Lys
1 5 10 15

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

Pro Leu Ala Lys Ala Leu His Asp Gln Asn Lys Ile Arg Ala Val Ile
35 40 45

Arg Gly Thr Gly Ser Asn Gln Asp Gly Arg Thr Ala Gly Ile Thr Val
50 55 60

Pro Asn Gly Ala Ala Gln
65 70

<210> 180
<211> 51
<212> PRT
<213> Penicillium coprobium PF1169

<400> 180

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

Gln Gly Gly Thr Gly Gln Val Val Met Glu Ser Asp Leu Met Gln Thr
20 25 30

Glu Phe Leu Glu Ala Ala Asn Gly His Arg Met Asn Asp Cys Gly Val
35 40 45

Val Thr Ser
50

<210> 181
<211> 64
<212> PRT
<213> Penicillium coprobium PF1169

<400> 181

Leu Leu Gly Leu Arg Leu Lys Trp Lys Glu Tyr His Gln Asp Phe Asn

1 5 10 15

Ala Ala His Arg Val Leu Pro Leu Pro Ser Tyr Lys Trp Asp Leu Lys
20 25 30

Asn Tyr Trp Ile Pro Tyr Thr Asn Asn Phe Cys Leu Leu Lys Gly Ala
35 40 45

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

<210> 182
<211> 26
<212> PRT
<213> Penicillium coprobium PF1169

<400> 182

Ser Phe Arg Arg Gln Glu Asp Thr Trp Lys Val Leu Ser Asn Ala Thr
1 5 10 15

Ser Thr Leu Tyr Leu Ala Gly Ile Glu Ile
20 25

<210> 183
<211> 65
<212> PRT
<213> Penicillium coprobium PF1169

<400> 183

Ala Gly Gly Asn Thr Thr Val Ala Leu Glu Asp Ala Pro Ile Arg Thr
1 5 10 15

Arg Ser Gly Ser Asp Pro Arg Ser Leu His Pro Ile Ala Ile Ser Ala
20 25 30

Lys Ser Lys Val Ser Leu Arg Gly Asn Leu Glu Asn Leu Leu Ala Tyr
35 40 45

Leu Asp Thr His Pro Asp Val Ser Leu Ser Asp Leu Ser Tyr Thr Thr
50 55 60

Thr
65

<210> 184
<211> 96
<212> PRT
<213> Penicillium coprobium PF1169

<400> 184

Phe Asp Ala Ala Phe Phe Asn Met Ser Pro Arg Glu Ala Gln Gln Thr
1 5 10 15

Asp Pro Met Gln Arg Leu Ala Ile Val Thr Ala Tyr Glu Ala Leu Glu
20 25 30

Arg Ala Gly Tyr Val Ala Asn Arg Thr Ala Ala Thr Asn Leu His Arg
35 40 45

Ile Gly Thr Phe Tyr Gly Gln Ala Ser Asp Asp Tyr Arg Glu Val Asn
50 55 60

Thr Ala Gln Glu Ile Ser Thr Tyr Phe Ile Pro Gly Gly Cys Arg Ala
65 70 75 80

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

<210> 185
<211> 58
<212> PRT
<213> Penicillium coprobium PF1169

<400> 185

Phe Leu Gln Ile Ser Gly Pro Ser Phe Ser Ile Asp Thr Ala Cys Ser
1 5 10 15

Ser Ser Leu Ala Thr Ile Gln Val Cys Thr His Leu Phe His Val His
20 25 30

Leu Asn Arg Gln Leu Thr Ile Ala Ala Cys Thr Ser Leu Trp Asn Gly
35 40 45

Glu Thr Asp Thr Val Val Ala Gly Gly Met
50 55

<210> 186
<211> 59
<212> PRT

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<213> Penicillium coprobium PF1169

<400> 186

Val Tyr Ser Gly Ser Met Thr Asn Asp Tyr Glu Leu Leu Ser Thr Arg
1 5 10 15

Asp Ile Tyr Asp Met Pro His Asn Ser Ala Thr Gly Asn Gly Arg Thr
20 25 30

Met Leu Ala Asn Arg Leu Ser Trp Phe Phe Asp Leu Gln Gly Pro Ser
35 40 45

Ile Met Met Asp Thr Ala Cys Ser Ser Ser Leu
50 55

<210> 187
<211> 31
<212> PRT
<213> Penicillium coprobium PF1169

<400> 187

Leu Phe Leu Phe Pro Asp Gly Ser Gly Ser Ala Thr Ser Tyr Ala Thr
1 5 10 15

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

<210> 188
<211> 26
<212> PRT
<213> Penicillium coprobium PF1169

<400> 188

Ala Lys His Pro Pro Ala Thr Ser Ile Leu Leu Gln Gly Asn Pro Lys
1 5 10 15

Thr Ala Thr Gln Ser Phe Ile Phe Val Pro
20 25

<210> 189
<211> 38
<212> PRT
<213> Penicillium coprobium PF1169

<400> 189

Gly Asn Gly Ser Ala Met Ile Ser Asn Arg Ile Ser Trp Phe Phe Asp
1 5 10 15

Leu Lys Gly Pro Ser Leu Ser Leu Asp Thr Ala Cys Ser Ser Ser Leu
20 25 30

Val Ala Leu His Leu Ala
35

<210> 190
<211> 76
<212> PRT
<213> Penicillium coprobium PF1169

<400> 190

Ala Ile His His Gly Val Gln Ala Ile Lys Leu Gly Glu Ser Arg Val
1 5 10 15

Ala Ile Val Gly Gly Val Asn Ala Leu Cys Gly Pro Gly Leu Thr Arg
20 25 30

Val Leu Asp Lys Ala Gly Ala Ile Ser Ser Asp Gly Ser Cys Lys Ser
35 40 45

Phe Asp Asp Asp Ala His Gly Tyr Ala Arg Gly Glu Gly Ala Gly Ala
50 55 60

Leu Val Leu Lys Ser Leu His Gln Ala Leu Leu Asp
65 70 75

<210> 191
<211> 65
<212> PRT
<213> Penicillium coprobium PF1169

<400> 191

Val Trp Ile Glu Ile Gly Pro His Pro Val Cys Leu Gly Phe Val Lys
1 5 10 15

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

Glu Asn Ala Trp Cys Thr Leu Ala Gln Ser Leu Thr Thr Leu His Asn
35 40 45

Ala Gly Val Pro Val Gly Trp Ser Glu Phe His Arg Pro Phe Glu Arg
50 55 60

Ala
65

<210> 192
<211> 53
<212> PRT
<213> Penicillium coprobium PF1169

<400> 192

Thr Ser Asp Asp Tyr Arg Glu Val Asn Ser Gly Gln Asp Ile Asp Thr
1 5 10 15

Tyr Phe Ile Pro Gly Gly Asn Arg Ala Phe Thr Pro Gly Arg Ile Asn
20 25 30

Tyr Tyr Phe Lys Phe Ser Gly Pro Ser Val Ser Val Asp Thr Ala Cys
35 40 45

Ser Ser Ser Leu Ala
50

<210> 193
<211> 40
<212> PRT
<213> Penicillium coprobium PF1169

<400> 193

Val Asp Thr Ala Cys Ser Ser Ser Leu Tyr Ala Leu His Ser Ala Cys
1 5 10 15

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

Ala Asn Leu Ile Gln Ser Pro Glu
35 40

<210> 194
<211> 68
<212> PRT
<213> Penicillium coprobium PF1169

<400> 194

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

Ala Met Arg Gly Asn Lys Ala Val Ile Ala Cys Val Asn Ser Glu Ser
20 25 30

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

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

Ala Tyr His Ser
65

<210> 195
<211> 62
<212> PRT
<213> Penicillium coprobium PF1169

<400> 195

Phe Leu Asp Asp Leu Ala Phe Thr Val Asn Glu Arg Arg Ser Ile Phe
1 5 10 15

Pro Trp Lys Ala Ala Val Val Gly Asp Thr Met Glu Gly Leu Ala Ala
20 25 30

Ser Leu Ala Gln Asn Ile Lys Pro Arg Ser Val Leu Arg Met Pro Thr
35 40 45

Leu Gly Phe Val Phe Thr Gly Gln Gly Ala Gln Trp Pro Gly
50 55 60

<210> 196
<211> 76
<212> PRT
<213> Penicillium coprobium PF1169

<400> 196

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

Leu His Gln Ala Val Gln Ser Leu Arg Ser Gly Glu Thr Asp Val Ala
20 25 30

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

Glu Ser Lys Leu Lys Met Leu Ser Pro Asn Gly Arg Ser Arg Met Trp
50 55 60

Asp Lys Asp Ala Asp Gly Tyr Ala Arg Gly Asp Gly
65 70 75

<210> 197
<211> 79
<212> PRT
<213> Penicillium coprobium PF1169

<400> 197

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

Thr Cys Val Gln Met Ala Leu Thr Lys Tyr Trp Thr Ser Leu Gly Val
20 25 30

Thr Pro Ser Phe Val Met Gly His Ser Leu Gly Glu Phe Ala Ala Leu
35 40 45

Asn Ala Ala Gly Val Leu Thr Ile Ser Asp Thr Ile Tyr Leu Ala Gly
50 55 60

Arg Arg Ala Gln Leu Leu Thr Glu Gln Ile Glu Gly Gly Thr His
65 70 75

<210> 198
<211> 40
<212> PRT
<213> Penicillium coprobium PF1169

<400> 198

Phe Asn Leu Lys Gly Ile Ser Gln Ser Ile Ala Ser Ala Cys Ala Thr
1 5 10 15

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

Gln Asp Leu Met Leu Ala Gly Gly

35 40

<210> 199
<211> 70
<212> PRT
<213> Penicillium coprobium PF1169

<400> 199

Gly Arg Phe Leu Ser Ser Asp Gly Arg Cys His Thr Phe Asp Glu Lys
1 5 10 15

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

Pro Leu Ala Lys Ala Leu His Asp Gln Asn Lys Ile Arg Ala Val Ile
35 40 45

Arg Gly Thr Gly Ser Asn Gln Asp Gly Arg Thr Ala Gly Ile Thr Val
50 55 60

Pro Asn Gly Ala Ala Gln
65 70

<210> 200
<211> 284
<212> PRT
<213> Penicillium coprobium PF1169

<400> 200

Leu Ser Val Lys Arg Val Gly Ile His Asp Asp Phe Phe Glu Leu Gly
1 5 10 15

Gly His Ser Leu Leu Ala Val Lys Leu Val Asn His Leu Lys Lys Val
20 25 30

Phe Gly Thr Glu Leu Ser Val Ala Leu Leu Ala Gln Tyr Ser Thr Val
35 40 45

Glu Ser Leu Gly Glu Ile Ile Arg Glu Asn Lys Glu Ile Lys Pro Ser
50 55 60

Ile Val Ile Glu Leu Arg Ser Gly Thr Tyr Glu Gln Pro Leu Trp Leu
65 70 75 80

Phe His Pro Ile Gly Gly Ser Thr Phe Cys Tyr Met Glu Leu Ser Arg
85 90 95

His Leu Asn Pro Asn Arg Thr Leu Arg Ala Ile Gln Ser Pro Gly Leu
100 105 110

Ile Glu Ala Asp Ala Ala Glu Val Ala Ile Glu Glu Met Ala Thr Leu
115 120 125

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

Gly Gly Trp Cys Phe Gly Gly Ala Ile Ala Tyr Glu Ile Ser Arg Gln
145 150 155 160

Leu Arg Gln Met Gly Gln Gln Val Thr Gly Ile Val Met Ile Asp Thr
165 170 175

Arg Ala Pro Ile Pro Glu Asn Val Pro Glu Asp Ala Asp Asp Ala Met
180 185 190

Leu Leu Ser Trp Phe Ala Arg Asp Leu Ala Val Pro Tyr Gly Lys Lys
195 200 205

Leu Thr Ile Ser Ala Gln Tyr Leu Arg Glu Leu Ser Pro Asp His Met
210 215 220

Phe Asp His Val Leu Lys Glu Ala Lys Ala Ile Asn Val Ile Pro Leu
225 230 235 240

Asp Ala Asn Pro Ser Asp Phe Arg Leu Tyr Phe Asp Thr Tyr Leu Ala
245 250 255

Asn Gly Val Ala Leu Gln Thr Tyr Phe Pro Glu Pro Glu Asp Phe Pro
260 265 270

Ile Leu Leu Val Lys Ala Lys Asp Glu Ser Glu Asp
275 280

<210> 201
<211> 73
<212> PRT
<213> Penicillium coprobium PF1169

<400> 201

Pro Met Asn Lys Asp Lys Val Tyr Trp Ser Ala Ile Ile Arg Thr Leu
1 5 10 15

Val Ala Lys Glu Met Arg Val Glu Pro Glu Thr Ile Asp Pro Glu Gln
20 25 30

Lys Phe Thr Thr Tyr Gly Leu Asp Ser Ile Val Ala Leu Ser Val Ser
35 40 45

Gly Asp Leu Glu Asp Leu Thr Lys Leu Glu Leu Glu Pro Thr Leu Leu
50 55 60

Trp Asp Tyr Pro Thr Ile Asn Ala Leu
65 70

<210> 202
<211> 63
<212> PRT
<213> Penicillium coprobium PF1169

<400> 202

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

Arg Tyr Ile Gln Gly Ala Asp Ile Val Arg Ile Ser Asp Gly Ile Ala
20 25 30

Arg Thr Ser Arg Phe Arg Ser Leu Pro Arg Thr Lys Leu Arg Pro Val
35 40 45

Ser Asp Gly Pro Arg Leu Leu Pro Arg Pro Glu Gly Thr Tyr Leu
50 55 60

<210> 203
<211> 69
<212> PRT
<213> Penicillium coprobium PF1169

<400> 203

Leu Glu Val Val Trp Glu Cys Leu Glu Asn Ser Gly Glu Thr Gln Trp
1 5 10 15

Arg Gly Lys Glu Ile Gly Cys Phe Val Gly Val Phe Gly Glu Asp Trp

20 25 30

Leu Glu Met Ser His Lys Asp Pro Gln His Leu Asn Gln Met Phe Pro
35 40 45

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

Asp Leu Thr Gly Pro
65

<210> 204
<211> 96
<212> PRT
<213> Penicillium coprobium PF1169

<400> 204

Phe Asp Ala Ala Phe Phe Asn Met Ser Pro Arg Glu Ala Gln Gln Thr
1 5 10 15

Asp Pro Met Gln Arg Leu Ala Ile Val Thr Ala Tyr Glu Ala Leu Glu
20 25 30

Arg Ala Gly Tyr Val Ala Asn Arg Thr Ala Ala Thr Asn Leu His Arg
35 40 45

Ile Gly Thr Phe Tyr Gly Gln Ala Ser Asp Asp Tyr Arg Glu Val Asn
50 55 60

Thr Ala Gln Glu Ile Ser Thr Tyr Phe Ile Pro Gly Gly Cys Arg Ala
65 70 75 80

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

<210> 205
<211> 58
<212> PRT
<213> Penicillium coprobium PF1169

<400> 205

Phe Leu Gln Ile Ser Gly Pro Ser Phe Ser Ile Asp Thr Ala Cys Ser
1 5 10 15

Ser Ser Leu Ala Thr Ile Gln Val Cys Thr His Leu Phe His Val His
20 25 30

Leu Asn Arg Gln Leu Thr Ile Ala Ala Cys Thr Ser Leu Trp Asn Gly
35 40 45

Glu Thr Asp Thr Val Val Ala Gly Gly Met
50 55

<210> 206
<211> 52
<212> PRT
<213> Penicillium coprobium PF1169

<400> 206

Glu Leu Arg His Gly Lys Asn Ile Asp Lys Pro Glu Tyr Ser Gln Pro
1 5 10 15

Leu Cys Thr Ala Ile Gln Ile Ala Leu Val Glu Leu Leu Glu Ser Phe
20 25 30

Gly Val Val Pro Lys Ala Val Val Gly His Ser Ser Gly Glu Ile Ala
35 40 45

Ala Ala Tyr Val
50

<210> 207
<211> 59
<212> PRT
<213> Penicillium coprobium PF1169

<400> 207

Val Tyr Ser Gly Ser Met Thr Asn Asp Tyr Glu Leu Leu Ser Thr Arg
1 5 10 15

Asp Ile Tyr Asp Met Pro His Asn Ser Ala Thr Gly Asn Gly Arg Thr
20 25 30

Met Leu Ala Asn Arg Leu Ser Trp Phe Phe Asp Leu Gln Gly Pro Ser
35 40 45

Ile Met Met Asp Thr Ala Cys Ser Ser Ser Leu
50 55

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<210> 208
<211> 28
<212> PRT
<213> Penicillium coprobium PF1169

<400> 208

Pro Trp Pro Thr Thr Gly Leu Arg Arg Ala Ser Val Asn Ser Phe Gly
1 5 10 15

Tyr Gly Gly Thr Asn Ala His Cys Val Leu Asp Asp
20 25

<210> 209
<211> 71
<212> PRT
<213> Penicillium coprobium PF1169

<400> 209

Lys Ala Ser Leu Ser Leu Gln His Gly Met Ile Ala Pro Asn Leu Leu
1 5 10 15

Met Gln His Leu Asn Pro Lys Ile Lys Pro Phe Ala Ala Lys Leu Ser
20 25 30

Val Pro Thr Glu Cys Ile Pro Trp Pro Ala Val Pro Asp Gly Cys Pro
35 40 45

Arg Arg Ala Ser Val Asn Ser Phe Gly Phe Gly Gly Ala Asn Val His
50 55 60

Val Val Leu Glu Ser Tyr Thr
65 70

<210> 210
<211> 80
<212> PRT
<213> Penicillium coprobium PF1169

<400> 210

Leu Lys Gly Thr Gly Gly Gln Met Leu Gln Asn Val Val Leu Arg Val
1 5 10 15

Pro Val Ala Ile Asn Ala Pro Arg Ser Val Gln Val Val Val Gln Gln
20 25 30

Asp Gln Val Lys Val Val Ser Arg Leu Ile Pro Ser Glu Ala Ser Val
35 40 45

Leu Asp Asp Asp Ala Ser Trp Val Thr His Thr Thr Ala Tyr Trp Asp
50 55 60

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

<210> 211
<211> 38
<212> PRT
<213> Penicillium coprobium PF1169

<400> 211

Gly Asn Gly Ser Ala Met Ile Ser Asn Arg Ile Ser Trp Phe Phe Asp
1 5 10 15

Leu Lys Gly Pro Ser Leu Ser Leu Asp Thr Ala Cys Ser Ser Ser Leu
20 25 30

Val Ala Leu His Leu Ala
35

<210> 212
<211> 76
<212> PRT
<213> Penicillium coprobium PF1169

<400> 212

Ala Ile His His Gly Val Gln Ala Ile Lys Leu Gly Glu Ser Arg Val
1 5 10 15

Ala Ile Val Gly Gly Val Asn Ala Leu Cys Gly Pro Gly Leu Thr Arg
20 25 30

Val Leu Asp Lys Ala Gly Ala Ile Ser Ser Asp Gly Ser Cys Lys Ser
35 40 45

Phe Asp Asp Asp Ala His Gly Tyr Ala Arg Gly Glu Gly Ala Gly Ala
50 55 60

Leu Val Leu Lys Ser Leu His Gln Ala Leu Leu Asp
65 70 75

<210> 213
<211> 69
<212> PRT
<213> Penicillium coprobium PF1169

<400> 213

Arg Glu Trp Met Thr Ala Glu Gly Lys Asp His Asn Leu Ser Asp Ile
1 5 10 15

Leu Thr Thr Leu Ala Thr Arg Arg Asp His His Asp Tyr Arg Ala Ala
20 25 30

Leu Val Val Asp Asp Asn Arg Asp Ala Glu Leu Ala Leu Gln Ala Leu
35 40 45

Glu His Gly Val Asp Gln Thr Phe Thr Thr Gln Ser Arg Val Phe Gly
50 55 60

Ala Asp Ile Ser Lys
65

<210> 214
<211> 53
<212> PRT
<213> Penicillium coprobium PF1169

<400> 214

Thr Ser Asp Asp Tyr Arg Glu Val Asn Ser Gly Gln Asp Ile Asp Thr
1 5 10 15

Tyr Phe Ile Pro Gly Gly Asn Arg Ala Phe Thr Pro Gly Arg Ile Asn
20 25 30

Tyr Tyr Phe Lys Phe Ser Gly Pro Ser Val Ser Val Asp Thr Ala Cys
35 40 45

Ser Ser Ser Leu Ala
50

<210> 215
<211> 63
<212> PRT
<213> Penicillium coprobium PF1169

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<400> 215

Ala Gly Ile Pro Leu Ala Asn Ile Met Gly Thr Lys Thr Ser Cys Phe
1 5 10 15

Val Gly Ser Phe Ser Ala Asp Tyr Thr Asp Leu Leu Leu Arg Asp Pro
20 25 30

Glu Cys Val Pro Met Tyr Gln Cys Thr Asn Ala Gly Gln Ser Arg Ala
35 40 45

Met Thr Ala Asn Arg Leu Ser Tyr Phe Phe Asp Leu Lys Gly Pro
50 55 60

<210> 216
<211> 68
<212> PRT
<213> Penicillium coprobium PF1169

<400> 216

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

Ala Met Arg Gly Asn Lys Ala Val Ile Ala Cys Val Asn Ser Glu Ser
20 25 30

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

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

Ala Tyr His Ser
65

<210> 217
<211> 39
<212> PRT
<213> Penicillium coprobium PF1169

<400> 217

Asn Ala Ala Gly Ala His Phe Leu Thr Glu Asp Ile Gly Leu Phe Asp
1 5 10 15

Ala Pro Phe Phe Asn Ile Thr Leu Gln Glu Ala Gln Thr Met Asp Pro

20 25 30

Gln Gln Arg Ile Phe Leu Glu
35

<210> 218
<211> 76
<212> PRT
<213> Penicillium coprobium PF1169

<400> 218

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

Leu His Gln Ala Val Gln Ser Leu Arg Ser Gly Glu Thr Asp Val Ala
20 25 30

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

Glu Ser Lys Leu Lys Met Leu Ser Pro Asn Gly Arg Ser Arg Met Trp
50 55 60

Asp Lys Asp Ala Asp Gly Tyr Ala Arg Gly Asp Gly
65 70 75

<210> 219
<211> 61
<212> PRT
<213> Penicillium coprobium PF1169

<400> 219

Gly Leu Val Asn Ile Leu Arg Ser Trp Gly Ile Glu Pro Ser Thr Val
1 5 10 15

Val Gly His Ser Ser Gly Glu Ile Val Ala Ala Tyr Thr Ala Arg Ala
20 25 30

Ile Ser Met Arg Thr Ala Ile Ile Leu Ala Tyr Tyr Arg Gly Lys Val
35 40 45

Ala Gln Pro Leu Glu Gly Leu Gly Ala Met Val Ala Val
50 55 60

<210> 220
<211> 79
<212> PRT
<213> Penicillium coprobium PF1169

<400> 220

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

Thr Cys Val Gln Met Ala Leu Thr Lys Tyr Trp Thr Ser Leu Gly Val
20 25 30

Thr Pro Ser Phe Val Met Gly His Ser Leu Gly Glu Phe Ala Ala Leu
35 40 45

Asn Ala Ala Gly Val Leu Thr Ile Ser Asp Thr Ile Tyr Leu Ala Gly
50 55 60

Arg Arg Ala Gln Leu Leu Thr Glu Gln Ile Glu Gly Gly Thr His
65 70 75

<210> 221
<211> 81
<212> PRT
<213> Penicillium coprobium PF1169

<400> 221

Val Tyr Thr Gly Arg Ile Ser Leu Lys Asp Leu Gly Met Arg Cys Leu
1 5 10 15

Pro Leu Cys Leu Phe Leu Phe Leu Trp Thr Ile Tyr Phe Asn Thr Ala
20 25 30

Tyr Ser Tyr Gln Asp Ile Lys Asp Asp Cys Lys Leu Asn Val Asn Ser
35 40 45

Ser Tyr Val Leu Ala Gly Ser His Val Arg Gly Met Leu Leu Leu Gln
50 55 60

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

Ser

<210> 222
<211> 82
<212> PRT
<213> Penicillium coprobium PF1169

<400> 222

Arg His Phe Gly Leu Trp Asp Glu Pro Arg Glu Leu Glu Asp Val Glu
1 5 10 15

Phe Leu Leu Lys Ala Asp Val Arg Asn Asn Ser Ala Trp Asn His Arg
20 25 30

Tyr Met Leu Arg Phe Gly Pro Arg Asp Thr Ser Leu Pro Asp Ala Gly
35 40 45

Met Val Asn Ala Gly Asp Leu Ser Thr Ala Pro Ala Glu Lys Gly Arg
50 55 60

Leu Ser Val Val Asp Glu Asp Met Val Asp Gly Glu Leu Lys Phe Ala
65 70 75 80

Gln Glu

<210> 223
<211> 35
<212> PRT
<213> Penicillium coprobium PF1169

<400> 223

Ile Met Arg Gly Ala Gly Cys Ala Ile Asn Asp Leu Trp Asp Arg Asn
1 5 10 15

Leu Asp Pro His Val Glu Arg Thr Lys Phe Arg Pro Ile Ala Arg Gly
20 25 30

Ala Leu Ser
35

<210> 224
<211> 86
<212> PRT
<213> Penicillium coprobium PF1169

<400> 224

Phe Pro Thr Phe Pro Pro Lys Glu Ala Asp Phe Leu Met Glu Met Phe
1 5 10 15

Ala Gln Asp Ser Lys Asn Tyr His Val Trp Thr Tyr Arg His Trp Leu
20 25 30

Val Arg His Phe Gly Leu Trp Asp Glu Pro Arg Glu Leu Glu Asp Val
35 40 45

Glu Phe Leu Leu Lys Ala Asp Val Arg Asn Asn Ser Ala Trp Asn His
50 55 60

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

Gly Met Val Asn Ala Gly
85

<210> 225
<211> 82
<212> PRT
<213> Penicillium coprobium PF1169

<400> 225

Asn His Arg Tyr Met Leu Arg Phe Gly Pro Arg Asp Thr Ser Leu Pro
1 5 10 15

Asp Ala Gly Met Val Asn Ala Gly Asp Leu Ser Thr Ala Pro Ala Glu
20 25 30

Lys Gly Arg Leu Ser Val Val Asp Glu Asp Met Val Asp Gly Glu Leu
35 40 45

Lys Phe Ala Gln Glu Ala Ile Leu Arg Ala Pro Glu Asn Arg Ser Pro
50 55 60

Trp Trp Tyr Ala Arg Gly Val Leu Arg Ala Ala Gly Arg Gly Leu Gly
65 70 75 80

Glu Trp

<210> 226

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<211> 45
<212> PRT
<213> Penicillium coprobium PF1169

<400> 226

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

Ala Ser Ser Ala Leu Thr Ile Leu Pro Ala Trp Ala Ser Val Tyr Thr
20 25 30

Gly Arg Ile Ser Leu Lys Asp Leu Gly Met Arg Cys Leu
35 40 45

<210> 227
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<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 227
tacaggcggc ctaaattgtc 20

<210> 228
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 228
gaacacagcg caagagatca 20

<210> 229
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 229
cgcaagactt gaggaacaag 20

<210> 230
<211> 20
<212> DNA

<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 230
tgaggtcaac agtggacagg 20

<210> 231
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 231
cgcttttacg gcaatcatct 20

<210> 232
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 232
tgttcgtcgt ccttgtatgc 20

<210> 233
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 233
cagacgctgc ataggatcag 20

<210> 234
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 234
ttactagcct ctggggtgga 20

<210> 235
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 235
tctcttgcgc tgtgttcact 20

<210> 236
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 236
atgcggcctt tttcaacat 19

<210> 237
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 237
cgacgtaagg agctgtgagc 20

<210> 238
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 238
acctcgatcc tgctgcaa 18

<210> 239
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 239

ggttgtcagg atttgtcaga a 21

<210> 240
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 240
ttacttcatc cccggtggta 20

<210> 241
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 241
agagcatagc ccggttgtta 20

<210> 242
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 242
cccaccttga tttgctcagt 20

<210> 243
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 243
agagcatagc ccggttgtta 20

<210> 244
<211> 20
<212> DNA
<213> Artificial Sequence

<220>

<223> a primer sequence for PCR

<400> 244
gccaccttga tttgctcagt 20

<210> 245
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 245
aagaacacag agattggtgt gg 22

<210> 246
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 246
ccaggaagac acttggaagg 20

<210> 247
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 247
agagcatagc ccggttgtta 20

<210> 248
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 248
ccaccttcga tttgctcagt 20

<210> 249
<211> 20
<212> DNA

<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 249
cgcaagactt gaggaacaag 20

<210> 250
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 250
tccctctacg cagaagaacc 20

<210> 251
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 251
agagcatagc ccggttgtta 20

<210> 252
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 252
ccaccttcga tttgctcagt 20

<210> 253
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 253
gaggcgctgg tgtagagaat 20

<210> 254
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 254
tgtctcccgc tttgtctctt 20

<210> 255
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 255
agacgtggag ttcctcctga 20

<210> 256
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 256
caaacttcag ttcgccatca 20

<210> 257
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 257
caactttccc acccaaagaa 20

<210> 258
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 258

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aagcatgtat cggtggttcc 20

<210> 259
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 259
cgatacatgc ttcgttttgg 20

<210> 260
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 260
cagcagccct cagcacac 18

<210> 261
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 261
ggcgtctatc cgcaatacat 20

<210> 262
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 262
gagacaccgc atacccagat 20

<210> 263
<211> 406
<212> DNA
<213> Penicillium coprobium PF1169

<400> 263

cccagcccaa gacttgagta gactatattt attctctttg atatccatct cagcatcaag 60

tttttgacgt tgtattacta tcctcgtttg gaattctcct cccaggtctt gcttcattgc 120

ttatagcatt ctaccaaaaa cgtcactgtc atggacgggt ggtcagacat atcatcagcg 180

cctgccggat acaaggatgt tgtttggata gcagatcggg ctctgctagc ccaaggattg 240

ggatggtcaa tcaactacct ggccatgata taccaatcgc gcaaagaccg cacatacggc 300

atggccattt tgccactatg ttgcaacttt gcgtgggaat tcgtctacac tgtcatctat 360

ccttctcaaa atcccttcga gagagctgtc ctcacaacat ggatgg 406

<210> 264
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 264
cccagcccaa gacttgagta 20

<210> 265
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> a primer sequence for PCR

<400> 265
ccatccatgt tgtgaggaca 20

<210> 266
<211> 39008
<212> DNA
<213> Penicillium coprobium PF1169

<400> 266
gccagccaat gtctcgacga gactctcggt gtcaagctgc ttgaggaggc cattgtgaag 60

atcgaagagc gtatcaggtc gcacggcggt agctgcaccg tgaagatggc acccaaggcc 120

gtcaccgagc aggacgatgc gatcctgcag gagcttatgg agaagcgcga acgtgagaac 180

acccaggtca gcggagatga ggactctgaa agtgatgagg gtgttcccga gtaagcgacg 240

ggctacaaat tcgagtcgag gggcatacag cggtcaccag cgctaaaatt caaagctggt 300

atcaccgcta gaggggagtt ggtgaaagat ggatagaaaa aacttgcaca tatcggaaaa 360

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aaggctcgat gggccagtgt gctgatgggc aggattacag tcagaactcg cccaggtaag 420

tcgcctggac ttcggggtct ggatatgaca tattcacacc tgtgtatgcg gtattcccat 480

tgcggtcgaa atcctcgttc ccggcatcaa atacactggg tccgcacagg gtgcaagttc 540

tgatgcacat aatgtttgat gcaaccgata cgttcaatgc cagtcatgct tttagatgca 600

attatccctg tagaggccat gtagcaatgt atgtagcaat gtatgtagca atgtatatag 660

caatgtatgt agcaatgtat gtaagatatc ataacaatcg agctcatgaa atggcgggga 720

gagctgaagc ttatctaccg ccgccgatca ttggtgccct caaagccatc gagaacttcc 780

ctttcggcac ttctcttttt ccaccaactt tcattctacg cgatatggga cattgggcaa 840

agatctttac cgccgatcgt ggcaggaccc ggcatcgggt cgaggtggaa cgtcgtcggc 900

gtacgtcatt ttccaaacat gcggaacact actgacaagc cgcagtgcta ccggcctatg 960

cggccgatga gtctgacgcc tcggatgctt caaaggaaat tgcaaaggtt gctcttcggt 1020

tgaaatatca aattgagcag gttgtctcct gtgaagtgga ggagaacgtc ttgaccgacc 1080

caaacagccg tatcatcacg gatgatgtgg ttgcgactgc taagcaggcc ggtggagatg 1140

aatacaaagc atgcattgtt tattgtctcc tggtttgtct gcgatggttc aaaatccaat 1200

catccgtcga gctttgggat tccgatctcc atgagattcg agctgtggct tgcgaggtca 1260

tcgccaagcg catgtaatgc ccctttttca ttccatgttc tcggccattt cctgacccaa 1320

acagtatcga atccgagcag aaccaagaat acgtgctaaa agacatttta ctcaagcgat 1380

actcaatctt cagtgaaggt gtggagactg atcccgccaa tgtcattgaa cgatcggtag 1440

atctccatgc tttaaggatc atcagctgtg ctgcgtacca gaagtgtatc cagtatctct 1500

ggagaggttg gatctgccag gaagaaggca acccaactaa ctttgtcgaa tacagtgaga 1560

agtcaaaccc caattattgg gttcatttcc atcctgatcg gatgcggact cctctgtatc 1620

agaatgtctg ccaaattttg ttttccttga tttaccttgc gacttatacc gcagttatca 1680

ataccgtgaa tcccaccggt gacctggatg tagctgaagc catactgtat gttatgactc 1740

tcgcgttcat ctgcgacgag gcggtcaaat tctggaaggt tggatggaat tatctcgaat 1800

tctggaatgc gttcaactca acgctctact ctatcctggc agtgtctctt gtcttgcgct 1860

ttattgcctt ggcacactca tcatctacgc acgatgaaac aaggcaggca tacaatgaac 1920

tcagctacaa cttcctcgcc tttgcgggcc ctatgttctg gatgcggatg atgctatatc 1980

ttgactcgtt ccgcttcttc ggtgccatgt tcgtggtcct tcgagtgatg atgaaagaaa 2040

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gcatggccca agtggatgct gatatcccca tccaccgaaa tattctccag ggaatgatca 2160

atagtatcat gcaaagccct gagtttgaca cttttcagga atttgcattt ccctttggta 2220

tcatcctcta ttatgtgttc aacttcattg ttatgactgg taagtctgta ttacatttgt 2280

ttggggtgtc gctaaacatt tttagttctg ttgaatattc tcattgcctt gtacaacagc 2340

gcatatgaag atatctctgg caatgccacg gacgagttca tggccatctt cgcgcagaaa 2400

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Gly Leu Lys Ala Arg Gly Val Glu Arg Gly Asp Cys Val Leu Val Gln

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Ala Gly Gly Val Tyr Met Gly Phe Asp Val Ala Ser Arg Pro His Glu
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Lys Pro Cys Ala Asp Pro Tyr Arg Asp Ala Met Lys Ala Tyr Pro Val
755 760 765

Ala Leu Ser Ala Ser Ala Ser Arg Trp Tyr Ser Ser Val Tyr Pro Gly
770 775 780

Glu Val Met Thr Gly Tyr Asp Gln Gln Glu Leu Thr Gly Glu Tyr Trp
785 790 795 800

Val Glu Asn Met Leu Arg Pro Val Gln Phe Ser Gln Ala Leu Glu Ala
805 810 815

Ala Ala Arg Asp Ala Gly Pro Pro Asp Leu Ile Ile Glu Ile Gly Pro
820 825 830

His Pro Thr Leu Arg Gly Pro Val Leu Gln Thr Leu Ser Lys Met His
835 840 845

Ser Ala His Ser Ala Ile Pro Tyr Leu Ala Leu Ala Glu Arg Gly Lys
850 855 860

Pro Gly Leu Asp Thr Trp Ala Thr Ala Leu Gly Ser Ser Trp Ala His
865 870 875 880

Leu Gly Pro Asn Val Val Arg Leu Thr Asp Tyr Val Ser Leu Phe Asp
885 890 895

Pro Asn His Trp Pro Val Leu Val Glu Ser Leu Pro Phe Tyr Pro Phe
900 905 910

Asp His Thr Gln Thr Tyr Trp Thr Gln Ser Arg Met Ser Ser Asn His
915 920 925

Asn His Arg Ala Thr Ser Pro Asn Ala Leu Leu Gly Ser Leu Ser Pro
930 935 940

Glu Thr Gly Ala Glu Lys Phe Arg Trp Arg Asn Tyr Leu Arg Pro Glu
945 950 955 960

Glu Leu Pro Trp Leu Ala Asp Arg Arg Ala Asp Ser Gly Ser Val Phe
965 970 975

Pro Glu Thr Gly Tyr Ile Ser Met Ala Leu Glu Ala Gly Met Ile Met
980 985 990

Ala Gln Thr Gln Gly Leu Arg Leu Leu Asn Val Lys Asp Leu Thr Ile
995 1000 1005

His Thr Gln Leu Pro Ile Gln Asn Asp Pro Ile Gly Thr Glu Val
1010 1015 1020

Leu Val Thr Val Gly Ser Ile His Ser His Asp Gly Ala Ile Thr
1025 1030 1035

Ala Trp Phe Cys Cys Glu Ala Val Val Ser Gly Glu Leu Val Gln
1040 1045 1050

Cys Ala Thr Ala Lys Met Ile Met His Pro Gly Asp Ser Asp Arg

1055 1060 1065

Ala Leu Leu Pro Pro Gln Gly Gln Leu Pro Gln Ala Leu Glu Pro
1070 1075 1080

Val Asp Ser Thr Glu Phe Tyr Asp Ser Leu Arg Arg Ala Asp Tyr
1085 1090 1095

His Cys Thr Gly Pro Phe Ser Thr Leu Thr Gly Leu Arg Lys Arg
1100 1105 1110

Arg Asp Leu Ala Thr Gly Ser Val Pro Val Pro Ser Asn Asp Ser
1115 1120 1125

Asp Glu Pro Met Ala Leu His Pro Ala Ile Leu Asp Leu Gly Val
1130 1135 1140

Gln Thr Met Ile Ala Ala Ile Gly Gly Leu Glu Glu Thr Leu Leu
1145 1150 1155

Thr Gly Pro Phe Leu Ser Arg Asn Val Asp Ser Thr Trp Ile Asn
1160 1165 1170

Pro Val Leu Cys Ala Ser Asp Trp Gln Gly Lys Glu Leu Thr Val
1175 1180 1185

Ala Ser Tyr Leu Thr Cys Val Asn Gly Asp Arg Ile Arg Gly Asp
1190 1195 1200

Ile Asp Ile Phe Thr Met Asn Gly Glu Lys Ala Val Gln Leu Glu
1205 1210 1215

Gly Val Ser Leu Ile Cys Gln Pro Ser Gly Thr Ala Pro Asn Asn
1220 1225 1230

Leu Gln Val Leu Ser Gln Thr Ala Trp Gly Pro Leu Glu Pro Thr
1235 1240 1245

Leu Lys Lys Gly Ser Arg Lys Leu Pro Ala Thr Met Leu Gln Leu
1250 1255 1260

His Ser Leu Arg Glu Glu Leu Ala Leu Leu Tyr Leu Lys Gln Ala
1265 1270 1275

Arg Asn Gly Leu Thr Asp Leu Glu Arg Ser Gly Leu Asp Phe Asp
1280 1285 1290

Gly Ala Arg Leu Leu Ala Trp Met Asn Gln Cys Ile Ala Asn Ala
1295 1300 1305

Ser Gln Glu Pro Asp Pro Val Gly Glu Ser Glu Cys Leu Asp Gln
1310 1315 1320

Lys Ile Glu Asp Phe Thr Ala Gly Val Ser Pro Ser Leu Leu Asn
1325 1330 1335

Asp Pro Gly Leu Thr Ala Ile Ala Ala Val Gly Gln Arg Leu Pro
1340 1345 1350

Arg Val Leu Arg Asp Ser Gly Leu Gln Ile Glu Ala Trp Pro Ala
1355 1360 1365

Ile Asp Glu Glu Ser Gln Tyr Leu Lys Glu Asp Leu Gln Val Leu
1370 1375 1380

Asp Leu Glu Asp Glu Leu Val Ser Val Val Ser Gln Ala Cys Phe
1385 1390 1395

Arg Phe Pro Gln Met Asn Ile Leu Gln Ile Gly Gln Phe Gly Gly
1400 1405 1410

His Val His Ser Gly Leu Lys Lys Met Gly Arg Thr Tyr Arg Ser
1415 1420 1425

Phe Thr Tyr Ala Gly Leu Ser Val Ser Gly Leu Gln Ala Ile Glu
1430 1435 1440

Glu Asp Leu Glu Gln Pro Gly Glu Val Ser His Lys Thr Leu Asp
1445 1450 1455

Ile Asn Glu Asp Pro Val Glu Gln Gly Cys Arg Glu Gln Phe Tyr
1460 1465 1470

Asp Met Val Leu Ile Thr Ala Ala Val Phe Leu Gln Glu Val Ala
1475 1480 1485

Val Ala His Val Arg Arg Leu Leu Lys Pro Gly Gly Phe Leu Val
1490 1495 1500

Leu Leu Val Arg Thr Asn Pro Ser Thr Thr Tyr Leu Asn Leu Leu
1505 1510 1515

Phe Gly Pro Pro Met Arg Cys Thr Glu Thr Gly Lys Gly Tyr Cys
1520 1525 1530

Ser Gly Glu Pro Ile Thr Thr Arg Arg Asp Trp Val Glu Leu Leu
1535 1540 1545

Ser Asn Gly Gly Phe Tyr Gly Leu Asp Ser Phe Asp Ala Ser Gln
1550 1555 1560

Glu Ser Glu Ser Leu Gly Asp Phe Ser Leu Leu Leu Cys Arg Thr
1565 1570 1575

Pro Asp Ser Pro Ala Glu Pro Gln Ser Arg Gly Asp Leu Leu Leu
1580 1585 1590

Leu Gly Gly Asp Ala Glu Glu Ala Asp Cys Leu Thr Ser Glu Leu
1595 1600 1605

Phe Glu Leu Val Gln Asp Asp Phe Val Lys Val Ala His Ala Pro
1610 1615 1620

Asp Leu Asp Leu Ile Glu Asp Arg Asp Leu Ser Lys Leu Thr Val
1625 1630 1635

Leu Tyr Leu Val Asp Asp Arg Asp Leu Thr Asn Ala Thr Leu Ser
1640 1645 1650

Glu Leu Cys Arg Leu Met Thr Val Ser Lys Arg Met Leu Val Val
1655 1660 1665

Thr Cys Glu Lys Val Asp His Pro Asp Ala Gly Leu Val Lys Gly
1670 1675 1680

Leu Leu Ser Thr Phe Leu Ala Ser Glu Arg Ser Ser Ser Leu Leu
1685 1690 1695

Gln Leu Leu His Ile Thr Asp Pro Val Gly Val Thr Thr Glu Ile
1700 1705 1710

Leu Ala Thr Ala Leu Gly His Phe Val Gln Ala Ser Ala Ala Gln
1715 1720 1725

Glu Asn Pro His Ser Cys Gly Leu Thr Asn Ile Glu Pro Glu Ile
1730 1735 1740

Gln Tyr Asp Gly Ser Met Phe Arg Val Pro Arg Gln Tyr His Asp
1745 1750 1755

His Ala Thr Gly Leu Arg His Leu Ala Arg Arg Gln Lys Val Thr
1760 1765 1770

Asp Cys Val Asp Leu Asp Lys Gly Val Val Gln Ile Leu Pro Ala
1775 1780 1785

Thr Thr Asp Lys Thr Cys Glu Gly Phe Arg Leu Leu Ser Met Ala
1790 1795 1800

Asp Pro Pro Ile Thr Ala Ser Tyr Gly Pro Thr Leu His Leu Arg
1805 1810 1815

Val Arg His Ser Ser Ile Ala Ala Val Arg Val Ala Gly Ala Ile
1820 1825 1830

Phe Leu Arg Leu Val Ile Gly Leu Asp Val Lys Ser Asn Lys Arg
1835 1840 1845

Met Ile Ala Leu Ser Ser His Ile Ala Ser His Val Ile Val Pro
1850 1855 1860

Asp Ser Trp Ala Trp Ser Val Pro Asp Thr Val Leu Glu Ala His
1865 1870 1875

Glu Gln Ser Tyr Leu Arg Ala Thr Ala Ala Ala Leu Leu Ala Gly
1880 1885 1890

Tyr Leu Val Glu Gln Val Pro Gln Ser Gly Thr Leu Val Val His
1895 1900 1905

Glu Ala Asp Gly Val Leu Gln Ser Val Phe His Gln Met Leu Thr

1910 1915 1920

Arg Arg Asp Gly Lys Val Ile Phe Ser Thr Ser Lys Ser Asn Pro
1925 1930 1935

Asp Lys Glu Arg Pro Met Leu Leu Leu His Glu His Ser Thr Ala
1940 1945 1950

Arg Gln Leu Ser Gln Val Leu Pro Ser Asp Val Ser Ala Ile Ala
1955 1960 1965

Ile Leu His Arg Arg Gly Gln Gly Val Tyr Asp Arg Met Leu Ser
1970 1975 1980

Leu Leu Pro Asp Asn Ala Thr Arg Ile His Leu Gln Asp Phe Tyr
1985 1990 1995

Leu Thr Ser Ala Ser Thr Gly Pro Ile Asn Ala Asp Asp Ser Ser
2000 2005 2010

Leu Ile Ala Lys Ala Phe Leu Thr Ala Cys Leu Val Ala Tyr Thr
2015 2020 2025

Gly Arg Glu Gly Leu Pro Pro Asn Ser Val Asp Ser Leu Pro Ile
2030 2035 2040

Ser Arg Ile Ser Glu Tyr Pro Ile Leu Asp Ser Gln Asp Ala Val
2045 2050 2055

Val Asp Trp Asp Ser Thr Thr Pro Val Leu Ala Gln Ile Pro Thr
2060 2065 2070

Ala Gly Ser Gln Val Gln Leu Ser Glu Lys Lys Thr Tyr Ile Leu
2075 2080 2085

Val Gly Leu Gly Ser Glu Leu Ala His Ala Ile Cys Leu Trp Leu
2090 2095 2100

Ala Thr His Gly Ala Lys Trp Ile Leu Leu Ala Gly Ser Arg Leu
2105 2110 2115

Asp Ser Asp Ala Trp Trp Leu Glu Glu Val Ser Arg Arg Gly Thr
2120 2125 2130

Arg Ile Ala Val Ser Lys Ile Asn Leu Ile Asp Gly Ile Ser Ala
2135 2140 2145

Thr Ser Leu His Gln Thr Ile Pro Tyr Ala Phe Pro Pro Val Val
2150 2155 2160

Gly Gly Val Leu Ile Gln Pro Pro Pro Leu Pro Asp Cys Ser Leu
2165 2170 2175

Ser Gln Leu Thr Ile Asp Ser Leu Arg Asn His Leu His Pro Val
2180 2185 2190

Leu Lys Gly Leu Gln Gln Leu Asp Glu Leu Tyr Lys Thr Pro Thr
2195 2200 2205

Leu Asp Phe Trp Val Leu Ile Gly Ser Ile Ala Gly Val Leu Gly
2210 2215 2220

His Ala Asp Gln Ala Met Thr Ala Ala Met Ser Glu Lys Met Ala
2225 2230 2235

Leu Leu Val Arg His Arg Arg Ala Gln Gly Arg Pro Ala Ser Leu
2240 2245 2250

Val His Leu Gly Glu Ile His Gly Ile Ser Ser Pro Ser Pro Ser
2255 2260 2265

Gln Pro Leu Trp Cys Gly Pro Val Ala Val Ser Gln Arg Asp Val
2270 2275 2280

Asp Glu Ile Leu Ala Glu Ala Ile Leu Cys Gly Arg Ser Asp Ser
2285 2290 2295

Asn Ser Asn Ala Glu Leu Ile Gly Gly Leu Arg His Gln Ser Leu
2300 2305 2310

Lys Cys Gly Tyr Gly Glu Cys Pro Ile Pro Lys Leu Trp Pro Phe
2315 2320 2325

Tyr Ser Tyr Thr Ala Thr Ala Ser Gln Asp Gln Ile Leu Ala Leu
2330 2335 2340

Ile Glu Thr Arg Ser Thr Lys Asp Leu Val Thr Ala Ala Thr Ser
2345 2350 2355

Leu Glu Glu Lys Ala Glu Ala Val Val Arg Pro Leu Met Glu Lys
2360 2365 2370

Ile Arg Ala Ser Leu Asn Leu Ala Glu Asp Ala Pro Leu Ser Ala
2375 2380 2385

Asp Thr Leu Ile Pro Glu Leu Gly Ile Asp Ser Leu Ile Ala Ile
2390 2395 2400

Gly Leu Ser Gln Trp Phe Thr Lys Glu Leu Ser Val Asp Ile Gly
2405 2410 2415

Val Ile Leu Ile Leu Ser Gly Val Ser Val Gly Glu Leu Ala His
2420 2425 2430

Ala Ala Ala Ser Lys Leu Cys Asn Val Ser Val Gly Lys Pro
2435 2440 2445

<210> 269
<211> 509
<212> PRT
<213> Penicillium coprobium PF1169

<400> 269

Met Asp Asn Met Asp Asn Met Asn Asn Thr Pro Leu Gly Phe Asn Trp
1 5 10 15

Ala Trp Ala Val Ile Ile Ser Phe Leu Gly Leu Leu Thr Phe Ser Phe
20 25 30

Val Ser Pro His Leu Phe Pro Ser Arg Leu Thr Val Ile Asn Gly Gly
35 40 45

Arg Ala Trp Asp Ile Phe Arg Thr Lys Ala Lys Lys Arg Phe Arg Ser
50 55 60

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

Phe Arg Ile Ile Thr Asp Asn Gly Pro Leu Leu Val Leu Ser Pro Gln

85 90 95

Tyr Ala Arg Glu Val Arg Ser Asp Asp Arg Leu Ser Leu Asp His Phe
100 105 110

Ile Ala Ser Glu Phe His Pro Asn Ile Pro Gly Phe Glu Pro Phe Lys
115 120 125

Leu Ile Leu Asp Pro Lys Asn Pro Leu Asn Thr Ile Leu Lys Ser Asn
130 135 140

Leu Thr Gln Ala Leu Glu Asp Leu Ser Ala Glu Val Thr Glu Ala Leu
145 150 155 160

Ser Ala Thr Cys Thr Asp Asp Pro Glu Trp His Glu Val Ser Val Ser
165 170 175

Gln Thr Ala Leu Lys Ile Ile Ala Gln Met Ala Ser Lys Ala Phe Ile
180 185 190

Gly Gln Glu Arg Cys Arg Asp Ala Lys Trp His Asn Ile Ile Ile Thr
195 200 205

Tyr Thr His Asn Val Tyr Gly Ala Ala Gln Ala Leu His Phe Trp Pro
210 215 220

Ser Phe Leu Arg Pro Ile Val Ala Gln Phe Leu Pro Ala Cys Arg Thr
225 230 235 240

Leu Gln Ala Gln Ile Ala Glu Ala Arg Glu Ile Leu Glu Pro Leu Val
245 250 255

Ala Gln Arg Arg Ala Glu Arg Ala Thr Arg Ala Ala Gln Glu Lys Pro
260 265 270

His Pro Ser Gly Gly Asp Ile Ile Asp Trp Leu Glu Gln Phe Tyr Gly
275 280 285

Asp Gln Pro Tyr Asp Pro Val Ala Ala Gln Leu Leu Leu Ser Phe Ala
290 295 300

Ala Ile His Gly Thr Ser Asn Leu Leu Ala Gln Ala Leu Ile Asp Leu
305 310 315 320

Cys Gly Gln Pro Glu Leu Val Gln Asp Leu Arg Glu Glu Ala Val Ser
325 330 335

Val Leu Gly Lys Glu Gly Trp Thr Arg Ala Ala Leu Tyr Gln Leu Lys
340 345 350

Leu Met Asp Ser Ala Leu Lys Glu Ser Gln Arg Leu Ala Pro Asn Arg
355 360 365

Leu Leu Ser Met Gly Arg Ile Ala Gln Gly Asp Met Asp Leu Ser Asp
370 375 380

Gly Leu Arg Ile His Arg Gly Thr Thr Leu Met Val Ser Ala His Asn
385 390 395 400

Met Trp Asp Pro Glu Ile Tyr Pro Asp Pro Arg Lys Tyr Asp Gly Tyr
405 410 415

Arg Phe His Lys Leu Arg Gln Thr Ser Gly Gln Glu Gly Gln His Gln
420 425 430

Leu Val Ser Ser Thr Pro Asp His Met Gly Phe Gly Tyr Gly Lys His
435 440 445

Ala Cys Pro Gly Arg Phe Phe Ala Ala Ala Gln Ile Lys Val Ala Leu
450 455 460

Cys Asn Ile Leu Leu Lys Tyr Asp Ile Glu Tyr Arg Gly Gly Lys Ser
465 470 475 480

Pro Gly Val Trp Gly Gln Gly Ile His Leu Phe Pro Asp Pro Thr Ser
485 490 495

Arg Ile His Val Arg Arg Arg Lys Glu Glu Ile Asn Leu
500 505

<210> 270
<211> 505
<212> PRT
<213> Penicillium coprobium PF1169

<400> 270

Met Ile Glu Leu Lys Asp Ala Ser Met Gly Ala Val Leu Leu Thr Cys
1 5 10 15

Val Leu Val Leu Ala Gly Leu Tyr Leu Ile Arg Leu Thr Leu Ser Ser
20 25 30

Asp Gln Leu Asp Lys Phe Pro Ser Ile Asn Pro Arg Lys Pro Trp Glu
35 40 45

Ile Val Asn Val Phe Ala Gln Arg Arg Phe Gln Gln Asp Gly Pro Arg
50 55 60

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

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

Lys Asp Glu Lys Leu Leu Asp His Tyr Arg Ser Met Ile Glu Asp Phe
100 105 110

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

Asn Thr Val Leu Arg Asp Val Ile Ser Val Ile Thr Arg Glu Leu Glu
130 135 140

Gln Leu Leu Ala Pro Leu Ser Asp Glu Val Ser Ala Ala Leu Val Asp
145 150 155 160

Thr Trp Thr Asp Ser Pro Asp Trp His Glu Val Ala Leu Leu Pro Ser
165 170 175

Met Leu Gly Leu Ile Ala Lys Val Ser Ser Leu Val Phe Val Gly Glu
180 185 190

Pro Leu Cys Arg His Pro Val Trp Leu Glu Thr Val Ile Asn Phe Thr
195 200 205

Leu Ile Arg His Asn Ala Ile Leu Ala Leu His Gln Cys Pro Ala Val
210 215 220

Leu Arg Pro Val Leu His Trp Val Leu Pro Pro Cys Gln Lys Leu Arg

225 230 235 240

Arg Glu Ile Arg Thr Ala Arg Thr Leu Ile Asp Ser Ala Leu Glu Lys
245 250 255

Ser Arg Lys Asn Pro Gln Thr Glu Lys Phe Ser Ser Val Ala Trp Val
260 265 270

Asp Ala Phe Ala Lys Gly Asn Lys Tyr Asn Ala Ala Met Val Gln Leu
275 280 285

Arg Leu Ala Asn Ala Ser Ile His Ser Ser Ala Asp Leu Leu Val Lys
290 295 300

Ile Leu Ile Asn Leu Cys Glu Gln Pro Glu Leu Ile Arg Asp Leu Arg
305 310 315 320

Asp Glu Ile Ile Ser Val Leu Gly Glu Asn Gly Trp Arg Ser Ser Thr
325 330 335

Leu Asn Gln Leu Lys Leu Leu Asp Ser Val Leu Lys Glu Ser Gln Arg
340 345 350

Leu His Pro Val Thr Thr Gly Ala Phe Ser Arg Phe Thr Arg Gln Asp
355 360 365

Ile Lys Leu Thr Asn Gly Thr Glu Ile Pro Ser Gly Thr Pro Ile Met
370 375 380

Val Thr Asn Asp Val Ala Gly Asp Ala Ser Ile Tyr Asp Asp Pro Asp
385 390 395 400

Val Phe Asp Gly Tyr Arg Tyr Phe Arg Met Arg Glu Gly Ala Asp Lys
405 410 415

Ala Arg Ala Pro Phe Thr Thr Thr Gly Gln Asn His Leu Gly Phe Gly
420 425 430

Tyr Gly Lys Tyr Ala Cys Pro Gly Arg Phe Phe Ala Ala Thr Glu Ile
435 440 445

Lys Ile Ala Leu Cys His Met Leu Leu Lys Tyr Glu Trp Arg Leu Val
450 455 460

Lys Asp Arg Pro His Gly Ile Val Thr Ser Gly Phe Ala Ala Phe Arg
465 470 475 480

Asp Pro Arg Ala Ser Ile Glu Val Arg Arg Arg Ala Val Ala Gly Glu
485 490 495

Glu Leu Glu Val Leu Thr Gly Lys Lys
500 505

<210> 271
<211> 241
<212> PRT
<213> Penicillium coprobium PF1169

<400> 271

Met Asp Gly Trp Ser Asp Ile Ser Ser Ala Pro Ala Gly Tyr Lys Asp
1 5 10 15

Val Val Trp Ile Ala Asp Arg Ala Leu Leu Ala Gln Gly Leu Gly Trp
20 25 30

Ser Ile Asn Tyr Leu Ala Met Ile Tyr Gln Ser Arg Lys Asp Arg Thr
35 40 45

Tyr Gly Met Ala Ile Leu Pro Leu Cys Cys Asn Phe Ala Trp Glu Phe
50 55 60

Val Tyr Thr Val Ile Tyr Pro Ser Gln Asn Pro Phe Glu Arg Ala Val
65 70 75 80

Leu Thr Thr Trp Met Val Leu Asn Leu Tyr Leu Met Tyr Thr Thr Ile
85 90 95

Lys Phe Ala Pro Asn Glu Trp Gln His Ala Pro Leu Val Gln Arg Ile
100 105 110

Leu Pro Val Ile Phe Pro Val Ala Ile Ala Ala Phe Thr Ala Gly His
115 120 125

Leu Ala Leu Ala Ala Thr Val Gly Val Ala Lys Ala Val Asn Trp Ser
130 135 140

Ala Phe Leu Cys Phe Glu Leu Leu Thr Ala Gly Ala Val Cys Gln Leu
145 150 155 160

Met Ser Arg Gly Ser Ser Arg Gly Ala Ser Tyr Thr Ile Trp Val Ser
165 170 175

Arg Phe Leu Gly Ser Tyr Ile Gly Ser Ile Phe Met His Val Arg Glu
180 185 190

Thr His Trp Pro Gln Glu Phe Asp Trp Ile Ser Tyr Pro Phe Val Ala
195 200 205

Trp His Gly Ile Met Cys Phe Ser Leu Asp Ile Ser Tyr Val Gly Leu
210 215 220

Leu Trp Tyr Ile Arg Arg Gln Glu Arg Gln Gly Gln Leu Lys Lys Ala
225 230 235 240

Met

<210> 272
<211> 464
<212> PRT
<213> Penicillium coprobium PF1169

<400> 272

Met Lys Val Ile Ile Val Gly Gly Ser Ile Ala Gly Leu Ala Leu Ala
1 5 10 15

His Cys Leu Asp Lys Ala Asn Ile Asp Tyr Val Ile Leu Glu Lys Lys
20 25 30

Lys Glu Ile Ala Pro Gln Glu Gly Ala Ser Ile Gly Ile Met Pro Asn
35 40 45

Gly Gly Arg Ile Leu Glu Gln Leu Gly Leu Tyr Asp Gln Ile Glu Glu
50 55 60

Leu Ile Glu Pro Leu Val Arg Ala His Val Thr Tyr Pro Asp Gly Phe
65 70 75 80

Asn Tyr Thr Ser Arg Tyr Pro Ala Leu Ile Gln Gln Arg Phe Gly Tyr
85 90 95

Pro Leu Ala Phe Leu Asp Arg Gln Lys Leu Leu Gln Ile Leu Ala Thr
100 105 110

Gln Pro Val Gln Ser Ser Arg Val Lys Leu Asp His Lys Val Glu Ser
115 120 125

Ile Glu Val Ser Pro Cys Gly Val Thr Val Ile Thr Ser Asn Gly His
130 135 140

Thr Tyr Gln Gly Asp Leu Val Val Gly Ala Asp Gly Val His Ser Arg
145 150 155 160

Val Arg Ala Glu Met Trp Arg Leu Ala Asp Ala Ser Gln Gly Asn Val
165 170 175

Cys Gly Asn Gly Asp Lys Ala Phe Thr Ile Asn Tyr Ala Cys Ile Phe
180 185 190

Gly Ile Ser Ser His Val Asp Gln Leu Asp Pro Gly Glu Gln Ile Thr
195 200 205

Cys Tyr Asn Asp Gly Trp Ser Ile Leu Ser Val Ile Gly Gln Asn Gly
210 215 220

Arg Ile Tyr Trp Phe Leu Phe Ile Lys Leu Glu Lys Glu Phe Val Tyr
225 230 235 240

Asp Gly Ser His Lys Thr Gln Leu His Phe Ser Arg Glu Asp Ala Arg
245 250 255

Ala His Cys Glu Arg Leu Ala Gln Glu Pro Leu Trp Lys Asp Val Thr
260 265 270

Phe Gly Gln Val Trp Ala Arg Cys Glu Val Phe Gln Met Thr Pro Leu
275 280 285

Glu Glu Gly Val Leu Gly Lys Trp His Trp Arg Asn Ile Ile Cys Ile
290 295 300

Gly Asp Ser Met His Lys Phe Ala Pro His Ile Gly Gln Gly Ala Asn
305 310 315 320

Cys Ala Ile Glu Asp Ala Ala Gln Leu Ser Asn Ser Leu His Thr Trp
325 330 335

Leu Ser Gly Ser Gly Lys Glu His Gln Leu Lys Thr Asp Asp Leu Thr
340 345 350

Glu Ile Leu Ala Gln Phe Ala Gln Thr Arg Leu Gln Arg Leu Gly Pro
355 360 365

Thr Ala Met Ala Ala Arg Ser Ala Met Arg Leu His Ala Arg Glu Gly
370 375 380

Leu Lys Asn Trp Ile Leu Gly Arg Tyr Phe Leu Pro Tyr Ala Gly Asp
385 390 395 400

Lys Pro Ala Asp Trp Ala Ser Arg Gly Ile Ala Gly Gly Asn Thr Leu
405 410 415

Asp Phe Val Glu Pro Pro Thr Arg Ala Gly Pro Gly Trp Ile Gln Phe
420 425 430

Ser Gln Ser Gly Lys Arg Thr Ser Phe Pro Met Ala Val Ala Gly Leu
435 440 445

Cys Leu Val Ser Ile Val Ala Arg Ile Met Tyr Leu Lys Leu Val Ala
450 455 460

<210> 273
<211> 317
<212> PRT
<213> Penicillium coprobium PF1169

<400> 273

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

Ile Ser Arg Phe Asp Lys Tyr Asn Cys Leu Phe Ala Ile Phe Pro Gly
20 25 30

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

Pro Val Pro Leu Asp Phe Val Leu Gly Arg Ala Gly Leu Ala Phe Met

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50 55 60

Tyr Thr Tyr Met Leu Ser Gly Ala Gly Met Val Trp Asn Asp Trp Ile
65 70 75 80

Asp Arg Asp Ile Asp Ala Gln Val Ala Arg Thr Lys Asn Arg Pro Leu
85 90 95

Ala Ser Gly Arg Leu Ser Thr Arg Ala Ala Leu Ile Trp Met Leu Val
100 105 110

Gln Tyr Ala Ala Ser Val Trp Leu Met Asp Arg Met Val Ser Gly Gln
115 120 125

Asp Val Trp Thr Tyr Met Leu Pro Leu Thr Thr Gly Ile Ile Leu Tyr
130 135 140

Pro Phe Gly Lys Arg Pro Thr Ser Arg Lys Leu Gly Val Tyr Pro Gln
145 150 155 160

Tyr Ile Leu Gly Ala Ser Ser Ala Leu Thr Ile Leu Pro Ala Trp Ala
165 170 175

Ser Val Tyr Thr Gly Arg Ile Ser Leu Lys Asp Leu Gly Met Arg Cys
180 185 190

Leu Pro Leu Cys Leu Phe Leu Phe Leu Trp Thr Ile Tyr Phe Asn Thr
195 200 205

Ala Tyr Ser Tyr Gln Asp Ile Lys Asp Asp Cys Lys Leu Asn Val Asn
210 215 220

Ser Ser Tyr Val Leu Ala Gly Ser His Val Arg Gly Met Leu Leu Leu
225 230 235 240

Gln Ala Ile Ala Val Val Leu Val Ile Pro Trp Ile Leu Tyr Thr Ser
245 250 255

Ala Ser Thr Trp Leu Trp Val Ser Trp Leu Gly Val Trp Thr Ala Ser
260 265 270

Leu Gly Glu Gln Leu Tyr Leu Phe Asp Val Lys Asp Pro Ser Ser Gly
275 280 285

Gly Lys Val His Arg Arg Asn Phe Ala Leu Gly Ile Trp Asn Val Leu
290 295 300

Ala Cys Phe Val Glu Leu Leu Tyr Ala Ser Gly Ser Leu
305 310 315

<210> 274
<211> 522
<212> PRT
<213> Penicillium coprobium PF1169

<400> 274

Met Ser Thr Gln Glu Val Cys Leu Pro Val Ser Gln Arg Asp Gln Val
1 5 10 15

Lys Glu Gly Pro Val Arg Leu His Gly Leu Cys Glu Asp Gly Met Cys
20 25 30

Asp Ala Arg Arg Thr Gly Asp Arg Ser Ala Tyr Pro Leu Ser Ser Leu
35 40 45

Asp His Asn Pro Leu Gly Met Asn Val Thr Phe Leu Leu Phe Phe Gln
50 55 60

Thr Thr Gln Pro Glu Lys Ser Ile Gly Val Leu Glu Asn Gly Ile Glu
65 70 75 80

Leu Leu Leu Lys Val His Pro Phe Leu Ala Gly Asp Val Thr Arg Arg
85 90 95

Thr Glu Ser Ser Gln Thr Lys Tyr Thr Trp Gln Ile Glu Pro Glu Ala
100 105 110

Ser Glu Ser Leu Val Gln Phe Pro Ile Leu Arg Ile Arg His Tyr Gln
115 120 125

Ala Glu Ser Phe Lys Glu Ile Gln Ser Lys Cys Leu Leu Thr Gly Thr
130 135 140

Glu Glu Gln Glu Ile Ile Ser Arg Leu Ala Pro Leu Pro Ile Asp Met
145 150 155 160

Asp Ile Ser Leu Pro Arg Arg Pro Ile Leu Arg Phe Gln Ala Asn Val
165 170 175

Met Arg Asp Gly Ile Ile Leu Ala Met Thr Phe His His Ser Ala Met
180 185 190

Asp Gly Ala Gly Ala Ala Arg Val Leu Gly Leu Leu Ala Asp Cys Cys
195 200 205

Arg Asp Pro Thr Ala Met Ser Ser Ala Ser Val Ser Pro Asp Arg Gln
210 215 220

Leu Arg Ser Glu Ile Glu Arg Leu Val Pro Glu Ser Ser Ser Gly Leu
225 230 235 240

Ser Arg Met Asp Phe Ser Lys His Tyr Cys Gly Leu Gly Asp Trp Ala
245 250 255

Ala Leu Leu Ala Lys Asn Trp Ser Gly Phe Val Arg Ala Arg Ala Thr
260 265 270

Glu Leu Val Thr Trp Arg Leu Lys Ile Pro Gly Pro Lys Ile Glu Tyr
275 280 285

Leu Lys Glu Ala Cys Asn Thr Leu Ile Lys Gly Gln Thr Ser Phe Gln
290 295 300

Ala Asp Gly Arg Pro Ser Pro Gly Phe Leu Ser Ser Asn Asp Ile Val
305 310 315 320

Ser Ala Leu Leu Ala Met Ile Leu Arg Gln Ala Gly Gln Leu Ala Gly
325 330 335

Lys Ser Thr Glu Leu Ser Ile Ala Val Asp Met Arg Gly Asn Phe Lys
340 345 350

Thr Pro Ala Phe Asp Asp Tyr Leu Gly Asn Met Val Leu Leu Thr Tyr
355 360 365

Thr Pro Ile Gln Ala Gly Arg Asn Glu Ala Leu Val Asp Gly Thr Asp
370 375 380

Pro Ser Val Glu Leu Arg Gln Glu Cys Leu Glu Asp Leu Thr Gln Ile

385 390 395 400

Ala Ala Arg Ile Arg Gln Ser Leu Leu Ala Val Asp Ala Glu Tyr Ile
405 410 415

Gln Asp Ala Leu Ser His Leu His Ser Gln Pro Asp Trp Ala Asp Ile
420 425 430

Gly Phe Arg Gly Val Pro Ile Pro Leu Ser Ser Phe Arg Asn Phe Glu
435 440 445

Ile Phe Gly Leu Asp Phe Gly Glu Ser Leu Gly Ala Gln Pro Arg Gly
450 455 460

Phe Gln Leu His Leu Pro Val Leu Gly Gly Met Cys Phe Ile Leu Pro
465 470 475 480

Lys Gly Gln Asp Asp Val Ala Ser Thr Glu Pro Trp Asp Leu His Leu
485 490 495

Thr Leu Asn Arg Asp Asp Gln Leu Leu Leu Ala Lys Asp Pro Leu Phe
500 505 510

Cys Trp Ala Ile Gly Ala Gln Ala Lys Glu
515 520

<210> 275
<211> 434
<212> PRT
<213> Penicillium coprobium PF1169

<400> 275

Met Asp Ser Leu Leu Thr Ser Pro Leu Trp Leu Lys Ile Ala His Glu
1 5 10 15

Leu Ala Leu Tyr Leu Ser Phe Ile Val Pro Thr Ala Phe Leu Ile Ile
20 25 30

Thr Thr Gln Lys Ser Ser Ile Ile Arg Trp Ala Trp Thr Pro Cys Leu
35 40 45

Leu Tyr Ile Leu Tyr Gln Phe Ser Leu Arg Val Pro Ser Leu Ser Thr
50 55 60

Ser Gln Phe Leu Lys Gly Val Ala Ala Gly Gln Ala Thr Val Ala Ala
65 70 75 80

Leu Gln Cys Leu Asn Leu Leu Leu Ile Thr Lys Leu Asp Gln Thr Asp
85 90 95

Leu Leu Arg Ala Asn Leu Tyr Ser Pro Ser Ala Gly Leu Leu Ser Arg
100 105 110

Leu Ala Gln Ser Cys Ala Leu Leu Val Asn Phe Arg Gly Ile Gly Thr
115 120 125

Ile Trp Glu Val Arg Asn Ile Pro Gln His Ala Ala Phe Val Gln Pro
130 135 140

Lys Gly Lys Asp Gln Ser Met Ser Arg Lys Arg Phe Val Leu Arg Glu
145 150 155 160

Ile Ala Ile Ile Val Trp Gln Tyr Leu Leu Leu Asp Phe Ile Tyr Glu
165 170 175

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

Gly Met Glu Ile Lys Tyr Leu Asp Ala Thr Phe Glu Gln Trp Met Gly
195 200 205

Arg Leu Ser Val Gly Ile Phe Ser Trp Leu Val Pro Ser Arg Val Cys
210 215 220

Leu Asn Ile Thr Ser Arg Leu Tyr Phe Leu Ile Leu Val Val Leu Gly
225 230 235 240

Ile Ser Ser Pro Glu Ser Cys Arg Pro Gly Phe Gly Arg Val Arg Asp
245 250 255

Val Cys Thr Ile Arg Gly Val Trp Gly Lys Phe Trp His Gln Ser Phe
260 265 270

Arg Trp Pro Leu Thr Ser Val Gly Asn Tyr Ile Ala Arg Asp Val Leu
275 280 285

Gly Leu Ala His Pro Ser Leu Leu Glu Arg Tyr Thr Asn Ile Phe Phe
290 295 300

Thr Phe Phe Thr Ser Gly Val Leu His Leu Val Cys Asp Ala Ile Leu
305 310 315 320

Gly Val Pro Pro Ser Ala Ser Gly Ala Met Gln Phe Phe Cys Ser Phe
325 330 335

Pro Leu Ala Ile Met Ile Glu Asp Gly Val Gln Glu Ile Trp Arg Arg
340 345 350

Ala Thr Gly Gln Thr Lys Asp Ser Asp Arg Ala Val Pro Phe Trp Gln
355 360 365

Arg Leu Val Gly Tyr Leu Trp Val Ala Val Trp Met Cys Val Thr Ser
370 375 380

Pro Phe Tyr Leu Tyr Pro Ala Ala Arg Gln His Ala Glu Lys Asn Trp
385 390 395 400

Ile Val Pro Phe Ser Ile Val Glu Glu Ile Gly Leu Gly Thr Ala Gln
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Lys Ile Leu Leu Gly Tyr Gly Leu Phe Val Tyr Trp Ala Val Gly Gly
420 425 430

Glu Ile

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<212> PRT
<213> Penicillium coprobium PF1169

<400> 276

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Ser Leu His Asn Pro Ile Pro Trp Gln Leu His Thr Tyr Val Trp Pro
20 25 30

Phe Leu Ile Ile Trp Pro Val Phe Phe Ala Phe Tyr Leu Ser Pro Glu
35 40 45

Arg Tyr Asp Thr Tyr Ile Gln Gly Gln Glu Trp Thr Phe Val Phe Ala
50 55 60

Gly Ser Ile Ile Thr Val Gln Ser Leu Phe Trp Leu Met Thr Lys Trp
65 70 75 80

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

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

Ala Glu Ile Cys Asn Leu Ile Arg Glu His Ile Gly Pro Lys Lys Thr
115 120 125

Leu Ser Phe Leu Phe Gln Lys Arg Arg Phe Leu Phe Tyr Pro Glu Thr
130 135 140

Arg Ser Phe Ala Pro Leu Ser Tyr Ala Leu Asp Ala Glu Pro Lys Pro
145 150 155 160

Ala Leu Lys Thr Phe Gln Gln Ser Glu Gly Phe Thr Ser Lys Ala Glu
165 170 175

Ile Glu Arg Val Gln Asn His Tyr Gly Asp Asn Thr Phe Asp Ile Pro
180 185 190

Val Pro Gly Phe Ile Glu Leu Phe Gln Glu His Ala Val Ala Pro Phe
195 200 205

Phe Val Phe Gln Ile Phe Cys Val Gly Leu Trp Met Leu Asp Glu Tyr
210 215 220

Trp Tyr Tyr Ser Leu Phe Thr Leu Phe Met Leu Val Met Phe Glu Ser
225 230 235 240

Thr Val Val Trp Gln Arg Gln Arg Thr Leu Ser Glu Phe Arg Gly Met
245 250 255

Ser Ile Lys Pro Tyr Asp Val Trp Val Tyr Arg Glu Arg Lys Trp Gln
260 265 270

Glu Ile Thr Ser Asp Lys Leu Leu Pro Gly Asp Leu Met Ser Val Asn
275 280 285

Arg Thr Lys Glu Asp Ser Gly Val Ala Cys Asp Ile Leu Leu Val Glu
290 295 300

Gly Ser Val Ile Val Asn Glu Ala Met Leu Ser Gly Glu Ser Thr Pro
305 310 315 320

Leu Leu Lys Asp Ser Ile Gln Leu Arg Pro Gly Asp Asp Leu Ile Glu
325 330 335

Pro Asp Gly Leu Asp Lys Leu Ser Phe Val His Gly Gly Thr Lys Val
340 345 350

Leu Gln Val Thr His Pro Asn Leu Thr Gly Asp Ala Gly Leu Lys Asn
355 360 365

Leu Ala Ser Asn Val Thr Met Pro Pro Asp Asn Gly Ala Leu Gly Val
370 375 380

Val Val Lys Thr Gly Phe Glu Thr Ser Gln Gly Ser Leu Val Arg Thr
385 390 395 400

Met Ile Tyr Ser Thr Glu Arg Val Ser Ala Asn Asn Val Glu Ala Leu
405 410 415

Leu Phe Ile Leu Phe Leu Leu Ile Phe Ala Ile Ala Ala Ser Trp Tyr
420 425 430

Val Trp Gln Glu Gly Val Ile Arg Asp Arg Lys Arg Ser Lys Leu Leu
435 440 445

Leu Asp Cys Val Leu Ile Ile Thr Ser Val Val Pro Pro Glu Leu Pro
450 455 460

Met Glu Leu Ser Leu Ala Val Asn Thr Ser Leu Ala Ala Leu Ser Lys
465 470 475 480

Tyr Ala Ile Phe Cys Thr Glu Pro Phe Arg Ile Pro Phe Ala Gly Arg
485 490 495

Val Asp Ile Ala Cys Phe Asp Lys Thr Gly Thr Leu Thr Gly Glu Asp
500 505 510

Leu Val Val Asp Gly Ile Ala Gly Leu Thr Leu Gly Glu Ala Gly Ser
515 520 525

Lys Val Glu Ala Asp Gly Ala His Thr Glu Leu Ala Asn Ser Ser Ala
530 535 540

Ala Gly Pro Asp Thr Thr Leu Val Leu Ala Ser Ala His Ala Leu Val
545 550 555 560

Lys Leu Asp Glu Gly Glu Val Val Gly Asp Pro Met Glu Lys Ala Thr
565 570 575

Leu Glu Trp Leu Gly Trp Thr Leu Gly Lys Asn Asp Thr Leu Ser Ser
580 585 590

Lys Gly Asn Ala Pro Val Val Ser Gly Arg Ser Val Glu Ser Val Gln
595 600 605

Ile Lys Arg Arg Phe Gln Phe Ser Ser Ala Leu Lys Arg Gln Ser Thr
610 615 620

Ile Ala Thr Ile Thr Thr Asn Asp Arg Asn Ala Ser Lys Lys Thr Lys
625 630 635 640

Ser Thr Phe Val Gly Val Lys Gly Ala Pro Glu Thr Ile Asn Thr Met
645 650 655

Leu Val Asn Thr Pro Pro Asn Tyr Glu Glu Thr Tyr Lys His Phe Thr
660 665 670

Arg Asn Gly Ala Arg Val Leu Ala Leu Ala Tyr Lys Tyr Leu Ser Ser
675 680 685

Glu Thr Glu Leu Ser Gln Ser Arg Val Asn Asn Tyr Val Arg Glu Glu
690 695 700

Ile Glu Ser Glu Leu Ile Phe Ala Gly Phe Leu Val Leu Gln Cys Pro
705 710 715 720

Leu Lys Asp Asp Ala Ile Lys Ser Val Gln Met Leu Asn Glu Ser Ser

725 730 735

His Arg Val Val Met Ile Thr Gly Asp Asn Pro Leu Thr Ala Val His
740 745 750

Val Ala Arg Lys Val Glu Ile Val Asp Arg Glu Val Leu Ile Leu Asp
755 760 765

Ala Pro Glu His Asp Asn Ser Gly Thr Lys Ile Val Trp Arg Thr Ile
770 775 780

Asp Asp Lys Leu Asn Leu Glu Val Asp Pro Thr Lys Pro Leu Asp Pro
785 790 795 800

Glu Ile Leu Lys Thr Lys Asp Ile Cys Ile Thr Gly Tyr Ala Leu Ala
805 810 815

Lys Phe Lys Gly Gln Lys Ala Leu Pro Asp Leu Leu Arg His Thr Trp
820 825 830

Val Tyr Ala Arg Val Ser Pro Lys Gln Lys Glu Glu Ile Leu Leu Gly
835 840 845

Leu Lys Asp Ala Gly Tyr Thr Thr Leu Met Cys Gly Asp Gly Thr Asn
850 855 860

Asp Val Gly Ala Leu Lys Gln Ala His Val Gly Val Ala Leu Leu Asn
865 870 875 880

Gly Ser Gln Glu Asp Leu Thr Lys Ile Ala Glu His Tyr Arg Asn Thr
885 890 895

Lys Met Lys Glu Leu Tyr Glu Lys Gln Val Ser Met Met Gln Arg Phe
900 905 910

Asn Gln Pro Ala Pro Pro Val Pro Val Leu Ile Ala His Leu Tyr Pro
915 920 925

Pro Gly Pro Thr Asn Pro His Tyr Glu Lys Ala Met Glu Arg Glu Ser
930 935 940

Gln Arg Lys Gly Ala Ala Ile Thr Ala Pro Gly Ser Thr Pro Glu Ala
945 950 955 960

Ile Pro Thr Ile Thr Ser Pro Gly Ala Gln Ala Leu Gln Gln Ser Asn
965 970 975

Leu Asn Pro Gln Gln Gln Lys Lys Gln Gln Ala Gln Ala Ala Ala Ala
980 985 990

Gly Leu Ala Asp Lys Leu Thr Ser Ser Met Met Glu Gln Glu Leu Asp
995 1000 1005

Asp Ser Glu Pro Pro Thr Ile Lys Leu Gly Asp Ala Ser Val Ala
1010 1015 1020

Ala Pro Phe Thr Ser Lys Leu Ala Asn Val Ile Ala Ile Pro Asn
1025 1030 1035

Ile Ile Arg Gln Gly Arg Cys Thr Leu Val Ala Thr Ile Gln Met
1040 1045 1050

Tyr Lys Ile Leu Ala Leu Asn Cys Leu Ile Ser Ala Tyr Ser Leu
1055 1060 1065

Ser Val Ile Tyr Leu Asp Gly Ile Lys Phe Gly Asp Gly Gln Val
1070 1075 1080

Thr Ile Ser Gly Met Leu Met Ser Val Cys Phe Leu Ser Ile Ser
1085 1090 1095

Arg Ala Lys Ser Val Glu Gly Leu Ser Lys Glu Arg Pro Gln Pro
1100 1105 1110

Asn Ile Phe Asn Val Tyr Ile Ile Gly Ser Val Leu Gly Gln Phe
1115 1120 1125

Ala Ile His Ile Ala Thr Leu Ile Tyr Leu Ser Asn Tyr Val Tyr
1130 1135 1140

Lys His Glu Pro Arg Asp Ser Asp Ile Asp Leu Glu Gly Glu Phe
1145 1150 1155

Glu Pro Ser Leu Leu Asn Ser Ala Ile Tyr Leu Leu Gln Leu Ile
1160 1165 1170

Gln Gln Ile Ser Thr Phe Ser Ile Asn Tyr Gln Gly Arg Pro Phe
1175 1180 1185

Arg Glu Ser Ile Arg Glu Asn Lys Gly Met Tyr Trp Gly Leu Ile
1190 1195 1200

Ala Ala Ser Gly Val Ala Phe Ser Cys Ala Thr Glu Phe Ile Pro
1205 1210 1215

Glu Leu Asn Glu Lys Leu Arg Leu Val Pro Phe Thr Asn Glu Phe
1220 1225 1230

Lys Val Thr Leu Thr Val Leu Met Ile Phe Asp Tyr Gly Gly Cys
1235 1240 1245

Trp Leu Ile Glu Asn Val Leu Lys His Leu Phe Ser Asp Phe Arg
1250 1255 1260

Pro Lys Asp Ile Ala Ile Arg Arg Pro Asp Gln Leu Lys Arg Glu
1265 1270 1275

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Glu Leu Gln Arg Lys Val
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atttaaatag ttagacaata gtatca 26

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gcgcggggta ccatgttgtc ttagcatttt catta 35

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<211> 40
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<210> 289
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<210> 291
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