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(54) Title: CONSERVED ESCHERICHIA COLI IMMUNOGENS

(57) Abstract: Homologs of the E. coli proteins orf353, bacterial lg-like domain (group 1) protein (orf405), flu antigen 43 (orfl 364), NodT-family outer-membrane-factor-lipoprotein efflux transporter (orfl 767), gspK (orf3515), gspJ (orf3516), toriB-dependent siderophore receptor (orO597), fibrial protein (orf3613), upec-948, upec- 1232. A chain precursor of the type- 1 fimbria! protein (upec- 1875), yapH homolog (upec-2820), hemolysin A (recp-3768), and Sel 1 repeat-containing protein (upec-521 1) from several pathogenic strains of E. coli have been identified with regions within the proteins that are conserved across all E. coli. Fragments corresponding to the conserved regions, especially immunogenic fragments such a linear B-epitopes, are provided. In addition, variants of the bacterial lg-l ike domain (group 1) protein (orf405), yapH homolog (upec2820) and two different fragments of hemolysin A (recp3768) are provided herein that have increased solubility as compared to the native protein where the variants still raise a substantially similar immune response in a subject as the corresponding native protein.

CONSERVED ESCHERICHIA COLI IMMUNOGENS

TECHNICAL FIELD

This invention relates to immunisation against pathogenic *Escherichia coli* strains.

BACKGROUND ART

E.coli strains have traditionally been classified as either commensal or pathogenic, and pathogenic strains are then sub-classified as intestinal or extraintestinal strains. Pathogenic *E.coli* are discussed in more detail in reference 1, and fall into a number of different pathotypes *i.e.* a group of *E.coli* strains that cause a common disease using a common set of virulence factors. Pathotyping of strains is a routine technique that can be performed genotypically or phenotypically. One recent genotype-based pathotyping method [2] uses a DNA microarray.

Among intestinal strains at least six well-described pathotypes are known: enteropathogenic (EPEC), enterohaemorrhagic (EHEC), enteroaggregative (EAEC), enteroinvasive (EIEC), enterotoxigenic (ETEC) and diffusely adherent (DAEC).

The extraintestinal pathogenic strains (or 'ExPEC' strains [3,4]) of *E.coli* include uropathogenic (UPEC) strains, neonatal meningitis (NMEC) strains, and septicemia-associated strains (SEPEC). ExPEC is the most common cause of urinary tract infections and one of the leading causes of neonatal meningitis and neonatal sepsis in humans, which can lead to serious complications and death. Other types of extraintestinal infections include osteomyelitis, pulmonary, intra-abdominal, soft tissue, and intravascular device-associated infections. Another ExPEC pathotype outside humans is avian pathogenic (APEC), causing extraintestinal infections in poultry.

Most previous ExPEC vaccines have been based on cell lysates or on cellular structures. SOLCOUROVAC™ includes ten different heat-killed bacteria including six ExPEC strains. URO-VAXOM™ is an oral tablet vaccine containing lyophilised bacterial lysates of 18 selected *E.coli* strains. Baxter Vaccines developed a UTI vaccine based on pili from 6 to 10 different strains. MedImmune developed a product called MEDI 516 based on the FimH adhesin complex. In contrast, references 5 and 6 disclose specific immunogens from ExPEC strains that can be used as the basis of defined vaccines against both NMEC and UPEC strains.

However, there remains a need for providing a vaccine that protects against a broad spectrum of intestinal and extraintestinal *E. coli* strains. *E. coli* is a versatile microorganism with an improved ability to adapt to new niches and to cause a broad spectrum of disease. Fitness, virulence and colonization factors can change in order to allow the microorganism to adapt to different tissues and hosts. Therefore, potential antigens are subject to high selective pressure and, as a result, may have sequence variability among different strains.

The database of genomes available at ncbi.nlm.nih.gov under genomes listed twenty one pathogenic and non-pathogenic *E. coli* genomes with as few as 4,126 proteins to as many as 5,339 proteins. However, such listings do not identify which are conserved across a significant fraction of the pathogenic *E. coli*, what are the conserved regions in the proteins that are so conserved, or which proteins among the thousands of potential proteins can be used in a vaccine to produce a sufficient immune response to protect against pathogenic *E. coli* which requires screening large numbers of proteins to identify the best candidates.

It is an object of the invention to provide further and better antigens for use in immunisation against pathogenic *E.coli* strains, and more particularly against intestinal pathotypes (*e.g.* EAEC, EIEC, EPEC and ETEC strains) as well as ExPEC pathotypes.

DISCLOSURE OF THE INVENTION

One of the many antigens disclosed in reference 5 is annotated as 'orf353' (SEQ IDs 705 & 706 therein), which is also known as: 'orf236' from *E. coli* NMEC strain IHE3034, 'c0368' from *E. coli* strain CFT073 and ecp_0248 from *E. coli* strain 536. Another such antigen disclosed in reference 5 is annotated as Bacterial Ig-like domain (group 1) protein (also as 'orf405', SEQ IDs 809 & 810), which is also known as: 'orf284' from *E. coli* NMEC strain IHE3034, 'c0415' from *E. coli* strain CFT073 and ecp_0367 from *E. coli* strain 536. Yet another such antigen disclosed in reference 5 is annotated as Flu antigen 43 protein (also as 'orf1364', SEQ IDs 2727 & 2728), which is also known as: 'orf1109' from *E. coli* NMEC strain IHE3034, 'c1273' from *E. coli* strain CFT073 and ecp_3009 from *E. coli* strain 536. Yet another such antigen disclosed in reference 5 is annotated as NodT-family outer-membrane-factor-lipoprotein efflux transporter protein (also as 'orf1767', SEQ IDs 3533 & 3534), which is also known as: 'orf1488' from *E. coli* NMEC strain IHE3034, 'c1765' from *E. coli* strain CFT073 and ecp_1346 from *E. coli* strain 536. Yet another such antigen disclosed in reference 5 is annotated as gspK general secretion pathway protein (also as 'orf3515', SEQ IDs 7029 & 7030), which is also known as: 'orf3332' from *E. coli* NMEC strain IHE3034, 'c3702' from *E. coli* strain CFT073 and ecp_3039 from *E. coli* strain 536. Yet another such antigen disclosed in reference 5 is annotated as gspJ general secretion pathway protein (also as 'orf3516', SEQ IDs 7029 & 7030), which is also known as: 'orf3333' from *E. coli* NMEC strain IHE3034 and ecp_3040 from *E. coli* strain 536. Yet another such antigen disclosed in reference 5 is annotated as tonB-dependent siderophore receptor (also as 'orf3597', SEQ IDs 7193 & 7194), which is also known as: 'orf3415' from *E. coli* NMEC strain IHE3034, 'c3775' from *E. coli* strain CFT073 and ecp_3121 from *E. coli* strain 536. Yet another such antigen disclosed in reference 5 is annotated as Fimbrial protein (also as 'orf3613', SEQ IDs 7225 & 7226), which is also known as: 'orf3431' from *E. coli* NMEC strain IHE3034 and 'c3791' from *E. coli* strain CFT073. Yet another such antigen disclosed in WO2008/020330 is annotated as Hemolysin A protein (also as 'recp3768', SEQ IDs 3), which is also known as: 'c3570' from *E. coli* strain CFT073 and ecp_3827 from *E. coli*

strain 536. 'upec948' protein from *E. coli* UPEC is also known as: 'c0975 from *E. coli* strain CFT073. 'upec1232' protein from *E. coli* UPEC is disclosed in reference 6 (SEQ ID 138) is also known as: 'c1275 from *E. coli* strain CFT073. Yet another such antigen disclosed in reference 6 is annotated as Type-1 fimbrial protein, A chain precursor (also as 'upec1875', SEQ ID 221), which is also known as: 'orf1642' from *E. coli* NMEC strain IHE3034 and 'c1936' from *E. coli* strain CFT073. Yet another such antigen disclosed in reference 6 is annotated as YapH homolog protein (also as 'upec2820', SEQ ID 307), which is also known as: 'c2895' from *E. coli* strain CFT073. Reference 5, reference 6, WO2008/020330, and other references discloses the sequences from NMEC strain IHE3034 or UPEC strains, and certain aspects of the present invention are based on variants of the ExPEC 'orf353', the Bacterial Ig-like domain (group 1) protein, Flu antigen 43 protein, NodT-family outer-membrane-factor-lipoprotein efflux transporter protein, gspK general secretion pathway protein, gspJ general secretion pathway protein, tonB-dependent siderophore receptor, Fimbrial protein, 'upec948' protein, 'upec1232', Type-1 fimbrial protein, A chain precursor, and YapH homolog protein that have been identified in further pathotypes, including APEC, UPEC, EAEC, EIEC, EPEC and ETEC strains. Unlike the disclosure of reference 5, these variants can be particularly useful for treating intestinal pathotypes. Thus the invention provides such variants, together with their use in immunising patients against *E.coli* infections. In addition, this disclosure includes fragments of the each of the proteins – bacterial Ig-like domain (group 1) protein (orf405), flu antigen 43 (orf1364), NodT-family outer-membrane-factor-lipoprotein efflux transporter (orf1767), gspK (orf3515), gspJ (orf3516), tonB-dependent siderophore receptor (orf3597), fibrial protein (orf3613), upec-948, upec-1232, A chain precursor of the type-1 fimbrial protein (upec-1875), yapH homolog (upec-2820), hemolysin A (recp-3768), and SelI repeat-containing protein (upec-5211) – of all *E. coli* pathotypes where the fragments are conserved across multiple strains and therefore can provide an immune response in a subject that provides protection across several strains.

Polypeptides used with the invention

The invention provides a polypeptide comprising an amino acid sequence that is derived from orf353, bacterial Ig-like domain (group 1) protein (orf405), flu antigen 43 (orf1364), NodT-family outer-membrane-factor-lipoprotein efflux transporter (orf1767), gspK (orf3515), gspJ (orf3516), tonB-dependent siderophore receptor (orf3597), fibrial protein (orf3613), upec-948, upec-1232, A chain precursor of the type-1 fimbrial protein (upec-1875), yapH homolog (upec-2820), hemolysin A (recp-3768), and SelI repeat-containing protein (upec-5211), each as more fully described herein.

orf353 protein

'orf353' protein from *E. coli* NMEC is disclosed in reference 5 (SEQ IDs 705 & 706) is also known as: 'orf236' from *E. coli* NMEC strain IHE3034, 'c0368' from CFT073 and ecp_0248 from 536.

When used according to the present invention, orf353 protein may take various forms. Preferred orf353 sequences have 50% or more identity (*e.g.* 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98%, 99%

or more) to SEQ ID NOs 1-2. This includes variants (*e.g.* allelic variants, homologs, orthologs, paralogs, mutants *etc*).

Other preferred orf353 sequences comprise at least *n* consecutive amino acids from SEQ ID SEQ ID NOs 1-2, wherein *n* is 7 or more (*eg.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). Preferred fragments comprise an epitope or immunogenic fragment from orf353. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or the N-terminus of SEQ ID SEQ ID NOs 1-2. Exemplary fragments are the conserved fragments SEQ ID NOs identified in the sequence alignment below.

```
Group A: strain IHE3034, RS218, APECO1, 536, UTI89 and F11  (SEQ ID NO: 1)
Strain O42  (SEQ ID NO: 2)

            1                                                  50
Group A     MLKMSLYVII LLFSLQFSAA ITGKESEVVS PLLMDVNPSL TMENISELST
strain O42  MLKISLYVII LLFSFQISAA ITSKESEVVS PLLMDVNSSL TMENISELST
  Consensus MLK-SLYVII LLFS-Q-SAA IT-KESEVVS PLLMDVN-SL TMENISELST
               SEQ ID NO: 211      SEQ ID NOs: 212-214     SEQ ID NO: 215
 B-Cell Ep.                       ********                    ****

            51                                                 100
Group A     SSEPSQQGVF PVICTRLHPG SVMKRQLLTG WGPVFIIGDD PFSLRWMSEH
strain O42  SSEPSQQGVF PVICTRLHPG SVMKRQLLTG WGPVFIIGDD PFSLRWMSEH
  Consensus SSEPSQQGVF PVICTRLHPG SVMKRQLLTG WGPVFIIGDD PFSLRWMSEH
B-Cell Ep.  ********

            101                                                150
Group A     LEILKSLNAL GLVVNVESVE RMEVLQQRAD GLLLLPVICD NFVQALQLNA
strain O42  LEILKSLNAL GLVVNVESVE RMEVLQQRAD GLLLLPVICD NFVQTLQLNA
  Consensus LEILKSLNAL GLVVNVESVE RMEVLQQRAD GLLLLPVICD NFVQ-LQLNA

            151       162
Group A     YPVLITEMEI SQ
strain O42  YPVLITEMEI SQ
  Consensus YPVLITEMEI SQ
            SEQ ID NO: 216

SEQ ID NO: 212  SAAIT(G/S)KESEVVSPLLMDVN
SEQ ID NO: 213  SAAITGKESEVVSPLLMDVN *
SEQ ID NO: 214  SAAITSKESEVVSPLLMDVN

B-Cell Epitopes
SEQ ID NO: 217  ITGKESEV
SEQ ID NO: 218  ELSTSSEPSQQG
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Orf405 protein

Bacterial Ig-like domain (group 1) protein is referred to herein as 'orf405.' 'orf405' protein from *E. coli* NMEC is disclosed in reference 5 (SEQ IDs 809 & 810) is also known as: 'orf284' from *E. coli* NMEC strain IHE3034, 'c0415' from CFT073 and ecp_0367 from 536.

When used according to the present invention, orf405 protein may take various forms. Preferred orf405 sequences have 50% or more identity (*e.g.* 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98%, 99%

or more) to SEQ ID NOs 3-18. This includes variants (*e.g.* allelic variants, homologs, orthologs, paralogs, mutants *etc*).

Other preferred orf405 sequences comprise at least *n* consecutive amino acids from SEQ ID NOs 3-18, wherein *n* is 7 or more (*eg.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). Preferred fragments comprise an epitope or immunogenic fragment from orf405. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or the N-terminus of SEQ ID NOs 3-18. Exemplary fragments are the conserved fragments SEQ ID NOs identified in the sequence alignment below. In addition, the three fragments tested for solubility and immunogenicity, 405A, 405B, and 405C, are underlined with 'A', 'B', and 'C', respectively.

```
strains B, C and 8739  (SEQ ID NO: 3)
strain H10407  (SEQ ID NO: 4)
strain 101-1  (SEQ ID NO: 5)
strain 536  (SEQ ID NO: 6)
strain F11  (SEQ ID NO: 7)
strain CFT073  (SEQ ID NO: 8)
Group A: strain IHE3034, UTI89, RS218 and APECO1  (SEQ ID NO: 9)
strain E2348-69  (SEQ ID NO: 10)
strains B171 and E22  (SEQ ID NO: 11)
strain B7A  (SEQ ID NO: 12)
strain E110019  (SEQ ID NO: 13)
strain HS  (SEQ ID NO: 14)
strain E24377A  (SEQ ID NO: 15)
strain O42  (SEQ ID NO: 16)
Group B: strain Sakai, EDL933, EC508, EC869, EC4024, EC4042, EC4045, EC4076,
EC4113, EC4115, EC4196, EC4206, EC4401, EC4486, EC4501 and TW14588  (SEQ ID NO:
17)
strain SECEC  (SEQ ID NO: 18)

strains B, C and 8739  MSHYKTGHKQ PRFRYSVLAR CVAWANISVQ VLFPLAVTFT PVMAARAQHA
strain H10407          MSHYKTGHKQ PRFRYSVLAR CVAWANISVQ VLFPLAVTFT PVMAARAQHA
strain 101-1           MSHYKTGHKQ PRFRYSVLAR CVAWANISVQ VLFPLAVTFT PVMAARAQHA
strain 536             MSRYKTDNKQ PRFRYSVLAR CVAWANISVQ VLFPLAVTFT PVMAARAQHA
strain F11             MSRYKTDNKQ PRFRYSVLAR CVAWANISVQ VLFPLAVTFT PVMAARAQHA
strain CFT073          MSRYKTDNKQ PRFRYSVLAR CVAWANISVQ VLFPLAVTFT PVMAARAQHA
Group A                MSRYKTDNKQ PRFRYSVLAR CVAWANISVQ VLFPLAVTFT PVMAARAQHA
strain E2348-69        MSRYKTGHKQ PRFRYSVLAR CVAWTNISVQ VLFPLAVTFT PVMAARAQHA
strains B171 and E22   MSRYKTGHKQ PLFRYSVLAR CVAWANISVQ VLFPLAVTFT PVMAAHAQHA
strain B7A             MSRYKTGHKQ PRFRYSVLAR CVAWANISVQ VLFPLAVTFT PVMAARAQHA
strain E110019         MSRYKTGHKQ PRFRYSVLAR CVAWANISVQ VLFPLAVTFT PVMAARAQHA
strain HS              MSRYKTDHKQ PRFRYSVLAR CVAWANISVQ VLFPLAVTFT PVMAARAQHA
strain E24377A         MSHYKTGHKQ PRFRYSVLAR CVAWANISVQ VLFPLAVTFT PVMAARAQHA
strain O42             MSRYKTGHKQ PRFRYSVLAR CVAWANISVQ VLFPLAVTFT PVMAARAQHA
Group B                MSRYKTGHKQ PRFRYSVLAR CVAWANISVQ VLFPLAVTFT PVMAARAQHA
strain SECEC           MSRYKTGHKQ PQFRYSVLAR CVAWANISVQ VLFPLAVTFT PVMAARAQHA
          . Consensus  MS-YKT--KQ P-FRYSVLAR CVAW-NISVQ VLFPLAVTFT PVMAA-AQHA
                                  SEQ ID NO: 219      SEQ ID NO: 220
Frag                                    AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA

                       51                                                100
strains B, C and 8739  VQPRLSMGNT TVTADNNVEK NVASFAANAG TFLSSQPDSD ATRNFITGMA
strain H10407          VQPRLSMGNT TVTADNNVEK NVASFAANAG TFLSSQPDSD ATRNFITGMA
strain 101-1           VQPRLSMGNT TVTADNNVEK NVASFAANAG TFLSSQPDSD ATRNFITGMA
strain 536             VQPRLSMENT TVTADNNVEK NVASLAANAG TFLSSQPDSD ATRNFITGMA
strain F11             VQPRLSMENT TVTADNNVEK NVASLAANAG TFLSSQPDSD ATRNFITGMA
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strain CFT073          VQPRLSMENT TVTADNNVEK NVASLAANAG TFLSSQPDSD ATRNFITGMA
Group A                VQPRLSMENT TVTADNNVEK NVASLAANAG TFLSSQPDSD ATRNFITGMA
strain E2348-69        VQPRLSMGNT TVTADNNVEK NVASFAANAG TFLSSQPDSD ATRNFITGMA
strains B171 and E22   VQPRLSMENT TVTADNNVEK NVASFAANAG TFLSSQPDSD ATRNFITGMA
strain B7A             VQPRLSMGNT TVTADNNVEK NVASFAANAG TFLSSQPDSD ATRNFITGMA
strain E110019         VQPRLSMGNT TVTADNNVEK NVASFAANAG TFLSSQPDSD ATRNFITGMA
strain HS              VQPRLSMGNT TVTADNNVEK NVASFAANAG TFLSSQPDSD ATRNFITGMA
strain E24377A         VQPRLSMGNT TVTADNNVEK NVASFAANAG TFLSSQPDSD ATRNFITGMA
strain O42             VQPRLSMENT TVAADNNVEK NVASFAANAG TFLSSQPDSD ATRNFITGMA
Group B                VQPRLSMGNT TVTADNNVEK NVASFAANAG TFLSSQPDSD ATRNFITGMA
strain SECEC           VQPRLSMGNT TVTADSNVEK NVASFAANAG TFLSSQPDSD ATRNFITGMA
           Consensus   VQPRLSM-NT TVtADnNVEK NVAS-AANAG TFLSSQPDSD ATRNFITGMA
                 SEQ ID NO: 221  SEQ ID NOs 222-5          SEQ ID NO: 683
B-Cell Ep.                     * **********              ********* ***
Frag                   AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA

                       101                                                150
strains B, C and 8739  TAKANQEIQE WLGKYGTARV KLNVDKDFSL KDSSLEMLYP IYDTPTNMLF
strain H10407          TAKANQEIQE WLGKYGTARV KLNVDKDFSL KDSSLEMLYP IYDTPTNMLF
strain 101-1           TAKANQEIQE WLGKYGTARV KLNVDKDFSL KDSSLEMLYP IYDTPTNMLF
strain 536             TAKANQEIQE WLGKYGTARV KLNVDKNFSL KDSSLEMLYP IYDTPTNMLF
strain F11             TAKANQEIQE WLGKYGTARV KLNVDKNFSL KDSSLEMLYP IYDTPTNMLF
strain CFT073          TAKANQEIQE WLGKYGTARV KLNVDKKFSL KDSSLEMLYP IYDTPTNMLF
Group A                TAKANQEIQE WLGKYGTARV KLNVDKNFSL KDSSLEMLYP IYDTPTNMLF
strain E2348-69        TAKANQEIQE WLGKYGTARV KLNVDKDFSL KDSSLEMLYP IYDTPTNMLF
strains B171 and E22   TAKANQEIQE WLGKYGTARV KLNVDKDFSL KDSSLEMLYP IYDTPTNMLF
strain B7A             TAKANQEIQE WLGKYGTARV KLNVDKDFSL KDSSLEMLYP IYDTPTNMLF
strain E110019         TAKANQEIQE WLGKYGTARV KLNVDKDFSL KDSSLEMLYP IYDTPTNMLF
strain HS              TAKANQEIQE WLGKYGTARV KLNVDKDFSL KDSSLEMLYP IYDTPTNMLF
strain E24377A         TAKANQEIQE WLGKYGTARV KLNVDKDFSL KDSSLEMLYP IYDTPTNMLF
strain O42             TAKANQEIQE WLGKYGTARV KLNVDKEFSL KDSSLEMLYP IYDTPTNMLF
Group B                TAKANQEIQE WLGKYGTARV KLNVDKDFSL KDSSLEMLYP IYDTPTNMLF
strain SECEC           TAKANQEIQE WLGKYGTARV KLNVDKDFSL KDSSLEMLYP IYDTPTNMLF
           Consensus   TAKANQEIQE WLGKYGTARV KLNVDK-FSL KDSSLEMLYP IYDTPTNMLF
                                                        SEQ ID NO: 226
B-Cell Ep.             *******
Frag                   AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA

                       151                                                200
strains B, C and 8739  TQGAIHRTDD RTQSNIGFGW RHFSGNDWMA GVNTFIDHDL SRSHTRIGVG
strain H10407          TQGAIHRTDD RTQSNIGFGW RHFSGNDWMA GVNTFIDHDL SRSHTRIGVG
strain 101-1           TQGAIHRTDD RTQSNIGFGW RHFSGNDWMA GVNTFIDHDL SRSHTRIGVG
strain 536             TQGAIHRTDD RTQSNIGFGW RHFSENDWMA GVNTFIDHDL SRSHTRIGVG
strain F11             TQGAIHRTDD RTQSNIGFGW RHFSENDWMA GVNTFIDHDL SRSHTRIGVG
strain CFT073          TQGAIHRTDD RTQSNIGFGW RHFSENDWMA GVNTFIDHDL SRSHTRIGVG
Group A                TQGAIHRTDD RTQSNIGFGW RHFSENDWMA GVNTFIDHDL SRSHTRIGVG
strain E2348-69        TQGAIHRTDD RTQSNIGFGW RHFSENDWMA GVNTFIDHDL SRSHTRIGVG
strains B171 and E22   TQGAIHRTDD RTQSNIGFGW RHFSGNDWMA GVNTFIDHDL SRSHTRIGVG
strain B7A             TQGAIHRTDD RTQSNIGFGW RHFSGNDWMA GVNTFIDHDL SRSHTRIGVG
strain E110019         TQGAIHRTDD RTQSNIGFGW RHFSGNDWMA GVNTFIDHDL SRSHTRIGVG
strain HS              TQGAIHRTDD RTQSNIGFGW RHFSGNDWMA GVNTFIDHDL SRSHTRIGVG
strain E24377A         TQGAIHRTDD RTQSNIGFGW RHFSGNDWMA GVNTFIDHDL SRSHTRIGVG
strain O42             TQGAIHRTDD RTQSNIGFGW RHFSGNDWMA GVNTFIDHDL SRSHTRIGVG
Group B                TQGAIHRTDD RTQSNIGFGW RHFSGNDWMA GVNTFIDHDL SRSHTRIGVG
strain SECEC           TQGAIHRTDD RTQSNIGFGW RHFSGNDWMA GVNTFIDHDL SRSHTRIGVG
           Consensus   TQGAIHRTDD RTQSNIGFGW RHFS-NDWMA GVNTFIDHDL SRSHTRIGVG
                                                        SEQ ID NO: 227
B-Cell Ep.                 ****** *****
Frag                   AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA

                       201                                                250
strains B, C and 8739  AEYWRDYLKL SANGYIRASG WKKSPDVEDY QERPANGWDI RAEGYLPAWP
strain H10407          AEYWRDYLKL SANGYIRASG WKKSPDIEDY QERPANGWDI RAEGYLPAWP
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strain 101-1            AEYWRDYLKL SANGYIRASG WKKSPDVEDY QERPANGWDI RAEGYLPAWP
strain 536              AEYWRDYLKL SANGYIRASG WKTSPDVEDY QERPANGWDI RAEGYLPAWP
strain F11              AEYWRDYLKL SANGYIRASG WKTSPDVEDY QERPANGWDI RAEGYLPAWP
strain CFT073           AEYWRDYLKL SANGYIRASG WKKSPDVEDY QERPANGWDI RAEGYLPAWP
Group A                 AEYWRDYLKL SANGYIRASG WKKSPDVEDY QERPANGWDI RAEGYLPAWP
strain E2348-69         AEYWRDYLKL SANGYIRASG WKKSPDVEDY QERPANGWDI RAEGYLPAWP
strains B171 and E22    AEYWRDYLKL SANGYIRASG WKKSPDIEDY QERPANGWDI RAEGYLPAWP
strain B7A              AEYWRDYLKL SANGYIRASG WKKSPDIEDY QERPANGWDI RAEGYLPAWP
strain E110019          AEYWRDYLKL SANGYIRASG WKKSPDIEDY QERPANGWDI RAEGYLPAWP
strain HS               AEYWRDYLKL SANGYIRASG WKKSPDIEDY QERPANGWDI RAEGYLPAWP
strain E24377A          AEYWRDYLKL SANGYIRASG WKKSPDVEDY QERPANGWDI RAEGYLPAWP
strain O42              AEYWRDYLKL SANGYIRASG WKKSPDVEDY QERPANGWDI RAEGYLPAWP
Group B                 AEYWRDYLKL SANGYIRASG WKKSPDIEDY QERPANGWDI RAEGYLPAWP
strain SECEC            AEYWRDYLKL SANGYIRASG WKKSPDIEDY QERPANGWDI RAEGYLPAWP
          Consensus     AEYWRDYLKL SANGYIRASG WK-SPD-EDY QERPANGWDI RAEGYLPAWP
                                                                SEQ ID NO: 228
B-Cell Ep.                          ** ********** ********** *   ******
Frag                    AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA

                        251                                               300
strains B, C and 8739   QLGASLMYEQ YYGDEVGLFG KDKRQKDPHA ISAEVTYTPV PLLTLSAGHK
strain H10407           QLGASLMYEQ YYGDEVGLFG KDKRQKDPHA ISAEVTYTPV PLLTLSAGHK
strain 101-1            QLGASLMYEQ YYGDEVGLFG KDKRQKDPHA ISAEVTYTPV PLLTLSAGHK
strain 536              QLGASLMYEQ YYGDEVGLFG KDKRQKDPHA ITAEVNYTPV PLLTLSAGHK
strain F11              QLGASLMYEQ YYGDEVGLFG KDKRQKDPHA ITAEVNYTPV PLLTLSAGHK
strain CFT073           QLGASLMYEQ YYGDEVGLFG KDKRQKDPHA ITAEVNYTPV PLLTLSAGHK
Group A                 QLGASLMYEQ YYGDEVGLFG KDKRQKDPHA ITAEVNYTPV PLLTLSAGHK
strain E2348-69         QLGASLMYEQ YYGDEVGLFG KDKRQKDPHA ITAEVNYTPV PLLTLSAGHK
strains B171 and E22    QLGASLMYEQ YYGDEVGLFG KDKRQKDPHA ISAEVTYTPV PLLTLSAGHK
strain B7A              QLGASLMYEQ YYGDEVGLFG KDKRQKDPHA ISAEVTYTPV PLLTLSAGHK
strain E110019          QLGASLMYEQ YYGDEVGLFG KDKRQKDPHA ISAEVTYTPV PLLTLSAGHK
strain HS               QLGASLMYEQ YYGDEVGLFG KDKRQKDPHA ISAEVTYTPV PLLTLSAGHK
strain E24377A          QLGASLMYEQ YYGDEVGLFG KDKRQKDPHA ISAEVTYTPV PLLTLSAGHK
strain O42              QLGASLMYEQ YYGDEVGLFG KDKRQKDPHA ITAEVNYTPV PLLTLSAGHK
Group B                 QLGASLMYEQ YYGDEVGLFG KDKRQKDPHA ISAEVTYTPV PLLTLSAGHK
strain SECEC            QLGASLMYEQ YYGDEVGLFG KDKRQKDPHA ISAEVTYTPV PLLTLSAGHK
          Consensus     QLGASLMYEQ YYGDEVGLFG KDKRQKDPHA I-AEV-YTPV PLLTLSAGHK
                                                                SEQ ID NO: 229
B-Cell Ep.              *                     ********** *                 ***
Frag                    AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA

                        301                                               350
strains B, C and 8739   QGKSGENDTR FGLEVNYRIG EPLAKQLDTD SIRERRVLAG SRYDLVERNN
strain H10407           QGKSGENDTR FGLEVNYRIG EPLAKQLDTD SIRERRVLAG SRYDLVERNN
strain 101-1            QGKSGENDTR FGLEVNYRIG EPLAKQLDTD SIRERRVLAG SRYDLVERNN
strain 536              QGKSGENDTR FGLEVNYRIG EPLEKQLDTD SIRERRMLAG SRYDLVERNN
strain F11              QGKSGENDTR FGLEVNYRIG EPLEKQLDTD SIRERRMLAG SRYDLVERNN
strain CFT073           QGKSGENDTR FGLEVNYRIG EPLEKQLDTD SIRERRMLAG SRYDLVERNN
Group A                 QGKSGENDTR FGLEVNYRIG EPLEKQLDTD SIRERRMLAG SRYDLVERNN
strain E2348-69         QGKSGENDTR FGLEVNYRIG EPLEKQLDTD SIRERRMLAG SRYDLVERNN
strains B171 and E22    QGKSGENDTR FGLEVNYRIG EPLEKQLDTD SIRERRMLAG SRYDLVERNN
strain B7A              QGKSGENDTR FGLEVNYRIG EPLEKQLDTD SIRERRMLAG SRYDLVERNN
strain E110019          QGKSGENDTR FGLEVNYRIG EPLAKQLDTD SIRERRVLAG SRYDLVERNN
strain HS               QGKSGENDTR FGLEVNYRIG EPLEKQLDTD SIRERRMLAG SRYDLVERNN
strain E24377A          QGKSGENDTR FGLEVNYRIG EPLAKQLDTD SIRERRVLAG SRYDLVERNN
strain O42              QGKSGENDTR FGLEVNYRIG EPLEKQLDTD SIRERRMLAG SRYDLVERNN
Group B                 QGKSGENDTR FGLEVNYRIG EPLAKQLDTD SIRERRVLAG SRYDLVERNN
strain SECEC            QGKSGENDTR FGLEVNYRIG EPLAKQLDTD SIRERRMLAG SRYDLVERNN
          Consensus     QGKSGENDTR FGLEVNYRIG EPL-KQLDTD SIRERR-LAG SRYDLVERNN
                                                  SEQ ID NO: 230   SEQ ID NO: 231
B-Cell Ep.              **********                  ****** **
Frag                    AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA
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                                351                                                 400
strains B, C and 8739           NIVLEYRKSE VIRIALPERI EGKGGQTLSL GLVVSKATHG LKNVQWEAPS
strain H10407                   NIVLEYRKSE VIRIALPERI EGKGGQTLSL GLVVSKATHG LKNVQWEAPS
strain 101-1                    NIVLEYRKSE VIRIALPERI EGKGGQTLSL GLVVSKATHG LKNVQWEAPS
strain 536                      NIVLEYRKSE VIRIALPERI EGKGGQTVSL GLVVSKATHG LKNVQWEAPS
strain F11                      NIVLEYRKSE VIRIALPERI EGKGGQTVSL GLVVSKATHG LKNVQWEAPS
strain CFT073                   NIVLEYRKSE VIRIALPERI EGKGGQTVSL GLVVSKATHG LKNVQWEAPS
Group A                         NIVLEYRKSE VIRIALPERI EGKGGQTVSL GLVVSKATHG LKNVQWEAPS
strain E2348-69                 NIVLEYRKSE VIRIALPERI EGKGGQTVSL GLVVSKATHG LKNVQWEAPS
strains B171 and E22            NIVLEYRKSE VIRIALPERI EGKGGQTLSL GLVVSKATHG LKNVQWEAPS
strain B7A                      NIVLEYRKSE VIRIALPERI EGKGGQTLSL GLVVSKATHG LKNVQWEAPS
strain E110019                  NIVLEYRKSE VIRIALPERI EGKGGQTLSL GLVVSKATHG LKNVQWEAPS
strain HS                       NIVLEYRKSE VIRIALPERI EGKGGQTLSL GLVVSKATHG LKNVQWEAPS
strain E24377A                  NIVLEYRKSE VIRIALPERI EGKGGQTLSL GLVVSKATHG LKNVQWEAPS
strain O42                      NIVLEYRKSE VIRIALPERI EGKGGQTLSL GLVVSKATHG LKNVQWEAPS
Group B                         NIVLEYRKSE VIRIALPERI EGKGGQTLSL GLVVSKATHG LKNVQWEAPS
strain SECEC                    NIVLEYRKSE VIRIALPDRI AGKGGQTVSL GLVVSKATHG LKNVQWEAPS
            Consensus           NIVLEYRKSE VIRIALP-RI eGKGGQT-SL GLVVSKATHG LKNVQWEAPS
                                                SEQ ID NO: 232-4      SEQ ID NO: 235
B-Cell Ep.                                        *  *******
Frag                            AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA

                                401                                                 450
strains B, C and 8739           LLAEGGKITG QGSQWQVTLP AYRPGKDNYY AISAVAYDNK GNASKRVQTE
strain H10407                   LLAEGGKITG QGSQWQVTLP AYRPGKDNYY AISAVAYDNK GNASKRVQTE
strain 101-1                    LLAEGGKITG QGSQWQVTLP AYRPGKDNYY AISAVAYDNK GNASKRVQTE
strain 536                      LLAAGGKITG QGNQWQVTLP AYQAGKDNYY AISAIAYDNK GNASKRVQTE
strain F11                      LLAAGGKITG QGNQWQVTLP AYQAGKDNYY AISAIAYDNK GNASKRVQTE
strain CFT073                   LLAAGGKITG QGNQWQVTLP AYQAGKDNYY AISAIAYDNK GNASKRVQTE
Group A                         LLAAGGKITG QGNQWQVTLP AYQAGKDNYY AISAIAYDNK GNASKRVQTE
strain E2348-69                 LLAAGGKITG QGNQWQVTLP AYQAGKDNYY AISAIAYDNK GNASKRVQTE
strains B171 and E22            LLAEGGKITG QGSQWQVTLP AYRPGKDNYY AISAVAYDNK GNASKRVQTE
strain B7A                      LLAEGGKITG QGSQWQVTLP AYRPGKDNYY AISAVAYDNK GNASKRVQTE
strain E110019                  LLAEGGKITG QGSQWQVTLP AYRPGKDNYY AISAVANDNK GNASKRVQTE
strain HS                       LLAEGGKITG QGSQWQVTLP AYRPGKDNYY AISAVAYDNK GNASKRVQTE
strain E24377A                  LLAEGGKITG QGSQWQVTLP AYRPGKDNYY AISAVAYDNK GNASKRVQTE
strain O42                      LLAEGGKITG QGSQWQVTLP AYRPGKDNYY AVSAIAYDNK GNASKRVQTE
Group B                         LLAEGGKITG QGSQWQVTLP AYRPGKDNYY AISAVAYDNK GNTSKRVQTE
strain SECEC                    LLAAGGKITG QGNQWQVTLP AYQAGKDNYY AISAVAYDNK GNASKRVQTE
            Consensus           LLA-GGKITG QG-QWQVTLP AY--GKDNYY A-SA-A-DNK GNASKRVQTE
                                                                        SEQ ID NO: 236
B-Cell Ep.                                                             ***  *******
Frag                            AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA

                                451                                                 500
strains B, C and 8739           VVITGAGMSA DRTALTLDGQ SRIQMLANGN EQRPLVLSLR DAEGQPVTGM
strain H10407                   VVITGAGMSA DRTALTLDGQ SRIQMLANGN EQRPLVLSLR DAEGQPVTGM
strain 101-1                    VVITGAGMSA DRTALTLDGQ SRIQMLANGN EQKPLVLSLR DAEGQPVTGM
strain 536                      VVISGAGMSA DRTALTLDGQ SRIQMLANGN EQKPLVLSLR DAEGQPVTGM
strain F11                      VVISGAGMSA DRTALTLDGQ SRIQMLANGN EQKPLVLSLR DAEGQPVTGM
strain CFT073                   VVISGAGMSA DRTALTLDGQ SRIQMLANGN EQKPLVLSLR DAEGQPVTGM
Group A                         VVISGAGMSA DRTALTLDGQ SRIQMLANGN EQKPLVLSLR DAEGQPVTGM
strain E2348-69                 VVISGAGMSA DRTALTLDGQ SRIQMLANGN EQKPLVLSLR DAEGQPVTGM
strains B171 and E22            VVITGAGMSA DRTALTLDGQ SRIQMLANGN EQRPLVLSLR DAEGQPVTGM
strain B7A                      VVITGAGMSA DRTALTLDGQ SRIQMLANGN EQRPLVLSLR DAEGQPVTGM
strain E110019                  VVITGAGMSA DRTALTLDGQ SRIQMLANGN EQRPLVLSLR DAEGQPVTGM
strain HS                       VVITGAGMSA DRTALTLDGQ SRIQMLANGN EQRPLVLSLR DAEGQPVTGM
strain E24377A                  VVITGAGMSA DRTALTLDGQ SRIQMLANGN EQRPLVLSLR DAEGQPVTGM
strain O42                      VVISGAGMSA DRTALTLDGQ SRIQMLANGN EQKPLVLSLR DAEGQPVTGM
Group B                         VVITGAGMSA DRTALTLDGQ SRIQMLANGN EQKPLVLSLR DAEGQPVTGM
strain SECEC                    VVITGAGMSA ERTALTLDGQ SRIQMLANGS EQKPLVLSLR DAEGQPVTGM
            Consensus           VVI-GAGMSA -RTALTLDGQ SRIQMLANG- EQ-PLVLSLR DAEGQPVTGM
                                              SEQ ID NO: 237        SEQ ID NO: 238
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B-Cell Ep.                                                          **********
Frag                    AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA

                        501                                                 550
strains B, C and 8739   KDQIKTELAF KPAGNIVTRS LKATKSQAKP TLGEFTETEA GVYQSVFTTG
strain H10407           KDQIKTELAF KPAGNIVTRS LKATKSQAKP TLGEFTETEA GVYQSVFTTG
strain 101-1            KDQIKTELTF KPAGNIVTRT LKATKSQAKP TLGEFTETEA GVYQSVFTTG
strain 536              KDQIKTELTF KPAGNIVTRS LKVTKSQAKP TLGEFTETEA GVYQSVFTTG
strain F11              KDQIKTELTF KPAGNIVTRS LKVTKSQAKP TLGEFTETEA GVYQSVFTTG
strain CFT073           KDQIKTELTF KPAGNIVTRT LKATKSQAKP TLGEFTETEA GVYQSVFTTG
Group A                 KDQIKTELTF KPAGNIVTRT LKATKSQAKP TLGEFTETEA GVYQSVFTTG
strain E2348-69         KDQIKTELTF KPAGNIVTRT LKATKSQAKP TLGEFTETEA GVYQSVFTTG
strains B171 and E22    KDQIKTELTF KPAGNIVTRT LKATKSQAKP TLGEFTETEA GVYQSVFTTG
strain B7A              KDQIKTELTF KPAGNIVTRT LKATKSQAKP TLGEFTETEA GVYQSVFTTG
strain E110019          KDQIKTELTF KPAGNIVTRT LKATKSQAKP TLGEFTETEA GVYQSVFTTG
strain HS               KDQIKTELTF KPAGNIVTRT LKATKSQAKP TLGEFTETEA GVYQSVFTTG
strain E24377A          KDQIKTELAF KPAGNIVTRS LKATKSQAKP TLGEFTETEA GVYQSVFTTG
strain O42              KDQIKTELTF KPAGNIVTRT LKATKSQAKP TLGEFTETEA GVYQSVFTTG
Group B                 KDQIKTELTF KPAGNIVTRS LKATKSQAKP TLGEFTETEA GVYQSVFTTG
strain SECEC            KDQIKTELTF KPAGNIVTRT LKATKSQAQP TLGEFTETEA GVYQSVFTTG
            Consensus   KDQIKTEL-F KPAGNIVTR- LK-TKSQA-P TLGEFTETEA GVYQSVFTTG
                                  SEQ ID NO: 239                SEQ ID NO: 240
B-Cell Ep.              ***                     * ********** **      ***
Frag                    AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA

                        551                                                 600
strains B, C and 8739   TQSGEATITV SVDGMSKTVT AELRATMMDV ANSTLSANEP SGDVVADGQQ
strain H10407           TQSGEATITV SVDGMSKTVT AELRATMMDV ANSTLSANEP SGDVVADGQQ
strain 101-1            TQSGEATITV SVDGMSKTVT AELRATMMDV ANSTLSANEP SGDVVADGQQ
strain 536              TQSGEATITV SVDGMSKTVT AELRATMMDV ANSTLSANEP SGDVVADGQQ
strain F11              TQSGEATITV SVDGMSKTVT AELRATMMDV ANSTLSANEP SGDVVADGQQ
strain CFT073           TQSGEATITV SVDDMSKTVT AELRATMMDV ANSTLSANEP SGDVVADGQQ
Group A                 TQSGEATITV SVDDMSKTVT AELRATMMDV SNSTLSANEP SGDVVADGQQ
strain E2348-69         TQSGEATITV SVDDMSKTVT AELRATMMNV ANSTLSANEP SGDVVADGRQ
strains B171 and E22    TQSGEATITV SVDGMSKTVT AELRATMMDV ANSTLSANEP SGDVVADGQQ
strain B7A              TQSGEATITV SVDGMSKTVT AELRATMMDV ANSTLSANEP SGDVVADGQQ
strain E110019          TQSGEATITV SVDGMSKTVT AELRATMMDV ANSTLSANEP SGDVVADGQQ
strain HS               TQSGEATITV SVDGMSKTVT AELRATMMDV ANSTLSANEP SGDVVADGQQ
strain E24377A          TQSGEATITV SVDGMSKTVT AELRATMMDV ANSTLSANEP SGDVVADGQQ
strain O42              TQSGEATITV SVDGMSKTVT AELRATMMDV ANSTLSANEP SGDVVADGQQ
Group B                 TQSGEATITV SVDGMSKTVT AELRATMMDV ANSTLSANEP SGDVVADGQQ
strain SECEC            TQSGEATITV SVDDMSKTVT AELRATMMDV ANSTLSANEP SGDVVADGQQ
            Consensus   TQSGEATITV SVD-MSKTVT AELRATMM-V -NSTLSANEP SGDVVADG-Q
                                     SEQ ID NO: 241        SEQ ID NO: 242
B-Cell Ep.              *******                 ******* ********
Frag                    AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAABBBBBB

                        601                                                 650
strains B, C and 8739   AYTLTLTAVD SEGNPVTGEA SRLRFVPQDT NGVTVGAISE IKPGVYSATV
strain H10407           AYTLTLTAVD SEGNPVTGEA SRLRFVPQDT NGVTVGAISE IKPGVYSATV
strain 101-1            AYTLTLTAVD SEGNPVTGEA SRLRFVPQDT NGVTVGAISE IKPGVYSATV
strain 536              AYTLTLTAVD SEGNPVTGEA SRLRLVPQDT NGVTVGAISE IKPGVYSATV
strain F11              AYTLTLTAVD SEGNPVTGEA SRLRLVPQDT NGVTVGAISE IKPGVYSATV
strain CFT073           AYTLTLTAVD SEGNPVTGEA SRLRLVPQDT NGVTVGAISE IKPGVYSATV
Group A                 AYTLTLTAVD SEGNPVTGEA SRLRLVPQDT NGVTVGAISE IKPGVYSATV
strain E2348-69         AYTLTLTAVD SEGNPVTGEA SRLRLVPQDT NGVTVGAISE IKPGGYSATV
strains B171 and E22    AYTLTLTAVD TDGNPVTGEA SRLRFVPQDT NGVTIGTISE IKPGVYSATV
strain B7A              AYTLTLTAVD TDGNPVTGEA SRLRFVPQDT NGVTIGTISE IKPGVYSATV
strain E110019          AYTLTLTAVD SEGNPVTGEA SRLRFVPQDT NGVTVGAISE IKPGVYSATV
strain HS               AYTLTLTAVD TDGNPVTGEA SRLRFVPQDT NGVTIGTISE IKPGVYSATV
strain E24377A          AYTLTLTAVD SEGNPVTGEA SRLRFVPQDT NGVTVGAISE IKPGVYSATV
strain O42              AYTLTLTAVD SEGNPVTGEA SRLRLVPQDT NGVTVGAISE IKPGVYSATV
Group B                 AYTLTLTAVD SEGNPVTGEA SRLRFVPQDT NGVTVGAISE IKPGVYSAAV
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strain SECEC          SHTLTLTAVD TDGNPVTGEA SRLRLVPQDT NGVTVGAISE IKPGVYSATV
          Consensus   --TLTLTAVD --GNPVTGEA SRLR-VPQDT NGVT-G-ISE IKPG-YSA-V
                                 SEQ ID NO: 243  SEQ ID NO: 244
B-Cell Ep.                       ********        ****  ****       **********
Frag                  BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB

                      651                                                 700
strains B, C and 8739 SSTRAGNVVV RAFSEQYQLG TLQQTLKFVA GPLDAAHSSI TLNPDKPVVG
strain H10407         SSTRAGNVVV RAFSEQYQLG TLQQTLKFVA GPLDAAHSSI PLNPDKPVVG
strain 101-1          SSTRAGNVVV RAFSEQYQLG TLQQTLKFVA GPLDAAHSSI TLNPDKPVVG
strain 536            SSTRAGNVVV RAFSEQYQLG TLQQTLKFVA GPLDAAHSSI TLNPDKPVVG
strain F11            SSTRAGNVVV RAFSEQYQLG TLQQTLKFVA GPLDAAHSSI TLNPDKPVVG
strain CFT073         SSTRAGNVVV RAFSEQYQLG TLQQTLKFVA GPLDAAHSSI TLNPDKPVVG
Group A               SSTRAGNVVV RAFSEQYQLG TLQQTLKFVA GPLDAAHSSI TLNPDKPVVG
strain E2348-69       SSTRAGNVVV RVFSEQYQLG TLQQTLKFVA GPLDAAHSSI TLNPDKPVVG
strains B171 and E22  SSTRAGNVVV RAFSEQYQLG TLQQTLKFVA GPLDAAHSSI TLNPDKPVVG
strain B7A            SSTRAGNVVV RAFSEQYQLG TLQQTLKFVA GPLDAAHSSI TLNPDKPVVG
strain E110019        SSTRAGNVVV RAFSEQYQLG TLQQTLKFVA GPLDAAHSSI TLNPDKPVVG
strain HS             SSTRAGNVVV RAFSEQYQLG TLQQTLKFVA GPLDAAHSSI TLNPDKPVVG
strain E24377A        SSTRAGNVVV RAFSEQYQLG TLQQTLKFVA GPLDAAHSSI TLNPDKPVVG
strain O42            SSTRAGNVVV RAFSEQYQLG TLQQTLKFVA GPLDAAHSSI TLNPDKPVVG
Group B               SSTRAGNVVV RAFSEQYQLG TLQQTLKFVA GPLDAAHSSI TLNPDKPVVG
strain SECEC          SSTRAGNVVV RAFSEQYQLG TLQQTLKFVA GPLDAAHSSI TLNPDKPVVG
          Consensus   SSTRAGNVVV R-FSEQYQLG TLQQTLKFVA GPLDAAHSSI -LNPDKPVVG
                    SEQ ID NO: 245        SEQ ID NO: 246          SEQ ID NO: 247
B-Cell Ep.           *****                                        *********
Frag                  BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB

                      701                                                 750
strains B, C and 8739 GTVTAIWTAK DAYDNPVTSL TPEAPSLAGA AAVGSTASGW TNNGDGTWTA
strain H10407         GTVTAIWTAK DAYDNPVTSL TPEAPSLAGA AAVGSTASGW TNNGDGTWTA
strain 101-1          GTVTAIWTAK DANDNPVTGL NPDAPSLSGA AAVGSTASGW TDNGDGTWTA
strain 536            GTVTAIWTAK DANDNPVTGL NPDAPSLSGA AAAGSTASGW TDNGDGTWTA
strain F11            GTVTAIWTAK DANDNPVTGL NPDAPSLSGA AAAGSTASGW TDNGDGTWTA
strain CFT073         GTVTAIWTAK DANDNPVTGL NPDAPSLSGA AAAGSTASGW TDNGDGTWTA
Group A               GTVTAIWTAK DANDNPVTGL NPDAPSLSGA AAAGSTASGW TDNGDGTWTA
strain E2348-69       GTVTAIWTAK DANDNPVTGL NPDAPSLSGA AAAGSTASGW TDNGDGTWTA
strains B171 and E22  GTVTAIWTVK DAYDNPVTSL TPEAPSLAGA AAVGSTASGW TNNGDGTWTA
strain B7A            GTVTAIWTVK DAYDNPVTSL TPEAPSLAGA AAVGSTASGW TNNGDGTWTA
strain E110019        GTVTAIWTAK DANDNPVTGL NPDAPSLSGA AAAGSTASGW TDNGDGTWTA
strain HS             GTVTAIWTAK DANDNPVTGL NPDAPSLSGA AAAGSTASGW TDNGDGTWTA
strain E24377A        GTVTAIWTVK DAYDNPVTSL TPEAPSLAGA AAVGSTASGW TNNGDGTWTA
strain O42            GTVTAIWTAK DANDNPVTGL NPDAPSLSGA AAAGSTASGW TNNGDGTWTA
Group B               GTVTAIWTVK DAYDNPVTSL TPEAPSLAGA AAEGSTASGW TNNGDGTWTA
strain SECEC          GTVTAIWTAK DAYDNPVTSL TPEAPSLAGA AAVGSTASGW TNNGDGTWTA
          Consensus   GTVTAIWT-K DA-DNPVT-L -P-APSL-GA AA-GSTASGW T-NGDGTWTA
                                                                SEQ ID NO: 248
B-Cell Ep.           *                                  *******  *********
Frag                  BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB

                      751                                                 800
strains B, C and 8739 QITLGSTAGE LEVMPKLNGQ DAAANAAKVT VVADALSSNQ SKVSVAEDHV
strain H10407         QITLGSTAGE LEVMPKLNGQ DAAANAAKVT VVADALSSNQ SKVSVAEDHV
strain 101-1          QISLGTTAGE LEVMPKLNGQ DAAANAAKVT VVADALSSNQ SKVSVAEDHV
strain 536            QISLGTTAGE LDVMPKLNGQ DAAANAAKVT VVADALSSNQ SKVSVAEDHV
strain F11            QISLGTTAGE LDVMPKLNGQ DAAANAAKVT VVADALSSNQ SKVSVAEDHV
strain CFT073         QISLGTTAGE LDVMPKLNGQ DAAANAAKVT VVADALSSNQ SKVSVAEDHV
Group A               QISLGTTAGE LDVMPKLNGQ DAAANAAKVT VVADALSSNQ SKVSVAEDHV
strain E2348-69       QISLGTTAGE LDVMPKLNGQ DAAANAAKVT VVADALSSNQ SKVSVAEDHV
strains B171 and E22  QITLGSTAGE LEVMPKLNGQ DAAANAAKVT VVADALSSNQ SKVSVAEDHV
strain B7A            QITLGSTAGE LEVMPKLNGQ DAAANAAKVT VVADALSSNQ SKVSVAEDHV
strain E110019        QISLGTTAGE LEVIPKLNGQ DAAANAAKVT VVADALSSNQ SKVSVAEDHV
strain HS             QISLGTTAGE LEVIPKLNGQ DAAANAAKVT VVADALSSNQ SKVSVAEDHV
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strain E24377A          QITLGSTAGE LEVMPKLNGQ DAAANAAKVT VVADALSSNQ SKVSVAEDHV
strain O42              QITLGSTAGE LEVMPKLNGQ DAAANAAKVT VVADALSSNQ SKVSVAEDHV
Group B                 QITLGSTAGE LEVMPKLNGQ NAAANAAKVT VVADALSSNQ SKVSVAEDHV
strain SECEC            QITLGSTAGE LDVMPKLNGQ DAAANAAKVT VVADALSSNQ SKVSVAEDHV
            Consensus   QI-LG-TAGE L-V-PKLNGQ -AAANAAKVT VVADALSSNQ SKVSVAEDHV
                                                        SEQ ID NO: 249
B-Cell Ep.                   ******      ***** ******          ***** *****  ***
Frag                    BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB

                        801                                                 850
strains B, C and 8739   KAGESTTVTL IAKDAHGNTI SGLSLSASLT GTASEGATVS SWTEKGDGSY
strain H10407           KAGESTTVTL IAKDAHGNTI SGLSLSASLT GTASEGATVS SWTEKGDCSY
strain 101-1            KAGESTTVTL VAKDAHGNAI SGLSLSASLT GTASEGATVS SWTEKGDGSY
strain 536              KAGESTTVTL VAKDAHGNAI SGLSLSASLT GTASEGATVS SWTEKGDGSY
strain F11              KAGESTTVTL VAKDAHGNAI RGLSLSASLT GTASEGATVS SWTEKGDGSY
strain CFT073           KAGESTTVTL VAKDAHGNAI SGLSLSASLT GTASEGATVS SWTEKGDGSY
Group A                 KAGESTTVTL VAKDAHGNAI SGLSLSASLT GTASEGATVS SWTEKGDGSY
strain E2348-69         KAGESTTVTL VAKDAHGNAI SGLSLSASLT GTASEGATVS SWTEKGDGSY
strains B171 and E22    KAGESTTVTL IAKDAHGNAI SGLSLSASLT GTASEGATVS SWTEKGDGSY
strain B7A              KAGESTTVTL IAKDAHGNAI SGLSLSASLT GTASEGATVS SWTEKGDGSY
strain E110019          KAGESTTVTL VAKDAHGNAI SGLSLSASLT GTASEGATVS SWTEKGDGSY
strain HS               KAGESTTVTL IAKDAHGNAI SGLSLSASLT GAASEGATVS GWTEKGDGSY
strain E24377A          KAGESTTVTL VAKDAHGNAI SGLSLSASLT GTASEGATVS SWTEKGDGSY
strain O42              KAGESTTVTL IAKDAHGNAI SGLSLSASLT GTASEGATIS SWTEKGDGSY
Group B                 KAGESTTVTL VAKDAHGNAI SGLALSASLT GTASEGATVS SWTEKGNGSY
strain SECEC            KAGESTTVTL IAKDAHGNAI SGLSLSASLT GAASEGATVS SWTEKGDGSY
            Consensus   KAGESTTVTL -AKDAHGN-I -GL-LSASLT G-ASEGATvS sWTEKG--SY
                                                        SEQ ID NO: 250-253
B-Cell Ep.              ******                           ********* *******
Frag                    BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB

                        851                                                 900
strains B, C and 8739   VATLTTGGKT GELRVMPLFN GQPAATEAAQ LTVIAGEMSS ANSTLVAANK
strain H10407           VATLTTGGKT GELRVMPLFN GQPAATEAAQ LTVIAGEMSS ANSTLVADNK
strain 101-1            VATLTTGGKT GELRVMPLFN GQPAATEAAQ LTVIAGEMSS ANSTLVADNK
strain 536              VATLTTGGKT GELRVMPLFN GQPAATEAAQ LTVIAGEMSS ANSTLVADNK
strain F11              VATLTTGGKT GELRVMPLFN GQPAATEAAQ LTVIAGEMSS ANSTLVADNK
strain CFT073           VATLTTGGKT GELRVMPLFN GQPAATEAAQ LTVIAGEMSS ANSTLVADNK
Group A                 VATLTTGGKT GELRVMPLFN GQPAATEAAQ LTVIAGEMSS ANSTLVADNK
strain E2348-69         VATLTTGGKT GELRVMPLFN GQPAATEAAQ LTVIAGEMSS ANSTLVADNK
strains B171 and E22    VATLTTGGKT GELRVMPLFN GQPAATEAAQ LTVIAGEMSS ANSTLVADNK
strain B7A              VATLTTGGKT GELRVMPLFN GQPAATEAAQ LTVIAGEMSS ANSTLVADNK
strain E110019          VATLTTGGKT GELRVMPLFN GQPAATEAAQ LTVIAGEMSS ANSTLVADNE
strain HS               VATLTTGGKT GELLVMPLFN GQPAATEAAQ LTVIAGEMSS ANSTLVADNK
strain E24377A          VATLTTGGKT GELRVMPLFN GQPAATEAAQ LTVIAGEMSS ANSTLVADNK
strain O42              VATLTTGGKT GELRVMPLFN GQPAATEAAQ LTVIAGEMSS ANSTLVADNK
Group B                 VATLTTGGKT GELRVMPLFN GQPAATEAAQ LTVIAGEMSS ANSTLVADNK
strain SECEC            VATLTTGGKT GELLVMPLFN GQPAATEAAQ LTVIAGEMSS ANSTLVADNK
            Consensus   VATLTTGGKT GEL-VMPLFN GQPAATEAAQ LTVIAGEMSS ANSTLVA-N-
                         SEQ ID NO: 254            SEQ ID NO: 255
B-Cell Ep.                    ***** *           ********
Frag                    BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB

                        901                                                 950
strains B, C and 8739   APTVKMTTEL TFTVKDAYGN PVTGLKPDAP VFSGAASTGS ERPSAGNWTE
strain H10407           APTVKMTTEL TFTVKDAYGN PVTGLKPDAP VFSGAASTGS ERPSAGNWTE
strain 101-1            APTVKTTTEL TFTVKDAYGN PVTGMKPDAP VFSGAANTGS ERPSAGNWTE
strain 536              TPTVKTTTEL TFTVKDAYGN PVTGLKPDAP VFSGAASTGS ERPSAGNWTE
strain F11              TPTVKTTTEL TFTVKDAYGN PVTGLKPDAP VFSGAASTGS ERPSAGNWTE
strain CFT073           TPTVKTTTEL TFTVKDAYGN PVTGLKPDAP VFSGAASTGS ERPSAGNWTE
Group A                 TPTVKTTTEL TFTMKDAYGN PVTGLKPDAP VFSGAASTGS ERPSAGNWTE
strain E2348-69         TPTVKTTTEL TFTVKDAYGN PVTGLKPDAP VFSGAASTGS ERPSAGNWTE
strains B171 and E22    APTVKTTTEL TFTVKDAYGN PVTGMKPDAP VFSGAASTGT ERPSTGDWTE
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strain B7A              APTVKTTTEL TFTVKDAYGN PVTGMKPDAP VFSGAASTGT ERPSTGDWTE
strain E110019          APTVKTTTKL TFTVKDAYGN LVTGLKPDAP QFSGAASTGT ERPSTGDWTE
strain HS               APTVKTTTKL TFTVKDAYGN LVTGLKPDAP QFSGAASTGT ERPSTGDWTE
strain E24377A          APTVKTTTEL TFTVKDAYGN PVTGMKPDAP VFSGAASTGT ERPSTGDWTE
strain O42              TPTVKTTTEL TFTVKDAYGN PVTGLKPDAP VFSGAASTGS ARPSAGSWTE
Group B                 APTVKTTTEL TFTVKDAYGN PVTGLKPDAP VFSGAASTGS ERPSAGNWTE
strain SECEC            APTVKATTEL TFTAKDAYGN PVSGLKLDAP VFSGAASTGS ERPSAGSWTE
            Consensus   -PTVK-TT-L TFT-KDAYGN -V-G-K-DAP -FSGAASTG- -RPS-G-WTE
Frag                    BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB

                        951                                                1000
strains B, C and 8739   KGNGVYVATL TLGSAAGQLS VMPRVNGQNA VAQPLVLNVA GDASKAEIRD
strain H10407           KGNGVYVATL TLGSAAGQLS VMPRVNGQNA VAQPLVLNVA GDASKAEIRD
strain 101-1            KGNGVYVATL TLGSAAGQLS VMPRVNGQNA VAQPLVLNVA GDASKAEIRD
strain 536              KGNGVYVSTL TLGSAAGQLS VMPRVNGQNA VAQPLVLNVA GDASKAEIRD
strain F11              KGNGVYVSTL TLGSAAGQLS VMPRVNGQNA VAQPLVLNVA GDASKAEIRD
strain CFT073           KGNGVYVSTL TLGSAAGQLS VMPRVNGQNA VAQPLVLNVA GDASKAEIRD
Group A                 KGNGVYVSTL TLGSAAGQLS VMPRVNGQNA VAQPLVLNVA GDASKAEIRD
strain E2348-69         KGNGVYVSTL TLGSAAGQLS VMPRVNGQNA VAQPLVLNVA GDASKAEIRD
strains B171 and E22    TSNGVYVATL TLGSAAGQLS VMPRVNGQNA VAQPLVLNVA GDASKAEIRD
strain B7A              TSNGVYVATL TLGSAAGQLS VMPRVNGQNA VAQPLVLNVA GDASKAEIRD
strain E110019          TSNGVYVATL TLGSAAGQLS VMPRVNGQNA VAQPLVLNVA GDASKAEIRD
strain HS               TSNGVYVATL TLGSAAGQLS VMPRVNGQNA VAQPLVLNVA GDASKAEIRD
strain E24377A          TSNGVYVATL TLGSAAGQLS VMPRVNGQNA VAQPLVLNVA GDASKAEIRD
strain O42              QSNGVYVATL TLGSAAGQLS VMPRVNGQNA VAQPLVLNVA GDASRAVISD
Group B                 KGNGVYVSTL TLGSAAGQLS VMPRVNGQNA VAQPLVLNVA GDASKAEIRD
strain SECEC            QSNGVYVATL TLGSAAGQLS VMPRVNGQNA VAQPLVLNVA GDASKAEIRD
            Consensus   --NGVYV-TL TLGSAAGQLS VMPRVNGQNA VAQPLVLNVA GDAS-A-I-D
                                              SEQ ID NO: 256
B-Cell Ep.                                    ******* *
Frag                    BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB

                        1001                                               1050
strains B, C and 8739   MTVKVNNQLA NGQSANQITL TVVDSYGNPL QGQEVTLTLP QGVTSKTGNT
strain H10407           MTVKVNNQLA NGQSANQITL TVVDSYGNPL QGQEVTLTLP QGVTSKTGNT
strain 101-1            MTVKVNNQLA NGQSANQITL TVVDSYGNPL QGQEVTLTLP QGVTSKTGNT
strain 536              MTVKVNNQLA NGQSANQITL TVVDSYGNPL QGQEVTLTLP QGVTSKTGNT
strain F11              MTVKVNNQLA NGQSANQITL TVVDSYGNPL QGQEVTLTLP QGVTSKTGNT
strain CFT073           MTVKVNNQLA NGQSANQITL TVVDSYGNPL QGQEVTLTLP QGVTSKTGNT
Group A                 MTVKVNNQLA NGQSANQITL TVVDSYGNPL QGQEVTLTLP QGVTSKTGNT
strain E2348-69         MTVKVNNQLA NGQSANQITL TVVDSYGNPL QGQEVTLTLP QGVTSKTGNT
strains B171 and E22    MTVKVDNQLA NGQSTNQVTL TVVDTYGNPL QGQNVTLTLP KGVTSKTGNT
strain B7A              MTVKVDNQLA NGQSTNQVTL TVVDTYGNPL QGQNVTLTLP KGVTSKTGNT
strain E110019          MTVKVDNQLA NGQSTNQVTL TVVDTYGNPL QGQNVTLTLP KGVTSKTGNT
strain HS               MTVKVDNQLA NGQSTNQVTL TVVDTYGNPL QGQNVTLTLP KGVTSKTGNT
strain E24377A          MTVKVDNQLA NGQSTNLVTL TVVDTYGNPL QGQEVTLNLP QGVTSKTGNT
strain O42              MAVKVNNQLA NGQSANQVTL TVVDSYGNPL QGQEVTLTLP QGVTSKTGNT
Group B                 MTVKVNNQLA NGQSANQITL TVVDTYGNPL QGQEVTLTLP QGVTSKTGNT
strain SECEC            MTVKVDNQLA NGQSTNQVTL TVVDTYGNPL QGQEVTLTLP QGVTSKTGNT
            Consensus   M-VKV-NQLA NGQStN--TL TVVDsYGNPL QGQ-VTL-LP -GVTSKTGNT
                         SEQ ID NO: 257-9     SEQ ID NO: 260-62       SEQ ID NO: 263
B-Cell Ep.                  *** ******          ****** ***           **********
Frag                    BBBBBBBBCC CCCCCCCCCC CCCCCCCCCC CCCCCCCCCC CCCCCCCCCC

                        1051                                               1100
strains B, C and 8739   VTTNAAGKVD IELMSTVAGE HSITASVNNA QKTVTVKFKA DFSTGQATLE
strain H10407           VTTNAAGKVD IELMSTVAGE HSITASVNNA QKTVTVKFKA DFSTGQATLE
strain 101-1            VTTNAAGKVD IELMSTVAGE HSITASVNNA QKTVTVKFKA DFSTGQATLE
strain 536              VTTNAAGKVD IELMSTVAGE HNISASVNGA QKTVTVKFNA DASTGQANLQ
strain F11              VTTNAAGKVD IELMSTVAGE HNISASVNGA QKTVTVKFNA DASTGQANLQ
strain CFT073           VTTNAAGKVD IELMSTVAGE LEIEASVKNS QKTVKVKFKA DFSTGQASLE
Group A                 VTTNAAGKVD IELMSTVAGE LEIEASVKNS QKTVKVKFKA DFSTGQASLE
strain E2348-69         VTTNAAGKVD IELMSTVAGE LEIEASVKNS QKTVKVKFKA DFSTGQASLE
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strains B171 and E22   VTTDAAGKAD IELMSTVAGE HSITASVNNA QKTVTVKFKA DFSTGQASLE
strain B7A             VTTDAAGKAD IELMSTVAGE HSITASVNNA QKTVTVKFKA DFSTGQASLE
strain E110019         VTTDAAGKAD IELMSTVAGE HSITASVNNA QKTVTVKFKA DFSTGQASLE
strain HS              VTTDAAGKAD IELMSTVAGE HSITASVNNA QKTVTVKFKA DFSTGQASLE
strain E24377A         VTTNAAGKAD IELISTVAGE LEIAAAVKNS QKTVTVKFNA DASTGQANLQ
strain O42             VTTNAAGKAD IELISTVAGE LEIAAAVKNS QKTVTVKFNA DASTGQANLQ
Group B                VTTNAAGKAD IELMSTVAGE HNISASVNGA QKTVTVKFNA DASTGQANLQ
strain SECEC           VTTNAAGKAD IELISTVAGE LEIAAAVKNS QKTVTVKFNA DASTGQANLQ
            Consensus  VTT-AAGK-D IEL-STVAGE --I-A-V--- QKTV-VKF-A D-STGQA-L-
B-Cell Ep.             ***          ********
Frag                   CCCCCCCCCC CCCCCCCCCC CCCCCCCCCC CCCCCCCCCC CCCCCCCCCC

                       1101                                                1150
strains B, C and 8739  VDGSTPKVAN DNDAFTLTAT VKDQYGNLLP GAVVVFNLPW GVKPLADGNI
strain H10407          VDGSTPKVAN DNDAFTLTAT VKDQYGNLLP GAVVVFNLPR GVKPLADGNI
strain 101-1           VDGSTPKVAN DNDAFTLTAT VKDQYGNLLP GAVVVFNLPR GVKPLADGNI
strain 536             VDTAVQKVAN GKDAFTLTAT VKDQYGNLLP GAVVVFNLPR GVKPLADGNI
strain F11             VDTAVQKVAN GKDAFTLTAT VKDQYGNLLP GAVVVFNLPR GVKPLADGNI
strain CFT073          VDAAAQKVAN GKDAFTLTAT VKDQYGNLLP GAVVVFNLPR GVKPLADGNI
Group A                VDAAAQKVAN GKDAFTLTAT VKDQYGNLLP GAVVVFNLPR GVKPLADGNI
strain E2348-69        VDAAAQKVAN GKDAFTLTAT VKDQYGNLLP GAVVVFNLPR GVKPLADGNI
strains B171 and E22   VDSAAPKVAN GKDAFTLTAT VEDKNGNPVP GSLVTFNLPR GVKPLTGDNV
strain B7A             VDSAAPKVAN GKDAFTLTAT VEDKNGNPVP GSLVTFNLPR GVKPLTGDNV
strain E110019         VDSAAPKVAN GKDAFTLTAT VEDKNGNPVP GSLVTFNLPR GVKPLTGDNV
strain HS              VDSAAPKVAN GKDAFTLTAT VEDKNGNPVP GSLVTFNLPR GVKPLTGDNV
strain E24377A         VDTAVQKVAN GKDAFTLTAT VEDKNGNPVP GSLVTFNLPR GVKPLTGDNV
strain O42             VDTAVQKVAN GKDAFTLTAT VEDKNGNPVP GTLVTFNLPR GVKPLTGDNV
Group B                VDAAAQKVAN GKDAFTLTAN VEDKNGNPVP GSLVTFNLPR GVKPLTGDNV
strain SECEC           VDAAAQKVAN GKDAFTLTAN VEDKNGNPVP GSLVTFNLPR GVKPLTGDNV
            Consensus  VD----KVAN --DAFTLTA- V-D--GN--P G--V-FNLP- GVKPL---N-
Frag                   CCCCCCCCCC CCCCCCCCCC CCCCCCCCCC CCCCCCCCCC CCCCCCCCCC

                       1151                                                1200
strains B, C and 8739  MVNADKEGKA ELKVVSVTAG TYEITVSAGN DQPSNAQSVT FVADKTTATI
strain H10407          MVNADKEGKA ELKVVSVTAG TYEITASAGN DQPSNAQSVT FVADKTTATI
strain 101-1           MVNADKEGKA ELKVVSVTAG TYEITASAGN DQPSNAQSVT FVADKTTATI
strain 536             MVNADKEGKA ELKVVSVTAG TYEITASAGN DQPSNAQSVT FVADKTTATI
strain F11             MVNADKEGKA ELKVVSVTAG TYEITASAGN DQPSNAQSVT FVADKTTATI
strain CFT073          MVNADKEGKA ELKVVSVTAG TYEITASAGN DQPSNAQSVT FVADKTTATI
Group A                MVNADKEGKA ELKVVSVTAG TYEITASAGN DQPSNAQSVT FVADKTTATI
strain E2348-69        MVNADKEGKA ELKVGSVTAG TYEITASAGN DQPSNAQSVT FVADKTTATI
strains B171 and E22   WVKANGEGKA ELQVVSVTAG TYEITASAGN SQPSDTQTIT FVADKATATV
strain B7A             WVKANGEGKA ELQVVSVTAG TYEITASAGN SQPSDTQTIT FVADKATATV
strain E110019         WVKANGEGKA ELQVVSVTAG TYEITASAGN SQPSDTQTIT FVADKATATV
strain HS              WVKANDEGKA ELQVVSVTAG TYEITASAGN SQPSDTQTIT FVADKATATV
strain E24377A         WVKANDEGKA ELQVVSVTAG TYEITASAGN SQPSNTQTIT FVADKATATV
strain O42             WVKANDEGKA ELQVVSVTAG TYEITASAGN DQPSDAQTIT FVADKATATV
Group B                WVKANDEGKA ELQVVSVTAG TYEITASAGN SQPSNTQTIT FVADKATATV
strain SECEC           WVKANDEGKA ELQVVSVTAG TYEITASAGN DQPSDAQTIT FVADKTTATV
            Consensus  -V-A--EGKA EL-V-SVTAG TYEITaSAGN -QPS--Q--T FVADK-TAT-
                                   SEQ ID NO: 264-6
B-Cell Ep.                             **********
Frag                   CCCCCCCCCC CCCCCCCCCC CCCCCCCCCC CCCCCCCCCC CCCCCCCCCC

                       1201                                                1250
strains B, C and 8739  SSIEVIGNRA VADGKTKQTY KVTVTDANNN LLKDSDVTLT ASSENLVLDP
strain H10407          SSIEVIGNRA VADGKTKQTY KVTVTDANNN LLKDSDVTLT ASSENLVLDP
strain 101-1           SSIEVIGNRA VADGKTKQTY KVTVTDANNN LLKDSDVTLT ASSENLVLDP
strain 536             SSIEVIGNRA VADGKTKQTY KVTVTDANNN LLKDSEVTLT ASPENLVLTP
strain F11             SSIEVIGNRA VADGKTKQTY KVTVTDANNN LLKDSEVTLT ASPENLVLTP
strain CFT073          SSIEVIGNRA VADGKTKQTY KVTVTDANNN LLKDSEVTLT ASPENLVLTP
Group A                SSIEVIGNRA VADGKTKQTY KVTVTDANNN LLKDSEVTLT ASPENLVLTP
strain E2348-69        SSIEVIGNRA VADGKTKQTY KVTVTDANNN LLKDSEVTLT ASPENLVLTP
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strains B171 and E22   SGIEVMGNYA LADGKAKQTY KVTVTDANNN LVKDSEVTLT ASPASLNLEP
strain B7A             SGIEVMGNYA LADGKAKQTY KVTVTDANNN LVKDSEVTLT ASPASLNLEP
strain E110019         SGIEVMGNYA LADGKAKQTY KVTVTDANNN LVKDSEVTLT ASPASLNLEP
strain HS              SGIEVIGNYA LADGKAKQTY KVTVTDANNN LVKDSDVTLT ASPASLNLEP
strain E24377A         SGIEVMGNYA LADGKAKQTY KVTVTDANNN LVKDSEVTLT ASPASLNLEP
strain O42             SGIEVIGNYA LADGKAKQTY KVTVTDANNN LLKDSDVTLT ASPASLNLEP
Group B                SGIEVIGNYA LADGNAKQTY KVTVTDANNN LLKDSEVTLT ASPANLVLTP
strain SECEC           SGIEVIGNYA LADGKAKQTY KVTVTDANNN LLKDSEVTLT ASPANLALDP
           Consensus   S-IEV-GN-A -ADG--KQTY KVTVTDANNN L-KDS-VTLT AS---L-L-P
                                          SEQ ID NO: 267
B-Cell Ep.                                **** *******
Frag                   CCCCCCCCCC CCCCCCCCCC CCCCCCCCCC CCCCCCCCCC CCCCCCCCCC

                       1251                                                1300
strains B, C and 8739  KGTAKTNEQG QAVFTGSTTI AATYTLTAKV EQANGQVSTK TAESKFVADD
strain H10407          KGTAKTNEQG QAVFTGSTTI AATYTLTAKV EQANGQVSTK TAESKFVADD
strain 101-1           KGTAKTNEQG QAVFTGSTTI AATYTLTAKV EQANGQVSTK TAESKFVADD
strain 536             NGTATTNEQG QAIFTATTTV AATYTLTAKV EQADGQESTK TAESKFVADD
strain F11             NGTATTNEQG QAIFTATTTV AATYTLTAKV EQADGQESTK TAESKFVADD
strain CFT073          NGTATTNEQG QAIFTATTTV AATYTLTAKV EQADGQESTK TAESKFVADD
Group A                NGTATTNEQG QAIFTATTTV AATYTLTAKV EQADGQESTK TAESKFVADD
strain E2348-69        NGTATTNEQG QAIFTATTTV AATYTLTAKV EQADGQESTK TAESKFVADD
strains B171 and E22   NGTATTNEQG QAIFTATTTV AATYTLKAQV SQTNGQVSTK TAESKFVADD
strain B7A             NGTATTNEQG QAIFTATTTV AATYTLKAQV SQTNGQVSTK TAESKFVADD
strain E110019         NGTATTNEQG QAIFTATTTV AATYTLKAQV SQTNGQVSTK TAESKFVADD
strain HS              NGTATTNEQG QAIFTATTTV AATYTLKAQV SQTNGQVSTK TAESKFVADD
strain E24377A         NGTATTNEQG QAIFTATTTV AATYTLKAQV SQTNGQVSTK TAESKFVADD
strain O42             NGTATTNEQG QAIFTATTTV AATYTLKAQV SQTNGQVSTK TAESKFVADD
Group B                NGTAKTNEQG QAIFTATTTV AAKYTLTAKV SQADGQESTK TAESKFVADD
strain SECEC           DGTAKTNEQG QAIFTATTTV AAKYTLTAKV EQANGQESTK TAESKFVADD
           Consensus   -GTA-TNEQG QA-FT--TT- AA-YTL-A-V -Q--GQ-STK TAESKFVADD
                                                                 SEQ ID NO: 268
B-Cell Ep.                                                      *** *********
Frag                   CCCCCCCCCC CCCCCCCCCC CCCCCCCCCC CCCCCCCCCC CCCCCCCCCC

                       1301                                                1350
strains B, C and 8739  KNAVLAASPE RVDSLVADGK TTATMTVTLM AGVNPVGGSM WVDIEAPEGV
strain H10407          KNAVLAASPE RVDSLVADGK TTATMTVTLM AGVNPVGGSM WVDIEAPEGV
strain 101-1           KNAVLAASPE RVDSLVADGK TTATMTVTLM AGVNPVGGSM WVDIEAPEGV
strain 536             KNAELAATSD .VHSLVADGV TTATLTVTLF SANNPVGGTM WVDIEAPEGV
strain F11             KNAELAATSD .VHSLVADGV TTATLTVTLF SANNPVGGTM WVDIEAPEGV
strain CFT073          KNAVLAASPE RVDSLVADGK TTATLTVTLM SGVNPVGGTM WVDIEAPEGV
Group A                KNAVLAASPE RVDSLVADGK TTATLTVTLM SGVNPVGGTM WVDIEAPEGV
strain E2348-69        KNAVLAASPE RVDSLVADGK TTATLTVTLM SGVNPVGGTM WVDIEAPEGV
strains B171 and E22   KNAVLTASSD .MQSLVADGK STAKLEVTLM SANNPVGGNM WVDIQTPEGV
strain B7A             KNAVLTASSD .MQSLVADGK STAKLEVTLM SANNPVGGNM WVDIQTPEGV
strain E110019         KNAVLTASSD .MQSLVADGK STAKLEVTLM SANNPVGGNM WVDIQTPEGV
strain HS              KNAVLTASSD .MQSLVADGK STAKLEVTLM SANNPVGGNM WVDIQTPEGV
strain E24377A         KNAVLTASSD .MQSLVADGK STAKLEVTLM SANNPVGGNM WVDIQTPEGV
strain O42             KNAELTASSD .VQSLVADGK STAKLEVTLF SANNPVGGNV WVDIEAPEGV
Group B                TNAVLTASSD .VTSLVADGI STAKLEVTLM SANNPVGGNM WVDIKTPEGV
strain SECEC           KNAVLAASSD .VTSLVADGV QTATMTVTLF SANNPVGGNV WVDIEAPEGV
           Consensus   -NA-L-A--- ---SLVADG- -TA---VTL- ---NPVGG-- WVDI--PEGV
                                                                       ****
B-Cell Ep.
Frag                   CCCCCCCCCC CCCCCCCCCC CCCCCCCCCC CCCCCCCCCC CCCCCCCCCC

                       1351                                                1400
strains B, C and 8739  TEKDYQFLPS KADHFSGGKI TRTFSTSKPG VYTFTFNALT YGGYEMTPVK
strain H10407          TEKDYQFLPS KADHFSGGKI TRTFSTSKPG VYTFTFNALT YGGYEMTPVK
strain 101-1           TEKDYQFLPS KADHFSGGKI TRTFSTSKPG VYTFTFNALT YGGYEMTPVK
strain 536             TEADYQFLPS KNDHFASGKI TRTFSTNKPG TYTFTFNSLT YGGYEMKPVT
strain F11             TEADYQFLPS KNDHFASGKI TRTFSTNKPG TYTFTFNSLT YGGYEMKPVT
strain CFT073          TEADYQFLPS KNDHFASGKI TRTFSTNKPG TYTFTFNSLT YGGYEMKPVT
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Group A                 TEADYQFLPS KNDHFASGKI TRTFSTNKPG TYTFTFNSLT YGGYEMKPVT
strain E2348-69         TEADYQFLPS KNDHFASGKI TRTFSTNKPG TYTFTFNSLT YGGYEMKPVT
strains B171 and E22    TEKDYQFLPS KNDHFVSGKI TRKFSTSKPG VYTFTFNALT YGGYEMKPVT
strain B7A              TEKDYQFLSS KNDHFVSGKI TRKFSTSKPG VYTFTFNALT YGGYEMKPVT
strain E110019          TEKDYQFLPS KNDHFVSGKI TRKFSTSKPG VYTFTFNALT YGGYEMKPVT
strain HS               TEKDYQFLPS KNDHFVSGKI TRKFSTSKPG VYTFTFNALT YGGYEMKPVT
strain E24377A          TEKDYQFLPS KNDHFVSGKI TRKFSTSKPG VYTFTFNALT YGGYEMKPVT
strain O42              TEKDYQFLPS KNDHFVSGKI TRTFSTSKPG VYTFTFNALT YGGYEMKPVT
Group B                 TEKDYQFLPS KNDHFVSGKI TRTFSTSKPG VYTFTFNALT YGGYEMKPVT
strain SECEC            TEKDYQFLPS KNDHFVSGKI TRTFSTNKPG TYTFTFNSLT YGGYEMKPVT
          Consensus     TEkDYQFL-S K-DHF--GKI TR-FST-KPG -YTFTFN-LT YGGYEM-PV-
                        SEQ ID NO: 269-71
B-Cell Ep.              **
Frag                    CCCCCCCCCC CCCCCCCCCC CCCCCCCCCC CCCCCCCCCC CCCCCCCCCC

                        1401          1418
strains B, C and 8739   VTINAVAAET ENGEEEMP
strain H10407           VTINAVAAET ENGEEEMP
strain 101-1            VTINAVAAET ENGEEEMP
strain 536              VTINAVPADT EGAEEK~~
strain F11              VTINAVPADT EGAEEK~~
strain CFT073           VTINAVPADT EGAEEK~~
Group A                 VTINAVPADT EGAEEK~~
strain E2348-69         VTINAVPADT EGAEEK~~
strains B171 and E22    VTITAVDADT AKDEEAMK
strain B7A              VTITAVDADT AKDEEAMK
strain E110019          VTITAVDADT AKDEEAMK
strain HS               VTITAVDADT AKDEEAMK
strain E24377A          VTITAVDADT AKDEEAMK
strain O42              VTITAVDADT AKGEEAMK
Group B                 VTITAVDADT AKGEEAMN
strain SECEC            VTITAVDANT ATGEEAMK
          Consensus     VTI-AV-A-T ---EE---
Frag                    CCCCCCCCCC CCCCCCCC

SEQ ID NO: 222  NTTV(T/A)AD(N/S)NVEKNVAS
SEQ ID NO: 223  NTTVAADNNVEKNVAS
SEQ ID NO: 224  NTTVTADSNVEKNVAS
SEQ ID NO: 225  NTTVTADNNVEKNVAS
SEQ ID NO: 232  RI(E/A)GKGGQT
SEQ ID NO: 233  RIEGKGGQT
SEQ ID NO: 234  RIAGKGGQT
SEQ ID NO: 250  ASEGAT(V/I)S(S/G)WTEKG
SEQ ID NO: 251  ASEGATISSWTEKG
SEQ ID NO: 252  ASEGATVSGWTEKG
SEQ ID NO: 253  ASEGATVSSWTEKG
SEQ ID NO: 257  NQLA NGQS(T/A)N
SEQ ID NO: 258  NQLA NGQSTN
SEQ ID NO: 259  NQLA NGQSAN
SEQ ID NO: 260  TLTVVD(S/T)YGNPLQGQ
SEQ ID NO: 261  TLTVVDSYGNPLQGQ
SEQ ID NO: 262  TLTVVDTYGNPLQGQ
SEQ ID NO: 264  SVTAGTYEIT(A/V)SAGN
SEQ ID NO: 265  SVTAGTYEITASAGN
SEQ ID NO: 266  SVTAGTYEITVSAGN
SEQ ID NO: 269  PEGVTE(K/A)DYQFL
SEQ ID NO: 270  PEGVTEKDYQFL
SEQ ID NO: 271  PEGVTEADYQFL

B-Cell Epitopes
SEQ ID NO: 272  TTVTADNNVEK
SEQ ID NO: 273  FLSSQPDSDATR
SEQ ID NO: 274  TAKANQE
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SEQ ID NO: 275 IHRTDDRTQSN
SEQ ID NO: 276 SGWKKSPDVEDYQERPANGWDIR
SEQ ID NO: 277 YLPAWPQ
SEQ ID NO: 278 KDKRQKDPHAI
SEQ ID NO: 279 GHKQGKSGENDTR
SEQ ID NO: 280 KQLDTDSI
SEQ ID NO: 281 IEGKGGQT
SEQ ID NO: 282 DNKGNASKRV
SEQ ID NO: 283 DAEGQPVTGMKDQ
SEQ ID NO: 284 PTLGEFTETEAGV
SEQ ID NO: 285 TTGTQSGEAT
SEQ ID NO: 286 TLSANEPSGDVVADG
SEQ ID NO: 287 GNPVTGEA
SEQ ID NO: 288 PQDTNGVT
SEQ ID NO: 289 IKPGVYSATVSSTRA
SEQ ID NO: 290 LNPDKPVVGG
SEQ ID NO: 291 GSTASGWTNNGDGTWTA
SEQ ID NO: 292 GSTAGE
SEQ ID NO: 293 KLNGQDAAANA
SEQ ID NO: 294 LSSNQSKVSV
SEQ ID NO: 295 DHVKAGEST
SEQ ID NO: 296 ASEGATVSSWTEKG
SEQ ID NO: 297 TGGKTG
SEQ ID NO: 298 GQPAATEA
SEQ ID NO: 299 RVNGQNAV
SEQ ID NO: 300 QLANGQSTN
SEQ ID NO: 301 SYGNPLQGQ
SEQ ID NO: 302 GVTSKTGNTVTT
SEQ ID NO: 303 LMSTVAGE
SEQ ID NO: 304 TYEITASAGN
SEQ ID NO: 305 KQTYKVTVTDA
SEQ ID NO: 306 STKTAESKFVAD
SEQ ID NO: 307 PEGVTE

Orf1364 protein

Flu antigen 43 protein is referred to herein as 'orf1364.' 'orf1364' protein from *E. coli* NMEC is disclosed in reference 5 (SEQ IDs 2727 & 2728) is also known as: 'orf1109' from *E. coli* NMEC strain IHE3034, 'c1273' from CFT073 and ecp_3009 from 536.

When used according to the present invention, orf1364 protein may take various forms. Preferred orf1364 sequences have 50% or more identity (*e.g.* 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98%, 99% or more) to SEQ ID NOs 19-40. This includes variants (*e.g.* allelic variants, homologs, orthologs, paralogs, mutants *etc*).

Other preferred orf1364 sequences comprise at least *n* consecutive amino acids from SEQ ID NOs 19-40, wherein *n* is 7 or more (*eg.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). Preferred fragments comprise an epitope or immunogenic fragment from orf1364. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or the N-terminus of SEQ ID NOs 19-40. Exemplary fragments are the conserved fragments SEQ ID NOs identified in the sequence alignment below.

strain E110019 (SEQ ID NO: 19)

Group A: strain Sakai, EDL933, EC508, EC869, EC4024, EC4042, EC4045, EC4076, EC4113, EC4115, EC4196, EC4206, EC4401, EC4486, EC4501 and TW14588 (SEQ ID NO: 20)
strain B171 (SEQ ID NO: 21)
strain E22 (SEQ ID NO: 22)
strain B171 (SEQ ID NO: 23)
strain B171 (SEQ ID NO: 24)
strain E24377A and O42 (SEQ ID NO: 26)
strain E24377A (SEQ ID NO: 25)
Group B: strain UTI89, RS218 and IHE3034 (SEQ ID NO: 27)
strain E110019 (SEQ ID NO: 28)
strain E22 (SEQ ID NO: 29)
strain H10407 (SEQ ID NO: 30)
strain F11 and 536 (SEQ ID NO: 31)
strain SECEC (SEQ ID NO: 32)
strain H10407 (SEQ ID NO: 33)
strain W3110 and DH10B (SEQ ID NO: 34)
strain MG1655 (SEQ ID NO: 35)
strain O42 (SEQ ID NO: 36)
strain B7A (SEQ ID NO: 37)
strain CFT073 (SEQ ID NO: 38)
strain O42 (SEQ ID NO: 39)
strain CFT073 (SEQ ID NO: 40)

	1	50
strain E110019	MKRHLNTSYR	LVWNHITGTL VVASELARSR GKRAGVAVAL SLAAVTSVPA
Group A	MKRHLNTSYR	LVWNHITGTL VVASELARSR GKRAGVAVAL SLAAVTSVPA
strain B171	MKRHLNTSYR	LVWNHITGTL VVASELARSR GKRAGVAVAL SLAAVTSVPA
strain E22	MKRHLNTSYR	LVWNHITGTL VVASELARSR GKRAGVAVAL SLAAVTSVPA
strain B171	MKRHLNTSYR	LVWNHITGTL VVASELARSR GKRTGVAVAL SLAAVTSVPV
strain B171	MKRHLNTSYR	LVWNHITGTL VVASELARSR GKRTGVAVAL SLAAVTSVPV
strain E24377A and O42	MKRHLNTSYR	LVWNHITGTL VVASELARSR GKRTGVAVAL SLAAVTSVPV
strain E24377A	MKRHLNTSYR	LVWNHITGTL VVASELARSR GKRAGVAIAL SLAAVTSVPA
Group B	MKRHLNTSYR	LVWNHITGTL VVASELARSR GKGAGVAVAL SLAAVTSVPA
strain E110019	MKRHLNTSYR	LVWNHITGTL VVASELARSR GKRTGVAVAL SLAAVTSVPV
strain E22	MKRHLNTSYR	LVWNHITGTL VVASELARSR GKRAGVAVAL SLAAVTSVPA
strain H10407	MKRHLNTSYR	LVWNHITGTL VVASELARSR GKRAGVAIAL SLAAVTSVPA
strain F11 and 536	MKRHLNTSYR	LVWNHITGTL VVASELARSR GKRAGVAVAL SLAAVTSVPA
strain SECEC	MKRHLNTSYR	LVWNHITGTL VVASELARSR GKRAGVAVAL SLAAVTPVPA
strain H10407	MKRHLNTSYR	LVWNHITGTL VVASELARSR GKRTGVAVAL SLATATSVPA
strain W3110 and DH10B	MKRHLNTCYR	LVWNHMTGAF VVASELARAR GKRGGVAVAL SLAAVTSLPV
strain MG1655	MKRHLNTCYR	LVWNHMTGAF VVASELARAR GKRGGVAVAL SLAAVTSLPV
strain O42	MKRHLNTCYR	LVWNHITGAF VVASELARAR GKRGGVAVAL SLAAVTSLPV
strain B7A	MKRHLNTSYR	LVWNHITGTL VVASELARSR GKRAGVAVAL SLAAVTSVPA
strain CFT073	MKRHLNTSYR	LVWNHITGAF VVASELARAR GKRAGVAVAL SLAAATSLPA
strain O42	MKRHLNTCYR	LVWNHITGAF VVASELARAR GKRGGVAVAL SLAAVTSLPV
strain CFT073	MKRHLNTCYR	LVWNHITGAF VVASELARAR GKRGGVAVAL SLAAVTPLPV
Consensus	MKRHLNT-YR	LVWNH-TG-- VVASELAR-R GK--GVA-AL SLA--T--P-
B-Cell Ep.		*** *****

	51	100
strain E110019	LAADKVVQAG	ETVNDGTLTN HDNQIVFGTA NGMTISTGLE LGPDSEENTG
Group A	LAADKVVQAG	ETVNDGTLTN HDNQIVFGTA NGMTISTGLE LGPDSEENTG
strain B171	LAADTVVQAG	ETVNGGTLTN HDNQIVLGTA NGMTISTGLE LGPDSEENTG
strain E22	LAADTVVQAG	ETVNGGTLTN HDNQIVLGTA NGMTISTGLE LGPDSEENTG
strain B171	LAADTVVQAG	ETVSGGTLTN HDNQIVLGTA NGMTISTGLE YGPDNEANTG
strain B171	LAADTVVQAG	ETVSGGTLTN HDNQIVLGTA NGMTISTGLE YGPDNEANTG
strain E24377A and O42	LAADTVVQAG	ETVSGGTLTN HDNQIVFGTA NGMTISTGLE YGPDNEANTG
strain E24377A	LAADTVVQAG	ETVNDGTLTN HDNQIVLGTA NGMTISTGLE YGPDNEANTG
Group B	LAADTVVQAG	ETVNGGTLTN HDNQIVLGTA NGMTISTGLE YGPDNEANTG
strain E110019	LAADTVVQAG	ETVSGGTLTN HDNQIVFGTA NGMTISTGLE YGPDNEANTG
strain E22	LAADTVVQAG	ETVSGGTLVN HDNQIVFGTA NGMTISTGLE YGPDNEANTG
strain H10407	LAADTVVQAG	ETVSGGTLTN HDNQIVFGTA NGMTISSGLE YGPDNEANTG

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strain F11 and 536       LAADTVVQAG ETVNDGTLTN HDNQIVLGTA NGMTISTGLE YGPDNEANTG
strain SECEC             LAADTVVEAG ETVNGGTLTN HDNQIVFGTT NGMTISTGLE YGTDNEANTG
strain H10407            LAADSVVQAG ETVSGGTLEN HDNQIVFGTT NGITISTGLE YGPDNEANTG
strain W3110 and DH10B   LAADIVVHPG ETVNGGTLAN HDNQIVFGTT NGMTISTGLE YGPDNEANTG
strain MG1655            LAADIVVHPG ETVNGGTLAN HDNQIVFGTT NGMTISTGLE YGPDNEANTG
strain O42               LAADIVVHPG ETVNGGTLAN HDNQIVFGTT NGMTISTGLE YGPDNEANTG
strain B7A               LAADKVVQAG ETVNDGTLTN HDNQIVLGTA NGMTISTGLE YGPDNEANTG
strain CFT073            LAADSVVPAG ETVNGGTLIN HDRQFVSGTA DGMTVSTGLE LGADSDNNTG
strain O42               LAADIVVHPG ETVNGGTLVN HDNQFVSGTA DGVTVSTGLE LGPDSDDNTG
strain CFT073            LSADIVVHPG ETVNGGTLVN HDNQFVSGTA NGVTVSTGLE LGPDSDENTG
          Consensus      L-AD-VV--G ETV--GTL-N HD-Q-V-GT- -G-T-S-GLE -G-D---NTG
B-Cell Ep.                        * ********** ***** **********

                                 101                                       150
strain E110019           GQWIQNGGIA GNTTVTTNGR QVVLEGGTAS DTVIRDGGGQ SLNGLAVNTT
Group A                  GQWIQNGGIA GNTTVTTNGR QVVLEGGTAS DTVIRDGGGQ SLNGLAVNTT
strain B171              GQWIQNGGIA GNTTVTTNGR QVVLEGGTAS DTVIRDGGGQ SLNGLAVNTT
strain E22               GQWIQNGGIA GNTTVTTNGR QVVLEGGTAS DTVIRDGGGQ SLNGLAVNTT
strain B171              GQWIQNGGIA NNTTVTGGGL QRVNAGGSVS DTVISAGGGQ SLQGQAVNTT
strain B171              GQWIQNGGIA NNTTVTGGGL QRVNAGGSVS DTVISAGGGQ SLQGQAVNTT
strain E24377A and O42   GQWIQNGGIA NNTTVTGGGL QRVNAGGSVS DTVISAGGGQ SLQGQAVNTT
strain E24377A           GQWIQNGGIA NNTTVTGGGL QRVNAGGSVS DTVISAGGGQ SLQGQAVNTT
Group B                  GQWIQNGGIA NNTTVTGGGL QRVNAGGSVS DTVISAGGGQ SLQGQAVNTT
strain E110019           GQWIQNGGIA NNTTVTGGGL QRVNAGGSVS DTVISAGGGQ SLQGQAVNTT
strain E22               GQWIQNGGTA NNTTVTGGGL QRVNTGGSVS DTVISAGGGQ SLQGQAVNTT
strain H10407            GQWIQNGGIA NNTTVTGGGL QRVNAGGSVS DTVISAGGGQ SLQGQAVNTT
strain F11 and 536       GQWIQNGGIA NNTTVTGGGL QRVNAGGSVS DTVISAGGGQ SLQGQAVNTT
strain SECEC             GQWVQDGGTA SNTTISSGGL QFVGAGGKAT DTIINEGGGQ SLKGLALNTT
strain H10407            GQWVQDGGTA SNTTISSGGL QFVGAGGKAT DTIINEGGGQ SLKGLALNTT
strain W3110 and DH10B   GQWVQDGGTA NKTTVTSGGL QRVNPGGSVS DTVISAGGGQ SLQGRAVNTT
strain MG1655            GQWVQDGGTA NKTTVTSGGL QRVNPGGSVS DTVISAGGGQ SLQGRAVNTT
strain O42               GQWVQDGGTA NKTTVTSGGL QRVNPGGSVS DTVISAGGGQ SLQGRAVNTT
strain B7A               GQWIQNGGIA NNTTVTGGGL QRVNAGGSVS DTVISAGGGQ SLQGQAVNTT
strain CFT073            GQQIARGGTA RNTRVTANGL QDVMAGGSTS DTVISTGGGQ NLRGKASGTV
strain O42               GQQIARGGTA RNTTVTANGL QDVMAGGSAT DTVISAGGGQ NLRGQAYGTV
strain CFT073            GQWIKAGGTG RNTTVTANGR QIVQAGGTAS DTVIRDGGGQ SLNGLAVNTT
          Consensus      GQ----GG-- --T-----G- Q-V--GG--- DT-I--GGGQ -L-G-A--T-
B-Cell Ep.               ********** ********** ********** ********** *****

                                 151                                       200
strain E110019           LNNRGEQWVH EGGVATGTII NRDGYQSVKS GGLATGTIIN TGAEGGPDSD
Group A                  LNNRGEQWVH EGGVATGTII NRDGYQSVKS GGLATGTIIN TGAEGGPDSD
strain B171              LNNRGEQWVH EGGVATGTII NRDGYQSVKS GGLATGTIIN TGAEGGPDSD
strain E22               LNNRGEQWVH EGGVATGTII NRDGYQSVKS GGLATGTIIN TGAEGGPDSD
strain B171              LNG.GEQWVH EGGIATGTVI NEKGWQAVKS GAMATDTVVN TGAEGGPDAE
strain B171              LNG.GEQWVH EGGIATGTVI NEKGWQAVKS GAMATDTVVN TGAEGGPDAE
strain E24377A and O42   LNG.GEQWVH EGGIATGTVI NEKGWQAVKS GAMATDTVVN TGAEGGPDAE
strain E24377A           LNG.GEQWVH EGGIATGTVI NEKGWQAVKS GAMATDTVVN TGAEGGPDAE
Group B                  LNG.GEQWVH EGGIATGTVI NEKGWQAVKS GAMATDTVVN TGAEGGPDAE
strain E110019           LNG.GEQWVH EGGIATVTVI NEKGWQAVKS GAMATDTVVN TGAEGGPDAD
strain E22               LNG.GEQWVH EGGIATGTVI NEKGWQAIKS GAVATDTVVN TGAEGGPDAE
strain H10407            LNG.GEQWVH EGGIATGTVI NEKGWQAVKS GAMATDTVVN TGAEGGPDAE
strain F11 and 536       LNG.GEQWVH EGGIATGTVI NEKGWQAVKS GAMATDTVVN TGAEGGPDAE
strain SECEC             LNG.GEQWMH EGAIATGTVI NDKGWQVVKP GAVATDTVVN TGAEGGPDAE
strain H10407            LNG.GEQWMH EGAIATGTVI NDKGWQVVKP GAVATDTVVN TGAEGGPDAE
strain W3110 and DH10B   L.NGGEQWMH EGAIATGTVI NDKGWQVVKP GTVATDTVVN TGAEGGPDAE
strain MG1655            L.NGGEQWMH EGAIATGTVI NDKGWQVVKP GTVATDTVVN TGAEGGPDAE
strain O42               L.NGGEQWMH EGAIATGTVI NDKGWQVVKP GTVATDTVVN TGAEGGPDAE
strain B7A               L.NGGEQWVH EGGIATGTVI NEKGWQAIKS GAVATDTVVN TGAEGGPDAE
strain CFT073            L.NGGDQWIH AGGRASGTVI NQDGYQTIKH GGLVTGTIVN TGAEGGPDSE
strain O42               L.NGGEQWIH AGGSASGTVI NQSGYQTIKH GGQATGTIVN TGAEGGPESE
strain CFT073            LDNRGEQWVH GGGKAAGTII NQDGYQTIKH GGLATGTIVN TGAEGGPESE
          Consensus      L---G-QW-H -G--A--T-I N--G-Q--K- G---T-T--N TGAEGGP---
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B-Cell Ep.                                  **************************

                                  201                                 250
strain E110019                    NSYTGQKVQG TAESTTINKN GRQIILFSGL ARDTLIYAGG DQSVHGRALN
Group A                           NSYTGQKVQG TAESTTINKN GRQIILFSGL ARDTLIYAGG DQSVHGRALN
strain B171                       NSYTGQKVQG TAESTTINKN GRQIILFSGI ARDTLIYAGG DQSVHGRALN
strain E22                        NSYTGQKVQG TAESTTINKN GRQIILFSGI ARDTLIYAGG DQSVHGRALN
strain B171                       NGDTGQFVRG NAVRTTINKN GRQIVAAEGT ANTTVVYAGG DQTVHGHALD
strain B171                       NGDTGQFVRG NAVRTTINKN GRQIVAAEGT ANTTVVYAGG DQTVHGHALD
strain E24377A and O42            NGDTGQFVRG NAVRTTINEN GRQIVAAEGT ANTTVVYAGG DQTVHGHALD
strain E24377A                    NGDTGQFVRG NAVRTTINKN GRQIVAAEGT ANTTVVYAGG DQTVHGHALD
Group B                           NGDTGQTVYG DAVRTTINKN GRQIVAAEGT ANTTVVYAGG DQTVHGHALD
strain E110019                    NGDTGQFVRG NAVRTTINKN GRQIVAVEGT ANTTVVYAGG DQTVHGHALD
strain E22                        NGDTGQTVYG DAVRTTINKN GRQIVAAEGT ANTTVVYAGG DQTVHGHALD
strain H10407                     NGDTGQFVRG NAVRTTINKN GRQIVAAEGT ANTTVVYAGG DQTVHGHALD
strain F11 and 536                NGDTGQFVRG NAVRTTINEN GRQIVAAEGT ANTTVVYAGG DQTVHGYALD
strain SECEC                      NGDTGQFVRG NAVRTTINKN GRQIVTVEGT ANTTVVYAGG DQTVHGHALD
strain H10407                     NADTGQFVRG DAVRTTINKN GRQIVVATGV ANTTVVYAGG DQTVHGYALD
strain W3110 and DH10B            NGDTGQFVRG DAVRTTINKN GRQIVRAEGT ANTTVVYAGG DQTVHGHALD
strain MG1655                     NGDTGQFVRG DAVRTTINKN GRQIVRAEGT ANTTVVYAGG DQTVHGHALD
strain O42                        NGDTGQFVRG DAVRTTINKN GRQIVRAEGT ANTTVVYAGG DQTVHGHALD
strain B7A                        NGDTGQTVYG DAVRTTINKN GRQIVAAEGT ANTTVVYAGG DQTVHGHALD
strain CFT073                     NVSTGQMVGG IAESTTINKN GRQVIWSSGI ARDTLIYTGG DQTVHGEAHN
strain O42                        NVSSGQMVGG TAESTTINKN GRQVIWSSGM ARDTLIYAGG DQTVHGEAHN
strain CFT073                     NVSSGQMVGG TAESTTINKN GRQVIWSSGM ARDTLIYAGG DQTVHGEAHN
                Consensus         N---GQ-V-G -A--TTIN-N GRQ-----G- A--T--Y-GG DQ-VHG-A-
B-Cell Ep.                        ********    *********       ***** ***   **** ******

                                  251                                 300
strain E110019                    TTLNGGYQYV HRDGLALNTV INEGGWQVVK AGGAAGNTTI NQNGELRVHA
Group A                           TTLNGGYQYV HRDGLALNTV INEGGWQVVK AGGAAGNTTI NQNGELRVHA
strain B171                       TTLNGGYQYV HKDGLALNTV INEGGWQVVK AGGAVGNTTI NQNGELRVHA
strain E22                        TTLNGGYQYV HKDGLALNTV INEGGWQVVK AGGAVGNTTI NQNGELRVHA
strain B171                       TTLNGGYQYV HNGGTASGTV VNSDGWQIIK EGGLADFTTV NQKGKLQVNA
strain B171                       TTLNGGYQYV HNGGTASGTV VNSDGWQIIK EGGLADFTTV NQKGKLQVNA
strain E24377A and O42            TTLNGGYQYV HNGGTASDTV VNSDGWQIVK EGGLADFTTV NQKGKLQVNA
strain E24377A                    TTLNGGYQYV HNGGTASGTV VNSDGWQIIK EGGLADFTTV NQKGKLQVNA
Group B                           TTLNGGYQYV HNGGTASDTV VNSDGWQIIK EGGLADFTTV NQKGKLQVNA
strain E110019                    TTLNGGYQYV HNGGTASDTV VNSDGWQIVK EGGLADFTTV NQKGKLQVNA
strain E22                        TTLNGGYQYV HNGGTASGTV VNSDGWQIIK EGGLADFTTV NQKGKLQVNA
strain H10407                     TTLNGGYQYV HNGGTASGTV VNSDGWQIIK EGGLADFTTV NQKGKLQVNA
strain F11 and 536                TTLNGGNQYV HNGGTASGTV VNSDGWQIVK EGGLADFTIV NQKGKLQVNA
strain SECEC                      TTLNGGNQYV HNGGTTSDTV VNSDGWQIIK EGGLADFTTV NQKGKLQVNA
strain H10407                     TTLNGGNQYV HNGGTASDTV VNSDGWQIIK EGGLADFTTV NQKGKLQVNA
strain W3110 and DH10B            TTLNGGYQYV HNGGTASDTV VNSDGWQIVK NGGVAGNTTV NQKGRLQVDA
strain MG1655                     TTLNGGYQYV HNGGTASDTV VNSDGWQIVK NGGVAGNTTV NQKGRLQVDA
strain O42                        TTLNGGYQYV HNGGTASDTV VNSDGWQIVK NGGVAGNTTV NQKGRLQVDA
strain B7A                        TTLNGGYQYV HNGGTASGTV VNSDGWQIVK NGGVAGNTTV NQKGRLQVDA
strain CFT073                     TRLEGGNQYV HKYGLALNTV INEGGWQVVK AGGTAGNTTI NQNGELRVHA
strain O42                        TRLEGGNQYV HKYGLALNTV INEGGWQVIK EGGTTAHTTI NQKGKLQVNA
strain CFT073                     TRLEGGNQYV HNGGTATETL INRDGWQVIK EGGTAAHTTI NQKGKLQVNA
                Consensus         T-L-GG-QYV H--G----T- -N--GWQ--K -GG----T-- NQ-G-L-V-A
B-Cell Ep.                              *** ********** ***          ********* *** ******

                                  301                                 350
strain E110019                    GGEATAVTQN TGGALVTSTA ATVIGTNRLG NFTVENGKAD GVVLESGGRL
Group A                           GGEATAVTQN TGGALVTSTA ATVIGTNRLG NFTVENGKAD GVVLESGGRL
strain B171                       GGEATAVTQN TGGALVTSTA ATVTGANRLG HFSVGNGMAD NVVLENGGRL
strain E22                        GGEATAVTQN TGGALVTSTA ATVTGANRLG HFSVGNGMAD NVVLENGGRL
strain B171                       GGTATHVTLK QGGALVTSTA ATVLGSNRLG NFTVENGKAD GVVLESGGRL
strain B171                       GGTATHVTLK QGGALVTSTA ATVLGSNRLG NFTVENGKAD GVVLESGGRL
strain E24377A and O42            GGTATNVTLK QGGALVTSTA ATVTGSNRLG NFTVENGNAD GVVLESGGRL
strain E24377A                    GGTATNVTLK QGGALVTSTA ATVTGSNRLG NFTVENGKAD GVVLESGGRL
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Group B                 GGTATNVTLT QGGALVTSTA ATVTGSNRLG NFTVENGNAD GVVLESGGRL
strain E110019          GGTATNVTLK QGGALVTSTA ATVTGSNRLG NFTVENGNAD GVVLESGGRL
strain E22              GGTATNVTLK QGGALVTSTA ATVLGSNRLG NFTVENGKAD GVVLESGGRL
strain H10407           GGTATHVTLK QGGALVTSTA ATVLGSNRLG NFTVENGKAD GVVLESGGRL
strain F11 and 536      GGTATNVTLK QGGALVTSTA ATVTGSNRLG NFTVENGNAD GVVLESGGRL
strain SECEC            GGTATNVTLK QGGALVTSTA ATVTGSNRLG NFAVENGKAD GVVLESGGRL
strain H10407           GGTATNVTLK QGGALVTSTA ATVLGSNRLG NFTVENGKAD GVVLESGGRL
strain W3110 and DH10B  GGTATNVTLK QGGALVTSTA ATVTGINRLG AFSVVEGKAD NVVLENGGRL
strain MG1655           GGTATNVTLK QGGALVTSTA ATVTGINRLG AFSVVEGKAD NVVLENGGRL
strain O42              GGTATNVTLK QGGALVTSTA ATVTGINRLG AFSVVEGKAD NVVLENGGRL
strain B7A              GGTATNVTLK QGGALVTSTA ATVTGINRLG AFSVVEGKAD NVVLENGGRL
strain CFT073           GGEASDVTQN TGGALVTSTA ATVTGTNRLG AFSVVEGKAD NVVLENGGRL
strain O42              GGKASDVTQN TGGALVTSTA ATVTGTNRLG AFSVLAGKAD NVVLENGGRL
strain CFT073           GGKASDVTQN TGGALVTSTA ATVTGTNRLG AFSVVAGKAD NVVLENGGRL
          Consensus     GG-A--VT-- -GGALVTSTA ATV-G-NRLG -F-V--G-AD -VVLE-GGRL
                                   SEQ ID NO: 308
B-Cell Ep.              **********

                        351                                                400
strain E110019          DVLESHSAQN TLVDDGGTLA VSAGGKATSV TITSGGALIA DSGATVEGTN
Group A                 DVLESHSAQN TLVDDGGTLA VSAGGKATSV TITSGGALIA DSGATVEGTN
strain B171             DVLEGHSAQN TLVDDGGTLA VSAGGKATDV TMTSGGALIA DSGATVEGTN
strain E22              DVLEGHSAQN TLVDDGGTLA VSAGGKATDV TMTSGGALIA DSGATVEGTN
strain B171             DVLEGHSAQK TRVDDGGTLA VSAGGKATDV TMTSGSALIA DSGATVEGTN
strain B171             DVLEGHSAQK TRVDDGGTLA VSAGGKATDV TMTSGSALIA DSGATVEGTN
strain E24377A and O42  DVLEGHSAWK TLVDDGGTLA VSAGGKATDV TMTSGSALIA DSGATVEGTN
strain E24377A          DVLEGHSAWK TLVDDGGTLA VSAGGKATDV TMTSGGALIA DSGATVEGTN
Group B                 DVLEGHSAWK TLVDDGGTLA VSAGGKATDV TMTSGGALIA DSGATVEGTN
strain E110019          DVLEGHSAWK TRVDDGGTLA VSAGGKATGV TMTSGGALIA DSGATVEGTN
strain E22              DVLEGHSAWK TLVDDGGTLA VSAGGKATGV TMTSGGALIA DSGATVEGTN
strain H10407           DVLEGHSAQK TRVDDGGTLA VSAGGKATGV TMTSGGALIA DSGATVEGTN
strain F11 and 536      DVLEGHSAWK TLVDDGGTLA VSAGGKATDV TMTSGGALIA DSGATVEGTN
strain SECEC            DVLEGHSAQK TRVDDGGTLA VSAGGKATGV TMTSGGALIA DSGATVEGTN
strain H10407           DVLEGHSAWK TLVDDGGILA VSAGGKATDV TMTSGGALIA DSGATVEGTN
strain W3110 and DH10B  DVLTGHTATN TRVDDGGTLD VRNGGTATTV SMGNGGVLLA DSGAAVSGTR
strain MG1655           DVLTGHTATN TRVDDGGTLD VRNGGTATTV SMGNGGVLLA DSGAAVSGTR
strain O42              DVLTGHTATN TRVDDGGTLD VRNGGTATTV SMGNGGVLLA DSGAAVSGTR
strain B7A              DVLTGHTATN TRVDDGGTLD VRNGGTATTV SMGNGGVLLA DSGAAVSGTR
strain CFT073           DVLSGHTATR TLVDDGGTLD VRNGGTATAV SMGNGGVLLA DSGAAVSGTR
strain O42              DVLSGHTATN TRVDDGGTLD VRNGGAATTV SMGNGGVLLA DSGAAVSGTR
strain CFT073           DVLSGHTATN TRVDDGGTLD IRNGGAATTV SMGNGGVLLA DSGAAVSGTR
            Consensus   DVL--H-A-- T-VDDGG-L- ---GG-AT-V ----G--L-A DSGA-V-GT-
B-Cell Ep.                   ***** ********** ********** ***           ********

                        401                                                450
strain E110019          ASGK.FSIDG TSGQASGLLL ENGGSFTVNA GGQAGNTTVG HRGTLTLAAG
Group A                 ASGK.FSIDG TSGQASGLLL ENGGSFTVNA GGQAGNTTVG HRGTLTLAAG
strain B171             ASGK.FSIDG ISGQASGLLL ENGGSFTVNA GGQAGNTTVG HRGTLTLAAG
strain E22              ASGK.FSIDG ISGQASGLLL ENGGSFTVNA GGQAGNTTVG HRGTLTLAAG
strain B171             ASGK.FSIDG TSGQASGLLL ENGGSFTVNA GGLASNTTVG HRGTLTLAAG
strain B171             ASGK.FSIDG TSGQASGLLL ENGGSFTVNA GGLASNTTVG HRGTLTLAAG
strain E24377A and O42  ASGK.FSIDG TSGQASGLLL ENGGSFTVNA GGLASNTTVG HRGTLTLAAG
strain E24377A          ASGK.FSIDG TSGQASGLLL ENGGSFTVNA GGLASNTTVG HRGTLTLAAG
Group B                 ASGK.FSIDG ISGQASGLLL ENGGSFTVNA GGLASNTTVG HRGTLTLAAG
strain E110019          ASGK.FSIDG ISGQASGLLL ENGGSFTVNA GGQASNTTVG HRGTLMLAAG
strain E22              ASGK.FSIDG ISGQASGLLL ENGGSFTVNA GGQASNTTVG HRGTLMLAAG
strain H10407           ASGK.FSIDG TSGQASGLLL ENGGSFTVNA GGQASNTTVG HRGTLMLAAG
strain F11 and 536      ASGK.FSIDG ISGQASGLLL ENGGSFTVNA GGQAGNTTVG HRGTLTLAAG
strain SECEC            ASGK.FSIDG ISGQASGLLL ENGGSFTVNA GGQAGNTTVG HRGTLTLAAG
strain H10407           ASGK.FSIDG ISGQASGLLL ENGGSFTVNA GGQAGNTTVG HRGTLTLAAG
strain W3110 and DH10B  SDGKAFSIGG ..GQADALML EKGSSFTLNA GDTATDTTV. .NGGLFTARG
strain MG1655           SDGKAFSIGG ..GQADALML EKGSSFTLNA GDTATDTTV. .NGGLFTARG
strain O42              SDGKAFSIGG ..GQADALML EKGSSFTLNA GDTATDTTV. .NGGLFTARG
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strain B7A                SDGKAFSIGG ..GQADALML EKGSSFTLNA GDTATDTTV. .NGGLFTARG
strain CFT073             SDGTAFRIGG ..GQADALML EKGSSFTLNA GDTATDTTV. .NGGLFTARG
strain O42                SDGTAFRIGG ..GQADALML EKGSSFTLNA GDTATDTTV. .NGGLFTARG
strain CFT073             SDGKAFSIGG ..GQADALML EKGSSFTLNA GDTATDTTV. .NGGLFTARG
                Consensus --G--F-I-G --GQA--L-L E-G-SFT-NA G--A--TTV- --G-L--A-G
B-Cell Ep.                **********                ****  *********

                          451                                              500
strain E110019            GSLSGRTQLS KGASMVLNGD VVST..... .GDIV..... .........
Group A                   GSLSGRTQLS KGASMVLNGD VVST..... .GDIV..... .........
strain B171               GSLSGRTQLS KGASMVLNGD VVST..... .GDIV..... .........
strain E22                GSLSGRTQLS KGASMVLNGD VVST..... .GDIV..... .........
strain B171               GSLSGRTQLS KGASMVLNGD VVST..... .GDIV..... .........
strain B171               GSLSGRTQLS KGASMVLNGD VVST..... .GDIV..... .........
strain E24377A and O42    GSLSGRTQLS KGASMVLNGD VVST..... .GDIV..... .........
strain E24377A            GSLSGRTQLS KGASMVLNGD VVST..... .GDIV..... .........
Group B                   GSLSGRTQLS KGASMVLNGD VVST..... .GDIV..... .........
strain E110019            GSLSGRTQLS KGASMVLNGD VVST..... .GDIV..... .........
strain E22                GSLSGRTQLS KGASMVLNGD VVST..... .GDIV..... .........
strain H10407             GSLSGRTQLS KGASMVLNGD VVST..... .GDIV..... .........
strain F11 and 536        GSLSGRTQLS KGASMVLNGD VVST..... .GDIV..... .........
strain SECEC              GSLSGRTQLS KGASMVLNGD VVST..... .GDIV..... .........
strain H10407             GSLSGRTQLS KGASMVLNGD VVST..... .GDIV..... .........
strain W3110 and DH10B    GTLAGTTTLN NGAILTLSGK TVNNDTLTIR EGDALLQGGS LTGNGSVEKS
strain MG1655             GTLAGTTTLN NGAILTLSGK TVNNDTLTIR EGDALLQGGS LTGNGSVEKS
strain O42                GTLAGTTTLN NGAILTLSGK TVNNDTLTIR EGDALLQGGS LTGNGSVEKS
strain B7A                GTLAGTTTLN NGAILTLSGK TVNNDTLTIR EGDALLQGGS LTGNGSVEKS
strain CFT073             GSLAGTTTLN NGATFTLAGK TVNNDTLTIR EGDALLQGGA LTGNGRVEKS
strain O42                GSLAGTTTLN NGATLTLSGK TVNNDTLTIR EGDALLQGGA LTGNGRVEKS
strain CFT073             GTLAGTTTLN NGAILTLSGK TVNNDTLTIR EGDALLQGGS LTGNGSVEKS
                Consensus G-L-G-T-L- -GA---L-G- -V-------- -GD------- ----------
B-Cell Ep.                **********                                  **********

                          501                                              550
strain E110019            NAGEIRFDNQ T.TPNAA.LS R.AVAKSNSP VTFH..... ...KLTTT..
Group A                   NAGEIRFDNQ T.TPNAA.LS R.AVAKSNSP VTFH..... ...KLTTT..
strain B171               NAGEIRFDNQ T.TQDAV.LS R.AVAKGDSP VTFH..... ...KLTTN..
strain E22                NAGEIRFDNQ T.TQDAV.LS R.AVAKGDSP VTFH..... ...KLTTN..
strain B171               NAGEIRFDNQ T.TQDAV.LS R.AVAKGDSP VTFH..... ...KLTTS..
strain B171               NAGEIRFDNQ T.TQDAV.LS R.AVAKGDSP VTFH..... ...KLTTS..
strain E24377A and O42    NAGEIRFDNQ T.TPDAA.LS R.AVAKGDSP VTFH..... ...KLTTS..
strain E24377A            NAGEIRFDNQ T.TPDAV.LS R.AVAKGDSP VTFH..... ...KLTTS..
Group B                   NAGEIRFDNQ T.TPDAA.LS R.AVAKGDSP VTFH..... ...KLTTS..
strain E110019            NAGEIYFDNQ T.TPDAV.LS R.AVAKGNAP VTFH..... ...KLTTS..
strain E22                NAGEIYFDNQ T.TPDAV.LS R.AVAKGNAP VTFH..... ...KLTTS..
strain H10407             NAGEIHFDNQ T.TQDAV.LS R.AVAKSNSP VTFH..... ...KLTTT..
strain F11 and 536        NAGEIHFDNQ T.TPDAA.LS R.AVAKGDSP VTFH..... ...KLTTS..
strain SECEC              NAGEIRFDNQ T.TQDAV.LS R.AVAKGDAP VTFH..... ...KLTTS..
strain H10407             NAGEIHFDNQ T.TQDAV.LS R.AVAKSNSP VTFH..... ...KLTTT..
strain W3110 and DH10B    GSGTLTVSNT TLTQKAVNLN EGTLTLNDST VTTDVIAQRG TALKLTGSTV
strain MG1655             GSGTLTVSNT TLTQKAVNLN EGTLTLNDST VTTDVIAQRG TALKLTGSTV
strain O42                GSGTLTVSNT TLTQKAVNLN EGTLTLNDST VTTDVIAQRG TALKLTGSTV
strain B7A                GSGTLTVSNT TLTQKAVNLN EGTLTLNDST VTTDVIAQRG TALKLTGSTV
strain CFT073             GSGTLTVSNT TLTQKAVNLN EGTLTLNDST VTTDIIAHRG TALKLTGSTV
strain O42                GSGTLTVSNT TLTQKTVNLN EGTLTLNDST VTTDVIAQRG TALKLTGSTV
strain CFT073             GSGTLTVSNT TLTQKAVNLN EGTLTLNDST VTTDVIAQRG TALKLTGSTV
                Consensus --G-----N- T-T-----L- ---------- VT-------- ---KLT----
B-Cell Ep.                *******

                          551                                              600
strain E110019            .......... .......... .......... .......... ..........
Group A                   .......... .......... .......... .......... ..........
strain B171               .......... .......... .......... .......... ..........
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strain E22                 .......... .......... .......... .......... ..........
strain B171                .......... .......... .......... .......... ..........
strain B171                .......... .......... .......... .......... ..........
strain E24377A and O42     .......... .......... .......... .......... ..........
strain E24377A             .......... .......... .......... .......... ..........
Group B                    .......... .......... .......... .......... ..........
strain E110019             .......... .......... .......... .......... ..........
strain E22                 .......... .......... .......... .......... ..........
strain H10407              .......... .......... .......... .......... ..........
strain F11 and 536         .......... .......... .......... .......... ..........
strain SECEC               .......... .......... .......... .......... ..........
strain H10407              .......... .......... .......... .......... ..........
strain W3110 and DH10B     LNGAIDPTNV TLASGATWNI PDNATVQSVV DDLSHAGQIH FTSTRTGKFV
strain MG1655              LNGAIDPTNV TLASGATWNI PDNATVQSVV DDLSHAGQIH FTSTRTGKFV
strain O42                 LNGAIDPTNV TLASGATWNI PDNATVQSVV DDLSHAGQIH FTSTRTGKFV
strain B7A                 LNGAIDPTNV TLASGATWNI PDNATVQSVV DDLSHAGQIH FTSTRTGKFV
strain CFT073              LNGAIDPTNV TLTSGATWNI PDNATVQSVV DDLSHAGQIH FTSARTGKFV
strain O42                 LNGAIDPTNV TLTSGATWNI PDNATVQSVV DDLSHAGQIH FTSTRTGKFV
strain CFT073              LNGAIDPTNV TLASDATWNI PDNATVQSVV DDLSHAGQIH FTSSRTGTFV
                 Consensus ---------- ---------- ---------- ---------- ----------
B-Cell Ep.                    ******* **    **** *******       ******

                           601                                               650
strain E110019             .......NLT GQGGTINMRV RLD.GSNASD QLVINGGQAT GKTWLAFTNV
Group A                    .......NLT GQGGTINMRV RLD.GSNASD QLVINGGQAT GKTWLAFTNV
strain B171                .......NLT GQGGTINMRV RLD.GSNASD QLVINGGQAT GKTWLAFTNV
strain E22                 .......NLT GQGGTINMRV RLD.GSNASD QLVINGGQAT GKTWLAFTNV
strain B171                .......NLT GQGGTINMRV RLD.GSNTSD QLVINGGQAT GKTWLAFTNV
strain B171                .......NLT GQGGTINMRV RLD.GSNTSD QLVINGGQAT GKTWLAFTNV
strain E24377A and O42     .......NLT GQGGTINMRV RLD.GSNTSD QLVINGGQAT GKTWLAFTNV
strain E24377A             .......NLT GQGGTINMRV RLD.GSNTSD QLVINGGQAT GKTWLAFTNV
Group B                    .......NLT GQGGTINMRV RLD.GSNASD QLVINGGQAT GKTWLAFTNV
strain E110019             .......NLT GQGGTINMRV RLD.GSNASD QLVINGGQAT GKTWLAFTNV
strain E22                 .......NLT GQGGTINMRV RLD.GSNTSD QLVINGGQAT GKTWLAFTNV
strain H10407              .......NLT GQGGTINMRV SLD.GSNASD QLVINGGQAT GKTWLAFTNV
strain F11 and 536         .......NLT GQGGTINMRV RLD.GSNTSD QLVINGGQAT GKTWLAFTNV
strain SECEC               .......NLT GQGGTINMRV RLD.GSNASD QLVINGGQAT GKTWLAFTNV
strain H10407              .......NLT GQGGTINMRV SLD.GSNASD QLVINGGQAT GKTWLAFTNV
strain W3110 and DH10B     PATLKVKNLN GQNGTISLRV RPDMAQNNAD RLVIDGGRAT GKTILNLVNA
strain MG1655              PATLKVKNLN GQNGTISLRV RPDMAQNNAD RLVIDGGRAT GKTILNLVNA
strain O42                 PATLKVKNLN GQNGTISLRV RPDMAQNNAD RLVIDGGRAT GKTILNLVNA
strain B7A                 PATLKVKNLN GQNGTISLRV RPDMAQNNAD RLVIDGGRAT GKTILNLVNA
strain CFT073              PTTLQVKNLN GQNGTISLRV RPDMAQNNAD RLVIDGGRAT GKTILNLVNA
strain O42                 PATLQVKNLN GQNGTISLRV RPDMAQNNAD RLVIDGGRAT GKTILNLVNA
strain CFT073              PATLKVKNLN GQNGTISLRV RPDMAQNNAD RLVIDGGRAT GKTILNLVNA
                 Consensus -------NL- GQ-GTI--RV --D---N--D -LVI-GG-AT GKT-L---N-
B-Cell Ep.                        ** ****         ******                      *

                           651                                               700
strain E110019             GNSNLGVATT GQGIRVVDAQ NGATTEEGAF ALSRPLQAGA FNYTLNRDSD
Group A                    GNSNLGVATT GQGIRVVDAQ NGATTEEGAF ALSRPLQAGA FNYTLNRDSD
strain B171                GNSNLGVATS GQGIRVVDAQ NGATTEEGAF ALSRPLQAGA FNYTLNRDSD
strain E22                 GNSNLGVATS GQGIRVVDAQ NGATTEESAF ALSRPLHAGA FNYTLNRDSD
strain B171                GNSNLGVATS GQGIRVVDAQ NGATTEEGAF ALSRPLQAGA FNYTLNRDSD
strain B171                GNSNLGVATS GQGIRVVDAQ NGATTEEGAF ALSRPLQAGA FNYTLNRDSD
strain E24377A and O42     GNSNLGVATS GQGIRVVDAQ NGATTEEGAF ALSRPLQAGA FNYTLNRDSD
strain E24377A             GNSNLGVATS GQGIRVVDAQ NGATTEEGAF ALSRPLQAGA FNYTLNRDSD
Group B                    GNSNLGVATS GQGIRVVDAQ NGATTEEGAF ALSRPLQAGA FNYTLNRDSD
strain E110019             GNSNLGVATT GQGIRVVDAQ NGATTEEGVF ALSRPLQAGA FNYTLNRDSD
strain E22                 GNSNLGVATS GQGIRVVDAQ NGATTEEGAF ALSRPLQAGA FNYTLNRDSD
strain H10407              GNSNLGVATS GQGIRVVDAQ NGATTEEGAF ALSRPLQAGA FNYTLNRDSD
strain F11 and 536         GNSNLGVATT GQGIRVVDAQ NGATTEEGAF ALSRPLQAGA FNYTLNRDSD
strain SECEC               GNSNLGVATS GQGIRVVDAQ NGATTEEGAF ALSRPLQAGA FNYTLNRDSD
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strain H10407            GNSNLGVATS GQGIRVVDAQ NGATTEEGAF ALSRPLQAGA FNYTLNRDSD
strain W3110 and DH10B   GNSASGLATS GKGIQVVEAI NGATTEEGAF VQGNRLQAGA FNYSLNRDSD
strain MG1655            GNSASGLATS GKGIQVVEAI NGATTEEGAF VQGNRLQAGA FNYSLNRDSD
strain O42               GNSASGLATS GKGIQVVEAI NGATTEEGAF VQGNRLQAGA FNYSLNRDSD
strain B7A               GNSASGLATS GKGIQVVEAI NGATTEEGAF IQGNKLQAGA FNYSLNRDSD
strain CFT073            GNSGTGLATT GKGIQVVEAI NGATTEEGAF VQGNMLQAGA FNYTLNRDSD
strain O42               GNSGTGLATT GKGIQVVEAI NGATTEEGAF VQGNMLQAGA FNYTLNRDSD
strain CFT073            GNSASGLATS GKGIQVVEAI NGATTEEGAF VQGNRLQAGA FNYSLNRDSD
            Consensus    GNS--G-AT- G-GI-VV-A- NGATTEE--F -----L-AGA FNY-LNRDSD
B-Cell Ep.               ********** ***        ********** *               *****

                         701                                               750
strain E110019           EDWYLRSENA YRAEVPLYTS MLTQAMDYDR ILAGSRSHQT GVNGENNSVR
Group A                  EDWYLRSENA YRAEVPLYTS MLTQAMDYDR ILAGSRSHQT GVNGENNSVR
strain B171              EDWYLRSENA YRAEVPLYAS MLTQAMDYDR ILAGSRSHQT GVNGENNSVR
strain E22               EDWYLRSENA YRAEVPLYAS MLTQAMDYDR ILAGSRSHQS GVSGENNSVR
strain B171              EDWYLRSENA YRAEVPLYAS MLTQAMDYDR ILAGSRSHQT GVNGENNSVR
strain B171              EDWYLRSENA YRAEVPLYAS MLTQAMDYDR ILAGSRSHQT GVNGENNSVR
strain E24377A and O42   EDWYLRSENA YRAEVPLYTS MLTQAMDYDR ILAGSRSHQT GVNGENNSVR
strain E24377A           EDWYLRSENA YRAEVPLYAS MLTQAMDYDR ILAGSRSHQT GVSGENNSVR
Group B                  EDWYLRSENA YRAEVPLYAS MLTQAMDYDR ILAGSRSHQS GVSGENNSVR
strain E110019           EDWYLRSENA YRAEVPLYTS MLTQAMDYDR ILAGSRSHQT GVNGENNSVR
strain E22               EDWYLRSENA YRAEVPLYAS MLTQAMDYDR ILAGSRSHQS GVSGENNSVR
strain H10407            EDWYLRSENA YRAEVPLYTS MLTQAMDYDR ILAGSRSHQT GVNGENNSVR
strain F11 and 536       EDWYLRSENA YRAEVPLYAS MLTQAMDYDR ILAGSRSHQT GVNGENNSFR
strain SECEC             EDWYLRSENA YRAEVPLYAS MLTQAMDYDR ILAGSRSHQT GVNGENNSVR
strain H10407            EDWYLRSENA YRAEVPLYTS MLTQAMDYDR ILAGSRSHQT GVNGENNSVR
strain W3110 and DH10B   ESWYLRSENA YRAEVPLYAS MLTQAMDYDR IVAGSRSHQT GVNGENNSVR
strain MG1655            ESWYLRSENA YRAEVPLYAS MLTQAMDYDR IVAGSRSHQT GVNGENNSVR
strain O42               ESWYLRSENA YRAEVPLYAS MLTQAMDYDR ILAGSRSHQT GVSGENNSVR
strain B7A               ESWYLRSENA YRAEVPLYAS MLTQAMDYDR ILAGSRSHQT GVSGENNSVR
strain CFT073            ESWYLRSEER YRAEVPLYAS MLTQAMDYDR ILAGSRSHQT GVNGENNSVR
strain O42               ESWYLRSEER YRAEVPLYAS MLTQAMDYDR ILAGSRSHQT GVNGENNSVR
strain CFT073            ESWYLRSENA YRAEVPLYAS MLTQAMDYDR ILAGSRSHQT GVNGENNSVR
            Consensus    E-WYLRSE-- YRAEVPLY-S MLTQAMDYDR I-AGSRSHQt GVnGENNS-R
                                                SEQ ID NO: 309    SEQ ID NO: 310-313
B-Cell Ep.               ****                                     ****** ********

                         751                                               800
strain E110019           LSIQGGHLGH DNNGGIARGA TPESSGSYGF VRLEGDLLRT EVAGMSLTTG
Group A                  LSIQGGHLGH DNNGGIARGA TPESSGSYGF VRLEGDLLRT EVAGMSLTTG
strain B171              LSIQGGHLGH DNNGGIARGA TPESSGSYGL VRLEGDLLRT EVAGMSLTTG
strain E22               LSIQGGHLGH DNNGGIARGA TPESNGSYGF VRLEGDLLRT EVAGMSLTTG
strain B171              LSIQGGHLGH DNNGGIARGA TPESNGSYGF VRLEGDLLRT EVAGMSLTTG
strain B171              LSIQGGHLGH DNNGGIARGA TPESNGSYGF VRLEGDLLRT EVAGMSLTTG
strain E24377A and O42   LSIQGGHLGH DNNGGIARGA TPESSGSYGF VRLEGDLLRT EVAGMSLTTG
strain E24377A           LSIQGGHLGH DNNGGIARGA TPESSGSYGF VRLEGDLLRT EVAGMSLTTG
Group B                  LSIQGGHLGH DNNGGIARGA TPESNGSYGF VRLEGDLLRT EVAGMSLTTG
strain E110019           LSIQGGHLGH DNNGGIARGA TPESSGSYGF VRLEGDLLRT EVAGMSLTTG
strain E22               LSIQGGHLGH DNNGGIARGA TPESNGSYGF VRLEGDLLRT EVAGMSLTTG
strain H10407            LSIQGGHLGH DNNGGIARGA TPESSGSYGF VRLEGDLLRT EVAGMSLTTG
strain F11 and 536       LSIQGGHLGH VNNGGIARGA TPESSGSYGL VRLEGDLLRT EVAGMSLTTG
strain SECEC             LSIQGGHLGH DNNGGIARGA TPESSGSYGF VRLESDLLRT EVAGMSVTAG
strain H10407            LSIQGGHLGH DNNGGIARGA TPESSGSYGF VRLEGDLLRT EVAGMSVTAG
strain W3110 and DH10B   LSIQGGHLGH DNNGGIARGA TPESSGSYGF VRLEGDLMRT EVAGMSVTAG
strain MG1655            LSIQGGHLGH DNNGGIARGA TPESSGSYGF VRLEGDLMRT EVAGMSVTAG
strain O42               LSIQGGHLGH DNNGGIARGA TPESSGSYGF VRLEGDLLRT EVAGMSLTTG
strain B7A               LSIQGGHLGH DNNGGIARGA TPESSGSYGF VRLEGDLLRT EVAGMSVTAG
strain CFT073            LSIQGGHLGH DNNGGIARGA TPESSGSYGF VRLEGDLLRT EVAGMSLTTG
strain O42               LSIQGGHLGH DNNGGIARGA TPESSGSYGF VRLEGDLLRT EVAGMSLTTG
strain CFT073            LSIQGGHLGH DNNGGIARGA TPESSGSYGF VRLEGDLLRT DVAGMSVTAG
            Consensus    LSIQGGHLGH -NNGGIARGA TPES-GSYG- VRLE-DL-RT -VAGMS-T-G
                         SEQ ID NO: 314  SEQ ID NO: 315
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B-Cell Ep.                    **** ********** ********

                              801                                                 850
strain E110019                VYGAAGHSSV DVKDDDGSRA GTVRDDAGSL GGYLNLVHTS SGLWADIVAQ
Group A                       VYGAAGHSSV DVKDDDGSRA GTVRDDAGSL GGYLNLVHTS SGLWADIVAQ
strain B171                   VYGAAGHSSV DVKDDDGSRA GTVRDDAGSL GGYLNLTHTS SGLWADIVAQ
strain E22                    VYGAAGHSSV DVKNDDGSRA GTVRDDAGSL GGYLNLVHTS SGLWADIVAQ
strain B171                   VYGAAGHSSV DVKDDDGSRA GTVRDDAGSL GGYLNLTHTS SGLWADIVAQ
strain B171                   VYGAAGHSSV DVKDDDGSRA GTVRDDAGSL GGYLNLTHTS SGLWADIVAQ
strain E24377A and O42        VHGAAGHSSV DVKDDDGSRA GTVRDDAGSL GGYLNLTHTS SGLWADIVAQ
strain E24377A                VYGAAGHSSV DVKDDDGSRA GTARDDAGSL GGYLNLVHTS SGLWADIVAQ
Group B                       VYGAAGHSSV DVKDDDGSRA GTVRDDAGSL GGYLHLVHTS SGLWADIVAQ
strain E110019                VYGAAGHSSV DVKDDDGSRA GTVRDDAGSL GGYLNLVHTS SGLWADIVAQ
strain E22                    VYGAAGHSSV DVKDDDGSRA GTVRDDAGSL GGYLNLTHTS SGLWADIVAQ
strain H10407                 VYGAAGHSSV DVKDDDGSRA GTVRDDAGSL GGYLNLTHTS SGLWADIVAQ
strain F11 and 536            VYGAAGHSSV DVKDDDGSRA GTVRDDAGSL GGYLNLVHTS SGLWADIVAQ
strain SECEC                  VYSAAGHSSV DVKDDDGSRA GTVRDDAGSL GGYLNLVHTS SGLWADIMAQ
strain H10407                 VYGAAGHSSV DVKDDDGSRA GTVRDDAGSL GGYLNLVHTS SGLWADIVAQ
strain W3110 and DH10B        VYGAAGHSSV DVKDDDGSRA GTVRDDAGSL GGYLNLVHTS SGLWADIVAQ
strain MG1655                 VYGAAGHSSV DVKDDDGSRA GTVRDDAGCL GGYLNLVHTS SGLWADIVAQ
strain O42                    VYGAAGHSSV DVKDDDGSRA GTVRDDAGSL GGYLNLTHTS SGLWADIVAQ
strain B7A                    VYGAAGHSSV DVKDDDGSRA GTVRDDAGSL GGYLNLIHNA SGLWADIVAQ
strain CFT073                 VYGAAGHSSV DVKDDDGSRA GTVRDDAGSL GGYMNLTHTS SGLWADIVAQ
strain O42                    VYGAAGHSSV DVKDDDGSRA GTVRDDAGSL GGYMNLTHTS SGLWADIVAQ
strain CFT073                 IYGAAGHSSV DVKDDDGSRA GTVRDDAGSL GGYMNLTHTS SGLWADIVAQ
                    Consensus ---AAGHSSV DVK-DDGSRA GT-RDDAG-L GGY--L-H-- SGLWADI-AQ
                                SEQ ID NO: 316
B-Cell Ep.                    ********************* *****

                              851                                                 900
strain E110019                GTRHSMKASS DNNDFRARGW GWLGSLETGL PFSITDNLML EPQLQYTWQG
Group A                       GTRHSMKASS DNNDFRARGW GWLGSLETGL PFSITDNLML EPQLQYTWQG
strain B171                   GTRHSMKASS DNNDFRARGW GWLGSLETGL PFSITDNLML EPQLQYTWQG
strain E22                    GTHHSMKASS DNNDFRARGW GWLGSLETGL PFSITDNLML EPQLQYTWQG
strain B171                   GTRHSMKASS DNNDFRARGW GWLGSLETGL PFSITDNVML EPQLQYTWQG
strain B171                   GTRHSMKASS DNNDFRARGW GWLGSLETGL PFSITDNLML EPQLQYTWQG
strain E24377A and O42        GTRHSMKASS DNNDFRARGW GWLGSLETGL PFSITDNLML EPQLQYTWQG
strain E24377A                GTRHSMKASS DNNDFRARGW GWLGSLETGL PFSITDNLML EPQLQYTWQG
Group B                       GTRHSMKASS DNNDFRARGW GWLGSLETGL PFSITDNLML EPQLQYTWQG
strain E110019                GTRHSMKASS DNNDFRARGW GWLGSLETGL PFSITDNLML EPQLQYTWQG
strain E22                    GTRHSMKASS DNNDFRARGW GWLGSLETGL PFSITDNLML EPQLQYTWQG
strain H10407                 GTRHSMKASS DNNDFRARGW GWLGSLETGL PFSITDNLML EPQLHYTWQG
strain F11 and 536            GTRHSMKASS DNNDFRARGW GWLGSLETGL PFSITDNLML EPQLQYTWQG
strain SECEC                  GTRHSMKASS DNNDFRARGW GWLGSLETGL PFSITDNLML EPQLQYTWQG
strain H10407                 GTRHSMKAST DNNDFRARGW GWLGSLETGL PFSITDNLML EPQLQYTWQG
strain W3110 and DH10B        GTRHSMKASS DNNDFRARGW GWLGSLETGL PFSITDNLML EPQLQYTWQG
strain MG1655                 GTRHSMKASS DNNDFRARGW GWLGSLETGL PFSITDNLML EPQLQYTWQG
strain O42                    GTRHSMKASS DNNDFRARGW GWLGSLETGL PFSITDNLML EPQLHYTWQG
strain B7A                    GTRHSMKASS DNNDFRVRGW GWLGSLETGL PFSITDNLML EPQLQYTWQG
strain CFT073                 GTRHSMKASS DNNDFRARGR GWLGSLETGL PFSITDNLML EPRLQYTWQG
strain O42                    GTRHSMKASS GNNDFRARGW GWLGSLETGL PFSITDNLML EPRLQYTWQG
strain CFT073                 GTRHSMKASS GNNDFRARGR GWLGSLETGL PFSITDNLML EPRLQYTWQG
                    Consensus GT-HSMKAS- -NNDFR-RG- GWLGSLETGL PFSITDN-ML EP-L-YTWQG
                                                    SEQ ID NO: 317      SEQ ID NO:
318
B-Cell Ep.                     ********* *******

                              901                                                 950
strain E110019                LSLDDGQDNA GYVKFGHGSA QHVRAGFRLG SHNDMTFGEG TSSRDTLRDS
Group A                       LSLDDGQDNA GYVKFGHGSA QHVRAGFRLG SHNDMTFGEG TSSRDTLRDS
strain B171                   LSLDDGQDNA GYVKFGHGSA QHVRAGFRLG SHNDMTFGEG TSSRDTLRDS
strain E22                    LSLDDGQDNA GYVKFGHGSA QHVRAGFRLG SHNDMTFGEG TSSRDTLRDS
strain B171                   LSLDDGQDNA GYVKFGHGSA QHVRAGFRLG SHNDMSFGEG TSSRDTLRDS
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strain B171                LSLDDGQDNA GYVKFGHGSA QHVRAGFRLG SHNDMSFGEG TSSRDTLRDS
strain E24377A and O42     LSLDDGQDNA GYVKFGHGSA QHVRAGFRLG SHNDMSFGEG TSSRDTLRDS
strain E24377A             LSLDDGQDNA GYVKFGHGSA QHVRAGFRLG SHNDMNFGKG TSSRDTLRDS
Group B                    LSLDDGQDNA GYVKFGHGSA QHVRAGFRLG SHNDMNFGKG TSSRDTLHDS
strain E110019             LSLDDGQDNA GYVKFGHGST QHVRAGFRLG SHNDMTFGEG TSSRDTLRDS
strain E22                 LSLDDGQDNA GYVKFGHGSA QHVRAGFRLG SHNDMSFGEG TSSRDTLRDS
strain H10407              LSLDDGQDNA GYVKFGHGSA QHVRAGFRLG SHNDMTFGEG TSSRDTLRDS
strain F11 and 536         LSLDDGQDNA GYVKFGHGSA QHVRAGFRLG SHNDMNFGKG TSSRDTLRDS
strain SECEC               LSLDDGQDNA GYVKFGHGSA QHMRAGFRLG SHNDMSFGEG TSSRDTLRDS
strain H10407              LSLDDGKDNA GYVKFGHGSA QHVRAGFRLG SHNDMTFGEG TSSRAPLRDS
strain W3110 and DH10B     LSLDDGKDNA GYVKFGHGSA QHVRAGFRLG SHNDMTFGEG TSSRAPLRDS
strain MG1655              LSLDDGKDNA GYVKFGHGSA QHVRAGFRLG SHNDMTFGEG TSSRAPLRDS
strain O42                 LSLDDGQDNA GYVKFGHGSA QHVRAGFRLG SHNDMTFGEG TSSRDTLRDS
strain B7A                 LSLDDGQDNA SYVKFGHGSA QHVRAGFRLG SHHDMNFGKG TSSRDTLRGS
strain CFT073              LSLDDGKDNA GYVKFGHGSA QHVRAGFRLG SHNDMTFGEG TSSRAPLRDS
strain O42                 LSLDDGKDNA GYVKFGHGSA QHVRAGFRLG SHNDMTFGEG TSSRAPLRDS
strain CFT073              LSLDDGKDNA GYVKFGHGSA QHVRAGFRLG SHNDMTFGEG TSSRAPLRDS
                 Consensus LSLDDG-DNA -YVKFGHGS- QH-RAGFRLG SH-DM-FG-G TSSR--L--S
B-Cell Ep.                 ********* **                      ******* **********

                                  951                                          1000
strain E110019             AKHSVSELPV NWWVQPSVIR TFSSRGDMSM GTAAAGSNMT FSPSRNGTSL
Group A                    AKHSVSELPV NWWVQPSVIR TFSSRGDMSM GTAAAGSNMT FSPSRNGTSL
strain B171                AKHSVSELPV NWWVQPSVIR TVSSRGDMSM GTAAAGSNMT FSPSRNGTSL
strain E22                 AKHRVRELPV NWWVQPSVIR TVSSRGDMSM GTAAAGSNMT FSPSRNGTSL
strain B171                AKHRVRELPV NWWVQPSVIR TFSSRGDMSM GTAAAGSNMT FSPSRNGTSL
strain B171                AKHRVRELPV NWWVQPSVIR TFSSRGDMSM GTAAAGSNMT FSPSRNGTSL
strain E24377A and O42     AKHRVRELPV NWWVQPSVIR TFSSRGDMSM GTAAAGSNMT FSPSRNGTSL
strain E24377A             AKHSVRELPV NWWVQPSVIR TFSSRGDMSM GTAAAGSNMT FSPSRNGTSL
Group B                    AKHSVRELPV NWWVQPSVIR TFSSRGDMSM GTAAAGSNMT FSPSRNGTSL
strain E110019             AKHRVRELPV NWWVQPSVIR TFSSRGDMSM GTAAAGSNMT FSPSRNGTSL
strain E22                 AKHRVRELPV NWWVQPSVIR TFSSRGDMSM GTAAAGSNMT FSPSRNGTSL
strain H10407              TKHGVSELPV NWWVQPSVIR TFSSRGDMSM GTAAAGSNMT FSPSRNGTSL
strain F11 and 536         AKHSVRELPV NWWVQPSVIR TFSSRGDMSM GTAAAGSNMT FSPSQNGTTL
strain SECEC               AKHRVRELPV NWWVQPSVIR TFSSRGDMSM GTAAAGSNMT FSPSQNGTSL
strain H10407              AKHSMRELPV NWWVQPSVIR TFSSRGDMSM GTAAAGSNMT FSPSRNGTSL
strain W3110 and DH10B     AKHSVSELPV NWWVQPSVIR TFSSRGDMRV GTSTAGSGMT FSPSQNGTSL
strain MG1655              AKHSVSELPV NWWVQPSVIR TFSSRGDMRV GTSTAGSGMT FSPSQNGTSL
strain O42                 TKHGVSELPV NWWVQPSVIR TFSSRGDMSM GTAAAGSNMT FSPSQNGTSL
strain B7A                 AKHSVRELPV NWWVQPSVIR TFSSRGDMSM GTAAAGSNMT FSPSQNGTSL
strain CFT073              AKHSVRELPV NWWVQPSVIR TFSSRGDMRV GTSTAGSGMT FSPSQNGTSL
strain O42                 AKHSVRELPV NWWVQPSVIR TFSSRGDMRV GTSTAGSGMT FSPSQNGTSL
strain CFT073              AKHSVRELPV NWWVQPSVIR TFSSRGDMRV GTSTAGSGMT FSPSQNGTSL
                 Consensus -KH---ELPV NWWVQPSVIR T-SSRGDM-- GT--AGS-MT FSPS-NGT-L
                                    SEQ ID NO: 319
B-Cell Ep.                 ****                          **** ********** **********

                                  1001                                         1044
strain E110019             DLQAGLEARI RENITLGVQA GYAHSVSGSS AEGYNGQATL NMTF
Group A                    DLQAGLEARI RENITLGVQA GYAHSVSGSS AEGYNGQATL NMTF
strain B171                DLQAGLEARV RENITLGVQA GYAHSVSGSS AEGYNGQATL NMTF
strain E22                 DLQAGLEARV RENITLGVQA GYAHSVSGSS AEGYNGQATL NMTF
strain B171                DLQAGLEARV RENITLGVQA GYAHSVSGSS AEGYNGQATL NVTF
strain B171                DLQAGLEARV RENITLGVQA GYAHSVSGSS AEGYNGQATL NVTF
strain E24377A and O42     DLQAGLEARV RENITLGVQA GYAHSVSGSS AEGYNGQATL NVTF
strain E24377A             DLQAGLEARV RENITLGVQA GYAHSVSGSS AEGYNGQATL NVTF
Group B                    DLQAGLEARV RENITLGVQA GYAHSVSGSS AEGYNGQATL NVTF
strain E110019             DLQAGLEARV RENITLGVQA GYAHSVSGSS AEGYNGQATL NVTF
strain E22                 DLQAGLEARV RENITLGVQA GYAHSVSGSS AEGYNGQATL NVTF
strain H10407              DLQAGLEARV RENITLGVQA GYAHSVSGNS AEGYNGQATL NVTF
strain F11 and 536         DLQAGLEARV RENITLGVQA GYAHSVSGSS AEGYNGQATL NVTF
strain SECEC               DLQAGLEARV RENITLGVQA GYAHSVSGSS AEGYNGQATL NVTF
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strain H10407            DLQAGLEARV RENITLGVQA GYAHSVIGSS AEGYNGQATL NVTF
strain W3110 and DH10B   DLQAGLEARV RENITLGVQA GYAHSVSGSS AEGYNGQATL NVTF
strain MG1655            DLQAGLEARV RENITLGVQA GYAHSVSGSS AEGYNGQATL NVTF
strain O42               DLQAGLEARV RENITLGVQA GYAHSVSGSS AEGYNGQATL NVTF
strain B7A               DLQAGLEARV RENITLGVQA GYVHSVSGSS AEGYNGQATL NVTF
strain CFT073            DLQAGLEARV RENITLGVQA GYAHSINGSS AEGYNSQATL NVTF
strain O42               DLQAGLEARV RENITLGVQA GYAHSVSGSS AEGYNSQATL NVTF
strain CFT073            DLQAGLEARV RENITLGVQA GYAHSVSGSS AEGYNGQATL NVTF
             Consensus   DLQAGLEAR- RENITLGVQA GY-HS--G-S AEGYN-QATL N-TF
                        SEQ ID NO: 320 SEQ ID NO: 321
B-Cell Ep.                                  ******** *********
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SEQ ID NO: 310 SRSHQ(T/S)GV(N/S)GENNS
SEQ ID NO: 311 SRSHQTGVNGENNS
SEQ ID NO: 312 SRSHQSGVSGENNS
SEQ ID NO: 313 SRSHQTGVSGENNS

B-Cell Epitopes
SEQ ID NO: 322 RARGKRGG
SEQ ID NO: 323 GETVNGGTLAN
SEQ ID NO: 324 GLEYGPDNEANTGGQWVQDGGTANKTTVTSGGLQRVNPGGSVSDTVISAGGGQSLQGR
SEQ ID NO: 325 WQVVKPGTVATDTVVNTGAEGGPDAENGDTGQFV
SEQ ID NO: 326 AVRTTINKN
SEQ ID NO: 327 RAEGTANT
SEQ ID NO: 328 YAGGDQTVHG
SEQ ID NO: 329 QYVHNGGTASDTVVNS
SEQ ID NO: 330 GGVAGNTTVNQKGRLQVDAGGTATNVTLK
SEQ ID NO: 331 HTATNTRVDDGGTLDVRNGGTATTVSMG
SEQ ID NO: 332 GAAVSGTRSDGKAFSIGG
SEQ ID NO: 333 TLNAGDTATDTTV
SEQ ID NO: 334 GTLAGTTTLN
SEQ ID NO: 335 LTGNGSVEKSGSGTLTV
SEQ ID NO: 336 AIDPTNVTL
SEQ ID NO: 337 TWNIPDNATVQ
SEQ ID NO: 338 SHAGQI
SEQ ID NO: 339 NLNGQNG
SEQ ID NO: 340 DMAQNN
SEQ ID NO: 341 AGNSASGLATSGKG
SEQ ID NO: 342 NGATTEEGAFV
SEQ ID NO: 343 NRDSDESWY
SEQ ID NO: 344 HLGHDNNGGIARGATPESSGSY
SEQ ID NO: 345 YGAAGHSSVDVKDDDGSRAGTVRD
SEQ ID NO: 346 TRHSMKASSDNNDFRA
SEQ ID NO: 347 SLDDGKDNAGY
SEQ ID NO: 348 DMTFGEGTSSRAPLRDSAKHS
SEQ ID NO: 349 DMRVGTSTAGSGMTFSPSQNGTSL
SEQ ID NO: 350 YAHSVSGSSAEGYNGQAT

Orf1767 protein

NodT-family outer-membrane-factor-lipoprotein efflux transporter protein is referred to herein as 'orf1767.' 'orf1767' protein from *E. coli* NMEC is disclosed in reference 5 (SEQ IDs 3533 & 3534) is also known as: 'orf1488' from *E. coli* NMEC strain IHE3034, 'c1765' from CFT073 and ecp_1346 from 536.

When used according to the present invention, orf1767 protein may take various forms. Preferred orf1767 sequences have 50% or more identity (*e.g.* 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98%, 99% or more) to SEQ ID NOs 41-47. This includes variants (*e.g.* allelic variants, homologs, orthologs, paralogs, mutants *etc*).

Other preferred orf1767 sequences comprise at least *n* consecutive amino acids from SEQ ID NOs 41-47, wherein *n* is 7 or more (*eg.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). Preferred fragments comprise an epitope or immunogenic fragment from orf1767. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or the N-terminus of SEQ ID NOs 41-47. Exemplary fragments are the conserved fragments SEQ ID NOs identified in the sequence alignment below.

strain UTI89 and IHE3034 (SEQ ID NO: 41)
strain 536 and F11 (SEQ ID NO: 42)
strain SECEC (SEQ ID NO: 43)
strain APECO1 (SEQ ID NO: 44)
strain CFT073 (SEQ ID NO: 45)
strain E2348-69 (SEQ ID NO: 46)
Group A: strain Sakai, EDL933, EC508, EC869, EC4024, EC4042, EC4045, EC4076, EC4113, EC4115, EC4196, EC4206, EC4401, EC4486, EC4501 and TW14588 (SEQ ID NO: 47)

```
                                1                                                 50
strain UTI89 and IHE3034        MLRRSLIFLV LLSAGCVSLD PHYSTPESPI PATLPGAQGQ GKAISHDWQQ
strain 536 and F11              MLRRSLIFLV LLSAGCVSLD PHYSTPESPI PATLPGAQGQ GKAISHDWQQ
strain SECEC                    MLRRSLIFLV LLSAGCVSLD PHYSTPESPI PATLPGAQGQ GKAISHDWQQ
strain APECO1                   MLRRSLIFLV LLSAGCVSLD PHYSTPESPI PATLPGAQGQ GKAISHDWQQ
strain CFT073                   MLRRSLIFLV LLSAGCVSLD PHYSTPESPI PATLPGAQGQ GKAISHDWQQ
strain E2348-69                 MLRRSLIFLV LLSAGCVSLD PHYSTPESPI PATLPGAQGQ GKAISHDWQQ
Group A                         MLRRSLIFLV LLSAGCVSLD PHYSTPESPI PATLPGAQGQ GKAISHDWQQ
                    Consensus   MLRRSLIFLV LLSAGCVSLD PHYSTPESPI PATLPGAQGQ GKAISHDWQQ
                                                  SEQ ID NO: 351
B-Cell Ep.                                        * ********** ********** *****

                                51                                                100
strain UTI89 and IHE3034        VIHDPRLQQV VTIALNSNRD VQKAIADIDS ARALYGQTNA SLFPTVNAAL
strain 536 and F11              VIHDPRLQQV VTIALNSNRD VQKAIADIDS ARALYGQTNA SLFPTVNAAL
strain SECEC                    VIHDPRLQQV VTIALNSNRD VQKAIADIDS ARALYGQTNA SLFPTVNAAL
strain APECO1                   VIHDPRLQQV VTIALNSNRD VQKAIADIDS ARALYGQTNA SLFPTVNAAL
strain CFT073                   VIHDPRLQQV VTIALNRNRD VQKAIADIDS ARALYGQTNA SLFPTVNAAL
strain E2348-69                 VIHDPRLQQV VTIALNSNRD VQKAIADIDS ARALYGQTNA SLFPTVNAAL
Group A                         VIHDPRLQQV VTIALNSNRD VQKAIADIDS ARALYGQTNA SLFPTVNAAL
                    Consensus   VIHDPRLQQV VTIALN-NRD VQKAIADIDS ARALYGQTNA SLFPTVNAAL
                                                            SEQ ID NO: 352

                                101                                               150
strain UTI89 and IHE3034        SSTRSRSLAN GTGTTAEADG TVSSYTLDLF GRNQSLSRAA RETWLASEFT
strain 536 and F11              SSTRSRSLAN GTGTTAEADG TVSSYTLDLF GRNQSLSRAA RETWLASEFT
strain SECEC                    SSTRSRSLAN GTGTTAEADG TVSSYTLDLF GRNQSLSRAA RETWLASEFT
strain APECO1                   SSTRSRSLAN GTVTTAEADG TVSSYTLDLF GRNQSLSRAA RETWLASEFT
strain CFT073                   SSTRSRSLAN GTGTTAEADG TVSSYTLDLF GRNQSLSRAA RETWLASEFT
strain E2348-69                 SSTRSRSLAN GTGTTAEADG TVSSYTLDLF GRNQSLSRAA RETWLASEFT
Group A                         SSTRSRSLAN GTETTAEADG TVSSFTLDLF GRNQSLSRAA RETWLASEFT
                    Consensus   SSTRSRSLAN GT-TTAEADG TVSS-TLDLF GRNQSLSRAA RETWLASEFT
                                              SEQ ID NO: 353          SEQ ID NO: 354
B-Cell Ep.                        ****** ********** ***

                                151                                               200
strain UTI89 and IHE3034        AQNTRLTLIA EISTAWLTLA ADNSNLALAK ETMASAENSL KIIQRQQQVG
strain 536 and F11              AQNTRLTLIA EISTAWLTLA ADNSNLALAK ETMASAENSL KIIQRQQQVG
strain SECEC                    AQNTRLTLIA EISTAWLTLA ADNSNLALAK ETMASAENSL KIIQRQQQVG
strain APECO1                   AQNTRLTLIA EISTAWLTLA ADNSNLALAK ETMASAENSL KIIQRQQQVG
strain CFT073                   AQNTRLTLIA EISTAWLTLA ADNSNLALAK ETMASAENSL KIIQRQQQVG
strain E2348-69                 AQSTRLTLIA EISTAWLTLA ADNSNLALAK ETMASAENSL KIIQRQQQVG
Group A                         AQNTRLTLIA EISTAWLTLA ADNSNLALAK ETMTSAENSL KIIQRQQQVG
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                Consensus  AQ-TRLTLIA EISTAWLTLA ADNSNLALAK ETM-SAENSL KIIQRQQQVG
                                      SEQ ID NO: 355                SEQ ID NO: 356
B-Cell Ep.                                                                  ****

                           201                                              250
strain UTI89 and IHE3034   TAAATDVSEA MSVYQQARAS VASYQTQVMQ DKNALNLLAG TTLAENLLPG
strain 536 and F11         TAAATDVSEA MSVYQQARAS VASYQTQVMQ DKNALNLLAG TTLAENLLPG
strain SECEC               TAAATDVSEA MSVYQQARAS VASYQTQVMQ DKNALNLLAG TTLAENLLPG
strain APECO1              TAAATDVSEA MSVYQQARAS VASYQTQVMQ DKNALNLLAG TTLAENLLPG
strain CFT073              TAAATDVSEA MSVYQQARAS VASYQTQVMQ DKNALNLLAG TTLAENLLPG
strain E2348-69            TAAATDVSEA MSVYQQARAS VASYQTQVMQ DKNALNLLAG TTLAENLLPG
Group A                    TAAATDVSEA MSVYQQARAS VASYQTQVMQ DKNALNLLAG TTLEENLLPG
                Consensus  TAAATDVSEA MSVYQQARAS VASYQTQVMQ DKNALNLLAG TTL-ENLLPG
B-Cell Ep.                 *********          *** ***

                           251                                              300
strain UTI89 and IHE3034   TLESLPEQMI SLVPAGVSSD VLLRRPDIQE AEHNLKSANA DIGAARANFF
strain 536 and F11         TLESLPEQMI SLVPAGVSSD VLLRRPDIQE AEHNLKSANA DIGAARANFF
strain SECEC               TLESLPEQMI SLVPAGVSSD VLLRRPDIQE AEHNLKSANA DIGAARANFF
strain APECO1              TLESLPEQMI SLVPAGVSSD VLLRRPDIQE AEHNLKSANA DIGAARANFF
strain CFT073              TLESLPEQMI SLVPAGVSSD VLLRRPDIQE AEHNLKSANA DIGAARANFF
strain E2348-69            TLESLPEQMI SLVPAGVSSD VLLRRPDIQE AEHNLKSANA DIGAARANFF
Group A                    TLESLPEQMI SLVPAGVSSD VLLRRPDIQE AEHNLKSANA DIGAARANFF
                Consensus  TLESLPEQMI SLVPAGVSSD VLLRRPDIQE AEHNLKSANA DIGAARANFF
                                      SEQ ID NO: 357
B-Cell Ep.                                        **** ********** ****

                           301                                              350
strain UTI89 and IHE3034   PTISLTASAG VGSDALSSLF SHGMQIWSFA PSVTLPLFTG GSNLAQLRYA
strain 536 and F11         PTISLTASAG VGSDALSSLF SHGMQIWSFA PSVTLPLFTG GSNLAQLRYA
strain SECEC               PTISLTASAG VGSDALSSLF SHGMQIWSFA PSVTLPLFTG GSNLAQLRYA
strain APECO1              PTISLTASAG VGSDALSSLF SHGMQIWSFA PSVTLPLFTG GSNLAQLRYA
strain CFT073              PTISLTASAG VGSDALSSLF SHGMQIWSFA PSVTLPLFTG GSNLAQLRYA
strain E2348-69            PTISLTASAG VGSDALSSLF SHGMQIWSFA PSVTLPLFTG GSNLAQLRYA
Group A                    PTISLTASAG VGSDALSSLF SHGMQIWSFT PSVTLPLFTG GSNLAQLRYA
                Consensus  PTISLTASAG VGSDALSSLF SHGMQIWSF- PSVTLPLFTG GSNLAQLRYA
                                                                SEQ ID NO: 358
B-Cell Ep.                        *** ****

                           351                                              400
strain UTI89 and IHE3034   EAQKRGLIAT YEKTVQSAFK DVANALARRT TLEEQLDAQR QYVKAEQQTV
strain 536 and F11         EAQKRGLIAT YEKTVQSAFK DVANALARRT TLEEQLDAQR QYVKAEQQTV
strain SECEC               EAQKRGLIAT YEKTVQSAFK DVANALARRT TLEEQLDAQR QYVKAEQQTV
strain APECO1              EAQKRGLIAT YEKTVQSAFK DVANALARRT TLEEQLDAQR QYVKAEQQTV
strain CFT073              EAQKRGLIAT YEKNVQSAFK DVANALARRT TLEEQLDAQR QYVKAEQQTV
strain E2348-69            EAQKRGLIAT YEKTVQSAFK EVANALARRT TLEEQLDAQS QYVKAEQQTV
Group A                    EAQKRGLIAT YEKTVQRAFK DVANALARRT TLEEQLDAQR QYVKAEQQTV
                Consensus  EAQKRGLIAT YEK-VQ-AFK -VANALARRT TLEEQLDAQ- QYVKAEQQTV
                                                  SEQ ID NO: 359    SEQ ID NO: 360
B-Cell Ep.                                                          **********

                           401                                              450
strain UTI89 and IHE3034   DVGLRRYQAG VGDYLTVLTA QRSLWSAQQE LLALQLTDFT NRITLWQSLG
strain 536 and F11         DVGLRRYQAG VGDYLTVLTA QRSLWSAQQE LLALQLTDFT NRITLWQSLG
strain SECEC               DVGLRRYQAG VGDYLTVLTA QRSLWSAQQE LLALQLTDFT NRITLWQSLG
strain APECO1              DVGLRRYQAG VGDYLTVLTA QRSLWSAQQE LLALQLTDFT NRITLWQSLG
strain CFT073              DVGLRRYQAG VGDYLTVLTA QRSLWSAQQE LLALQLTDFT NRITLWQSLG
strain E2348-69            DVGLRRYQAG VGDYLTVLTA QRSLWSAQQE LLALQLTDFT NRITLWQSLG
Group A                    DVGLRRYQTG VGDYLTVLTA QRSLWSAQQE LLALQLTDFT NRITLWQSLG
                Consensus  DVGLRRYQ-G VGDYLTVLTA QRSLWSAQQE LLALQLTDFT NRITLWQSLG
                                      SEQ ID NO: 361

                           451
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strain UTI89 and IHE3034 GGMSSLK
strain 536 and F11       GGMSSLK
strain SECEC             GGMSSLK
strain APECO1            GGMSSLK
strain CFT073            GGMSSLK
strain E2348-69          GGMSSLK
Group A                  GGMSSLK
             Consensus   GGMSSLK
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B-Cell Epitopes
SEQ ID NO: 362  DPHYSTPESPIPATLPGAQGQGKAIS
SEQ ID NO: 363  SRSLANGTGTTAEADGTVS
SEQ ID NO: 364  QQVGTAAATDVSE
SEQ ID NO: 365  RASVAS
SEQ ID NO: 366  DIQEAEHNLKSANADIGA
SEQ ID NO: 367  SAGVGSD
SEQ ID NO: 368  QYVKAEQQTV
```

Orf3515 protein

gspK general secretion pathway protein is referred to herein as 'orf3515.' 'orf3515' protein from *E. coli* NMEC is disclosed in reference 5 (SEQ IDs 7029 & 7030) is also known as: 'orf3332' from *E. coli* NMEC strain IHE3034, 'c3702' from CFT073 and ecp_3039 from 536.

When used according to the present invention, orf3515 protein may take various forms. Preferred orf3515 sequences have 50% or more identity (*e.g.* 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98%, 99% or more) to SEQ ID NOs 48-60. This includes variants (*e.g.* allelic variants, homologs, orthologs, paralogs, mutants *etc*).

Other preferred orf3515 sequences comprise at least *n* consecutive amino acids from SEQ ID NOs 48-60, wherein *n* is 7 or more (*eg.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). Preferred fragments comprise an epitope or immunogenic fragment from orf3515. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or the N-terminus of SEQ ID NOs 48-60. Exemplary fragments are the conserved fragments SEQ ID NOs identified in the sequence alignment below.

```
strain 536  (SEQ ID NO: 48)
strain SECEC  (SEQ ID NO: 49)
strain E22 and B7A  (SEQ ID NO: 50)
strain HS  (SEQ ID NO: 51)
strain E24377A  (SEQ ID NO: 52)
strain 53638  (SEQ ID NO: 53)
strain H10407  (SEQ ID NO: 54)
strain E2348-69  (SEQ ID NO: 55)
Group A: strain APECO1, UTI89, RS218 and IHE3034  (SEQ ID NO: 56)
strain E110019  (SEQ ID NO: 57)
strain F11  (SEQ ID NO: 58)
strain 101-1  (SEQ ID NO: 59)
strain 042  (SEQ ID NO: 60)
```

```
                          1                                                 50
strain 536                MITLPPKRGM ALVVVLVLLA VMMLVTITLS GRMQQQLGRT RSQQEYQQAL
strain SECEC              MITLPPKRGM ALVVVLVLLA VMMLVTITLS GRMQQQLGRT RSQQEYQQAL
strain E22 and B7A        MITSPPKRGM ALVVVLVLLA VMMLVTITLS GRMQQQLGRT RSQQEYQQAL
strain HS                 MITSPPKRGM ALVVVLVLLA VMMLVTITLS GRMQQQLGRT RSQQEYQQAL
strain E24377A            MITSPPKRGM ALVVVLVLLA VMMLVIITLS GRMQQQLGRT RSQQEYQQAL
```

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strain 53638            MITSPPKRGM ALVVVLVLLA VMMLVTITLS GRMQQQLGRT RSQQEYQQAL
strain H10407           MITSPPKRGM ALVVVLVLLA VMMLVTITLS GRMQQQLGRT RSQQEYQQAL
strain E2348-69         MITSPPKRGM ALVVVLVLLA VMMLVTITLS SRMQQQLGRT RSQQEYQQAL
Group A                 MITSPPKRGM ALVVVLVLLA VMMLVTITLS GRMQQQLGRT RSQQEYQQAL
strain E110019          MITSPPKRGM ALVVVLVLLA VMMLVTITLS GRMQQQLGRT RSQQEYQQAL
strain F11              MITSPPKRGM ALVVVLVLLA VIMLVTITLS GRMQQQLGRT RSQQEYQLAL
strain 101-1            MITLPPKRGM ALVVVLVLLA VMMLVTITLS GRMQQQLGRT RSQQEYQQAL
strain 042              MIISPPKRGM ALAVVLVLLA VMMLVTITLS ARMQQQLGRT RSQQEYQQAL
                Consensus MI--PPKRGM AL-VVLVLLA V-MLV-ITLS -RMQQQLGRT RSQQEYQ-AL
                                                          SEQ ID NO: 369
B-Cell Ep.                                                 ***** ******

                                51                                        100
strain 536              WYSASAESLA LSALSLSLKN EKRVHLAQPW ASGPRFFPLP QGQIAVTLRD
strain SECEC            WYSASAESLA LSALSLSLKN EKRVHLAQPW ASGPRFFPLP QGQIAVTLRD
strain E22 and B7A      WYSASAESLA LSALSLSLKN EKRVHLEQPW ASGPRFFPLP QGQIAVTLRD
strain HS               WYSASAESLA LSALSLSLKN EKRVHLEQPW ASGPRFFPLP QGQIAVTLRD
strain E24377A          WYSASAESLA LSALSLSLKN EKRVHLEQPW ASGPRFFPLP QGQIAVTLRD
strain 53638            WYSASAESLA LSALSLSLKN EKRVHLAQPW TSGPRFFPLP QGQIAVTLRD
strain H10407           WYSASAESLA LSALSLSLKN EKRVHLAQPW ASGPRFFPLP QGQIAVTLRD
strain E2348-69         WYSASAESLA LSALSLSLKN EKRVHLAQPW ASGPRFFPLP QGQIAVTLRD
Group A                 WYSASAESLA LSALSLSLKN EKRVHLAQPW ASGPRFFPLP QGQIAVTLRD
strain E110019          WYSASAESLA LSALSLSLKN EKRVHLTQPW ASGPRFFPLP QGQIAVTLRD
strain F11              WYSASAESLA LSALSLSLKN EKRVHLAQPW ASGPRFFPLP QGQIAVTLRD
strain 101-1            WYSASAESLA LSALSLSLKN EKRVHLAQPW ASGPRFFPLP QGQIAVTLRD
strain 042              WYSASAESLA LSALSLSLKN EKRVHLAQPW ASGPRFFPLP QGQIAVTLRD
                Consensus WYSASAESLA LSALSLSLKN EKRVHL-QPW -SGPRFFPLP QGQIAVTLRD
                          SEQ ID NO: 370                    SEQ ID NO: 371
B-Cell Ep.                                          ** *********

                                101                                       150
strain 536              AQACFNLNAL AQPTTASRPI AVQQLIALIS RLDVPAYRAE LIAESLWEFI
strain SECEC            AQACFNLNAL AQPTTTSRPL AVQQLIALIS RLDVPAYRAE LIAESLWEFI
strain E22 and B7A      AQACFNLNAL AQPTTASRPL AVQQLIALIT RLDVPAYRAE LIAESLWEFI
strain HS               AQACFNLNAL AQPTTASRPL AVQQLIALIT RLDVPAYRAE LIAESLWEFI
strain E24377A          AQACFNLNAL AQPTTASRPL AVQQLIALIS RLDVPAYRAE LIAESLWEFI
strain 53638            AQACFNLNAL AQPTTASRPL AVQQLIALIS RLDVPAYRAE LIAESLWEFI
strain H10407           AQACFNLNAL AQPTTASRPL AVQQLIALIS RLDVPAYRAE LIAESLWEFI
strain E2348-69         AQACFNLNAL AQPTTASRPL AVQQLIALIS RLDVPAYRAE LIAESLWEFI
Group A                 AQACFNLNAL AQPTTASRPL AVQQLIALIS RLDVPAYRAE LIAESLWEFI
strain E110019          AQACFNLNAL AQPTTASRPL AVQQLIALIS RLDVPAYRAE LIAESLWEFI
strain F11              AQACFNLNAL AQPTTASRPL AVQQLISLIS RLDVPAYRAE LIAESLWEFI
strain 101-1            AQACFNLNAL AQPTTASRPL AVQQLIALIT RLGVPAYRAE LIAESLWEFI
strain 042              AQACFNLNAL AQPTTATRPL AVQQLIALIT RLDVPAYRAE LIAESLWEFI
                Consensus AQACFNLNAL AQPTT--RP- AVQQLI-LI- RL-VPAYRAE LIAESLWEFI
                                                          SEQ ID NO: 372
B-Cell Ep.                      *********

                                151                                       200
strain 536              DEDRSVQTRL GREDSEYLAR SVPFYAANQP LADISEMRVV QGMDAGLYQK
strain SECEC            DEDRSVQTRL GREDSEYLAR SVPFYAANQP LADISEMRVV QGMDAGLYQK
strain E22 and B7A      DEDRSVQTRL GREDSEYLAR SVPFYAANQP LADISEMRVV QGMDAGLYQK
strain HS               DEDRSVQTRL GREDSEYLAR SVPFYAANQP LADISEMRVV QGMDAGLYQK
strain E24377A          DEDRSVQTRL GREDSEYLAR SVPFYAANQP LADISEMRVV QGMDAGLYQK
strain 53638            DEDRSVQTRL GREDSEYLAR SVPFYAANQP LADISEMRVV QGMDAGLYQK
strain H10407           DEDRSVQTRL GREDSEYLAR SVPFYAANQP LADISEMRVV QGMDAGLYQK
strain E2348-69         DEDRSVQTRL GREDSEYLAR SVPFYAANQP LADISEMRVV QGMDAGLYQK
Group A                 DEDRSVQTRL GREDSEYLAR SVPFYAANQP LADISEMRVV QGMDAGLYQK
strain E110019          DEDRSVQTRL GREDSEYLAR SVPFYAANQP LADISEMRVV QGMDDGLYQK
strain F11              DEDRSVQTRL GREDSEYLAR SVPFYAANQP LADISEMRVV QGMDAGLYQK
strain 101-1            DEDRSVQTRL GREDSEYLAR SVPFYAANQP LADISEMRVV QGMDAGLYQK
strain 042              DEDRSIQTRL GREDSEYLAR SVPFYAANQP LADISEMRVV QGMDAGLYQK
                Consensus DEDRS-QTRL GREDSEYLAR SVPFYAANQP LADISEMRVV QGMD-GLYQK
```

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                                                    SEQ ID NO: 373
B-Cell Ep.                              ** ******* ******* **

                                201                                                 250
strain 536                      LKPLVCALPM ARQQININTL DVTQSVILEA LFDPWLSPVQ ARALLQQRPA
strain SECEC                    LKPLVCALPM ARQQININTL DVTQSVILEA LFDPWLSPVQ ARALLQQRPA
strain E22 and B7A              LKPLVCALPM TRQQININTL DVTQSVILEA LFDPWLSPVQ ARALLQQRPA
strain HS                       LKPLVCALPM TRQQININTL DVTQSVILEA LFDPWLSPVQ ARALLQQRPA
strain E24377A                  LKPLVCALPM TRQQININTL DVTQSVILEA LFDPWLSPVQ ARALLQQRPA
strain 53638                    LKPLVCALPM TRQQININTL DVTQSVILEA LFDPWLSPVQ ARALLQQRPA
strain H10407                   LKPLVCALPM TRQQININTL DVTQSVILEA LFDPWLSPVQ ARALLQQRPA
strain E2348-69                 LKPLVCALPM ARQQININTL DVTQSVILEA LFDPWLSPVQ ARALLQQRPA
Group A                         LKPLVCALPM ARQQININTL DVTQSVILEA LFDPWLSPVQ ARALLQQRPA
strain E110019                  LKPLVCALPM TRQQININTL DVTQSVLLEA LFDPWLSPVQ ARALLQQRPA
strain F11                      LKPLVCALPM ARQQININTL DVTQSVILEA LFDPWLSPVQ ARALLQQRPA
strain 101-1                    LKPLVCALPM TRQQININTL DVTQSVILEA LFDPWLSPVQ ARALLQQRPA
strain O42                      LKPLVCALPM ARQQININTL DVTQSVILEA LFDPWLSPVQ ARALLQQRPA
                    Consensus   LKPLVCALPM -RQQININTL DVTQSV-LEA LFDPWLSPVQ ARALLQQRPA
                               SEQ ID NO: 374  SEQ ID NO: 375          SEQ ID NO: 376
B-Cell Ep.                                                                       ***

                                251                                                 300
strain 536                      KGWEDVDQFL AQPLLADVDE RTKKQLKTVL SVDSNYFWLR SDITVNEIEL
strain SECEC                    KGWEDVDQFL AQPLLADVDE RTKKQLKTIL SVDSNYFWLR SDITVNEIEL
strain E22 and B7A              KGWEDVDQFL AQPLLADVDE RTKKQLKTVL SVDSNYFWLR SDITVNEIEL
strain HS                       KGWEDVDQFL AQPLLADVDE RTKKQLKTVL SVDSNYFWLR SDITVNEIEL
strain E24377A                  KGWEDVDQFL AQPLLADVDE RTKKQLKTVL SVDSNYFWLR SDITVNEIEL
strain 53638                    KGWEDVDQFL AQPLLADVDE RTKKQLKTVL SVDSNYFWLR SDITVNEIEL
strain H10407                   KGWEDVDQFL AQPLLADVDE RTKKQLKTVL SVDSNYFWLR SDITVNEIEL
strain E2348-69                 KGWEDVDQFL AQPLLADVDE RTKKQLKTIL SVDSNYFWLR SDITVNEIEL
Group A                         KGWEDVDQFL AQPLLADVDE RTKKQLKTIL SVDSNYFWLR SDITVNEIEL
strain E110019                  KGWEDVDQFL AQPLLADVDE RTKKQLKTVL SVDSNYFWLR SDITVNEIEL
strain F11                      KGWEDVDQFL AQPLLADVDE RTKKQLKTIL SVDSNYFWLR SDITVNEIEL
strain 101-1                    KGWEDVDQFL AQPLLADVDE RTKKQLKTVL SVDSNYFWLR SDITVNEIEL
strain O42                      KGWEDVDQFL AQPLLADVDD RTKKQLKTVL SVDSNYFWLR SDITVNEIEL
                    Consensus   KGWEDVDQFL AQPLLADVD- RTKKQLKT-L SVDSNYFWLR SDITVNEIEL
                                                                 SEQ ID NO: 377
B-Cell Ep.                      *****              ** ****

                                301                         325
strain 536                      TMNSLIVRMG PQHFSVLWHQ TGESE
strain SECEC                    TMNSLIVRMG PQHFSVLWHQ TGESE
strain E22 and B7A              TMNSLIVRMG PQHFSVLWHQ TGESE
strain HS                       TMNSLIVRMG PQHFSVLWHQ TGESE
strain E24377A                  TMNSLIVRMG PQHFSVLWHQ TGESE
strain 53638                    TMNSLIVRMG PQHFSVLWHQ TGESE
strain H10407                   TMNSLIVRMG PQHFSVLWHQ TGESE
strain E2348-69                 TMNSLIVRMG PQHFSVLWHQ TGESE
Group A                         TMNSLIVRMG PQHFSVLWHQ TGESE
strain E110019                  TMNSLIVRMG PQHFSVLWHQ TGESE
strain F11                      TMNSLIIRMG PQHFSVLWHQ TGESE
strain 101-1                    TMNSLIVRMG SQHFSVIWHQ TGESE
strain O42                      TMNSLIVRMG PQHFSVLWHQ TGESE
                    Consensus   TMNSLI-RMG -QHFSV-WHQ TGESE

B-Cell Epitopes
SEQ ID NO: 378  QLGRTRSQQEY
SEQ ID NO: 379  PWASGPRFFPL
SEQ ID NO: 380  AQPTTASRP
SEQ ID NO: 381  RLGREDSEY
SEQ ID NO: 382  YAANQPLA
SEQ ID NO: 383  RPAKGWED
SEQ ID NO: 384  DERTKK
```

Orf3516 protein

gspJ general secretion pathway protein is referred to herein as 'orf3516.' 'orf3516' protein from *E. coli* NMEC is disclosed in reference 5 (SEQ IDs 7031 & 7032) is also known as: 'orf3333' from *E. coli* NMEC strain IHE3034 and ecp_3040 from 536.

When used according to the present invention, orf3516 protein may take various forms. Preferred orf3516 sequences have 50% or more identity (*e.g.* 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98%, 99% or more) to SEQ ID NOs 61-71. This includes variants (*e.g.* allelic variants, homologs, orthologs, paralogs, mutants *etc*).

Other preferred orf3516 sequences comprise at least *n* consecutive amino acids from SEQ ID NOs 61-71, wherein *n* is 7 or more (*eg.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). Preferred fragments comprise an epitope or immunogenic fragment from orf3516. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or the N-terminus of SEQ ID NOs 61-71. Exemplary fragments are the conserved fragments SEQ ID NOs identified in the sequence alignment below.

```
Group A: strain E22, E24377A and B7A  (SEQ ID NO: 61)
strain E110019  (SEQ ID NO: 62)
strain H10407  (SEQ ID NO: 63)
strain HS and 53638  (SEQ ID NO: 64)
Group B: strain APEC01, UTI89, RS218 and IHE3034  (SEQ ID NO: 65)
strain F11  (SEQ ID NO: 66)
strain SECEC  (SEQ ID NO: 67)
strain 536  (SEQ ID NO: 68)
strain E2348-69  (SEQ ID NO: 69)
strain 101-1  (SEQ ID NO: 70)
strain O42  (SEQ ID NO: 71)

                                1                                                50
Group A                         MLVAIAIFAS LALMAQQVTN GVTRVNSAVA GHDQKLNLMQ QTMSFLTHDL
strain E110019                  MLVAIAIFAS LALMAQQVTN GVTRVNNAVA GHDQKLNLMQ QTMSFLTHDL
strain H10407                   MLVAIAIFAS LALMAQQVTN GVTRVNSAVA DHDQKLNLMQ QTMSFLTHDL
strain HS and 53638             MLVAIAIFAS LALMAQQVTN GVTRVNSAVA GHDQKLNLMQ QTMSFLTHDL
Group B                         MLVAIAIFAS LALMAQQVTN GVTRVNSAVA GHDQKLNLMQ QTMSFLTHDL
strain F11                      MLVAIAIFAS LALMAQQVTN GVTRVNSAVA GHDQKLNLMQ QTMSFLNHDL
strain SECEC                    MLVAIAIFAS LALMAQQVTN GVTRVNSAVA GHDQKLNLMQ QTMSFLNHDL
strain 536                      MLVAIAIFAS LALMAQQVTN GVTRVNSAVA GHDQKLNLMQ QTMSFLNHDL
strain E2348-69                 MLVAIAIFAS LALMAQQVTN GVTRVNSAVA GHDQKLNLMQ QTMSFLNHDL
strain 101-1                    MLVAIAIFAL LALMAQQVTN GVTRVNSAVA GHDQKLNLMQ QTMSFLTHDL
strain O42                      MLVAIAIFAS LALMAQQVTN GVTRVNSAIG EHDQKLNLMQ QTMSFLTHDL
                 Consensus      MLVAIAIFA- LALMAQQVTN GVTRVN-A-- -HDQKLNLMQ QTMSFL-HDL
                                           SEQ ID NO: 385          SEQ ID NO: 386
B-Cell Ep.                                      ** ****   *** ***

                                51                                               100
Group A                         TQMMPRPVRG DQGQREPALL AGAGVLASES EGMRFVRGGV VNPLMRLPRS
strain E110019                  TQMMPRPVRG EQGQREPALL AGAGVLASES EGMRFVRGGV VNPLMRLPRS
strain H10407                   TQMMPRPVRG DQGQREPALL AGAGVLASES EGMRFVRGGV VNPLMRLPRS
strain HS and 53638             TQMMPRPVRG DQGQREPALL AGAGVLASES EGMRFVRGGV VNPLMRMPRS
Group B                         TQMMPRPVRG DQGQREPALL AGAGVLVSES GGMRFVRGGV VNPLMRLPRS
strain F11                      TQMMPRPVRG DQGQREPALL AGAGVLASES EGMRFVRGGV VNPLMRLPRS
strain SECEC                    TQMMPRPVRG DQGQREPALL AGAGVLASES EGMRFVRGGV VNPLMRLPRS
strain 536                      TQMMPRPVRG DQGQREPALL AGAGVLASES EGMRFVRGGV VNPLMRLPRS
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strain E2348-69          TQMMPRPVRG DQGQREPALL AGAGVLASES EGIRFVRGGV VNPLMRLPRS
strain 101-1             TQMMPRPVRG DQGQREPALL AGAGVLASES GGMRFVRGGV VNLLMRLPRS
strain O42               TQMMPRPVRG DQGQREPALL AGPGVLASES EGMRFVRGGV VNPLMRLPRS
              Consensus  TQMMPRPVRG -QGQREPALL AG-GVL-SES -G-RFVRGGV VN-LMR-PRS
                        SEQ ID NO: 387 SEQ ID NO: 388
B-Cell Ep.                   ****** ********

                         101                                                150
Group A                  NLLTVGYRIH DGYLERLAWP LTDAAGSVKP TMQKLIPADS LRLQFYDGTR
strain E110019           NLLTVGYRIH DGYLERLAWP LTDAAGSVKP TMQKLIPADS LRLQFYDGTR
strain H10407            NLLTVGYRIH DGYLERLAWP LTDAAGSVKP TMQKLIPADS LRLQFYDGTR
strain HS and 53638      NLLTVGYRIH DGYLERLSWP LTDAAGSVKP TMQKLIPADS LHLQFYDGTR
Group B                  NLLTVGYRIH DGYLERLAWP LTDAAGSVKP TTQKLIPADS LRLQFYDGTR
strain F11               NLLTVGYRIH GGYLERLAWP LTDAAGSVKP TTQKLIPADS LRLQFHDGTR
strain SECEC             NLLTVGYRIH GGYLERLAWP LTDAAGSVKP TTQKLIPADS LRLQFHDGTR
strain 536               NLLTVGYRIH GGYLERLAWP LTDAAGSVKP TTQKLIPADS LRLQFYDGTR
strain E2348-69          NLLTVGYRIH GGYLERLAWP LTDAAGSVKP TTQKLIPADS LRLQFHDGTC
strain 101-1             NLLTVGYRIH GGYLERLAWP LTDAAGSVKP TTQKLIPADS LRLQFHDGTR
strain O42               NLLTVGYRIH GGYLERLAWP LTDAADSVKP TTQKLIPADS LRLQFYDGTR
              Consensus  NLLTVGYRIH -GYLERL-WP LTDAAgSVKP T-QKLIPADS L-LQF-DGT-
                        SEQ ID NO: 389       SEQ ID NO: 390-391
B-Cell Ep.                                    ********* *                  **

                         151                                    189
Group A                  WQESWSSVQA IPVAVRMTLH SPQWGEIERI WLLRGPQ~~
strain E110019           WQESWSSVQA IPVAVRMTLH SPQWGEIERI WLLRGPQLS
strain H10407            WQESWSSVQA IPVAVRMTLH SPQWGEIERI WLLRGPQ~~
strain HS and 53638      WQESWSSVQA IPVAVRMTLH SPQWGEIERI WLLRGPQLS
Group B                  WQESWSSVQA IPVAVRITLH SPQWGEIERI WLLRGPQLS
strain F11               WQESWSSVQA IPVAVRITLH SPQWGEIERI WLLRGPQLS
strain SECEC             WQESWSSVQA IPVAVRITLH SPQWGEIERI WLLRGPQLS
strain 536               WQESWSSVQA VPVAVRITLH SPQWGEIERI WLLRGPQLS
strain E2348-69          WQESWSSVQA IPVAVRITLH SPQWGEIERI WLLRGPQLS
strain 101-1             WQESWSSVQA IPVAVRITLH SPQWGEIERI WLLRGPQLS
strain O42               WQESWSSVQA IPVAVRMTLH SPQWGEIERI WLLRGPQLS
              Consensus  WQESWSSVQA -PVAVR-TLH SPQWGEIERI WLLRGPQ~~
                        SEQ ID NO: 393            SEQ ID NO: 394
B-cell Ep.               *******
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SEQ ID NO: 390 WPLTDAA(G/D)SVKPT
SEQ ID NO: 391 WPLTDAAGSVKPT
SEQ ID NO: 392 WPLTDAADSVKPT
B-Cell Epitopes
SEQ ID NO: 395 TNGVTR
SEQ ID NO: 396 AVAGHD
SEQ ID NO: 397 PRPVRGDQGQREPA
SEQ ID NO: 398 TRWQESWSS

Orf3597 protein

tonB-dependent siderophore receptor protein is referred to herein as 'orf3597.' 'orf3597' protein from *E. coli* NMEC is disclosed in reference 5 (SEQ IDs 7193 & 7194) is also known as: 'orf3415' from *E. coli* NMEC strain IHE3034, 'c3775' from CFT073 and ecp_3121 from 536.

When used according to the present invention, orf3597 protein may take various forms. Preferred orf3597 sequences have 50% or more identity (*e.g.* 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98%, 99% or more) to SEQ ID NOs 72-79. This includes variants (*e.g.* allelic variants, homologs, orthologs, paralogs, mutants *etc*).

Other preferred orf3597 sequences comprise at least *n* consecutive amino acids from SEQ ID NOs 72-79, wherein *n* is 7 or more (*eg.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). Preferred fragments comprise an epitope or immunogenic fragment from orf3597. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or the N-terminus of SEQ ID NOs 72-79. Exemplary fragments are the conserved fragments SEQ ID NOs identified in the sequence alignment below.

strain E2348-69 (SEQ ID NO: 72)
strain F11 (SEQ ID NO: 73)
Group A: strain APECO1, UTI89, CFT073, RS218 and IHE3034 (SEQ ID NO: 74)
strain SECEC (SEQ ID NO: 75)
Group B: strain EC508, EC869, EC4024, EC4042, EC4045, EC4076, EC4113, EC4115, EC4196, EC4206, EC4401 and EC4486 (SEQ ID NO: 76)
strain O42 (SEQ ID NO: 77)
Group C: strain Sakai, EDL933, EC4501 and TW14588 (SEQ ID NO: 78)
strain 536 (SEQ ID NO: 79)

```
                                1                                                  50
strain E2348-69                 MAMFTPSFSG LKGRALFSLL FAAPMIHATD SVTTKDGETI TVTADANTAT
strain F11                      MAMFTPSFSG LKGRALFSLL FAAPMIHATD SVTTKDGETI TVTADANTAT
Group A                         MAMFTPSFSG LKGRALFSLL FAAPMIHATD SVTTKDGETI TVTADANTAT
strain SECEC                    MAMFTPSFSG LKGRALFSLL FAAPMIHATD SVTTKDGETI TVTADANTAT
Group B                         MAKFTPSFSG IKGRALFSLL FAAPMIHATD TATTKDGETI TVTADANTAT
strain O42                      MAKFTPSFSG IKGRALFSLL FAAPMIHATD TATTKDGETI TVTADANTAT
Group C                         MAKFTPSFSG IKGRALFSLL FAAPMIHATD TATTKDGETI TVTADANTAT
strain 536                      MAKFTPSFSG IKGRALFSLL FAAPMIHATD TATTKDGETI TVTADANTAT
                    Consensus   MA-FTPSFSG -KGRALFSLL FAAPMIHATD --TTKDGETI TVTADANTAT
                                           SEQ ID NO: 399          SEQ ID NO: 400
B-Cell Ep.                                                 ********** **********

                                51                                                 100
strain E2348-69                 EATDGYQPLS TSTATLTDMP MLDIPQVVNT VSDQVLENQN ATTLDEALYN
strain F11                      EATDGYQPLS TSTATLTDMP MLDIPQVVNT VSDQVLENQN ATTLDEALYN
Group A                         EATDGYQPLS TSTATLTDMP MLDIPQVVNT VSDQVLENQN ATTLDEALYN
strain SECEC                    EATDGYQPLS TSTATLTDMP MLDIPQVVNT VSDQVLENQN ATTLDEALYN
Group B                         EATDGYQPLS TSTATLTDMP MLDIPQVVNT VSDQVLENQN ATTLDEALYN
strain O42                      EATDGYQPLS TSTATLTDMP MLDIPQVVNT VSDQVLENQN ATTLDEALYN
Group C                         EATDGYQPLS TSTATLTDMP MLDIPQVVNT VSDQVLENQN ATTLDEALYN
strain 536                      EATDGYQPLS TSTATLTDMP MLDIPQVVNT VSDQVLENQN ATTLDEALYN
                    Consensus   EATDGYQPLS TSTATLTDMP MLDIPQVVNT VSDQVLENQN ATTLDEALYN
B-Cell Ep.                      ********** ******                 ****** ****

                                101                                                150
strain E2348-69                 VSNVVQTNTL GGTQDAFVRR GFGANRDGSI MTNGLRTVLP RSFNAATERV
strain F11                      VSNVVQTNTL GGTQDAFVRR GFGANRDGSI MTNGLRTVLP RSFNAATERV
Group A                         VSNVVQTNTL GGTQDAFVRR GFGANRDGSI MTNGLRTVLP RSFNAATERV
strain SECEC                    VSNVVQTNTL GGTQDAFVRR GFGANRDGSI MTNGLRTVLP RSFNAATERV
Group B                         VSNVVQTNTL GGTQDAFVRR GFGANRDGSI MTNGLRTVLP RSFNAATERV
strain O42                      VSNVVQTNTL GGTQDAFVRR GFGANRDGSI MTNGLRTVLP RSFNAATERV
Group C                         VSNVVQTNTL GGTQDAFVRR GFGANRDGSI MTNGLRTVLP RSFNAATERV
strain 536                      VSNVVQTNTL GGTQDAFVRR GFGANRDGSI MTNGLRTVLP RSFNAATERV
                    Consensus   VSNVVQTNTL GGTQDAFVRR GFGANRDGSI MTNGLRTVLP RSFNAATERV
B-Cell Ep.                         *** ******       ********

                                151                                                200
strain E2348-69                 EVLKGPASTL YGILDPGGLI NVVTKRPEKT FHGSVSATSS SFGGGTGQLD
strain F11                      EVLKGPASTL YGILDPGGLI NVVTKRPEKT FHGSVSATSS SFGGGTGQLD
Group A                         EVLKGPASTL YGILDPGGLI NVVTKRPEKT FHGSVSATSS SFGGGTGQLD
strain SECEC                    EVLKGPASTL YGILDPGGLI NVVTKRPEKT FHGSVSATSS SFGGGTGQLD
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Group B                 EVLKGPASTL YGILDPGGLI NVVTKRPEKT FHGSVSATSS SFGGGTGQLD
strain O42              EVLKGPASTL YGILDPGGLI NVVTKRPEKT FHGSVSATSS SFGGGTGQLD
Group C                 EVLKGPASTL YGILDPGGLI NVVTKRPEKT FHGSVSATSS SFGGGTGQLD
strain 536              EVLKGPASTL YGILDPGGLI NVVTKRPEKT FHGSVSATSS SFGGGTGQLD
            Consensus   EVLKGPASTL YGILDPGGLI NVVTKRPEKT FHGSVSATSS SFGGGTGQLD
B-Cell Ep.                                    ****** ********** **********

                        201                                               250
strain E2348-69         ITGPIEGTQL AYRLTGEVQD EDYWRNFGKE RSTFIAPSLT WFGDNATVTM
strain F11              ITGPIEGTQL AYRLTGEVQD EDYWRNFGKE RSTFIAPSLT WFGDNATVTM
Group A                 ITGPIEGTQL AYRLTGEVQD EDYWRNFGKE RSTFIAPSLT WFGDNATVTM
strain SECEC            ITGPIEGTQL AYRLTGEVQD EDYWRNFGKE RSTFIAPSLT WFGDNATVTM
Group B                 ITGPIEGTQL AYRLTGEVQD EDYWRNFGKE RSTFIAPSLT WFGDNATVTM
strain O42              ITGPIEGTQL AYRLTGEVQD EDYWRNFGKE RSTFIAPSLT WFGDNATVTM
Group C                 ITGPIEGTQL AYRLTGEVQD EDYWRNFGKE RSTFIAPSLT WFGDNATVTM
strain 536              ITGPIEGTQL AYRLTGEVQD EDYWRNFGKE RSTFIAPSLT WFGDNATVTM
            Consensus   ITGPIEGTQL AYRLTGEVQD EDYWRNFGKE RSTFIAPSLT WFGDNATVTM
B-Cell Ep.              *******         *****  ******

                        251                                               300
strain E2348-69         LYSHRDYKTP FDRGTIFDLT TKQPVNVDRK IRFDEPFNIT DGQSDLAQLN
strain F11              LYSHRDYKTP FDRGTIFDLT TKQPVNVDRK IRFDEPFNIT DGQSDLAQLN
Group A                 LYSHRDYKTP FDRGTIFDLT TKQPVNVDRK IRFDEPFNIT DGQSDLAQLN
strain SECEC            LYSHRDYKTP FDRGTIFDLT TKQPVNVDRK IRFDEPFNIT DGKSDLAQLN
Group B                 LYSHRDYKTP FDRGTIFDLT TKQPVNVDRK IRFDEPFNIT DGQSDLAQLN
strain O42              LYSHRDYKTP FDRGTIFDLT TKQPVNVDRK IRFDEPFNIT DGQSDLAQLN
Group C                 LYSHRDYKTP FDRGTIFDLT TKQPVNVDRK IRFDEPFNIT DGQSDLAQLN
strain 536              LYSHRDYKTP FDRGTIFDLT TKQPVNVDRK IRFDEPFNIT DGQSDLAQLN
            Consensus   LYSHRDYKTP FDRGTIFDLT TKQPVNVDRK IRFDEPFNIT DG-SDLAQLN
B-Cell Ep.                ***** **          ******          **** ******

                        301                                               350
strain E2348-69         AEYHLNSQWT ARFDYSYSQD KYSDNQARVT AYDATTGTLT RRVDATQGST
strain F11              AEYHLNSQWT ARFDYSYSQD KYSDNQARVT AYDATTGTLT RRVDATQGST
Group A                 AEYHLNSQWT ARFDYSYSQD KYSDNQARVT AYDATTGTLT RRVDATQGST
strain SECEC            AEYHLNSQWT ARFDYSYSQD KYSDNQARVT AYDATTGTLT RRVDATQGST
Group B                 AEYHLNSQWT ARFDYSYSQD KYSDNQARVT AYDATTGTLT RRVDATQGST
strain O42              AEYHLNSQWT ARFDYSYSQD KYSDNQARVT AYDATTGTLT RRVDATQGST
Group C                 AEYHLNSQWT ARFDYSYSQD KYSDNQARVT AYDATTGTLT RRVDATQGST
strain 536              AEYHLNSQWT ARFDYSYSQD KYSDNQARVT AYDATTGTLT RRVDATQGST
            Consensus   AEYHLNSQWT ARFDYSYSQD KYSDNQARVT AYDATTGTLT RRVDATQGST
                              SEQ ID NO: 401
B-Cell Ep.                      ***** ********** **********   ********

                        351                                               400
strain E2348-69         QRMHATRADL QGNVDIAGFY NEILGGVSYE YYDLLRTDMI RCKKAKDFNI
strain F11              QRMHATRADL QGNVDIAGFY NEILGGVSYE YYDLLRTDMI RCKKAKDFNI
Group A                 QRMHATRADL QGNVDIAGFY NEILGGVSYE YYDLLRTDMI RCKKAKDFNI
strain SECEC            QRMHATRADL QGNVDIAGFY NEILGGVSYE YYDLLRTDMI RCKKAKDFNI
Group B                 QRMHSTRADL QGNVDIAGFY NEILGGVSYE YYDLLRTDMI RCKNAKDFNI
strain O42              QRMHSTRADL QGNVDIAGFY NEILGGVSYE YYDLLRTDMI RCKNAKDFNI
Group C                 QRMHSTRADL QGNVDIAGFY NEILGGVSYE YYDLLRTDMI RCKNAKDFNI
strain 536              QRMHATRADL QGNVDIAGFY NEILGGVSYE YYDLLRTDMI RCKKAKDFNI
            Consensus   QRMH-TRADL QGNVDIAGFY NEILGGVSYE YYDLLRTDMI RCK-AKDFNI
                              SEQ ID NO: 402
B-Cell Ep.              ***

                        401                                               450
strain E2348-69         YNPVYGNTSK CTTVSASDSD QTIKQESYSA YAQDALYLTD NWIAVAGIRY
strain F11              YNPVYGNTSK CTTVSASDSD QTIKQESYSA YAQDALYLTD NWIAVAGIRY
Group A                 YNPVYGNTSK CTTVSASDSD QTIKQENYSA YAQDALYLTD NWIAVAGIRY
strain SECEC            YNPVYGNTSK CTTVSASDSD QTIKQESYSA YAQDALYLTD NWIAVAGIRY
Group B                 YNPVYGNTSK CTTVSASDSD QTIKQESYSA YAQDALYLTD NWIAVAGIRY
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strain O42              YNPVYGNTSK CTTVSASDSD QTIKQESYSA YAQDALYLTD NWIAVAGIRY
Group C                 YNPVYGNTSK CTTVSASDSD QTIKQESYSA YAQDALYLTD NWIAVAGIRY
strain 536              YNPVYGNTSK CTTVSASDSD QTIKQESYSA YAQDALYLTD NWIAVAGIRY
                Consensus YNPVYGNTSK CTTVSASDSD QTIKQE-YSA YAQDALYLTD NWIAVAGIRY
                              SEQ ID NO: 403              SEQ ID NO: 404
B-Cell Ep.                  ******** ********** ********** *

                        451                                             500
strain E2348-69         QYYTQYAGKG RPFNVNTDSR DEQWTPKLGL VYKLTPSVSL FANYSQTFMP
strain F11              QYYTQYAGKG RPFNVNTDSR DEQWTPKLGL VYKLTPSVSL FANYSQTFMP
Group A                 QYYTQYAGKG RPFNVNTDSR DEQWTPKLGL VYKLTPSVSL FANYSQTFMP
strain SECEC            QYYTQYAGKG RPFNVNTDSR DEQWTPKLGL VYKLTPSVSL FANYSQTFMP
Group B                 QYYTQYAGKG RPFNVNTDSR DEQWTPKLGL VYKLTPSVSL FANYSQTFMP
strain O42              QYYTQYAGKG RPFNVNTDSR DEQWTPKLGL VYKLTPSVSL FANYSQTFMP
Group C                 QYYTQYAGKG RPFNVNTDSR DEQWTPKLGL VYKLTPSVSL FANYSQTFMP
strain 536              QYYTQYAGKG RPFNVNTDSR DEQWTPKLGL VYKLTPSVSL FANYSQTFMP
                Consensus QYYTQYAGKG RPFNVNTDSR DEQWTPKLGL VYKLTPSVSL FANYSQTFMP
B-Cell Ep.                  ****** ********** *****

                        501                                             550
strain E2348-69         QSSIASYIGD LPPESSNAYE VGAKFELFDG ITADIALFDI HKRNVLYTES
strain F11              QSSIASYIGD LPPESSNAYE VGAKFELFDG ITADIALFDI HKRNVLYTES
Group A                 QSSIASYIGD LPPESSNAYE VGAKFELFDG ITADIALFDI HKRNVLYTES
strain SECEC            QSSIASYIGD LPPESSNAYE VGAKFELFDG ITADIALFDI HKRNVLYTES
Group B                 QSSIASYIGD LPPESSNAYE VGAKFELFDG ITADIALFDI HKRNVLYTES
strain O42              QSSIASYIGD LPPESSNAYE VGAKFELFDG ITADIALFDI HKRNVLYTES
Group C                 QSSIASYIGD LPPESSNAYE VGAKFELFDG ITADIALFDI HKRNVLYTES
strain 536              QSSIASYIGD LPPESSNAYE VGAKFELFDG ITADIALFDI HKRNVLYTES
                Consensus QSSIASYIGD LPPESSNAYE VGAKFELFDG ITADIALFDI HKRNVLYTES
B-Cell Ep.                    ** **********                                  *

                        551                                             600
strain E2348-69         VGDETIAKTA GRVRSRGVEV DLAGALTENI NIIASYGYTD AKVLEDPDYA
strain F11              VGDETIAKTA GRVRSRGVEV DLAGALTENI NIIASYGYTD AKVLEDPDYA
Group A                 IGDETIAKTA GRVRSRGVEV DLAGALTENI NIIASYGYTD AKVLEDPDYA
strain SECEC            VGDETIAKTA GRVRSRGVEV DLAGALTENI NIIASYGYTD AKVLEDPDYA
Group B                 IGDETIAKTA GRVRSRGVEV DLAGALTENI NIIASYGYTD AKVLEDPDYA
strain O42              IGDETIAKTA GRVRSRGVEV DLAGALTENI NIIASYGYTD AKVLEDPDYA
Group C                 IGDETIAKTA GRVRSRGVEV DLAGALTENI NIIASYGYTD AKVLEDPDYA
strain 536              VGDETIAKTA GRVRSRGVEV DLAGALTENI NIIASYGYTD AKVLEDPDYA
                Consensus -GDETIAKTA GRVRSRGVEV DLAGALTENI NIIASYGYTD AKVLEDPDYA
                                  SEQ ID NO: 405
B-Cell Ep.                  *********                                  **********

                        601                                             650
strain E2348-69         GKPLPNVPRH TGSLFLTYDI HNMPGNNTLT FGGGGHGVSR RSATNGADYY
strain F11              GKPLPNIPRH TGSLFLTYDI HNMPGNNTLT FGGGGHGVSR RSATNGADYY
Group A                 GKPLPNVPRH TGSLFLTYDI HNMPGNNTLT FGGGGHGVSR RSATNGADYY
strain SECEC            GKPLPNVPRH TGSLFLTYDI HNMPGNNTLT FGGGGHGVSR RSATNGADYY
Group B                 GKPLPNVPRH TGSLFLTYDI HNMPGNNTLT FGGGGHGVSR RSATNGADYY
strain O42              GKPLPNVPRH TGSLFLTYDI HNMPGNNTLT FGGGGHGVSR RSATNGADYY
Group C                 GKPLPNVPRH TGSLFLTYDI HNMPGNNTLT FGGGGHCVSR RSATNGADYY
strain 536              GKPLPNVPRH TGSLFLTYDI HNMPGNNTLT FGGGGHGVSR RSATNGADYY
                Consensus GKPLPN-PRH TGSLFLTYDI HNMPGNNTLT FGGGGH-VSR RSATNGADYY
                                  SEQ ID NO: 406          SEQ ID NO: 407
B-Cell Ep.                  **********          ********* ********** **********

                        651                                             700
strain E2348-69         LPGYFVADAF AAYKMKLQYP VTLQLNVKNL FDKTYYTSSI ATNNLGNQIG
strain F11              LPGYFVADAF AAYKMKLQYP VTLQLNVKNL FDKTYYTSSI ATNNLGNQIG
Group A                 LPGYFVADAF AAYKMKLQYP VTLQLNVKNL FDKTYYTSSI ATNNLGNQIG
strain SECEC            LPGYFVADAF AAYKMKLQYP VTLQLNVKNL FDKTYYTSSI ATNNLGNQIG
Group B                 LPGYFVADAF AAYKMKLQYP VTLQLNVKNL FDKTYYTSSI ATNNLGNQIG
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strain O42              LPGYFVADAF AAYKMKLQYP VTLQLNVKNL FDKTYYTSSI ATNNLGNQIG
Group C                 LPGYFVADAF AAYKMKLQYP VTLQLNVKNL FDKTYYTSSI ATNNLGNQIG
strain 536              LPGYFVADAF AAYKMKLQYP VTLQLNVKNL FDKTYYTSSI ATNNLGNQIG
              Consensus LPGYFVADAF AAYKMKLQYP VTLQLNVKNL FDKTYYTSSI ATNNLGNQIG
B-Cell Ep.                                                        * **********

                                  701        713
strain E2348-69                   DPREVQFTVK MEF
strain F11                        DPREVQFTVK MEF
Group A                           DPREVQFTVK MEF
strain SECEC                      DPREVQFTVK MEF
Group B                           DPREVQFTVK MEF
strain O42                        DPREVQFTVK MEF
Group C                           DPREVQFTVK MEF
strain 536                        DPREVQFTVK MEF
              Consensus           DPREVQFTVK MEF
B-Cell Ep.                        *****
```

B-Cell Epitopes

SEQ ID NO: 408 SVTTKDGETITVTADANTATEATDGYQPLSTSTATL
SEQ ID NO: 409 VLENQNATTL
SEQ ID NO: 410 NTLGGTQDA
SEQ ID NO: 411 GANRDGSI
SEQ ID NO: 412 KRPEKTFHGSVSATSSSFGGGTGQLDITGPIEG
SEQ ID NO: 413 GEVQDEDYWRN
SEQ ID NO: 414 DYKTPFD
SEQ ID NO: 415 KQPVNV
SEQ ID NO: 416 FNITDGQSDL
SEQ ID NO: 417 SYSQDKYSDNQARVTAYDATTGTLT
SEQ ID NO: 418 VDATQGSTQRM
SEQ ID NO: 419 PVYGNTSKCTTVSASDSDQTIKQESYSAY
SEQ ID NO: 420 QYAGKGRPFNVNTDSRDEQWT
SEQ ID NO: 421 GDLPPESSNAYE
SEQ ID NO: 422 SVGDETIAKT
SEQ ID NO: 423 AKVLEDPDYAGKPLPNVPRH
SEQ ID NO: 424 NMPGNNTLTFGGGGHGVSRRSATNGADYY
SEQ ID NO: 425 IATNNLGNQIGDPREV

Orf3613 protein

Fimbrial protein is referred to herein as 'orf3613.' 'orf3613' protein from *E. coli* NMEC is disclosed in reference 5 (SEQ IDs 7225 & 7226) is also known as: 'orf3431' from *E. coli* NMEC strain IHE3034 and 'c3791' from CFT073.

When used according to the present invention, orf3613 protein may take various forms. Preferred orf3613 sequences have 50% or more identity (*e.g.* 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98%, 99% or more) to SEQ ID NOs 80-81. This includes variants (*e.g.* allelic variants, homologs, orthologs, paralogs, mutants *etc*).

Other preferred orf3613 sequences comprise at least *n* consecutive amino acids from SEQ ID NOs 80-81, wherein *n* is 7 or more (*eg.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). Preferred fragments comprise an epitope or immunogenic fragment from orf3613. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15,

20, 25 or more) from the C-terminus and/or the N-terminus of SEQ ID NOs 80-81. Exemplary fragments are the conserved fragments SEQ ID NOs identified in the sequence alignment below.

```
Group A: strain UTI89, CFT073, APECO1, RS218 and IHE3034  (SEQ ID NO: 80)
Strain O42  (SEQ ID NO: 81)

                          1                                                50
Group A                   MLKKTLLSMF ATALLSGVAF NALADDANQG SGKITFKGEV IDAPCSIAPG
strain O42                MFKKTLLSMF ATALLSGVAF NALADDANQG SGKITFKGEV IDAPCSIAPG
               Consensus  M-KKTLLSMF ATALLSGVAF NALADDANQG SGKITFKGEV IDAPCSIAPG
                                        SEQ ID NO: 426
B-Cell Ep.                                 ******* *****          ******

                          51                                              100
Group A                   DEDQTINLGE VADTVLKSGQ KSLPVDVTIH LQDCILSDGT NTVDKVKITF
strain O42                DEDQTINLGE VADTVLKSGQ KSLPVDVTIH LQDCILSDGT NTVDKVKITF
               Consensus  DEDQTINLGE VADTVLKSGQ KSLPVDVTIH LQDCILSDGT NTVDKVKITF
B-Cell Ep.                *******

                          101                                             150
Group A                   SSASVDATDS NLLKNTLEGN IGGATDVGVR LVKSDNTNVT LGTPITINFP
strain O42                SSASVDATDS NLLKNTLEGN IGGATDVGVR LVKSDNTNVT LGTPITINFP
               Consensus  SSASVDATDS NLLKNTLEGN IGGATDVGVR LVKSDNTNVT LGTPITINFP
B-Cell Ep.                  ********        *** ******                    ***

                          151                                 187
Group A                   TTNSYQELNF KARMESLGRT ATPGNVQAQA NYVLDYK
strain O42                TTNSYQELNF KARMESLGRT ATPGNVQAQA NYVLDYK
               Consensus  TTNSYQELNF KARMESLGRT ATPGNVQAQA NYVLDYK
B-Cell Ep.                *****           **** *********

B-Cell Epitopes
SEQ ID NO: 427  ADDANQGSGKIT
SEQ ID NO: 428  CSIAPGDEDQTIN
SEQ ID NO: 429  ASVDATDS
SEQ ID NO: 430  EGNIGGATD
SEQ ID NO: 431  NFPTTNSY
SEQ ID NO: 432  LGRTATPGNVQAQ
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Recp3768 protein

Hemolysin A protein is referred to herein as 'recp3768.' 'recp3768' protein from *E. coli* UPEC is disclosed in reference WO2008/020330 (SEQ IDs 3) is also known as: 'c3570' from CFT073 and ecp_3827 from 536.

When used according to the present invention, recp3768 protein may take various forms. Preferred recp3768 sequences have 50% or more identity (*e.g.* 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98%, 99% or more) to SEQ ID NOs 101-105. This includes variants (*e.g.* allelic variants, homologs, orthologs, paralogs, mutants *etc*).

Other preferred recp3768 sequences comprise at least *n* consecutive amino acids from SEQ ID NOs 101-105, wherein *n* is 7 or more (*eg.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). Preferred fragments comprise an epitope or immunogenic fragment from recp3768. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10,

15, 20, 25 or more) from the C-terminus and/or the N-terminus of SEQ ID NOs 101-105. Exemplary fragments are the conserved fragments SEQ ID NOs identified in the sequence alignment below.

```
Strain 536  (SEQ ID NO: 101)
Strain 536  (SEQ ID NO: 102)
Strain CFT073  (SEQ ID NO: 103)
Group A: strain RS218, UTI89 and F11  (SEQ ID NO: 104)
Strain E110019  (SEQ ID NO: 105)
                                1                                                50
strain 536                      MPTITTAQIK STLQSAKQSA ANKLHSAGQS TKDALKKAAE QTRNAGNRLI
strain 536                      MPTITTAQIK STLQSAKQSA ANKLHSAGQS TKDALKKAAE QTRNAGNRLI
strain CFT073                   MPTITTAQIK STLQSAKQSS ANKLHSAGQS TKDALKKAAE QTRNAGNRLI
Group A                         MPTITTAQIK STLQSAKQSA ANKLHSAGQS TKDALKKAAE QTRNAGNRLI
strain E110019                  MPTITTAQIK STLQSAKQSA ENKLHSAGQS TKDALKKAAE KTRNAGNRLI
                      Consensus MPTITTAQIK STLQSAKQS- -NKLHSAGQS TKDALKKAAE -TRNAGNRLI
                                     SEQ ID NO: 433          SEQ ID NO: 434
B-Cell Ep.                           ******* ********** ********** *****

                                51                                               100
strain 536                      LLIPKDYKGQ GSSLNDLVRT ADELGIEVQY DEKNGTAITK QVFGTAEKLI
strain 536                      LLIPKDYKGQ GSSLNDLVRT ADELGIEVQY DEKNGTAITK QVFGTAEKLI
strain CFT073                   LLIPKDYKGQ GSSLNDLVRT ADELGIEVQY DEKNGTAITK QVFGTAEKLI
Group A                         LLIPKDYKGQ GSSLNDLVRT ADELGIEVQY DEKNGTAITK QVFGTAEKLI
strain E110019                  LLIPKDYKGQ GSSLNDLVRT ADELGIEVQY DEKNGTAITK QVFGTAEKLI
                      Consensus LLIPKDYKGQ GSSLNDLVRT ADELGIEVQY DEKNGTAITK QVFGTAEKLI
                                          SEQ ID NO: 435
B-Cell Ep.                       ***** ***                ** ********

                                101                                              150
strain 536                      GLTERGVTIF APQLDKLLQK YQKAGNKLGG SAENIGDNLG KAGSVLSTFQ
strain 536                      GLTERGVTIF APQLDKLLQK YQKAGNKLGG SAENIGDNLG KAGSVLSTFQ
strain CFT073                   GLTERGVTIF APQLDKLLQK YQKAGNKLGG SAENIGDNLG KAGSVLSTFQ
Group A                         GLTERGVTIF APQLDKLLQK YQKAGNKLGG SAENIGDNLG KAGSVLSTFQ
strain E110019                  GLTERGVTIF APKLDKLLQK YQKAGNKLGG SAENIGDNLG KAGGILSTFQ
                      Consensus GLTERGVTIF AP-LDKLLQK YQKAGNKLGG SAENIGDNLG KAG--LSTFQ
                                                    SEQ ID NO: 436
B-Cell Ep.                                          ********* ********** *

                                151                                              200
strain 536                      NFLGTALSSM KIDELIKKQK SGSNVSSSEL AKASIELINQ LVDTAASINN
strain 536                      NFLGTALSSM KIDELIKKQK SGGNVSSSEL AKASIELINQ LVDTAASLNN
strain CFT073                   NFLGTALSSM KIDELIKRQK SGSNVSSSEL AKASIELINQ LVDTAASINN
Group A                         NFLGTALSSM KIDELIKKQK SGSNVSSSEL AKASIELINQ LVDTAASINN
strain E110019                  NFLGTALSSM KIDELIKKQK SGGNVSSSEM AEASIELINQ LVDTAASLNN
                      Consensus NFLGTALSSM KIDELIK-QK SG-NVSSSE- A-ASIELINQ LVDTAAS-NN
                                  SEQ ID NO: 437                   SEQ ID NO: 438
B-Cell Ep.                              ***** **********

                                201                                              250
strain 536                      NVNSFSQQLN KLGSVLSNTK HLNGVGNKLQ NLPNLDNIGA GLDTVSGILS
strain 536                      NVNSFSQQLN KLGSVLSNTK HLNGVGNKLQ NLPNLDNIGA GLDTVSGILS
strain CFT073                   NVNSFSQQLN KLGSVLSNTK HLTGVGNKLQ NLPNLDNIGA GLDTVSGILS
Group A                         NVNSFSQQLN KLGSVLSNTK HLNGVGNKLQ NLPNLDNIGA GLDTVSGILS
strain E110019                  NVNSFSQQLN TLGSVLSNTK HLNGVGNKLQ NLPNLDNIGA GLDTVSGILS
                      Consensus NVNSFSQQLN -LGSVLSNTK HL-GVGNKLQ NLPNLDNIGA GLDTVSGILS
                               SEQ ID NO: 439 SEQ ID NO: 440     SEQ ID NO: 441

                                251                                              300
strain 536                      VISASFILSN ADADTGTKAA AGVELTTKVL GNVGKGISQY IIAQRAAQGL
strain 536                      AISASFILSN ADADTGTKAA AGVELTTKVL GNVGKGISQY IIAQRAAQGL
strain CFT073                   AISASFILSN ADADTGTKAA AGVELTTKVL GNVGKGISQY IIAQRAAQGL
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Group A                 AISASFILSN ADADTGTKAA AGVELTTKVL GNVGKGISQY IIAQRAAQGL
strain E110019          TISASFILSN ADADTRTKAA AGVELTTKVL GNVGKGISQY IIAQRAAQGL
                Consensus -ISASFILSN ADADT-TKAA AGVELTTKVL GNVGKGISQY IIAQRAAQGL
                           SEQ ID NO: 442        SEQ ID NO: 443
B-Cell Ep.                        ********** **                          ****

                          301                                             350
strain 536              STSAAAAGLI ASAVTLAISP LSFLSIADKF KRANKIEEYS QRFKKLGYDG
strain 536              STSAAAAGLI ASVVTLAISP LSFLSIADKF KRANKIEEYS QRFKKLGYDG
strain CFT073           STSAAAAGLI ASVVTLAISP LSFLSIADKF KRANKIEEYS QRFKKLGYDG
Group A                 STSAAAAGLI ASVVTLAISP LSFLSIADKF KRANKIEEYS QRFKKLGYDG
strain E110019          STSAAAAGLI ASAVILAISP LSFLSIADKF KRANKIEEYS QRFKKLGYDG
                Consensus STSAAAAGLI AS-V-LAISP LSFLSIADKF KRANKIEEYS QRFKKLGYDG
                                              SEQ ID NO: 444
B-Cell Ep.              *****

                          351                                             400
strain 536              DSLLAAFHKE TGAIDASLTT ISTVLASVSS GISAAATTSL VGAPVSALVG
strain 536              DSLLAAFHKE TGAIDASLTT ISTVLASVSS GISAAATTSL VGAPVSALVG
strain CFT073           DSLLAAFHKE TGAIDASLTT ISTVLASVSS GISAAATTSL VGAPVSALVG
Group A                 DSLLAAFHKE TGAIDASLTT ISTVLASVSS GISAAATTSL VGAPVSALVG
strain E110019          DSLLAAFHKA TGAIDASLTT ISTVLASVSS GISAAATTSL VGAPVSALVG
                Consensus DSLLAAFHK- TGAIDASLTT ISTVLASVSS GISAAATTSL VGAPVSALVG
                                    SEQ ID NO: 445
B-Cell Ep.                                      * *****

                          401                                             450
strain 536              AVTGIISGIL EASKQAMFEH VASKMADVIA EWEKKHGKNY FENGYDARHA
strain 536              AVTGIISGIL EASKQAMFEH VASKMADVIA EWEKKHGKNY FENGYDARHA
strain CFT073           AVTGIISGIL EASKQAMFEH VASKMADVIA EWEKKHGKNY FENGYDARHA
Group A                 AVTGIISGIL EASKQAMFEH VASKMADVIA EWEKKHGKNY FENGYDARHA
strain E110019          AVTGIISGIL EASKQAMFEH VASKMADVIA EWEKKHGKNY FENGYDARHA
                Consensus AVTGIISGIL EASKQAMFEH VASKMADVIA EWEKKHGKNY FENGYDARHA
B-Cell Ep.                                              ******** *******

                          451                                             500
strain 536              AFLEDNFKIL SQYNKEYSVE RSVLITQQHW DTLIGELAGV TRNGDKTLSG
strain 536              AFLEDNFEIL SQYNKEYSVE RSVLITQQHW DTLIGELAGV TRNGDKTLSG
strain CFT073           AFLEDNFKIL SQYNKEYSVE RSVLITQQHW DTLIGELAGV TRNGDKTLSG
Group A                 AFLEDNFKIL SQYNKEYSVE RSVLITQQHW DMLIGELASV TRNGDKTLSG
strain E110019          AFLEDNFKIL SQYNKKYSVE RSVLITQQHW DTLIGELAGV TRNGDKTLSG
                Consensus AFLEDNF-IL SQYNK-YSVE RSVLITQQHW D-LIGELA-V TRNGDKTLSG
                                    SEQ ID NO: 446          SEQ ID NO: 447
B-Cell Ep.                                                  ** *********

                          501                                             550
strain 536              KSYIDYYEEG KRLEKKPDEF QKQVFDPLKG NIDLSDSKSS TLLKFVTPLL
strain 536              KSYIDYYEEG KRLEKEPDEF QKQVFDPLKG NIDLSVIKSS TLLKFITPLL
strain CFT073           KSYIDYYEEG KRLEKKPDEF QKQVFDPLKG NIDLSDSKSS TLLKFVTPLL
Group A                 KSYIDYYEEG KRLERRPKEF QQQIFDPLKG NIDLSDSKSS TLLKFVTPLL
strain E110019          KSYIDYYEEG KRLEKKTDEF QKQVFDPLKG NIDLSDSKSS TLLKFVTPLL
                Consensus KSYIDYYEEG KRLE----EF Q-Q-FDPLKG NIDLS--KSS TLLKF-TPLL
                                              SEQ ID NO: 448
B-Cell Ep.                 ****** ********** **          ********          *

                          551                                             600
strain 536              TPGEEIRERR QSGKYEYITE LLVKGVDKWT VKGVQDKGSV YDYSNLIQHA
strain 536              TPGKEIRERR QSGKYEYITE LLVKGVDKWT VKGVQDKGSV YDYSNLIQHA
strain CFT073           TPGEEIRERR QSGKYEYITE LLVKGVDKWT VKGVQDKGSV YDYSNLIQHA
Group A                 TPGEEIRERR QSGKYEYITE LLVKGVDKWT VKGVQDKGSV YDYSNLIQHA
strain E110019          TPGEEIRERR QSGKYEYITE LLVKGVDKWT VKGVQDKGAV YDYSNLIQHA
                Consensus TPG-EIRERR QSGKYEYITE LLVKGVDKWT VKGVQDKG-V YDYSNLIQHA
                                    SEQ ID NO: 449                  SEQ ID NO: 450
B-Cell Ep.                 ********** *****                ********** *
```

```
                                601                                                 650
strain 536                      SVGNNQYREI RIESHLGDGD DKVFLAAGSA NIYAGKGHDV VYYDKTDTGY
strain 536                      SVGNNQYREI RIESHLGDGD DKVFLSAGSA NIYAGKGHDV VYYDKTDTGY
strain CFT073                   SVGNNQYREI RIESHLGDGD DKVFLSAGSA NIYAGKGHDV VYYDKTDTGY
Group A                         SVGNNQYREI RIESHLGDGD DKVFLSAGSA NIYAGKGHDV VYYDKTDTGY
strain E110019                  SVGNNQYRGI RIESHLGDGD DKVFLSAGSA NIYAGKGHDV VYYDKTDTGY
                    Consensus   SVGNNQYR-I RIESHLGDGD DKVFL-AGSA NIYAGKGHDV VYYDKTDTGY
                                           SEQ ID NO: 451          SEQ ID NO: 452
B-Cell Ep.                      *******       ****** *                    ********

                                651                                                 700
strain 536                      LTIDGTKATE AGNYTVTRVL GGDVKVLQEV VKEQEVSVGK RTEKTQYRSY
strain 536                      LTIDGTKATE AGNYTVTRVL GGDVKVLQEV VKEQEVSVGK RTEKTQYRSY
strain CFT073                   LTIDGTKATE AGNYTVTRVL GGDVKILQEV VKEQEVSVGK RTEKTQYRSY
Group A                         LTIDGTKATE AGNYTVTRVL GGDVKVLQEV VKEQEVSVGK RTEKTQYRSY
strain E110019                  LTIDGTKATE AGNYTVTRVL GGDVKVLQEV AKEQEVSVGK RTEKTQYRSY
                    Consensus   LTIDGTKATE AGNYTVTRVL GGDVK-LQEV -KEQEVSVGK RTEKTQYRSY
                                                                   SEQ ID NO: 453
B-Cell Ep.                      *   ****** ****                    ****** *******

                                701                                                 750
strain 536                      EFTHINGTDL TETDNLYSVE ELIGTNRADK FFGSKFTDIF HGADGDDHIE
strain 536                      EFTHINGTDL TETDNLYSVE ELIGTNRADK FFGSKFTDIF HGADGDDHIE
strain CFT073                   EFTHINGKNL TETDNLYSVE ELIGTTRADK FFGSKFTDIF HGADGDDHIE
Group A                         EFTHINGKNL TETDNLYSVE ELIGTTRADK FFGSKFTDIF HGADGDDHIE
strain E110019                  EFTHINGKNL TETDNLYSVE ELIGTTRADK FFGSKFTDIF HGADGDDLIE
                    Consensus   EFTHING--L TETDNLYSVE ELIGT-RADK FFGSKFTDIF HGADGDD-IE
                                           SEQ ID NO: 454          SEQ ID NO: 455
B-Cell Ep.                           **** ***                                **********

                                751                                                 800
strain 536                      GNDGNDRLYG DKGNDTLRGG NGDDQLYGGD GNDKLTGGVG NNYLNGGDGD
strain 536                      GNDGNDRLYG DKGNDTLRGG NGDDQLYGGD GNDKLTGGVG NNYLNGGDGD
strain CFT073                   GNDGNDRLYG DKGNDTLRGG NGDDQLYGGD GNDKLIGGTG NNYLNGGDGD
Group A                         GNDGNDRLYG DKGNDTLRGG NGDDQLYGGD GNDKLIGGTG NNYLNGGDGD
strain E110019                  GNDGNDRLYG DKGNDTLSGG NGDDQLYGGD GNDKLIGGAG NNYLNGGDGD
                    Consensus   GNDGNDRLYG DKGNDTL-GG NGDDQLYGGD GNDKL-GG-G NNYLNGGDGD
                                  SEQ ID NO: 456        SEQ ID NO: 457      SEQ ID NO: 458
B-Cell Ep.                      ********** ********** ********** ********** **********

                                801                                                 850
strain 536                      DELQVQGNSL AKNVLSGGKG NDKLYGSEGA DLLDGGEGND LLKGGYGNDI
strain 536                      DELQVQGNSL AKNVLSGGKG NDKLYGSEGA DLLDGGEGND LLKGGYGNDI
strain CFT073                   DELQVQGNSL AKNVLSGGKG NDKLYGSEGA DLLDGGEGND LLKGGYGNDI
Group A                         DELQVQGNSL AKNVLSGGKG NDKLYGSEGA DLLDGGEGND LLKGGYGNDI
strain E110019                  DELQVQGNSL AKNVLSGGKG NDKLYGSEGA DLLDGGEGND LLKGGYGNDI
                    Consensus   DELQVQGNSL AKNVLSGGKG NDKLYGSEGA DLLDGGEGND LLKGGYGNDI
B-Cell Ep.                      *****         ****** ********** ********** *********

                                851                                                 900
strain 536                      YRYLSGYGHH IIDDDGGKDD KLSLADIDFR DVAFKREGND LIMYKAEGNV
strain 536                      YRYLSGYGHH IIDDDGGKDD KLSLADIDFR DVAFKREGND LIMYKAEGNV
strain CFT073                   YRYLSGYGHH IIDDDGGKDD KLSLADIDFR DVAFRREGND LIMYKAEGNV
Group A                         YRYLSGYGHH IIDDEGGKDD KLSLADIDFR DVAFKREGND LIMYKAEGNV
strain E110019                  YRYLSGYGHH IIDDDGGKED KLSLADIDFR DVAFKREGND LIMYKAEGNV
                    Consensus   YRYLSGYGHH IIDD-GGK-D KLSLADIDFR DVAF-REGND LIMYKAEGNV
                                                      SEQ ID NO: 459      SEQ ID NO: 460
B-Cell Ep.                             ********* **

                                901                                                 950
strain 536                      LSIGHKNGIT FRNWFEKESG DISNHQIEQI FDKDGRVITP DSLKKAFEYQ
strain 536                      LSIGHKNGIT FRNWFEKESG DISNHQIEQI FDKDGRVITP DSLKKAFEYQ
```

```
strain CFT073          LSIGHKNGIT FRNWFEKESG DISNHQIEQI FDKDGRVITP DSLKKALEYQ
Group A                LSIGHKNGIT FKNWFEKESD DLSNHQIEQI FDKDGRVITP DSLKKAFEYQ
strain E110019         LSIGHENGIT FRNWFEKESG DISNHQIEQI FDKGGRIITP DSLKKALEYQ
            Consensus  LSIGH-NGIT F-NWFEKES- D-SNHQIEQI FDK-GR-ITP DSLKKA-EYQ
                                               SEQ ID NO: 461
B-Cell Ep.                          ***** *****          ****** ****   ***

                       951                                                1000
strain 536             QSNNQANYVY GEYASTYADL DNLNPLINEI SKIISAAGNF DVKEERSAAS
strain 536             QSNNQANYVY GEYASTYADL DNLNPLINEI SKIISAAGNF DVKEERSAAS
strain CFT073          QSNNKASYVY GNDALAYGSQ DNLNPLINEI SKIISAAGNF DVKEERAAAS
Group A                QSNNKVSYVY GHDASTYGSQ DNLNPLINEI SKIISAAGNF DVKEERSAAS
strain E110019         QRNNKASYVY GNDALAYGSQ DNLNLLINEI SKIISAAGNF DVKEERTAAS
            Consensus  Q-NN---YVY G--A--Y--- DNLN-LINEI SKIISAAGNF DVKEER-AAS
                                                        SEQ ID NO: 462
B-Cell Ep.             *********    ********                    ** *******

                       1001                 1024
strain 536             LLQLSGNASD FSYGRNSITL TASA
strain 536             LLQLSGNASD FSYGRNSITL TASA
strain CFT073          LLQLSGNASD FSYGRNSITL TASA
Group A                LLQLSGNASD FSYGRNSITL TASA
strain E110019         LLQLSGNASD FSYGRNSITL TTSA
            Consensus  LLQLSGNASD FSYGRNSITL T-SA
                            SEQ ID NO: 463
B-Cell Ep.                  ***** ***
```

B-Cell Epitopes

SEQ ID NO: 464 QSAKQSAANKLHSAGQSTKDALKKAAEQTRNA
SEQ ID NO: 465 DYKGQGSS
SEQ ID NO: 466 QYDEKNGTAI
SEQ ID NO: 467 QKAGNKLGGSAENIGDNLGK
SEQ ID NO: 468 IKKQKSGSNVSSSEL
SEQ ID NO: 469 ADADTGTKAAAG
SEQ ID NO: 470 AQGLSTSAA
SEQ ID NO: 471 SGISAA
SEQ ID NO: 472 EKKHGKNYFENGYDA
SEQ ID NO: 473 GVTRNGDKTLS
SEQ ID NO: 474 DYYEEGKRLEKKPDEFQK
SEQ ID NO: 475 IDLSDSKS
SEQ ID NO: 476 LTPGEEIRERRQSGKY
SEQ ID NO: 477 VKGVQDKGSVY
SEQ ID NO: 478 SVGNNQY
SEQ ID NO: 479 HLGDGDD
SEQ ID NO: 480 YDKTDTGYL
SEQ ID NO: 481 GTKATEAGNY
SEQ ID NO: 482 EVSVGKRTEKTQY
SEQ ID NO: 483 GTDLTET
SEQ ID NO: 484 HGADGDDHIEGNDGNDRLYGDKGNDTLRGGNGDDQLYGGDGNDKLTGGVGNNYLNGGDGDDELQV
SEQ ID NO: 485 LSGGKGNDKLYGSEGADLLDGGEGNDLLKGGYGN
SEQ ID NO: 486 IDDDGGKDDKL
SEQ ID NO: 487 EKESGDISNH
SEQ ID NO: 488 GRVITPDSLK
SEQ ID NO: 489 EYQQSNNQANYV
SEQ ID NO: 490 YASTYADL
SEQ ID NO: 491 NFDVKEERS
SEQ ID NO: 492 GNASDFSY

Upec948 protein

'upec948' protein from *E. coli* UPEC is also known as: 'c0975 from CFT073.

When used according to the present invention, upec948 protein may take various forms. Preferred upec948 sequences have 50% or more identity (*e.g.* 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98%, 99% or more) to SEQ ID NOs 82-84. This includes variants (*e.g.* allelic variants, homologs, orthologs, paralogs, mutants *etc*).

Other preferred upec948 sequences comprise at least *n* consecutive amino acids from SEQ ID NOs 82-84, wherein *n* is 7 or more (*eg.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). Preferred fragments comprise an epitope or immunogenic fragment from upec948. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or the N-terminus of SEQ ID NOs 82-84. Exemplary fragments are the conserved fragments SEQ ID NOs identified in the sequence alignment below.

```
Group A: strain RS218, E2348-69 and CFT073  (SEQ ID NO: 82)
Strain HS  (SEQ ID NO: 83)
Strain B and C  (SEQ ID NO: 84)

                        1                                                  50
Group A                 VSLSTALRMT CRRRLLSLIV GPASLNRFIP PFQHFGQRHN VSNGWRPVKN
strain HS               VSLSTALRMT CRRRLLSLIV GPASLNRFIP PFQHFGQRHN VSNGWRPVKD
strain B and C          VSLSTALRMT CRRRLLSLIV GPASLNRFIP PVQHFGQRHN VSNGWRPVKN
             Consensus  VSLSTALRMT CRRRLLSLIV GPASLNRFIP P-QHFGQRHN VSNGWRPVK-
                             SEQ ID NO: 493                    SEQ ID NO: 494
B-Cell Ep.                                                     ** **********

                        51                                                 100
Group A                 GGDICHQIVN RQAVGKPAST DFFNKKVTTS TDMAVRSAGS ISAISCAVSA
strain HS               GGDICHQIVN RQAVGKPAST DFFNKKVTTS TDMAVRSAGS ISAISCAVSA
strain B and C          GGDICHQIVN RQAVGKPAST DFFNKKVTTS TDMAVRSAGS ISAISCAVSA
             Consensus  GGDICHQIVN RQAVGKPAST DFFNKKVTTS TDMAVRSAGS ISAISCAVSA
                                   SEQ ID NO: 495
B-Cell Ep.              ***          ******** **     **** ******

                        101                                                150
Group A                 GLEMRGITVI IAFTSISIMA CRRVPRSAPD CGLRSTISVI SVLPRLMGVS
strain HS               GLEMRGITVI IAFTSISIMA CRRVPRSAPD CGLRSTISVI SVLPRMMGVS
strain B and C          GLEMRGITVI IAFTSISIMA CRRVPRSAPD CGLRSTISVI SVLPRMMGVS
             Consensus  GLEMRGITVI IAFTSISIMA CRRVPRSAPD CGLRSTISVI SVLPR-MGVS
B-Cell Ep.                                   ******* **

                        151
Group A                 S
strain HS               S
strain B and C          S
             Consensus  S

B-Cell Epitopes
SEQ ID NO: 496  HNVSNGWRPVKNGGD
SEQ ID NO: 497  AVGKPASTDF
SEQ ID NO: 498  VTTSTDMAVR
SEQ ID NO: 499  VPRSAPDCG
```

Upec1232 protein

'upec1232' protein from *E. coli* UPEC is disclosed in reference 6 (SEQ ID 138) is also known as: 'c1275 from CFT073.

When used according to the present invention, upec1232 protein may take various forms. Preferred upec1232 sequences have 50% or more identity (*e.g.* 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98%, 99% or more) to SEQ ID NOs 85-91. This includes variants (*e.g.* allelic variants, homologs, orthologs, paralogs, mutants *etc*).

Other preferred upec1232 sequences comprise at least *n* consecutive amino acids from SEQ ID NOs 85-91, wherein *n* is 7 or more (*eg.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). Preferred fragments comprise an epitope or immunogenic fragment from upec1232. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or the N-terminus of SEQ ID NOs 85-91. Exemplary fragments are the conserved fragments SEQ ID NOs identified in the sequence alignment below.

```
strain H10407  (SEQ ID NO: 85)
strain H10407  (SEQ ID NO: 86)
strain B7A  (SEQ ID NO: 87)
strain O42  (SEQ ID NO: 88)
strain CFT073  (SEQ ID NO: 89)
strain O42  (SEQ ID NO: 90)
strain CFT073  (SEQ ID NO: 91)

                                1                                          50
strain H10407                   MIHLFKTCMI TTFILGLMWS APLRAQDQRY ISIRNTDTIW LPGNICAYQF
strain H10407                   MIHLFKTCMI TTFILGLMWS APLRAQDQRY ISIRNTDTIW LPGNICAYQF
strain B7A                      MIHLFKTCMI TAFILGLTWS APLRAQDQRY ISIRNTDTIW LPGNICAYQF
strain O42                      MIHLFKTCMI TAFILGLTWS APLRAQDQRY ISIRNTDTIW LPGNICAYQF
strain CFT073                   MIHLFKTCMI TAFILGLTWS APLRAQDQRY ISIRNTDTIW LPGNICAYQF
strain O42                      MIHLFKTCMI TAFILGLTWS APLRAQDQRY ISIRNTDTIW LPGNICAYQF
strain CFT073                   MIHLFKTCMI TAFILGLTWS APLRAQDQRY ISIRNTDTIW LPGNICAYQF

strain H10407                   MIHLFKTCMI TTFILGLMWS APLRAQDQRY ISIRNTDTIW LPGNICAYQF
strain H10407                   MIHLFKTCMI TTFILGLMWS APLRAQDQRY ISIRNTDTIW LPGNICAYQF
strain B7A                      MIHLFKTCMI TAFILGLTWS APLRAQDQRY ISIRNTDTIW LPGNICAYQF
strain O42                      MIHLFKTCMI TAFILGLTWS APLRAQDQRY ISIRNTDTIW LPGNICAYQF
strain CFT073                   MIHLFKTCMI TAFILGLTWS APLRAQDQRY ISIRNTDTIW LPGNICAYQF
strain O42                      MIHLFKTCMI TAFILGLTWS APLRAQDQRY ISIRNTDTIW LPGNICAYQF
strain CFT073                   MIHLFKTCMI TAFILGLTWS APLRAQDQRY ISIRNTDTIW LPGNICAYQF
                    Consensus   MIHLFKTCMI T-FILGL-WS APLRAQDQRY ISIRNTDTIW LPGNICAYQF
                                SEQ ID NO: 500                  SEQ ID NO: 501

                                51                                         100
strain H10407                   RLDNGGNDEG FGPLTITLQL KDKYGQTLVT RKMETEAFGD SNATRTTDAF
strain H10407                   RLDNGGNDEG FGPLTITLQL KDKYGQTLVT RKMETEAFGD SNATRTTDAF
strain B7A                      RLDNGGNDEG FGPLTITLQL KDKYGQTLVT RKMETEAFGD SNATRTTDAF
strain O42                      RLDNGGNDEG FGPLTITLQL KDKYGQTLVT RKMETEAFGD SNATRTTDAF
strain CFT073                   RLDNGGNDEG FGPLTITLQL KDKYGQTLVT RKMETEAFGD SNATRTTDAF
strain O42                      RLDNGGNDEG FGPLTITLQL KDKYGQTLVT RKMETEAFGD SNATRTTDAF
strain CFT073                   RLDNGGNDEG FGPLTITLQL KDKYGQTLVT RKMETEAFGD SNATRTTDAF
                    Consensus   RLDNGGNDEG FGPLTITLQL KDKYGQTLVT RKMETEAFGD SNATRTTDAF
B-Cell Ep.                        ******** **                       ****** ******

                                101                                        150
strain H10407                   LETECVENVA TTEIIKATEE SNGHRVSLPL SVFDPQDYHP LLITVSGKNV
strain H10407                   LETECVENVA TTEIIKATEE SNGHRVSLPL SVFNPQDYHP LLITVSGKNV
strain B7A                      LETECVENVA TTEIIKATEE SNGHRVSLPL SVFNPQDYHP LLITVSGKNV
strain O42                      LETECVENVA TTEIIKATEE SNGHRVSLPL SVFNPQDYHP LLITVSGKNV
strain CFT073                   LETECVENVA TTEIIKATEE SNGHRVSLPL SVFDPQDYHP LLITVSGKNV
strain O42                      LETECVENVA TTEIIKATEE SNGHRVSLPL SVFDPQDYHP LLITVSGKNV
```

```
strain CFT073          LETECVENVA TTEIIKATEE SNGHRVSLPL SVFDPQDYHP LLITVSGKNV
            Consensus  LETECVENVA TTEIIKATEE SNGHRVSLPL SVF-PQDYHP LLITVSGKNV
                                                                 SEQ ID NO: 502
B-Cell Ep.                                *****  *****        ******

                           151
strain H10407              N
strain H10407              N
strain B7A                 N
strain O42                 N
strain CFT073              N
strain O42                 N
strain CFT073              N
            Consensus      N

B-Cell Epitopes
SEQ ID NO: 503  DNGGNDEGFG
SEQ ID NO: 504  TEAFGDSNATRT
SEQ ID NO: 505  KATEESNGHR
SEQ ID NO: 506  FDPQDY
```

Upec1875 protein

Type-1 fimbrial protein, A chain precursor, is referred to herein as 'upec1875.' 'upec1875' protein from *E. coli* UPEC is disclosed in reference 6 (SEQ ID 221) is also known as: 'orf1642' from *E. coli* NMEC strain IHE3034, 'c1936' from CFT073.

When used according to the present invention, upec1875 protein may take various forms. Preferred upec1875 sequences have 50% or more identity (*e.g.* 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98%, 99% or more) to SEQ ID NOs 92-98. This includes variants (*e.g.* allelic variants, homologs, orthologs, paralogs, mutants *etc*).

Other preferred upec1875 sequences comprise at least *n* consecutive amino acids from SEQ ID NOs 92-98, wherein *n* is 7 or more (*eg.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). Preferred fragments comprise an epitope or immunogenic fragment from upec1875. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or the N-terminus of SEQ ID NOs 92-98. Exemplary fragments are the conserved fragments SEQ ID NOs identified in the sequence alignment below.

```
Group A: strain E22, E110019, B7A and B171  (SEQ ID NO: 92)
Group B: strain EDL933, SAKAI, EC508, EC869, EC4024, EC4042, EC4045, EC4076,
EC4113, EC4115, EC4196, EC4206, EC4401, EC4486, EC4501 and TW14588  (SEQ ID NO:
93)
strain SECEC  (SEQ ID NO: 94)
strain O42  (SEQ ID NO: 95)
Group C: strain IHE3034, RS218, UTI89, F11 and APECO1  (SEQ ID NO: 96)
strain CFT073  (SEQ ID NO: 97)
strain E2348-69  (SEQ ID NO: 98)

                           1                                              50
Group A                    MKLKHVGMIV VSVLAMSSAA VSAAEGDESV TTTVNGGVIH FKGEVVNAAC
Group B                    MKLKHVGMIV VSVLAMSSAA VSAAEGDESV TTTVNGGVIH FKGEVVNAAC
strain SECEC               MKLKHVGMIV VSVLAMSSAA VSAAEGDESV TTTVNGGVIH FKGEVVNAAC
strain O42                 MKLKHVGMIV VSVLAMSSAA VSAAEGDESV TTTVNGGVIH FKGEVVNAAC
Group C                    MKLKHVGIIV VSVLAMSSAA VSAAEGDESV TTTVNGGVIH FKGEVVNAAC
strain CFT073              MKLKHVGIIV VSVLAMSSAA VSAAEGDESV TTTVNGGVIH FKGEVVNAAC
```

```
strain E2348-69          MKLKHVGIIV VSVLAMSSAA VSAAEGDESV MTTVNGGVIH FKGEVVNAAC
            Consensus    MKLKHVG-IV VSVLAMSSAA VSAAEGDESV -TTVNGGVIH FKGEVVNAAC
                                    SEQ ID NO: 507          SEQ ID NO: 508
B-Cell Ep.                          ********** ****

                         51                                                100
Group A                  AIDSESMNQT VELGQVRSSR LAKAGDLSSA VGFNIKLNDC DTNVSSNAAV
Group B                  AIDSESMNQT VELGQVRSSR LAKAGDLSSA VGFNIKLNDC DTNVSSNAAV
strain SECEC             AIDSESMNQT VELGQVRSSR LAKAGDLSSA VGFNIKLNDC DTNVSSNAAV
strain O42               AIDSESMNQT VELGQVRSSR LAKAGDLSSA VGFNIKLNDC DTNVSSNAAV
Group C                  AIDSESMNQT VELGQVRSSR LAKAGDLSSA VGFNIKLNDC DTNVSSNAAV
strain CFT073            AIDSESMNQT VELGQVRSSR LAKAGDLSSA VGFNIKLNDC DTNVSSNAAV
strain E2348-69          AIDSESMNQT VELGQVRSSR LAKAGDLSSA VGFNIKLNDC DTNVSSNAAV
            Consensus    AIDSESMNQT VELGQVRSSR LAKAGDLSSA VGFNIKLNDC DTNVSSNAAV
B-Cell Ep.                                                            *******

                         101                                               150
Group A                  AFLGTTVTSN DDTLALQSSA AGSAQNVGIQ ILDRTGEVLI LDGATFSAKT
Group B                  AFLGTTVTSN DDTLALQSSA AGSAQNVGIQ ILDRTGEVLI LDGATFSAKT
strain SECEC             AFLGTTVTSN DDTLALQSSA AGSAQNVGIQ ILDRTGEVLI LDGATFSAKT
strain O42               AFLGTTVTSN DDTLALQSSA AGSAQNVGIQ ILDRTGEVLI LDGGTFSAKT
Group C                  AFLGTTVTSN DDTLALQSSA AGSAQNVGIQ ILDRTGEVLV LDGATFSAKT
strain CFT073            AFLGTTVTSN DDTLALQSSA AGSAQNVGIQ ILDSTGEVLV LDGATFSAKT
strain E2348-69          AFLGTTVTSN DDTLALQSSA AGSAQNVGIQ ILDRTGEVLV LDGATFSAKT
            Consensus    AFLGTTVTSN DDTLALQSSA AGSAQNVGIQ ILD-TGEVL- LDG-TFSAKT
B-Cell Ep.                    ***** *****    ** ******

                         151                                       187
Group A                  DLIDGTNILP FQARYIALGQ SVAGTANADA TFKVQYL
Group B                  DLIDGTNILP FQARYIALGQ SVAGTANADA TFKVQYL
strain SECEC             DLIDGTNILP FQARYIALGQ SVAGTANADA TFKVQYL
strain O42               DLIDGTNILP FQARYIALGQ SVAGTANADA TFKVQYL
Group C                  DLIDGTNILP FQARYIALGQ SVAGTANADA TFKVQYL
strain CFT073            DLIDGTNILP FQARYIALGQ SVAGTANADA TFKVQYL
strain E2348-69          DLIDGTNILS FQARYIALGQ SVAGTANADA TFKVQYL
            Consensus    DLIDGTNIL- FQARYIALGQ SVAGTANADA TFKVQYL
                      SEQ ID NO: 509          SEQ ID NO: 510
B-Cell Ep.                                    **********
```

B-Cell Epitopes

SEQ ID NO: 511 VSAAEGDESVTTTV
SEQ ID NO: 512 DTNVSSN
SEQ ID NO: 513 TVTSNDDTLA
SEQ ID NO: 514 SAAGSAQN
SEQ ID NO: 515 SVAGTANADA

Upec2820 protein

YapH homolog protein is referred to herein as 'upec2820.' 'upec2820' protein from *E. coli* NMEC is disclosed in reference 6 (SEQ ID 307) is also known as: 'c2895' from CFT073.

When used according to the present invention, upec2820 protein may take various forms. Preferred upec2820 sequences have 50% or more identity (*e.g.* 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98%, 99% or more) to SEQ ID NOs 99-100. This includes variants (*e.g.* allelic variants, homologs, orthologs, paralogs, mutants *etc*).

Other preferred upec2820 sequences comprise at least *n* consecutive amino acids from SEQ ID NOs 99-100, wherein *n* is 7 or more (*eg.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100,

150, 200, 250 or more). Preferred fragments comprise an epitope or immunogenic fragment from upec2820. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or the N-terminus of SEQ ID NOs 99-100. Exemplary fragments are the conserved fragments SEQ ID NOs identified in the sequence alignment below.

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strain CFT073  (SEQ ID NO: 99)
strain SECEC  (SEQ ID NO: 100)

                                1                                                  50
strain CFT073                   MNKVYKVIWN HTTQKWDVVS ELTSCRKKCK STRLGIALSA MVLGGAIAIN
strain SECEC                    MNKIYKVIWN HTTQKWDVVS ELTSCRKKCK STRLGIALSA MVLGGAIAIN
                Consensus       MNK-YKVIWN HTTQKWDVVS ELTSCRKKCK STRLGIALSA MVLGGAIAIN
                                           SEQ ID NO: 516

                               51                                                  100
strain CFT073                   CNNAMADVIL SPDWRPGTNN SGVGAATVSG KTEYITGPNV VQSGGSGLIW
strain SECEC                    CNNAMADVIL SPDWRPGTNN SGVGAATVSG KTEYITGPNV VQSGGSGLIW
                Consensus       CNNAMADVIL SPDWRPGTNN SGVGAATVSG KTEYITGPNV VQSGGSGLIW
B-Cell Ep.                             ******** ********** ********** *****

                               101                                                 150
strain CFT073                   MTVEQAILNG YTTGDNLSGL IYVNTGEKTK TITVKDEVTG ASQTLQVFDT
strain SECEC                    MTVEQAILNG YTTGDNLSGL IYVNTGEKTK TITVKDEVTG AYQTLQVFDT
                Consensus       MTVEQAILNG YTTGDNLSGL IYVNTGEKTK TITVKDEVTG A-QTLQVFDT
B-Cell Ep.                             ******         ****** ********** ***

                               151                                                 200
strain CFT073                   DSFSQRDAGT GGNETIPGFS GTADFFNATR FVTANNGGTA ILDVGSPAIG
strain SECEC                    DSFSQRDAGT GGNETIPGFS GTADFFNATR FVTANNGGTA ILDVGSPAIG
                Consensus       DSFSQRDAGT GGNETIPGFS GTADFFNATR FVTANNGGTA ILDVGSPAIG
                                           SEQ ID NO: 517
B-Cell Ep.                     ********** ********** **           *******

                               201                                                 250
strain CFT073                   NFFKNTQLAV ADGEGSSVVW NSVNDFYFQP GATMQGGGVT QKIIDSMKYA
strain SECEC                    NFFKNTQLAV ADGEGSSVVW NSVNDFYFQP GATMQGGGVT QKIIDSMKYA
                Consensus       NFFKNTQLAV ADGEGSSVVW NSVNDFYFQP GATMQGGGVT QKIIDSMKYA
B-Cell Ep.                        ** ********                   **********

                               251                                                 300
strain CFT073                   GTITDWAGKV HHINSLDDLK QYNQYLIKSL EDKTLSYKQY DAEFNKALIV
strain SECEC                    GTITDWAGKV HHINSLDDLK QYNQYLIKSL EDKTLSYKQY DAEFNKALIV
                Consensus       GTITDWAGKV HHINSLDDLK QYNQYLIKSL EDKTLSYKQY DAEFNKALIV

                               301                                                 350
strain CFT073                   TKHNYNVDMT AGGRIDSTPY KENVGLLAVL HATNNARAIL GKTGKLTGVL
strain SECEC                    TKHNYNVDMT AGGRIDSTPY KENVGLLAVL HATNNARAIL GKTGKLTGVL
                Consensus       TKHNYNVDMT AGGRIDSTPY KENVGLLAVL HATNNARAIL GKTGKLTGVL
B-Cell Ep.                        *** ********** **

                               351                                                 400
strain CFT073                   PAYGNGGGIV ATNGGTGVNE GVIDAIGTEM IAYQDSTIVN DGTLFVWDNN
strain SECEC                    PAYGNGGGIV ATNGGTGVNE GVIDAIGTEM IAYQDSTIVN DGTLFVWDNN
                Consensus       PAYGNGGGIV ATNGGTGVNE GVIDAIGTEM IAYQDSTIVN DGTLFVWDNN
B-Cell Ep.                     ********** ********** *                             *

                               401                                                 450
strain CFT073                   DKYALQAEGM VAGSNGSSAI NNGVINIRPF KNAFAPEGIN TAIVVSNGGM
strain SECEC                    DKYALQAEGM VAGSNGSSAI NNGVINIRPF KNAFAPEGIN TAIVVSNGGM
                Consensus       DKYALQAEGM VAGSNGSSAI NNGVINIRPF KNAFAPEGIN TAIVVSNGGM
B-Cell Ep.                     *****    * **********                *******          ***
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                                  451                                                 500
strain CFT073                     ATNKGTINIT ADASTNDNNG KTRGVNVGAG GSFINSAFGS INVGIAEDKT
strain SECEC                      ATNKGTINIT ADASTNDNNG KTRGVNVGAG GSFINSAFGS INVGIAEDKT
                 Consensus        ATNKGTINIT ADASTNDNNG KTRGVNVGAG GSFINSAFGS INVGIAEDKT
B-Cell Ep.                        ********** ********** **********                  *****

                                  501                                                 550
strain CFT073                     ATHSAVGSVA IEVQNGANKV VNEGTIFLGR GAQGNYGILA KDAGTVDVVN
strain SECEC                      ATHSAVGSVA IEVQNGANKV VNEGTIFLGR GAQGNYGILA KDAGSVDVVN
                 Consensus        ATHSAVGSVA IEVQNGANKV VNEGTIFLGR GAQGNYGILA KDAG-VDVVN
B-Cell Ep.                        ******        ******* *                      *******

                                  551                                                 600
strain CFT073                     KGTITIDGHD SDAPALNVGM LANNSSGMKN SGIINVNGLN STGLQVINAG
strain SECEC                      KGTITIDGYD SDAPALNVGM LANNSSGMKN SGIINVNGLN STGLQVINAG
                 Consensus        KGTITIDG-D SDAPALNVGM LANNSSGMKN SGIINVNGLN STGLQVINAG
                          SEQ ID NO: 518                SEQ ID NO: 519
B-Cell Ep.                           ******* *****

                                  601                                                 650
strain CFT073                     QLNSDGTINV GGKGISSGFR NYGAWVEGAG SNVNVSGKIS LAGTGAVGVF
strain SECEC                      QLNSDGTINV GGEGISSGFR NYGAWVEGAR SNVNVSGKIN LSGTGAVGVF
                 Consensus        QLNSDGTINV GG-GISSGFR NYGAWVEGA- SNVNVSGKI- L-GTGAVGVF
                                                SEQ ID NO: 520
B-Cell Ep.                        ********** ********      ******* *****

                                  651                                                 700
strain CFT073                     AKDGGSLTLS GNGAVLFGSS DQIGFYVYGK DSAIHNTGSG VMDVSTENST
strain SECEC                      AKDGGSLTLS GNGAVLFGSS DQIGFYVYGK DSAIHNTGSG VMDVSTENST
                 Consensus        AKDGGSLTLS GNGAVLFGSS DQIGFYVYGK DSAIHNTGSG VMDVSTENST
                      SEQ ID NO: 521
B-Cell Ep.                        **********                          ********* *******

                                  701                                                 750
strain CFT073                     LFRIASGATF QGTADASSAL TASGKNSYAL IATGKSDGGV ASTVTSGGMT
strain SECEC                      LFRIASGATF QGTADASSAL TASGKNSYAL IATGKSDGGV ASTVTSGGMT
                 Consensus        LFRIASGATF QGTADASSAL TASGKNSYAL IATGKSDGGV ASTVTSGGMT
B-Cell Ep.                              *** ********** ******       ******** *******

                                  751                                                 800
strain CFT073                     INLTGEGATA TLIEGGAQGT IESNAIINMD NASAIAGIAD GNGYDISGKL
strain SECEC                      INLTGEGATA TLIEGGAQGT IESNAIINMD NASAIAGIAD GNGYDISGKL
                 Consensus        INLTGEGATA TLIEGGAQGT IESNAIINMD NASAIAGIAD GNGYDISGKL
B-Cell Ep.                           ******* ********** **                ****  ******

                                  801                                                 850
strain CFT073                     INPKDKTTLL TAGAQLSSTQ DKVTGYIARN GATLNNTGNI IFTGKNTVGV
strain SECEC                      INPKDKTTLL TAGAQLSSTQ DKVTGYIARN GATLNNTGNI IFTGKNTVGV
                 Consensus        INPKDKTTLL TAGAQLSSTQ DKVTGYIARN GATLNNTGNI IFTGKNTVGV
B-Cell Ep.                        ********       ****** ****                        ****

                                  851                                                 900
strain CFT073                     RVEEGAVGTN SGNITVQDGG VGLIANATQD VTTINNSGNL VLKGGDNANR
strain SECEC                      RVEEGAVGTN SGNITVQDGG VGLIANATQD VTTINNSGNL VLKGGDNANR
                 Consensus        RVEEGAVGTN SGNITVQDGG VGLIANATQD VTTINNSGNL VLKGGDNANR
B-Cell Ep.                        ********** *********          *** ******          ******

                                  901                                                 950
strain CFT073                     TTGIKASGTT TTVNMTAGTI SLQGQGAIGV EASNKGTVNL DGSAVPNFAA
strain SECEC                      TTGIKASGTT TTVNMTAGTI SLQGQGAIGV EASNKGTVNL DGSAVPNFAS
                 Consensus        TTGIKASGTT TTVNMTAGTI SLQGQGAIGV EASNKGTVNL DGSAVPNFA-
B-Cell Ep.                        ********** *****             **** ********** **********
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                                951                                                1000
strain CFT073                   DGSGITDQIA FRIIGDGATI KTNIAPGTLL DASGERSVLF RIEDGAKQAG
strain SECEC                    DGSGITDQIA FRIIGDGATI KTNIAPGTLL DASGERSVLF RIEDGAKQAG
            Consensus           DGSGITDQIA FRIIGDGATI KTNIAPGTLL DASGERSVLF RIEDGAKQAG
                                      SEQ ID NO: 522
B-Cell Ep.                      ******            *** *****   ** *****

                                1001                                               1050
strain CFT073                   SLLMKTSGTG SRGIWATGKG SNVLADAGSD FQILGAQAQG LYVTGGATAT
strain SECEC                    SLLMKTSGTG SRGIWATGKG SNVLADAGSD FQILGAQAQG LYVTGGATAT
            Consensus           SLLMKTSGTG SRGIWATGKG SNVLADAGSD FQILGAQAQG LYVTGGATAT
                                    **** ********** ******                      *****

                                1051                                               1100
strain CFT073                   LKQGASVNLV GDGAVVAEVD GNEYALDGSI TQTNTGSVIT NEADISSPLN
strain SECEC                    LKQGASVNLV GDGAVVAEVD GNEYALDGSI TQTNTGSVIT NEADISSPLN
            Consensus           LKQGASVNLV GDGAVVAEVD GNEYALDGSI TQTNTGSVIT NEADISSPLN
B-Cell Ep.                      ****          ******* ******* ** **********  *********

                                1101                                               1150
strain CFT073                   NAKGFITRNQ GLLINNGNID FTTGTDNIGV WVDNGRFENT GSRIAVNGVA
strain SECEC                    NAKGFITRNQ GLLINSGNID FTTGTDNIGV WVDNGRFENT GSRIAVNGVA
            Consensus           NAKGFITRNQ GLLIN-GNID FTTGTDNIGV WVDNGRFENT GSRIAVNGVA
                                                      SEQ ID NO: 523
B-Cell Ep.                      *                  ** *******       ****** ****

                                1151                                               1200
strain CFT073                   LFVEGAQSQI TSTGGDIVAV DGEAAIKLGA GASLNLAGSG LGTIEGQKNA
strain SECEC                    LFVEGEHAQI TSTGGDIVAV DGEAAIKLGA GASLNLAGSG LGTIEGQKNA
            Consensus           LFVEG---QI TSTGGDIVAV DGEAAIKLGA GASLNLAGSG LGTIEGQKNA
                                          SEQ ID NO: 524
B-Cell Ep.                        **** **********                          *********

                                1201                                               1250
strain CFT073                   HGILLDTGAV GLVIDGAKIN VNAAGAVGHG IENRAEIEGI QLTNTTEINV
strain SECEC                    HGILLDTGAV GLVIDGAKIN VNAAGAVGHG IENRAEIEGI QLTNTTEINV
            Consensus           HGILLDTGAV GLVIDGAKIN VNAAGAVGHG IENRAEIEGI QLTNTTEINV
                                                   ******* ******

                                1251                                               1300
strain CFT073                   ADGIGVRTSA SLAKTNSGTI NVDGSGIALA FQKADGSETD NNLDMSDSAG
strain SECEC                    ADGIGVRTSA SLAKTNSGTI NVDGSGIALA FQKADGSETD NNLDMSDSGG
            Consensus           ADGIGVRTSA SLAKTNSGTI NVDGSGIALA FQKADGSETD NNLDMSDS-G
B-Cell Ep.                            ********** ****          ******** ******

                                1301                                               1350
strain CFT073                   LVINLKGTDG TGIFANTKDG AVVKSGASVN VIQADGGSAL VVNNAASEVV
strain SECEC                    LVINLKGTGG TGIFANTKDG AVVKSGASVN VTQADGGSAL VVNNAASEVV
            Consensus           LVINLKGT-G TGIFANTKDG AVVKSGASVN V-QADGGSAL VVNNAASEVV
                                          SEQ ID NO: 525       SEQ ID NO: 526
B-Cell Ep.                        **** ********** ****         ******

                                1351                                               1400
strain CFT073                   QSGNLISASL SHAVVDASKA QSFTNKGQIK AASTTGTAMA FDDAVNTTVL
strain SECEC                    QSGNLISASL SHAVVDASKA QSFTNKGQIK AASATGTAMA FDDAVNTTVL
            Consensus           QSGNLISASL SHAVVDASKA QSFTNKGQIK AAS-TGTAMA FDDAVNTTVL
                                                                   SEQ ID NO: 527
B-Cell Ep.                              **** ********** **********          **

                                1401                                               1450
strain CFT073                   NDSGAEIQGV VALNGGDNTF TNKGSITGTV SAKEGNNTFL FDDGSTLTGE
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strain SECEC                NDSGAEIQGV VALNGGDNTF TNKGSITGTV SAKEGNNTFL FDDGSILTGE
                 Consensus  NDSGAEIQGV VALNGGDNTF TNKGSITGTV SAKEGNNTFL FDDGS-LTGE
B-Cell Ep.                  *******     ******** ********** ******         ******

                            1451                                            1500
strain CFT073               VTAGNGNNNV TLNGKTHVDQ VTAGTGKNTF TIKGEGATWN LLDGGQGDSD
strain SECEC                VAAGNGNNNV TLNGKAHVDK VTAGTGKNTF TIKGEGATWN LLDGGQGDSD
                 Consensus  V-AGNGNNNV TLNGK-HVD- VTAGTGKNTF TIKGEGATWN LLDGGQGDSD
                              SEQ ID NO: 528          SEQ ID NO: 529
B-Cell Ep.                  ********** *** ****** ********** *******     *********

                            1501                                            1550
strain CFT073               SLIFDNAIHT LDSVVKLQNF EHVGLKNSSL VTLKEALVLT DGGNGPGSVD
strain SECEC                SLIFDNAIHT LDSAVKLRNF EHVGLKNSSL VTLKEALVLT DGGTGPGSVD
                 Consensus  SLIFDNAIHT LDS-VKL-NF EHVGLKNSSL VTLKEALVLT DGG-GPGSVD
                                                    SEQ ID NO: 530
B-Cell Ep.                  *                                          **********

                            1551                                            1600
strain CFT073               IESGSELAII PAVAGNFTFD PLLTGKGTLS ARLDADTSAF EFSHNVGDQF
strain SECEC                IESGSELAII PAVAGNFTFD PLLTGKGTLS ARLDADTSAF EFSHNVGDQF
                 Consensus  IESGSELAII PAVAGNFTFD PLLTGKGTLS ARLDADTSAF EFSHNVGDQF
                              SEQ ID NO: 531
B-Cell Ep.                  ****                                 *******

                            1601                                            1650
strain CFT073               AGTLKLGTSS FALEGLNTSG LTHAMLMSET GNITTVGSGV QQIGGLGFNG
strain SECEC                AGTLKLGTSS FALEGLNTSG LTHAMLMSET GNITTVGSGV QQIGGLGFNG
                 Consensus  AGTLKLGTSS FALEGLNTSG LTHAMLMSET GNITTVGSGV QQIGGLGFNG
B-Cell Ep.                                                   ********* **

                            1651                                            1700
strain CFT073               GTLIFGSVMP GDTIASNSIE TSAAGTLDIR GKGTIQVTMP DEVINDIPAV
strain SECEC                GTLIFGSVMP GDTIASNSIE TSAAGTLDIR GKGTIQVTMP DEVINDIPAV
                 Consensus  GTLIFGSVMP GDTIASNSIE TSAAGTLDIR GKGTIQVTMP DEVINDIPAV
B-Cell Ep.                        ** ********** ******

                            1701                                            1750
strain CFT073               DTRKNLLEQD DAQTLVTLVN AAGTVTGTGG QLQLVDENGQ AISHSQTFDV
strain SECEC                DTRKNLLEQD DAQTLVTLVN AAGTVTGTGG QLQLVDENGQ AISHSQTFDV
                 Consensus  DTRKNLLEQD DAQTLVTLVN AAGTVTGTGG QLQLVDENGQ AISHSQTFDV
B-Cell Ep.                      **** ***          ********       **** ***   ****

                            1751                                            1800
strain CFT073               TQGGEVVAQG NYDYKLLGSS DGIKGDGLYI GYGLKSLDLQ GTGDKALVLT
strain SECEC                TQGGEVVAQG NYDYKLLGSS DGVKGDGLYI GYGLKSLDLQ GTGDKALVLT
                 Consensus  TQGGEVVAQG NYDYKLLGSS DG-KGDGLYI GYGLKSLDLQ GTGDKALVLT
                                                              SEQ ID NO: 532
B-Cell Ep.                  ********** *         * *****             ** ****

                            1801                                            1850
strain CFT073               PRANAQGLQT DLGAQLTGAG DLAIEAAGQV VTLSNGGNNY TGDTLVRSGT
strain SECEC                PRANAQGLQT DLGAQLTGAG DLAIEAAGQV VTLSNGGNNY TGDTLVRSGT
                 Consensus  PRANAQGLQT DLGAQLTGAG DLAIEAAGQV VTLSNGGNNY TGDTLVRSGT
                             ********* * *******                 ******* ******

                            1851                                            1900
strain CFT073               LQMANDNVLG ATGNLNVASN AVFRTNGYSQ TVGALQTETG AHIQLDSGSV
strain SECEC                LQMANDNVLG ATGSLNVASN AVFRTDGYSQ TVGALQTETG AHIQLDSGSV
                 Consensus  LQMANDNVLG ATG-LNVASN AVFRT-GYSQ TVGALQTETG AHIQLDSGSV
                                        SEQ ID NO: 533       SEQ ID NO: 534
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B-Cell Ep.                                          **** **********

                          1901                                      1950
strain CFT073             LTVSGTQRQP GDDNGGIIEN NVLSGEGTLA VTGSNLTVHG TNIGFTGNAS
strain SECEC              LTVSGTQRQP GDDNGGIIEN NVLTGDGTLA VTGSNLTVHG TNIGFTGNVS
          Consensus       LTVSGTQRQP GDDNGGIIEN NVL-G-GTLA VTGSNLTVHG TNIGFTGN-S
                                                                SEQ ID NO: 535
B-Cell Ep.                   ******* *******

                          1951                                      2000
strain CFT073             LTQGALVEMN GAQGLGSQGS ISFESLNDRL AIDIADGSGV SSNLSKSLSG
strain SECEC              LTRGSLVEMN GAQGLGSQGS ISFESLNDRL AIDIADGSGV SSNLSKSLSG
          Consensus       LT-G-LVEMN GAQGLGSQGS ISFESLNDRL AIDIADGSGV SSNLSKSLSG
                                          SEQ ID NO: 536
B-Cell Ep.                          ********* *              ****** *** ******

                          2001                                      2050
strain CFT073             EGSVGILNTT DLTLSGDNSN FSGEFRVQKD AALRASDEKH LGTGLIDSDG
strain SECEC              KGSVGILNTT DLTLSGDNRN FSGEFRVQKD AALRASDEKH LGTGLIDSDG
          Consensus       -GSVGILNTT DLTLSGDN-N FSGEFRVQKD AALRASDEKH LGTGLIDSDG
                             SEQ ID NO: 537             SEQ ID NO: 538
B-Cell Ep.                ***          ******** **

                          2051                                      2100
strain CFT073             VTWLTASGNW LLKNDITGSG ALVKQGAGNL IINHELTYTG DTTVESGVLI
strain SECEC              VTWLTASGNW LLKNDITGSG ALVKQGAGNL IINHELTYTG DTTVENGVLI
          Consensus       VTWLTASGNW LLKNDITGSG ALVKQGAGNL IINHELTYTG DTTVE-GVLI
B-Cell Ep.                                                  **** *****

                          2101                                      2150
strain CFT073             VGDDSVTRAA GATLSGSKNI HVLNGGTLSG LGTVSGQVNN QGTLASLNAL
strain SECEC              VGDDSVTRAA GATLSGSKNI HVLNGGTLSG LGTVSGQVNN QGTLASLNAL
          Consensus       VGDDSVTRAA GATLSGSKNI HVLNGGTLSG LGTVSGQVNN QGTLASLNAL
                                    SEQ ID NO: 539
B-Cell Ep.                   ******* ******                ******** ***

                          2151                                      2200
strain CFT073             SGYETAEVGN FTVGSLTNTG VIRLAGGKTG NTLTVNGDYT GGGTLIINTV
strain SECEC              SGYETAEAGN FTVGSLTNTG VIRLAGGKTG NTLTVNGDYT GGGTLIINTV
          Consensus       SGYETAE-GN FTVGSLTNTG VIRLAGGKTG NTLTVNGDYT GGGTLIINTV
                                    SEQ ID NO: 540
B-Cell Ep.                 *******                ***** ********** **

                          2201                                      2250
strain CFT073             LGDDTSTTDK LIVTGNTSGD TGVVVNNVRG QGAQTADGIE IVHVGGQSDG
strain SECEC              LGDDTSATDK LIVTGNTSGD TGVVVNNVRG QGAQTADGIE IVHVGGQSDG
          Consensus       LGDDTS-TDK LIVTGNTSGD TGVVVNNVRG QGAQTADGIE IVHVGGQSDG
                                    SEQ ID NO: 541
B-Cell Ep.                 *******        ***** ***    *** *******        *******

                          2251                                      2300
strain CFT073             NFRLQNRAVA GAWEYFLHKG NAGGTDGNWY LRSELPPEPQ PQPQPQPQPQ
strain SECEC              NFRLQNRAVA GAWEYFLHKG NAGGTDGNWY LRSELPPE.. ..........
          Consensus       NFRLQNRAVA GAWEYFLHKG NAGGTDGNWY LRSELPPE-- ----------
B-Cell Ep.                **                  * **********    ******* **********

                          2301                                      2350
strain CFT073             PQPQPQPQPQ PQPHPTPDKP VQKVYRPEAG SYIANIAAAN TLFNIRMHDR
strain SECEC              PQPQPQPQPQ PQPHPTPDKP VQKVYRPEAG SYIANIAAAN TLFNIRMHDR
          Consensus       PQPQPQPQPQ PQPHPTPDKP VQKVYRPEAG SYIANIAAAN TLFNIRMHDR
                                    SEQ ID NO: 542
B-Cell Ep.                ********** ********** ********** *                  **
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                                2351                                                2400
strain CFT073                   EGETYYTDVF TGEKKATSMW MRHIGGHNRW KDSSSQLNTQ SNRYVVQLGG
strain SECEC                    EGETYYTDVF TGEKKATSMW MRHIGGHNRW KDSSSQLNTQ SNRYVVQLGG
                Consensus       EGETYYTDVF TGEKKATSMW MRHIGGHNRW KDSSSQLNTQ SNRYVVQLGG
B-Cell Ep.                      ******   * ******             *** **********

                                2401                                                2450
strain CFT073                   SIAQWTDGQD RLQQGIMAGY GNEKSSTTSS LSGYKSKGAI NGYSTGLYGT
strain SECEC                    SIAQWTDGQD RLQLGIMAGY GNEKSSTTSS LSGYKSKGAI NGYSTGLYGT
                Consensus       SIAQWTDGQD RLQ-GIMAGY GNEKSSTTSS LSGYKSKGAI NGYSTGLYGT
                                                        SEQ ID NO: 543
B-Cell Ep.                        ******** **       ** ********** ********** ***      **

                                2451                                                2500
strain CFT073                   WQQNDGNDNG AYVDTWIQYG WFNNTVNGEK LAAESWKSRG FTGSVEAGYT
strain SECEC                    WQQNDGNDNG AYVDTWIQYG WFNNTVNGEK LAAESWKSRG FTGSVEAGYT
                Consensus       WQQNDGNDNG AYVDTWIQYG WFNNTVNGEK LAAESWKSRG FTGSVEAGYT
B-Cell Ep.                      ********** **             ****** ********** ********

                                2501                                                2550
strain CFT073                   FKAGEFTGSQ GSHYDWYIQP QSQITWMNVR ASEHTEKNGT KVQLSGDGNI
strain SECEC                    FKAGEFTGSQ GSHYDWYIQP QSQITWMNVR ASEHTEKNGT KVQLSGDGNI
                Consensus       FKAGEFTGSQ GSHYDWYIQP QSQITWMNVR ASEHTEKNGT KVQLSGDGNI
                                   ******* ***                    ********** **********

                                2551                                                2600
strain CFT073                   QSRLGVRTYL KGKSASDDNK AHQFEPFVEV NWIHNTRSWG VKMDNTALSQ
strain SECEC                    QSRLGVRTYL KGKSASDDNK AHQFEPFVEV NWIHNTRSWG VKMDNTALSQ
                Consensus       QSRLGVRTYL KGKSASDDNK AHQFEPFVEV NWIHNTRSWG VKMDNTALSQ
B-Cell Ep.                      *          ********** ***                      *****

                                2601                                                2649
strain CFT073                   DGATNIAEVK TGVQGKLSDN LNVWGNVGVQ AGDKGYSDAQ AMLGIKYIF
strain SECEC                    DGATNIAEVK TGVQGKLSDN LNVWGNVGVQ AGDKGYSDAQ AMLGIKYIF
                Consensus       DGATNIAEVK TGVQGKLSDN LNVWGNVGVQ AGDKGYSDAQ AMLGIKYIF
B-Cell Ep.                      ********   ********           *** ********
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B-Cell Epitopes

SEQ ID NO: 544 DWRPGTNNSGVGAATVSGKTEYITGPNVVQSGG
SEQ ID NO: 545 YTTGDN
SEQ ID NO: 546 TGEKTKTITVKDEVTGASQ
SEQ ID NO: 547 DSFSQRDAGTGGNETIPGFSGT
SEQ ID NO: 548 TANNGGT
SEQ ID NO: 549 AVADGEGSSV
SEQ ID NO: 550 GATMQGGGVT
SEQ ID NO: 551 DMTAGGRIDSTPYKE
SEQ ID NO: 552 PAYGNGGGIVATNGGTGVNEG
SEQ ID NO: 553 NDKYAL
SEQ ID NO: 554 MVAGSNGSSAI
SEQ ID NO: 555 AFAPEGI
SEQ ID NO: 556 GGMATNKGTINITADASTNDNNGKTRGVNVGAG
SEQ ID NO: 557 AEDKTATHSAV
SEQ ID NO: 558 QNGANKVV
SEQ ID NO: 559 AGTVDVV
SEQ ID NO: 560 TITIDGHDSDAPA
SEQ ID NO: 561 QLNSDGTINVGGKGISSG
SEQ ID NO: 562 AWVEGAGSNVNV
SEQ ID NO: 563 AKDGGSLTLS
SEQ ID NO: 564 SAIHNTGSGVMDVSTE
SEQ ID NO: 565 ATFQGTADASSALTASGKN
SEQ ID NO: 566 TGKSDGGVASTVTSG
SEQ ID NO: 567 TGEGATATLIEGGAQGTIE

SEQ ID NO: 568 GIADGNGYDI
SEQ ID NO: 569 INPKDKTT
SEQ ID NO: 570 QLSSTQDKVT
SEQ ID NO: 571 TVGVRVEEGAVGTNSGNITVQDG
SEQ ID NO: 572 TQDVTTINN
SEQ ID NO: 573 GDNANRTTGIKASGTTTTVNM
SEQ ID NO: 574 AIGVEASNKGTVNLDGSAVPNFAADGSGIT
SEQ ID NO: 575 ATIKTNIA
SEQ ID NO: 576 LLDASGE
SEQ ID NO: 577 SGTGSRGIWATGKGSNVLAD
SEQ ID NO: 578 GATATLKQG
SEQ ID NO: 579 AVVAEVDGNEYALD
SEQ ID NO: 580 SITQTNTGSVITNEADISSPLNN
SEQ ID NO: 581 IDFTTGTDN
SEQ ID NO: 582 GRFENTGSRI
SEQ ID NO: 583 QSQITSTGGDIVAV
SEQ ID NO: 584 LGTIEGQKN
SEQ ID NO: 585 AGAVGHGIENRAE
SEQ ID NO: 586 SLAKTNSGTINVDG
SEQ ID NO: 587 KADGSETDNNLDMS
SEQ ID NO: 588 GTDGTGIFANTKDGAVVK
SEQ ID NO: 589 IQADGG
SEQ ID NO: 590 ASKAQSFTNKGQIKAASTTGTAMA
SEQ ID NO: 591 VLNDSGAEI
SEQ ID NO: 592 LNGGDNTFTNKGSITGTVSAKEGN
SEQ ID NO: 593 STLTGEVTAGNGNNNVTLN
SEQ ID NO: 594 KTHVDQVTAGTGKNTFTIKGEGA
SEQ ID NO: 595 LDGGQGDSDS
SEQ ID NO: 596 DGGNGPGSVDIESG
SEQ ID NO: 597 LDADTSA
SEQ ID NO: 598 NITTVGSGVQQ
SEQ ID NO: 599 MPGDTIASNSIETSAAGT
SEQ ID NO: 600 LEQDDAQ
SEQ ID NO: 601 GTVTGTGG
SEQ ID NO: 602 ENGQAIS
SEQ ID NO: 603 TFDVTQGGEVVAQGN
SEQ ID NO: 604 SDGIKG
SEQ ID NO: 605 LQGTGD
SEQ ID NO: 606 RANAQGLQTD
SEQ ID NO: 607 GAQLTGA
SEQ ID NO: 608 SNGGNNYTGDTLV
SEQ ID NO: 609 GYSQTVGALQTETG
SEQ ID NO: 610 SGTQRQPGDDNGGI
SEQ ID NO: 611 AQGLGSQGSI
SEQ ID NO: 612 ADGSGVSSN
SEQ ID NO: 613 SKSLSGEGS
SEQ ID NO: 614 TLSGDNSNFS
SEQ ID NO: 615 TYTGDTTVE
SEQ ID NO: 616 DSVTRAAGATLSG
SEQ ID NO: 617 TVSGQVNNQGT
SEQ ID NO: 618 GYETAEV
SEQ ID NO: 619 GGKTGNTLTVNGDYTGG
SEQ ID NO: 620 GDDTSTT
SEQ ID NO: 621 NTSGDTGV
SEQ ID NO: 622 VRGQGAQTAD
SEQ ID NO: 623 GGQSDGNF
SEQ ID NO: 624 GNAGGTDGNWY
SEQ ID NO: 625 ELPPEPQPQPQPQPQPQPQPQPQPQPQPHPTPDKPVQKVYRPEAGS
SEQ ID NO: 626 DREGETYY
SEQ ID NO: 627 FTGEKKA
SEQ ID NO: 628 NRWKDSSSQLNTQ
SEQ ID NO: 629 AQWTDGQDRL
SEQ ID NO: 630 GYGNEKSSTTSSLSGYKSKGAINGY

SEQ ID NO: 631 GTWQQNDGNDNGAY
SEQ ID NO: 632 TVNGEKLAAESWKSRGFTGSVEAG
SEQ ID NO: 633 GEFTGSQGSH
SEQ ID NO: 634 ASEHTEKNGTKVQLSGDGNIQ
SEQ ID NO: 635 KGKSASDDNKAHQ
SEQ ID NO: 636 TALSQDGATNIAE
SEQ ID NO: 637 TGVQGKLS
SEQ ID NO: 638 GVQAGDKGYSD

Upec-5211 polypeptide

Sell repeat-containing protein is referred to herein as 'upec-5211.' 'upec-5211' polypeptide from *E. coli* is also known as: 'c5321' from CFT073; 'ECED1_5081' from ED1a and 'EFER_4303' from *E. fergusonii* ATCC 35469.

When used according to the present invention, upec-5211 polypeptide may take various forms. Preferred upec-5211 sequences have 50% or more identity (*e.g.*, 60%, 65%, 70%, 75%, 80%, 85%, 87.5%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more) to SEQ ID NOs 653-655. This includes variants (*e.g.*, allelic variants, homologs, orthologs, paralogs, mutants *etc*).

Other preferred upec-5211 sequences comprise at least *n* consecutive amino acids from SEQ ID NOs 653-655, wherein *n* is 7 or more (*eg.* 8, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more). Preferred fragments comprise an epitope or immunogenic fragment from upec-5211. Other preferred fragments lack one or more amino acids (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or the N-terminus of SEQ ID NOs 653-655. Exemplary fragments are the conserved fragments SEQ ID NOs identified in the sequence alignment below.

```
Strains CFT073 and 83972  (SEQ ID NO: 653)
Strain ED1a  (SEQ ID NO: 654)
Escherichia fergusonii ATCC 35469  (SEQ ID NO: 655)

strain CFT073 and 83972  MKKSLLAVML TGLFALVSLP ALGNVNLEQL KQKAESGEAK AQLELGYRYF
strain ED1a              MKKSLLAVML TGLFALVSLP ALGNVNLEQL KQKAESGEAK AQLELGYRYF
E. fergusonii            MKKSLLAALL TGLFALVSLP ALGNVNFEQL KQKAERGEAK AQLELGYRYF
               Consensus  MKKSLLA +L TGLFALVSLP ALGNVN EQL KQKAE GEAK AQLELGYRYF
                                    SEQ ID NO: 656                SEQ ID NO: 657
B-Cell Ep.                                                                    *

strain CFT073 and 83972  QGNETTKDLT QAMDWFRRAA EQGYTPAEYV LGLRYMNGEG VPQDYAQAVI
strain ED1a              QGNETTKDLT LAMDWFRRAA EQGYTPAEYV LGLRYMNGEG VPQDYAQAVI
E. fergusonii            QGNETTKDLT QAIDWFRRAA EQGYTPAEFV LGLRYMNGEG VPKDYAQAVI
               Consensus  QGNETTKDLT  A+DWFRRAA EQGYTPAE+V LGLRYMNGEG VP+DYAQAVI
B-Cell Ep.               **********          * *******           *** ******

strain CFT073 and 83972  WYKKAALKGL PQAQQNLGVM YHEGNGVKVD KAESVKWFRL AAEQGRDSGQ
strain ED1a              WYKKAALKGL PQAQQNLGVM YHEGNGVKVD KAESVKWFRL AAEQGRDSGQ
E. fergusonii            WYKKAALKGL PQAQQNLGVM YHDGKGVKID KAESVKWFRL AAEQGRDSGQ
               Consensus  WYKKAALKGL PQAQQNLGVM YH+G GVK+D KAESVKWFRL AAEQGRDSGQ
                                SEQ ID NO: 658
B-Cell Ep.                       * *****                                ********

strain CFT073 and 83972  QSMGDAYFEG DGVTRDYVMA REWYSKAAEQ GNVWSCNQLG YMYSRGLGVE
strain ED1a              QSMGDAYFEG DGVTRDYVMA REWYSKAAEQ GNVWSCNQLG YMYSRGLGVE
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E. fergusonii            QSMGDAYFEG DGVTRDYVMA REWYSKAAEQ GNVWSCNQLG YIYSKGLGVE
              Consensus  QSMGDAYFEG DGVTRDYVMA REWYSKAAEQ GNVWSCNQLG Y+YS+GLGVE
                                 SEQ ID NO: 659
B-Cell Ep.               ********** ****           ****** ***

strain CFT073 and 83972  RNDAISAQWY RKSATSGDEL GQLHLADMYY FGIGVTQDYT QSRVLFSQSA
strain ED1a              RNDAISAQWY RKSATSGDEL GQLHLADMYY FGIGVTQDYT QSRVLFSQSA
E. fergusonii            KNDAISAQWY RKSATSGDEL GQLHLADMYY FGIGVTQDYT QSRILFTQSA
              Consensus  +NDAISAQWY RKSATSGDEL GQLHLADMYY FGIGVTQDYT QSR+LF+QSA
                                              SEQ ID NO: 660
B-Cell Ep.                        * **********                 *****

strain CFT073 and 83972  EQGNSIAQFR LGYILEQGLA GAKEPLKALE WYRKSAEQGN SDGQYYLAHL
strain ED1a              EQGNSIAQFR LGYILEQGLA GAKEPLKALE WYRKSAEQGN SDGQYYLAHL
E. fergusonii            EQGNAIAQYR LGYILEEGLA GAKEPLKALE WYRKSAEQGN AIGQYYLAEI
              Consensus  EQGN+IAQ+R LGYILE+GLA GAKEPLKALE WYRKSAEQGN + GQYYLA +
                                                 SEQ ID NO: 661
B-Cell Ep.                                  ** ******

strain CFT073 and 83972  YDKGAEGVAK NREQAISWYT KSAEQGDATA QANLGAIYFR LGSEEEHKKA
strain ED1a              YDKGAEGVAK NREQAISWYT KSAEQGDATA QANLGAIYFR LGSEEEHKKA
E. fergusonii            YIRRAEGIPY NREQAIYWYT KSAEQGDTDA QVNLGALLYR HGSEEEQRRA
              Consensus  Y + AEG+   NREQAI WYT KSAEQGD  A Q NLGA+ +R  GSEEE ++A

strain CFT073 and 83972  VEWFRKAAAK GEKAAQFNLG NALLQGKGVK KDEQQAAIWM RKAAEQGLSA
strain ED1a              VEWFRKAAAK GEKAAQFNLG NALLQGKGVK KDEQQAAIWM RKAAEQGLSA
E. fergusonii            VDWYRKAAEE GVAMAQFNLG NALLQGKGVK KDEQQAAIWM RKAAEQGFSS
              Consensus  V+W+RKAA + G   AQFNLG NALLQGKGVK KDEQQAAIWM RKAAEQG S+
                                                 SEQ ID NO: 662
B-Cell Ep.                                          *** *****

strain CFT073 and 83972  AQVQLGEIYY YGLGVERDYV QAWAWFDTAS TNDMNLFGTE NRNITEKKLT
strain ED1a              AQVQLGEIYY YGLGVERDYV QAWAWFDTAS TNDMNLFGTE NRNITEKKLT
E. fergusonii            AQVQLGEIYY YGLGVERDYV QAWAWFDTAS TNDMNLFGTE NRNITEKKLT
              Consensus  AQVQLGEIYY YGLGVERDYV QAWAWFDTAS TNDMNLFGTE NRNITEKKLT
                                                 SEQ ID NO: 663
B-Cell Ep.                                          *** **          *****

strain CFT073 and 83972  AKQLQQAELL SQQYIEKYAP EAWARMQKLK AQSAVKTGNK
strain ED1a              TKQLQQAELL SQQYIEKYAT EAWARMQKLK AQSAVKTGNK
E. fergusonii            AKQLQQAELL SQQYIEKYAP EAWARMQKLN ARSTVTTGNK
              Consensus   KQLQQAELL SQQYIEKYA  EAWARMQKL  A+S V TGNK
                             SEQ ID NO: 664
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B-Cell Epitopes

SEQ ID NO: 665 FQGNETTKDLT
SEQ ID NO: 666 AEQGYTPA
SEQ ID NO: 667 GEGVP(K/Q)DYA
SEQ ID NO: 668 LPQAQQ
SEQ ID NO: 669 EQGRDSGQQSMGDAYFEGDGVT
SEQ ID NO: 670 SKAAEQGNV
SEQ ID NO: 671 YRKSATSGDEL
SEQ ID NO: 672 TQDYT
SEQ ID NO: 673 LAGAKEPL
SEQ ID NO: 674 GVKKDEQQ
SEQ ID NO: 675 TASTN
SEQ ID NO: 676 NRNIT

Specific Polypeptides used with the invention

An aspect of the invention includes an isolated or recombinant polypeptide comprising an E. coli protein selected from the group consisting of orf353, bacterial Ig-like domain (group 1) protein (orf405), flu antigen 43 (orf1364), NodT-family outer-membrane-factor-lipoprotein efflux transporter (orf1767), gspK (orf3515), gspJ (orf3516), tonB-dependent siderophore receptor (orf3597), fibrial protein (orf3613), upec-948, upec-1232, A chain precursor of the type-1 fimbrial protein (upec-1875), yapH homolog (upec-2820), and hemolysin A (recp-3768).

In certain embodiments, the isolated or recombinant polypeptide may have an amino acid sequence having at least *a%* identity to SEQ ID NOs: 1-105.

In certain embodiments, the polypeptide comprises an amino acid that when aligned with any of SEQ ID NOs: 1-105 using a pairwise alignment algorithm, each moving window of x amino acids from N terminus to C terminus has at least x•y identical aligned amino acids, where: *x* is selected from 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100, 150, 200; *y* is selected from 0.50, 0.60, 0.70, 0.75, 0.80, 0.85, 0.90, 0.91, 0.92, 0.93, 0.94, 0.95, 0.96, 0.97, 0.98, 0.99; and if $x \cdot y$ is not an integer then it is rounded up to the nearest integer.

In certain embodiments, the isolated or recombinant polypeptide will include at least *b* consecutive amino acids of any of SEQ ID NOs: 1-105, wherein the at least *b* consecutive amino acids is immunogenic.

In certain embodiments where the isolated or recombinant polypeptide is orf353, the isolated or recombinant polypeptide will comprise less than 160, less than 150, less than 140 or less than 130 amino acids from SEQ ID NOs: 1-2. Preferred examples will include SEQ ID NOs: 211-218.

In certain embodiments where the isolated or recombinant polypeptide is bacterial Ig-like domain (group 1) protein (orf405), the isolated or recombinant polypeptide will comprise less than 1410, less than 1400, less than 1390 or less than 1380 amino acids from SEQ ID NOs: 3-18. Preferred examples will include SEQ ID NOs: 219-307 & 683.

In certain embodiments where the isolated or recombinant polypeptide is flu antigen 43 (orf1364), the isolated or recombinant polypeptide will comprise less than 1040, less than 1030, less than 1020 or less than 1010 amino acids from SEQ ID NOs: 19-40. Preferred examples will include SEQ ID NOs: 308-350.

In certain embodiments where the isolated or recombinant polypeptide is NodT-family outer-membrane-factor-lipoprotein efflux transporter (orf1767), the isolated or recombinant polypeptide will comprise less than 450, less than 440, less than 430 or less than 420 amino acids from SEQ ID NOs: 41-47. Preferred examples will include SEQ ID NOs: 351-368.

In certain embodiments where the isolated or recombinant polypeptide is gspK (orf3515), the isolated or recombinant polypeptide will comprise less than 320, less than 310, less than 300 or

less than 290 amino acids from SEQ ID NOs: 48-60. Preferred examples will include SEQ ID NOs: 369-384.

In certain embodiments where the isolated or recombinant polypeptide is gspJ (orf3516), the isolated or recombinant polypeptide will comprise less than 180, less than 170, less than 160 or less than 150 amino acids from SEQ ID NOs: 61-71. Preferred examples will include SEQ ID NOs: 385-398.

In certain embodiments where the isolated or recombinant polypeptide is tonB-dependent siderophore receptor (orf3597), the isolated or recombinant polypeptide will comprise less than 710, less than 700, less than 690 or less than 680 amino acids from SEQ ID NOs: 72-79. Preferred examples will include SEQ ID NOs: 399-425.

In certain embodiments where the isolated or recombinant polypeptide is fibrial protein (orf3613), the isolated or recombinant polypeptide will comprise less than 180, less than 170, less than 160 or less than 150 amino acids from SEQ ID NOs: 80-81. Preferred examples will include SEQ ID NO: 426-432.

In certain embodiments where the isolated or recombinant polypeptide is upec-948, the isolated or recombinant polypeptide will comprise less than 150, less than 140, less than 130 or less than 120 amino acids from SEQ ID NOs: 82-84. Preferred examples will include SEQ ID NOs: 493-499.

In certain embodiments where the isolated or recombinant polypeptide is upec-1232, the isolated or recombinant polypeptide will comprise less than 150, less than 140, less than 130 or less than 120 amino acids from SEQ ID NOs: 85-91. Preferred examples will include SEQ ID NOs: 500-506.

In certain embodiments where the isolated or recombinant polypeptide is A chain precursor of the type-1 fimbrial protein (upec-1875), the isolated or recombinant polypeptide will comprise less than 180, less than 170, less than 160 or less than 150 amino acids from SEQ ID NOs: 92-98. Preferred examples will include SEQ ID NOs: 507-515.

In certain embodiments where the isolated or recombinant polypeptide is yapH homolog (upec-2820), the isolated or recombinant polypeptide will comprise less than 2640, less than 2620, less than 2600 or less than 2580 amino acids from SEQ ID NOs: 99-100. Preferred examples will include SEQ ID NOs: 516-638.

In certain embodiments where the isolated or recombinant polypeptide is hemolysin A (recp-3768), the isolated or recombinant polypeptide will comprise less than 1020, less than 1010, less than 1000 or less than 990 amino acids from SEQ ID NOs: 101-105. Preferred examples will include SEQ ID NOs: 433-492. In certain embodiments, the isolated or recombinant polypeptide includes a fragment of an E. coli hemolysin A (recp-3768) wherein the fragment contains a deletion relative to the E. coli AcfD protein which increases solubility of the fragment as

compared to the full length protein and wherein the fragment raises a substantially similar immune response in a subject as the E. coli AcfD protein.

In certain embodiments which may be combined with any of the preceding embodiments, the polypeptide does not comprise the corresponding full length protein (e.g., orf353, bacterial Ig-like domain (group 1) protein (orf405), flu antigen 43 (orf1364), NodT-family outer-membrane-factor-lipoprotein efflux transporter (orf1767), gspK (orf3515), gspJ (orf3516), tonB-dependent siderophore receptor (orf3597), fibrial protein (orf3613), upec-948, upec-1232, A chain precursor of the type-1 fimbrial protein (upec-1875), yapH homolog (upec-2820), and hemolysin A (recp-3768)). Examples of such corresponding full length proteins include SEQ ID NOs: 1-105.

An aspect of the invention includes an isolated or recombinant polypeptide comprising an *Escherichia* Sell repeat-containing protein (upec-5211).

In certain embodiments, the isolated or recombinant polypeptide may have an amino acid sequence having at least *a%* identity to SEQ ID NOs: 653-655.

In certain embodiments, the polypeptide comprises an amino acid that when aligned with any of SEQ ID NOs: 653-655 using a pairwise alignment algorithm, each moving window of x amino acids from N terminus to C terminus has at least x•y identical aligned amino acids, where: *x* is selected from 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100, 150, 200; *y* is selected from 0.50, 0.60, 0.70, 0.75, 0.80, 0.85, 0.90, 0.91, 0.92, 0.93, 0.94, 0.95, 0.96, 0.97, 0.98, 0.99; and if *x·y* is not an integer then it is rounded up to the nearest integer.

In certain embodiments, the isolated or recombinant polypeptide will include at least *b* consecutive amino acids of any of SEQ ID NOs: 653-655, wherein the at least *b* consecutive amino acids is immunogenic.

In certain embodiments, the isolated or recombinant polypeptide will comprise less than 480, less than 470, less than 460, less than 450, less than 425, less than 400, less than 350, less than 200,or less than 250 amino acids from SEQ ID NOs: 653-655. Preferred examples will include SEQ ID NOs: 656-676.

Any of the polypeptides disclosed herein have utility as components of vaccines. Thus in another embodiment, the isolated or recombinant polypeptide will be with an adjuvant.

Another aspect of the invention includes a polynucleotide encoding any of the foregoing polypeptides. In certain embodiments, the polynucleotide has at *a%* sequence identity to a nucleic acid sequence selected from the group consisting of SEQ ID NOs:106-210.

Another aspect of the invention includes an immunogenic polypeptide which includes a fragment of an orf405 protein wherein the fragment contains a deletion relative to the E. coli orf405 which increases solubility of the fragment as compared to the full length protein and wherein the fragment raises a substantially similar immune response in a subject as the E. coli orf405. One

example of such is SEQ ID NO:642. In certain embodiments, the fragment of an orf405 protein has less than 1200 amino acids, less than 1100 amino acids, less than 1000 amino acids, less than 950 amino acids, less than 900 amino acids, less than 850 amino acids, less than 800 amino acids, less than 750 amino acids, less than 700 amino acids, less than 650 amino acids, less than 600 amino acids, less than 590 amino acids, or less than 580 amino acids of the orf405 protein. In certain embodiments with may be combined with any of the foregoing embodiments, the fragment of orf405 with increased solubility has (a) the amino acid sequence selected from the group consisting of SEQ ID NOs 3-18; (b) from 1 to 10 single amino acid alterations compared to SEQ ID NOs: 3-18; at least *a%* sequence identity to any one of SEQ ID NOs: 3-18; and/or (d) when aligned with any of SEQ ID NOs: 3-18 using a pairwise alignment algorithm, each moving window of x amino acids from N terminus to C terminus has at least x•y identical aligned amino acids, where: *x* is selected from 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100, 150, 200; *y* is selected from 0.50, 0.60, 0.70, 0.75, 0.80, 0.85, 0.90, 0.91, 0.92, 0.93, 0.94, 0.95, 0.96, 0.97, 0.98, 0.99; and if *x·y* is not an integer then it is rounded up to the nearest integer. In certain embodiments with may be combined with any of the foregoing embodiments, the fragment of orf405 with increased solubility is isolated, purified, or recombinant. In certain embodiments with may be combined with any of the foregoing embodiments, the immunogenic polypeptide may be combined with an adjuvant.

Another aspect of the invention includes an immunogenic polypeptide comprising a fragment of a flu antigen 43 (orf1364) protein wherein the fragment contains a deletion relative to the E. coli flu antigen 43 (orf1364)which increases solubility of the fragment as compared to the full length protein and wherein the fragment raises a substantially similar immune response in a subject as the E. coli flu antigen 43 (orf1364). One example of such is SEQ ID NO:652. In certain embodiments, the E. coli flu antigen 43 has less than 950 amino acids, less than 900 amino acids, less than 850 amino acids, less than 800 amino acids, less than 750 amino acids, less than 700 amino acids, less than 650 amino acids, less than 600 amino acids, less than 550 amino acids, less than 500 amino acids, less than 450 amino acids, less than 440 amino acids, or less than 430 amino acids of the flu antigen 43 (orf1364) protein. In certain embodiments with may be combined with any of the foregoing embodiments, the fragment of flu antigen 43 (orf1364) with increased solubility has (a) the amino acid sequence selected from the group consisting of SEQ ID NOs 19-40; (b) from 1 to 10 single amino acid alterations compared to SEQ ID NOs: 19-40; (c) at least *a%* sequence identity to any one of SEQ ID NOs: 19-40; and/or (d) when aligned with any of SEQ ID NOs: 19-40 using a pairwise alignment algorithm, each moving window of x amino acids from N terminus to C terminus has at least x•y identical aligned amino acids, where: *x* is selected from 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100, 150, 200; *y* is selected from 0.50, 0.60, 0.70, 0.75, 0.80, 0.85, 0.90, 0.91, 0.92, 0.93, 0.94, 0.95, 0.96, 0.97, 0.98, 0.99; and if *x·y* is not an integer then it is rounded up to the nearest integer. In certain embodiments

with may be combined with any of the foregoing embodiments, the fragment of flu antigen 43 (orf1364) with increased solubility is isolated, purified, or recombinant. In certain embodiments with may be combined with any of the foregoing embodiments, the immunogenic polypeptide may be combined with an adjuvant.

Another aspect of the invention includes an immunogenic polypeptide comprising a fragment of an yapH homolog (upec-2820) protein wherein the fragment contains a deletion relative to the E. coli yapH homolog (upec-2820) which increases solubility of the fragment as compared to the full length protein and wherein the fragment raises a substantially similar immune response in a subject as the E. coli yapH homolog (upec-2820). Examples of such are SEQ ID NO:644, SEQ ID NO:646, SEQ ID NO: 648, or SEQ ID NO: 650. In certain embodiments, the fragment of an *E. coli* yapH homolog has less than 2500 amino acids, less than 2000 amino acids, less than 1750 amino acids, less than 1500 amino acids, less than 1400 amino acids, less than 1300 amino acids, less than 1200 amino acids, less than 1100 amino acids, less than 1000 amino acids, less than 900 amino acids, less than 850 amino acids, less than 800 amino acids, less than 750 amino acids, less than 700 amino acids, less than 650 amino acids, less than 600 amino acids, less than 550 amino acids, less than 500 amino acids, less than 450 amino acids, less than 400 amino acids, or less than 390 amino acids of the yapH homolog (upec-2820) protein. In certain embodiments with may be combined with any of the foregoing embodiments, the fragment of yapH homolog (upec-2820) with increased solubility has (a) the amino acid sequence selected from the group consisting of SEQ ID NOs 99-100; (b) from 1 to 10 single amino acid alterations compared to SEQ ID NOs: 99-100; (c) at least *a%* sequence identity to any one of SEQ ID NOs: 99-100; and/or (d) when aligned with any of SEQ ID NOs: 99-100 using a pairwise alignment algorithm, each moving window of x amino acids from N terminus to C terminus has at least x•y identical aligned amino acids, where: *x* is selected from 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100, 150, 200; *y* is selected from 0.50, 0.60, 0.70, 0.75, 0.80, 0.85, 0.90, 0.91, 0.92, 0.93, 0.94, 0.95, 0.96, 0.97, 0.98, 0.99; and if $x \cdot y$ is not an integer then it is rounded up to the nearest integer. In certain embodiments with may be combined with any of the foregoing embodiments, the fragment of yapH homolog (upec-2820) with increased solubility is isolated, purified, or recombinant. In certain embodiments with may be combined with any of the foregoing embodiments, the immunogenic polypeptide may be combined with an adjuvant.

Another aspect of the invention includes an immunogenic polypeptide comprising a fragment of an hemolysin A (recp3768) protein wherein the fragment contains a deletion relative to the E. coli hemolysin A (recp3768) which increases solubility of the fragment as compared to the full length protein and wherein the fragment raises a substantially similar immune response in a subject as the E. coli hemolysin A (recp3768). One example of such is SEQ ID NO:640. In certain embodiments, the fragment of an *E. coil* hemolysin A has less than 1000 amino acids, less than 950 amino acids, less than 900 amino acids, less than 850 amino acids, less than 800

amino acids, less than 750 amino acids, less than 700 amino acids, less than 650 amino acids, less than 600 amino acids, less than 550 amino acids, less than 500 amino acids, less than 450 amino acids, less than 400 amino acids, less than 390 amino acids, less than 380 amino acids, less than 350 amino acids, less than 300 amino acids, less than 250 amino acids, less than 240 amino acids, less than 230 amino acids, or less than 220 amino acids of the hemolysin A (recp3768) protein. In certain embodiments with may be combined with any of the foregoing embodiments, the fragment of the hemolysin A (recp3768) with increased solubility has (a) the amino acid sequence selected from the group consisting of SEQ ID NOs 101-105; (b) from 1 to 10 single amino acid alterations compared to SEQ ID NOs: 101-105; (c) at least *a%* sequence identity to any one of SEQ ID NOs: 101-105; and/or (d) when aligned with any of SEQ ID NOs: 101-105 using a pairwise alignment algorithm, each moving window of x amino acids from N terminus to C terminus has at least x•y identical aligned amino acids, where: *x* is selected from 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100, 150, 200; *y* is selected from 0.50, 0.60, 0.70, 0.75, 0.80, 0.85, 0.90, 0.91, 0.92, 0.93, 0.94, 0.95, 0.96, 0.97, 0.98, 0.99; and if $x \cdot y$ is not an integer then it is rounded up to the nearest integer. In certain embodiments with may be combined with any of the foregoing embodiments, the fragment of hemolysin A (recp3768) with increased solubility is isolated, purified, or recombinant. In certain embodiments with may be combined with any of the foregoing embodiments, the immunogenic polypeptide may be combined with an adjuvant.

The preferred pairwise alignment algorithm for determining percent identity is the Needleman-Wunsch global alignment algorithm [7], using default parameters (*e.g.* with Gap opening penalty = 10.0, and with Gap extension penalty = 0.5, using the EBLOSUM62 scoring matrix). This algorithm is conveniently implemented in the *needle* tool in the EMBOSS package [8].

These polypeptides include variants of SEQ ID NOs 1 to 105, including allelic variants, polymorphic forms, homologs, orthologs, paralogs, mutants, *etc.*, as well as variants of SEQ ID NOs 653 to 655.

The value of *a* may be selected from 50%, 60%, 65%, 70%, 75%, 80%, 85%, 87.5%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5% or more.

The value of *b* may be selected from 7, 8, 9, 10, 12, 14, 16, 18, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 150, 200, 250 or more. Preferred fragments of comprise an epitope or immunogenic fragment from SEQ ID NOs 1 to 105, as well as an epitope or immunogenic fragment from SEQ ID NOs 653 to 655. Other preferred fragments lack one or more amino acids (*e.g.* 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the C-terminus and/or one or more amino acids (*e.g.* 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25 or more) from the N-terminus of SEQ ID NOs 1 to 105, preferably while retaining at least one epitope or immunogenic fragment of SEQ ID NOs 1 to 105, or from the N-terminus of SEQ ID NOs 653 to 655, preferably while retaining at least one epitope or

immunogenic fragment of SEQ ID NOs 653 to 655. Other fragments omit one or more protein domains *e.g.* omission of a signal peptide, of a cytoplasmic domain, of a transmembrane domain, of an extracellular domain, *etc.* The hemolysin A (recp3768) fragment (B4) was obtained by deleting the amino-terminal hydrophobic domain required for membrane insertion and pore formation (the hydrophobic α-helix region), carboxyl-terminal signal sequence and domains required for pore-forming activity after post-translational acylation. The soluble fragment obtained is a carboxyl-terminal β-sheet and glycine-rich region required for binding to calcium. The flu antigen 43 (orf1364) fragment was obtained by deleting the carboxyl-terminal β-barrel domain while retaining the passenger domain (amino acids 53-620). The orf405 fragment was obtained by deletion of a putative amino-terminal translocator domain while retaining four predicted immunoglobulin-binding-like domains (amino acids 595-1008).

An epitope within a fragment may be a B-cell epitope and/or a T-cell epitope. Such epitopes can be identified empirically (*e.g.* using PEPSCAN [9,10] or similar methods), or they can be predicted (*e.g.* using the Jameson-Wolf antigenic index [11], matrix-based approaches [12], MAPITOPE [13], TEPITOPE [14,15], neural networks [16], OptiMer & EpiMer [17, 18], ADEPT [19], Tsites [20], hydrophilicity [21], antigenic index [22] or the methods disclosed in references 23-24, *etc.*). Epitopes are the parts of an antigen that are recognised by and bind to the antigen binding sites of antibodies or T-cell receptors, and they may also be referred to as "antigenic determinants".

Immunogenic fragments of SEQ ID NOs 1 to 105 or of SEQ ID NOs 653 to 655 discussed above include, without limitation, immunogenic fragments that, when administered to a subject in a suitable composition which can include an adjuvant (including without limitation any of the adjuvants listed or discussed in the section "Immunogenic compositions and medicaments" below), or a suitable carrier coupled to the polypeptide, induces an antibody or T-cell mediated immune response that recognizes the isolated full length polypeptide SEQ ID NOs 1 to 105 or of SEQ ID NOs 653 to 655, respectively, from which the immunogenic fragment is derived.

A polypeptide of the invention may, compared to any one of SEQ ID NOs 1 to 105 or of SEQ ID NOs 653 to 655, include one or more (*e.g.* 1, 2, 3, 4, 5, 6, 7, 8, 9, *etc.*) amino acid substitutions, such as conservative substitutions (*i.e.* substitutions of one amino acid with another which has a related side chain). Genetically-encoded amino acids are generally divided into four families: (1) acidic *i.e.* aspartate, glutamate; (2) basic *i.e.* lysine, arginine, histidine; (3) non-polar *i.e.* alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan; and (4) uncharged polar *i.e.* glycine, asparagine, glutamine, cysteine, serine, threonine, tyrosine. Phenylalanine, tryptophan, and tyrosine are sometimes classified jointly as aromatic amino acids. In general, substitution of single amino acids within these families does not have a major effect on the biological activity.

A polypeptide may include one or more (*e.g.* 1, 2, 3, 4, 5, 6, 7, 8, 9, *etc.*) single amino acid deletions relative to any one of SEQ ID NOs 1 to 105 or of SEQ ID NOs 653 to 655. Similarly, a polypeptides may include one or more (*e.g.* 1, 2, 3, 4, 5, 6, 7, 8, 9, *etc.*) insertions (*e.g.* each of 1, 2, 3, 4 or 5 amino acids) relative to any one of SEQ ID NOs 1 to 105 or of SEQ ID NOs 653 to 655.

Within group (c), deletions or substitutions may be at the N-terminus and/or C-terminus, or may be between the two termini. Thus a truncation is an example of a deletion. Truncations may involve deletion of up to 40 (or more) amino acids at the N-terminus and/or C-terminus. As mentioned above, for instance, truncation to remove the N-terminus up to the GGGSG sequence can be used.

In general, when a polypeptide of the invention comprises a sequence that is not identical to a complete one of SEQ ID NOs 1 to 105 or of SEQ ID NOs 653 to 655 (*e.g.* when it comprises a sequence listing with <100% sequence identity thereto, or when it comprises a fragment thereof) it is preferred that the polypeptide can elicit an antibody that recognises a polypeptide consisting of the complete SEQ ID sequence *i.e.* the antibody binds to one or more of said SEQ ID NOs 1 to 105 or of SEQ ID NOs 653 to 655. Such antibody may bind specifically to SEQ ID NOs 1 to 105 or to SEQ ID NOs 653 to 655, respectively while not binding to other proteins that are not homologs with affinity significantly higher than the antibody's non-specific affinity to human serum albumin as a non-specific binding reference standard.

A polypeptide of the invention may include a metal ion *e.g.* a metal ion that is coordinated by one or more amino acids in the polypeptide chain. For instance, the polypeptide may include a monovalent, divalent or trivalent metal cation. Divalent cations are typical, such as Mn^{2+}, Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, *etc.* The divalent cation is preferably Zn^{2+}. The ion may be coordinated by a HEAGH or HEVGH amino acid sequence.

Polypeptides used with the invention can take various forms (*e.g.* native, fusions, glycosylated, non-glycosylated, lipidated, non-lipidated, phosphorylated, non-phosphorylated, myristoylated, non-myristoylated, monomeric, multimeric, particulate, denatured, *etc.*). For instance, a polypeptide of the invention may have a lipidated N-terminal cysteine.

Polypeptides used with the invention can be prepared by various means (*e.g.* recombinant expression, purification from cell culture, chemical synthesis, *etc.*). Recombinantly-expressed proteins are preferred.

Polypeptides used with the invention are preferably provided in purified or substantially purified form *i.e.* substantially free from other polypeptides (*e.g.* free from naturally-occurring polypeptides), particularly from other *E.coli* or host cell polypeptides, and are generally at least

about 50% pure (by weight), and usually at least about 90% pure *i.e.* less than about 50%, and more preferably less than about 10% (*e.g.* 5%) of a composition is made up of other expressed polypeptides. Thus the antigens in the compositions are separated from the whole organism with which the molecule is expressed.

Polypeptides used with the invention are preferably *E.coli* polypeptides. Such polypeptides may be further selected from NMEC, APEC, UPEC, EAEC, EIEC, EPEC and ETEC *E. coli* polypeptides.

The term "polypeptide" refers to amino acid polymers of any length. The polymer may be linear or branched, it may comprise modified amino acids, and it may be interrupted by non-amino acids. The terms also encompass an amino acid polymer that has been modified naturally or by intervention; for example, disulfide bond formation, glycosylation, lipidation, acetylation, phosphorylation, or any other manipulation or modification, such as conjugation with a labeling component. Also included are, for example, polypeptides containing one or more analogs of an amino acid (including, for example, unnatural amino acids, *etc.*), as well as other modifications known in the art. Polypeptides can occur as single chains or associated chains.

The invention provides polypeptides comprising a sequence -P-Q- or -Q-P-, wherein: -P- is an amino acid sequence as defined above and -Q- is not a sequence as defined above *i.e.* the invention provides fusion proteins. Where the N-terminus codon of -P- is not ATG, but this codon is not present at the N-terminus of a polypeptide, it will be translated as the standard amino acid for that codon rather than as a Met. Where this codon is at the N-terminus of a polypeptide, however, it will be translated as Met. Examples of -Q- moieties include, but are not limited to, histidine tags (*i.e.* His_n where n = 3, 4, 5, 6, 7, 8, 9, 10 or more), a maltose-binding protein, or glutathione-S-transferase (GST).

The invention also provides an oligomeric protein comprising a polypeptide of the invention. The oligomer may be a dimer, a trimer, a tetramer, *etc.* The oligomer may be a homo-oligomer or a hetero-oligomer. Polypeptides in the oligomer may be covalently or non-covalently associated.

The invention also provides *E. coli* polypeptides which are fragments of the full length orf405, flu antigen 43 (orf1364), yapH homolog (upec-2820), and hemolysin A (recp3768) (of which SEQ ID NOs: 3-18, SEQ ID NOs: 19-40, SEQ ID NOs: 99-100, and SEQ ID NO 101-105, respectively, are representative examples) which have increased solubility over the full length protein while raising a substantially similar immune response in a subject as that raised by the full length protein. Examples of such immunogenic polypeptide fragments include any of SEQ ID NOs 640, 642, 644, 646, 648, 650 and 652. Increased solubility may be measured by any means available to one of skill in the art. One simple method involves overexpression of the

fragment in bacteria and running comparative samples of total bacterial lysate versus bacterial lysate supernatant after centrifugation or samples of bacterial lysate pellet after centrifugation versus samples of bacterial lysate supernatant after centrifugation. One of skill in the art would grow and express such immunogenic polypeptide fragments using standard techniques (e.g., transform BL21(DE3) bacteria with a pET21 expression vector expressing the fragment, grow the bacteria to 0.6 OD_{600} in LB and induce with 1 mM IPTG, and culture for 3 hours after induction), Such samples may be run on SDS PAGE (e.g., 4-12% MOPS) and roughly quantified by scanning the resulting stained gel and measuring the relative size of the bands. The increased solubility as used herein is as determined at 25° C. Such increased solubility can be a 10% increase in soluble polypeptide, a 20% increase in soluble polypeptide, a 30% increase in soluble polypeptide, a 50% increase in soluble polypeptide, a 75% increase in soluble polypeptide, a 100% increase (i.e., two-fold) in soluble polypeptide, a three-fold increase in soluble polypeptide, a four-fold increase in soluble polypeptide, a five-fold increase in soluble polypeptide, a seven-fold increase in soluble polypeptide, or a ten-fold increase in soluble polypeptide.

Comparison of the immune response raised in a subject by the polypeptide with the immune response raised by the full length protein may be carried out use by any means available to one of skill in the art. One simple method as used in the examples below involves immunization of a model subject such as mouse and then challenge with a lethal dose of *E. coli*. For proper comparison, one of skill in the art would naturally select the same adjuvant such as Freund's complete adjuvant. In such a test the immunogenic polypeptide fragments of the present invention will raise a substantially similar immune response in a subject (i.e., will provide substantially the same protection against the lethal challenge) if, for example, the polypeptide provides at least 70% of the protection provided by the full length protein, at least 80% of the protection provided by the full length protein, at least 85% of the protection provided by the full length protein, at least 90% of the protection provided by the full length protein, at least 95% of the protection provided by the full length protein, at least 97% of the protection provided by the full length protein, at least 98% of the protection provided by the full length protein, or at least 99% of the protection provided by the full length protein.

The corresponding protein against which the immunogenic polypeptide fragment would be compared (for both solubility and immune response raised) may be any representative corresponding *E. coli* protein including without limitation SEQ ID NOs 1-105 and SEQ ID NOs 653-655. In preferred embodiments, the protein will be the corresponding full length protein from which the immunogenic polypeptide fragment is obtained.

In some embodiments, the immunogenic polypeptide will contain a deletion relative to the corresponding *E. coli* protein which results in the increased solubility. The deletion may include

removal of substantially all of the highly hydrophobic or transmembrane regions of the full length sequences, e.g., the amino terminal pore-forming domain for the hemolysin A (recp3768) protein, the β-barrel domain for the flu antigen 43 (orf1364) protein, and putative translocator domain for the orf405 protein.

The invention also provides a process for producing a polypeptide of the invention, comprising the step of culturing a host cell transformed with nucleic acid of the invention under conditions which induce polypeptide expression. The polypeptide may then be purified *e.g.* from culture supernatants.

The invention provides an *E.coli* cell, containing a plasmid that encodes a polypeptide of the invention. The chromosome of the *E.coli* cell may include a homolog of the applicable protein (e.g., orf353, bacterial Ig-like domain (group 1) protein (orf405), flu antigen 43 (orf1364), NodT-family outer-membrane-factor-lipoprotein efflux transporter (orf1767), gspK (orf3515), gspJ (orf3516), tonB-dependent siderophore receptor (orf3597), fibrial protein (orf3613), upec-948, upec-1232, A chain precursor of the type-1 fimbrial protein (upec-1875), yapH homolog (upec-2820), and hemolysin A (recp-3768)), or such a homolog may be absent, but in both cases the polypeptide of the invention can be expressed from the plasmid. The plasmid may include a gene encoding a marker, *etc.* These and other details of suitable plasmids are given below.

Although expression of the polypeptides of the invention may take place in an *E.coli* strain, the invention will usually use a heterologous host for expression. The heterologous host may be prokaryotic (*e.g.* a bacterium) or eukaryotic. Suitable hosts include, but are not limited to, *Bacillus subtilis, Vibrio cholerae, Salmonella typhi, Salmonella typhimurium, Neisseria lactamica, Neisseria cinerea, Mycobacteria* (*e.g. M.tuberculosis*), yeasts, *etc.*

The invention provides a process for producing a polypeptide of the invention, comprising the step of synthesising at least part of the polypeptide by chemical means.

Any and all of the foregoing proteins, polypeptides, hybrid polypeptides, epitopes and immunogenic fragments may be in any one of a number of forms including, without limitation, recombinant, isolated or substantially purified (from materials co-existing with such proteins, polypeptides, hybrid polypeptides, epitopes and immunogenic fragments in their natural state).

Nucleic acids

The invention also provides nucleic acid encoding polypeptides and hybrid polypeptides of the invention. It also provides nucleic acid comprising a nucleotide sequence that encodes one or more polypeptides or hybrid polypeptides of the invention.

The invention also provides nucleic acid comprising nucleotide sequences having sequence identity to such nucleotide sequences. Identity between sequences is preferably determined by

the Smith-Waterman homology search algorithm as described above. Such nucleic acids include those using alternative codons to encode the same amino acid.

The invention also provides nucleic acid which can hybridize to these nucleic acids. Hybridization reactions can be performed under conditions of different "stringency". Conditions that increase stringency of a hybridization reaction of widely known and published in the art (*e.g.* page 7.52 of Sambrook *et al* (2001) *Molecular Cloning: A laboratory Manual*, 3rd edition (Cold Spring Harbor Laboratory Press). Examples of relevant conditions include (in order of increasing stringency): incubation temperatures of 25°C, 37°C, 50°C, 55°C and 68°C; buffer concentrations of 10 x SSC, 6 x SSC, 1 x SSC, 0.1 x SSC (where SSC is 0.15 M NaCl and 15 mM citrate buffer) and their equivalents using other buffer systems; formamide concentrations of 0%, 25%, 50%, and 75%; incubation times from 5 minutes to 24 hours; 1, 2, or more washing steps; wash incubation times of 1, 2, or 15 minutes; and wash solutions of 6 x SSC, 1 x SSC, 0.1 x SSC, or de-ionized water. Hybridization techniques and their optimization are well known in the art (*e.g.* see refs 25, 26, Sambrook *et al* (2001), *etc.*].

In some embodiments, nucleic acid of the invention hybridizes to a target under low stringency conditions; in other embodiments it hybridizes under intermediate stringency conditions; in preferred embodiments, it hybridizes under high stringency conditions. An exemplary set of low stringency hybridization conditions is 50°C and 10 x SSC. An exemplary set of intermediate stringency hybridization conditions is 55°C and 1 x SSC. An exemplary set of high stringency hybridization conditions is 68°C and 0.1 x SSC.

The invention includes nucleic acid comprising sequences complementary to these sequences (*e.g.* for antisense or probing, or for use as primers).

Nucleic acids of the invention can be used in hybridisation reactions (*e.g.* Northern or Southern blots, or in nucleic acid microarrays or 'gene chips') and amplification reactions (*e.g.* PCR, SDA, SSSR, LCR, TMA, NASBA, *etc.*) and other nucleic acid techniques.

Nucleic acid according to the invention can take various forms (*e.g.* single-stranded, double-stranded, vectors, primers, probes, labelled *etc.*). Nucleic acids of the invention may be circular or branched, but will generally be linear. Unless otherwise specified or required, any embodiment of the invention that utilizes a nucleic acid may utilize both the double-stranded form and each of two complementary single-stranded forms which make up the double-stranded form. Primers and probes are generally single-stranded, as are antisense nucleic acids.

Nucleic acids of the invention are preferably provided in purified or substantially purified form *i.e.* substantially free from other nucleic acids (*e.g.* free from naturally-occurring nucleic acids), particularly from other *E.coli* or host cell nucleic acids, generally being at least about 50% pure

(by weight), and usually at least about 90% pure. Nucleic acids of the invention are preferably *E.coli* nucleic acids.

Nucleic acids of the invention may be prepared in many ways *e.g.* by chemical synthesis (*e.g.* phosphoramidite synthesis of DNA) in whole or in part, by digesting longer nucleic acids using nucleases (*e.g.* restriction enzymes), by joining shorter nucleic acids or nucleotides (*e.g.* using ligases or polymerases), from genomic or cDNA libraries, *etc.*

Nucleic acid of the invention may be attached to a solid support (*e.g.* a bead, plate, filter, film, slide, microarray support, resin, *etc.*). Nucleic acid of the invention may be labelled *e.g.* with a radioactive or fluorescent label, or a biotin label. This is particularly useful where the nucleic acid is to be used in detection techniques *e.g.* where the nucleic acid is a primer or as a probe.

The term "nucleic acid" includes in general means a polymeric form of nucleotides of any length, which contain deoxyribonucleotides, ribonucleotides, and/or their analogs. It includes DNA, RNA, DNA/RNA hybrids. It also includes DNA or RNA analogs, such as those containing modified backbones (*e.g.* peptide nucleic acids (PNAs) or phosphorothioates) or modified bases. Thus the invention includes mRNA, tRNA, rRNA, ribozymes, DNA, cDNA, recombinant nucleic acids, branched nucleic acids, plasmids, vectors, probes, primers, *etc.*. Where nucleic acid of the invention takes the form of RNA, it may or may not have a 5' cap.

Nucleic acids of the invention may be part of a vector *i.e.* part of a nucleic acid construct designed for transduction/transfection of one or more cell types. Vectors may be, for example, "cloning vectors" which are designed for isolation, propagation and replication of inserted nucleotides, "expression vectors" which are designed for expression of a nucleotide sequence in a host cell, "viral vectors" which is designed to result in the production of a recombinant virus or virus-like particle, or "shuttle vectors", which comprise the attributes of more than one type of vector. Preferred vectors are plasmids, as mentioned above. A "host cell" includes an individual cell or cell culture which can be or has been a recipient of exogenous nucleic acid. Host cells include progeny of a single host cell, and the progeny may not necessarily be completely identical (in morphology or in total DNA complement) to the original parent cell due to natural, accidental, or deliberate mutation and/or change. Host cells include cells transfected or infected *in vivo* or *in vitro* with nucleic acid of the invention.

Where a nucleic acid is DNA, it will be appreciated that "U" in a RNA sequence will be replaced by "T" in the DNA. Similarly, where a nucleic acid is RNA, it will be appreciated that "T" in a DNA sequence will be replaced by "U" in the RNA.

The term "complement" or "complementary" when used in relation to nucleic acids refers to Watson-Crick base pairing. Thus the complement of C is G, the complement of G is C, the

complement of A is T (or U), and the complement of T (or U) is A. It is also possible to use bases such as I (the purine inosine) *e.g.* to complement pyrimidines (C or T).

Nucleic acids of the invention can be used, for example: to produce polypeptides; as hybridization probes for the detection of nucleic acid in biological samples; to generate additional copies of the nucleic acids; to generate ribozymes or antisense oligonucleotides; as single-stranded DNA primers or probes; or as triple-strand forming oligonucleotides.

The invention provides a process for producing nucleic acid of the invention, wherein the nucleic acid is synthesised in part or in whole using chemical means.

The invention provides vectors comprising nucleotide sequences of the invention (*e.g.* cloning or expression vectors) and host cells transformed with such vectors.

Nucleic acid amplification according to the invention may be quantitative and/or real-time.

For certain embodiments of the invention, nucleic acids are preferably at least 7 nucleotides in length (*e.g.* 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 45, 50, 55, 60, 65, 70, 75, 80, 90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, 225, 250, 275, 300 nucleotides or longer).

For certain embodiments of the invention, nucleic acids are preferably at most 500 nucleotides in length (*e.g.* 450, 400, 350, 300, 250, 200, 150, 140, 130, 120, 110, 100, 90, 80, 75, 70, 65, 60, 55, 50, 45, 40, 39, 38, 37, 36, 35, 34, 33, 32, 31, 30, 29, 28, 27, 26, 25, 24, 23, 22, 21, 20, 19, 18, 17, 16, 15 nucleotides or shorter).

Primers and probes of the invention, and other nucleic acids used for hybridization, are preferably between 10 and 30 nucleotides in length (*e.g.* 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 nucleotides).

Immunogenic compositions and medicaments

Polypeptides of the invention are useful as active ingredients (immunogens) in immunogenic compositions, and such compositions may be useful as vaccines. Vaccines according to the invention may either be prophylactic (*i.e.* to prevent infection) or therapeutic (*i.e.* to treat infection), but will typically be prophylactic.

Immunogenic compositions will be pharmaceutically acceptable. They will usually include components in addition to the antigens *e.g.* they typically include one or more pharmaceutical carrier(s), excipient(s) and/or adjuvant(s). A thorough discussion of carriers and excipients is available in ref.155. Thorough discussions of vaccine adjuvants are available in refs. 27 and 28.

Compositions will generally be administered to a mammal in aqueous form. Prior to administration, however, the composition may have been in a non-aqueous form. For instance,

although some vaccines are manufactured in aqueous form, then filled and distributed and administered also in aqueous form, other vaccines are lyophilised during manufacture and are reconstituted into an aqueous form at the time of use. Thus a composition of the invention may be dried, such as a lyophilised formulation.

The composition may include preservatives such as thiomersal or 2-phenoxyethanol. It is preferred, however, that the vaccine should be substantially free from (*i.e.* less than 5μg/ml) mercurial material *e.g.* thiomersal-free. Vaccines containing no mercury are more preferred. Preservative-free vaccines are particularly preferred.

To improve thermal stability, a composition may include a temperature protective agent.

To control tonicity, it is preferred to include a physiological salt, such as a sodium salt. Sodium chloride (NaCl) is preferred, which may be present at between 1 and 20 mg/ml *e.g.* about 10±2mg/ml NaCl. Other salts that may be present include potassium chloride, potassium dihydrogen phosphate, disodium phosphate dehydrate, magnesium chloride, calcium chloride, *etc.*

Compositions will generally have an osmolality of between 200 mOsm/kg and 400 mOsm/kg, preferably between 240-360 mOsm/kg, and will more preferably fall within the range of 290-310 mOsm/kg.

Compositions may include one or more buffers. Typical buffers include: a phosphate buffer; a Tris buffer; a borate buffer; a succinate buffer; a histidine buffer (particularly with an aluminum hydroxide adjuvant); or a citrate buffer. Buffers will typically be included in the 5-20mM range.

The pH of a composition will generally be between 5.0 and 8.1, and more typically between 6.0 and 8.0 *e.g.* 6.5 and 7.5, or between 7.0 and 7.8.

The composition is preferably sterile. The composition is preferably non-pyrogenic *e.g.* containing <1 EU (endotoxin unit, a standard measure) per dose, and preferably <0.1 EU per dose. The composition is preferably gluten free.

The composition may include material for a single immunisation, or may include material for multiple immunisations (*i.e.* a 'multidose' kit). The inclusion of a preservative is preferred in multidose arrangements. As an alternative (or in addition) to including a preservative in multidose compositions, the compositions may be contained in a container having an aseptic adaptor for removal of material.

Human vaccines are typically administered in a dosage volume of about 0.5ml, although a half dose (*i.e.* about 0.25ml) may be administered to children.

Immunogenic compositions of the invention may also comprise one or more immunoregulatory agents. Preferably, one or more of the immunoregulatory agents include one or more adjuvants. The adjuvants may include a TH1 adjuvant and/or a TH2 adjuvant, further discussed below.

Adjuvants which may be used in compositions of the invention include, but are not limited to:

A. Mineral-containing compositions

Mineral containing compositions suitable for use as adjuvants in the invention include mineral salts, such as aluminium salts and calcium salts (or mixtures thereof). Calcium salts include calcium phosphate (*e.g.* the "CAP" particles disclosed in ref. 29). Aluminum salts include hydroxides, phosphates, sulfates, *etc.*, with the salts taking any suitable form (*e.g.* gel, crystalline, amorphous, *etc.*). Adsorption to these salts is preferred. The mineral containing compositions may also be formulated as a particle of metal salt [30].

The adjuvants known as aluminum hydroxide and aluminum phosphate may be used. These names are conventional, but are used for convenience only, as neither is a precise description of the actual chemical compound which is present (*e.g.* see chapter 9 of reference 27). The invention can use any of the "hydroxide" or "phosphate" adjuvants that are in general use as adjuvants. The adjuvants known as "aluminium hydroxide" are typically aluminium oxyhydroxide salts, which are usually at least partially crystalline. The adjuvants known as "aluminium phosphate" are typically aluminium hydroxyphosphates, often also containing a small amount of sulfate (*i.e.* aluminium hydroxyphosphate sulfate). They may be obtained by precipitation, and the reaction conditions and concentrations during precipitation influence the degree of substitution of phosphate for hydroxyl in the salt.

A fibrous morphology (*e.g.* as seen in transmission electron micrographs) is typical for aluminium hydroxide adjuvants. The pI of aluminium hydroxide adjuvants is typically about 11 *i.e.* the adjuvant itself has a positive surface charge at physiological pH. Adsorptive capacities of between 1.8-2.6 mg protein per mg Al^{+++} at pH 7.4 have been reported for aluminium hydroxide adjuvants.

Aluminium phosphate adjuvants generally have a PO_4/Al molar ratio between 0.3 and 1.2, preferably between 0.8 and 1.2, and more preferably 0.95 ± 0.1. The aluminium phosphate will generally be amorphous, particularly for hydroxyphosphate salts. A typical adjuvant is amorphous aluminium hydroxyphosphate with PO_4/Al molar ratio between 0.84 and 0.92, included at 0.6mg Al^{3+}/ml. The aluminium phosphate will generally be particulate (*e.g.* plate-like morphology as seen in transmission electron micrographs). Typical diameters of the particles are in the range 0.5-20μm (*e.g.* about 5-10μm) after any antigen adsorption. Adsorptive capacities of between 0.7-1.5 mg protein per mg Al^{+++} at pH 7.4 have been reported for aluminium phosphate adjuvants.

The point of zero charge (PZC) of aluminium phosphate is inversely related to the degree of substitution of phosphate for hydroxyl, and this degree of substitution can vary depending on reaction conditions and concentration of reactants used for preparing the salt by precipitation. PZC is also altered by changing the concentration of free phosphate ions in solution (more phosphate = more acidic PZC) or by adding a buffer such as a histidine buffer (makes PZC more basic). Aluminium phosphates used according to the invention will generally have a PZC of between 4.0 and 7.0, more preferably between 5.0 and 6.5 *e.g.* about 5.7.

Suspensions of aluminium salts used to prepare compositions of the invention may contain a buffer (*e.g.* a phosphate or a histidine or a Tris buffer), but this is not always necessary. The suspensions are preferably sterile and pyrogen-free. A suspension may include free aqueous phosphate ions *e.g.* present at a concentration between 1.0 and 20 mM, preferably between 5 and 15 mM, and more preferably about 10 mM. The suspensions may also comprise sodium chloride.

The invention can use a mixture of both an aluminium hydroxide and an aluminium phosphate. In this case there may be more aluminium phosphate than hydroxide *e.g.* a weight ratio of at least 2:1 *e.g.* ≥5:1, ≥6:1, ≥7:1, ≥8:1, ≥9:1, *etc.*

The concentration of Al^{+++} in a composition for administration to a patient is preferably less than 10mg/ml *e.g.* ≤5 mg/ml, ≤4 mg/ml, ≤3 mg/ml, ≤2 mg/ml, ≤1 mg/ml, *etc.* A preferred range is between 0.3 and 1mg/ml. A maximum of 0.85mg/dose is preferred.

B. Oil Emulsions

Oil emulsion compositions suitable for use as adjuvants in the invention include squalene-water emulsions, such as MF59 [Chapter 10 of ref. 27; see also ref. 31] (5% Squalene, 0.5% Tween 80, and 0.5% Span 85, formulated into submicron particles using a microfluidizer). Complete Freund's adjuvant (CFA) and incomplete Freund's adjuvant (IFA) may also be used.

Various oil-in-water emulsion adjuvants are known, and they typically include at least one oil and at least one surfactant, with the oil(s) and surfactant(s) being biodegradable (metabolisable) and biocompatible. The oil droplets in the emulsion are generally less than 5μm in diameter, and ideally have a sub-micron diameter, with these small sizes being achieved with a microfluidiser to provide stable emulsions. Droplets with a size less than 220nm are preferred as they can be subjected to filter sterilization.

The emulsion can comprise oils such as those from an animal (such as fish) or vegetable source. Sources for vegetable oils include nuts, seeds and grains. Peanut oil, soybean oil, coconut oil, and olive oil, the most commonly available, exemplify the nut oils. Jojoba oil can be used *e.g.* obtained from the jojoba bean. Seed oils include safflower oil, cottonseed oil, sunflower seed oil, sesame seed oil and the like. In the grain group, corn oil is the most readily available, but the oil

of other cereal grains such as wheat, oats, rye, rice, teff, triticale and the like may also be used. 6-10 carbon fatty acid esters of glycerol and 1,2-propanediol, while not occurring naturally in seed oils, may be prepared by hydrolysis, separation and esterification of the appropriate materials starting from the nut and seed oils. Fats and oils from mammalian milk are metabolizable and may therefore be used in the practice of this invention. The procedures for separation, purification, saponification and other means necessary for obtaining pure oils from animal sources are well known in the art. Most fish contain metabolizable oils which may be readily recovered. For example, cod liver oil, shark liver oils, and whale oil such as spermaceti exemplify several of the fish oils which may be used herein. A number of branched chain oils are synthesized biochemically in 5-carbon isoprene units and are generally referred to as terpenoids. Shark liver oil contains a branched, unsaturated terpenoids known as squalene, 2,6,10,15,19,23-hexamethyl-2,6,10,14,18,22-tetracosahexaene, which is particularly preferred herein. Squalane, the saturated analog to squalene, is also a preferred oil. Fish oils, including squalene and squalane, are readily available from commercial sources or may be obtained by methods known in the art. Other preferred oils are the tocopherols (see below). Mixtures of oils can be used.

Surfactants can be classified by their 'HLB' (hydrophile/lipophile balance). Preferred surfactants of the invention have a HLB of at least 10, preferably at least 15, and more preferably at least 16. The invention can be used with surfactants including, but not limited to: the polyoxyethylene sorbitan esters surfactants (commonly referred to as the Tweens), especially polysorbate 20 and polysorbate 80; copolymers of ethylene oxide (EO), propylene oxide (PO), and/or butylene oxide (BO), sold under the DOWFAX™ tradename, such as linear EO/PO block copolymers; octoxynols, which can vary in the number of repeating ethoxy (oxy-1,2-ethanediyl) groups, with octoxynol-9 (Triton X-100, or t-octylphenoxypolyethoxyethanol) being of particular interest; (octylphenoxy)polyethoxyethanol (IGEPAL CA-630/NP-40); phospholipids such as phosphatidylcholine (lecithin); nonylphenol ethoxylates, such as the Tergitol™ NP series; polyoxyethylene fatty ethers derived from lauryl, cetyl, stearyl and oleyl alcohols (known as Brij surfactants), such as triethyleneglycol monolauryl ether (Brij 30); and sorbitan esters (commonly known as the SPANs), such as sorbitan trioleate (Span 85) and sorbitan monolaurate. Non-ionic surfactants are preferred. Preferred surfactants for including in the emulsion are Tween 80 (polyoxyethylene sorbitan monooleate), Span 85 (sorbitan trioleate), lecithin and Triton X-100.

Mixtures of surfactants can be used *e.g.* Tween 80/Span 85 mixtures. A combination of a polyoxyethylene sorbitan ester such as polyoxyethylene sorbitan monooleate (Tween 80) and an octoxynol such as t-octylphenoxypolyethoxyethanol (Triton X-100) is also suitable. Another useful combination comprises laureth 9 plus a polyoxyethylene sorbitan ester and/or an octoxynol.

Preferred amounts of surfactants (% by weight) are: polyoxyethylene sorbitan esters (such as Tween 80) 0.01 to 1%, in particular about 0.1 %; octyl- or nonylphenoxy polyoxyethanols (such as Triton X-100, or other detergents in the Triton series) 0.001 to 0.1 %, in particular 0.005 to 0.02%; polyoxyethylene ethers (such as laureth 9) 0.1 to 20 %, preferably 0.1 to 10 % and in particular 0.1 to 1 % or about 0.5%.

Preferred emulsion adjuvants have an average droplets size of <1μm *e.g.* ≤750nm, ≤500nm, ≤400nm, ≤300nm, ≤250nm, ≤220nm, ≤200nm, or smaller. These droplet sizes can conveniently be achieved by techniques such as microfluidisation.

Specific oil-in-water emulsion adjuvants useful with the invention include, but are not limited to:

- A submicron emulsion of squalene, Tween 80, and Span 85. The composition of the emulsion by volume can be about 5% squalene, about 0.5% polysorbate 80 and about 0.5% Span 85. In weight terms, these ratios become 4.3% squalene, 0.5% polysorbate 80 and 0.48% Span 85. This adjuvant is known as 'MF59' [32-33], as described in more detail in Chapter 10 of ref. 34 and chapter 12 of ref. 35. The MF59 emulsion advantageously includes citrate ions *e.g.* 10mM sodium citrate buffer.
- An emulsion of squalene, a tocopherol, and Tween 80. The emulsion may include phosphate buffered saline. It may also include Span 85 (*e.g.* at 1%) and/or lecithin. These emulsions may have from 2 to 10% squalene, from 2 to 10% tocopherol and from 0.3 to 3% Tween 80, and the weight ratio of squalene:tocopherol is preferably ≤1 as this provides a more stable emulsion. Squalene and Tween 80 may be present volume ratio of about 5:2. One such emulsion can be made by dissolving Tween 80 in PBS to give a 2% solution, then mixing 90ml of this solution with a mixture of (5g of DL-α-tocopherol and 5ml squalene), then microfluidising the mixture. The resulting emulsion may have submicron oil droplets *e.g.* with an average diameter of between 100 and 250nm, preferably about 180nm.
- An emulsion of squalene, a tocopherol, and a Triton detergent (*e.g.* Triton X-100). The emulsion may also include a 3d-MPL (see below). The emulsion may contain a phosphate buffer.
- An emulsion comprising a polysorbate (*e.g.* polysorbate 80), a Triton detergent (*e.g.* Triton X-100) and a tocopherol (*e.g.* an α-tocopherol succinate). The emulsion may include these three components at a mass ratio of about 75:11:10 (*e.g.* 750μg/ml polysorbate 80, 110μg/ml Triton X-100 and 100μg/ml α-tocopherol succinate), and these concentrations should include any contribution of these components from antigens. The emulsion may also include squalene. The emulsion may also include a 3d-MPL (see below). The aqueous phase may contain a phosphate buffer.

- An emulsion of squalane, polysorbate 80 and poloxamer 401 ("Pluronic™ L121"). The emulsion can be formulated in phosphate buffered saline, pH 7.4. This emulsion is a useful delivery vehicle for muramyl dipeptides, and has been used with threonyl-MDP in the "SAF-1" adjuvant [36] (0.05-1% Thr-MDP, 5% squalane, 2.5% Pluronic L121 and 0.2% polysorbate 80). It can also be used without the Thr-MDP, as in the "AF" adjuvant [37] (5% squalane, 1.25% Pluronic L121 and 0.2% polysorbate 80). Microfluidisation is preferred.

- An emulsion comprising squalene, an aqueous solvent, a polyoxyethylene alkyl ether hydrophilic nonionic surfactant (*e.g.* polyoxyethylene (12) cetostearyl ether) and a hydrophobic nonionic surfactant (*e.g.* a sorbitan ester or mannide ester, such as sorbitan monoleate or 'Span 80'). The emulsion is preferably thermoreversible and/or has at least 90% of the oil droplets (by volume) with a size less than 200 nm [38]. The emulsion may also include one or more of: alditol; a cryoprotective agent (*e.g.* a sugar, such as dodecylmaltoside and/or sucrose); and/or an alkylpolyglycoside. Such emulsions may be lyophilized.

- An emulsion of squalene, poloxamer 105 and Abil-Care [39]. The final concentration (weight) of these components in adjuvanted vaccines are 5% squalene, 4% poloxamer 105 (pluronic polyol) and 2% Abil-Care 85 (Bis-PEG/PPG-16/16 PEG/PPG-16/16 dimethicone; caprylic/capric triglyceride).

- An emulsion having from 0.5-50% of an oil, 0.1-10% of a phospholipid, and 0.05-5% of a non-ionic surfactant. As described in reference 40, preferred phospholipid components are phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine, phosphatidylinositol, phosphatidylglycerol, phosphatidic acid, sphingomyelin and cardiolipin. Submicron droplet sizes are advantageous.

- A submicron oil-in-water emulsion of a non-metabolisable oil (such as light mineral oil) and at least one surfactant (such as lecithin, Tween 80 or Span 80). Additives may be included, such as QuilA saponin, cholesterol, a saponin-lipophile conjugate (such as GPI-0100, described in reference 41, produced by addition of aliphatic amine to desacylsaponin via the carboxyl group of glucuronic acid), dimethyidioctadecylammonium bromide and/or N,N-dioctadecyl-N,N-bis (2-hydroxyethyl)propanediamine.

- An emulsion in which a saponin (*e.g.* QuilA or QS21) and a sterol (*e.g.* a cholesterol) are associated as helical micelles [42].

- An emulsion comprising a mineral oil, a non-ionic lipophilic ethoxylated fatty alcohol, and a non-ionic hydrophilic surfactant (*e.g.* an ethoxylated fatty alcohol and/or polyoxyethylene-polyoxypropylene block copolymer) [43].

- An emulsion comprising a mineral oil, a non-ionic hydrophilic ethoxylated fatty alcohol, and a non-ionic lipophilic surfactant (*e.g.* an ethoxylated fatty alcohol and/or polyoxyethylene-polyoxypropylene block copolymer) [43].

In some embodiments an emulsion may be mixed with antigen extemporaneously, at the time of delivery, and thus the adjuvant and antigen may be kept separately in a packaged or distributed vaccine, ready for final formulation at the time of use. In other embodiments an emulsion is mixed with antigen during manufacture, and thus the composition is packaged in a liquid adjuvanted form,. The antigen will generally be in an aqueous form, such that the vaccine is finally prepared by mixing two liquids. The volume ratio of the two liquids for mixing can vary (*e.g.* between 5:1 and 1:5) but is generally about 1:1. Where concentrations of components are given in the above descriptions of specific emulsions, these concentrations are typically for an undiluted composition, and the concentration after mixing with an antigen solution will thus decrease.

Where a composition includes a tocopherol, any of the α, β, γ, δ, ε or ξ tocopherols can be used, but α-tocopherols are preferred. The tocopherol can take several forms *e.g.* different salts and/or isomers. Salts include organic salts, such as succinate, acetate, nicotinate, *etc.* D-α-tocopherol and DL-α-tocopherol can both be used. Tocopherols are advantageously included in vaccines for use in elderly patients (*e.g.* aged 60 years or older) because vitamin E has been reported to have a positive effect on the immune response in this patient group [44]. They also have antioxidant properties that may help to stabilize the emulsions [45]. A preferred α-tocopherol is DL-α-tocopherol, and the preferred salt of this tocopherol is the succinate. The succinate salt has been found to cooperate with TNF-related ligands *in vivo*.

C. Saponin formulations [chapter 22 of ref. 27]

Saponin formulations may also be used as adjuvants in the invention. Saponins are a heterogeneous group of sterol glycosides and triterpenoid glycosides that are found in the bark, leaves, stems, roots and even flowers of a wide range of plant species. Saponin from the bark of the *Quillaia saponaria* Molina tree have been widely studied as adjuvants. Saponin can also be commercially obtained from *Smilax ornata* (sarsaprilla), *Gypsophilla paniculata* (brides veil), and *Saponaria officianalis* (soap root). Saponin adjuvant formulations include purified formulations, such as QS21, as well as lipid formulations, such as ISCOMs. QS21 is marketed as Stimulon™.

Saponin compositions have been purified using HPLC and RP-HPLC. Specific purified fractions using these techniques have been identified, including QS7, QS17, QS18, QS21, QH-A, QH-B and QH-C. Preferably, the saponin is QS21. A method of production of QS21 is disclosed in ref. 46. Saponin formulations may also comprise a sterol, such as cholesterol [47].

Combinations of saponins and cholesterols can be used to form unique particles called immunostimulating complexs (ISCOMs) [chapter 23 of ref. 27]. ISCOMs typically also include a phospholipid such as phosphatidylethanolamine or phosphatidylcholine. Any known saponin can be used in ISCOMs. Preferably, the ISCOM includes one or more of QuilA, QHA & QHC. ISCOMs are further described in refs. 47-48. Optionally, the ISCOMS may be devoid of additional detergent [49].

A review of the development of saponin based adjuvants can be found in refs. 50 & 51.

D. Virosomes and virus-like particles

Virosomes and virus-like particles (VLPs) can also be used as adjuvants in the invention. These structures generally contain one or more proteins from a virus optionally combined or formulated with a phospholipid. They are generally non-pathogenic, non-replicating and generally do not contain any of the native viral genome. The viral proteins may be recombinantly produced or isolated from whole viruses. These viral proteins suitable for use in virosomes or VLPs include proteins derived from influenza virus (such as HA or NA), Hepatitis B virus (such as core or capsid proteins), Hepatitis E virus, measles virus, Sindbis virus, Rotavirus, Foot-and-Mouth Disease virus, Retrovirus, Norwalk virus, human Papilloma virus, HIV, RNA-phages, Qß-phage (such as coat proteins), GA-phage, fr-phage, AP205 phage, and Ty (such as retrotransposon Ty protein p1). VLPs are discussed further in refs. 52-53. Virosomes are discussed further in, for example, ref. 54

E. Bacterial or microbial derivatives

Adjuvants suitable for use in the invention include bacterial or microbial derivatives such as non-toxic derivatives of enterobacterial lipopolysaccharide (LPS), Lipid A derivatives, immunostimulatory oligonucleotides and ADP-ribosylating toxins and detoxified derivatives thereof.

Non-toxic derivatives of LPS include monophosphoryl lipid A (MPL) and 3-O-deacylated MPL (3dMPL). 3dMPL is a mixture of 3 de-O-acylated monophosphoryl lipid A with 4, 5 or 6 acylated chains. A preferred "small particle" form of 3 De-O-acylated monophosphoryl lipid A is disclosed in ref. 55. Such "small particles" of 3dMPL are small enough to be sterile filtered through a 0.22μm membrane [55]. Other non-toxic LPS derivatives include monophosphoryl lipid A mimics, such as aminoalkyl glucosaminide phosphate derivatives *e.g.* RC-529 [56,57].

Lipid A derivatives include derivatives of lipid A from *Escherichia coli* such as OM-174. OM-174 is described for example in refs. 58 & 59.

Immunostimulatory oligonucleotides suitable for use as adjuvants in the invention include nucleotide sequences containing a CpG motif (a dinucleotide sequence containing an

unmethylated cytosine linked by a phosphate bond to a guanosine). Double-stranded RNAs and oligonucleotides containing palindromic or poly(dG) sequences have also been shown to be immunostimulatory.

The CpG's can include nucleotide modifications/analogs such as phosphorothioate modifications and can be double-stranded or single-stranded. References 60, 61 and 62 disclose possible analog substitutions *e.g.* replacement of guanosine with 2'-deoxy-7-deazaguanosine. The adjuvant effect of CpG oligonucleotides is further discussed in refs. 63-64.

The CpG sequence may be directed to TLR9, such as the motif GTCGTT or TTCGTT [65]. The CpG sequence may be specific for inducing a Th1 immune response, such as a CpG-A ODN, or it may be more specific for inducing a B cell response, such a CpG-B ODN. CpG-A and CpG-B ODNs are discussed in refs. 66-67. Preferably, the CpG is a CpG-A ODN.

Preferably, the CpG oligonucleotide is constructed so that the 5' end is accessible for receptor recognition. Optionally, two CpG oligonucleotide sequences may be attached at their 3' ends to form "immunomers". See, for example, refs. 65 & 68-69.

A useful CpG adjuvant is CpG7909, also known as ProMune™ (Coley Pharmaceutical Group, Inc.). Another is CpG1826. As an alternative, or in addition, to using CpG sequences, TpG sequences can be used [70], and these oligonucleotides may be free from unmethylated CpG motifs. The immunostimulatory oligonucleotide may be pyrimidine-rich. For example, it may comprise more than one consecutive thymidine nucleotide (*e.g.* TTTT, as disclosed in ref. 70), and/or it may have a nucleotide composition with >25% thymidine (*e.g.* >35%, >40%, >50%, >60%, >80%, *etc.*). For example, it may comprise more than one consecutive cytosine nucleotide (*e.g.* CCCC, as disclosed in ref. 70), and/or it may have a nucleotide composition with >25% cytosine (*e.g.* >35%, >40%, >50%, >60%, >80%, *etc.*). These oligonucleotides may be free from unmethylated CpG motifs. Immunostimulatory oligonucleotides will typically comprise at least 20 nucleotides. They may comprise fewer than 100 nucleotides.

A particularly useful adjuvant based around immunostimulatory oligonucleotides is known as IC-31™ [71]. Thus an adjuvant used with the invention may comprise a mixture of (i) an oligonucleotide (*e.g.* between 15-40 nucleotides) including at least one (and preferably multiple) CpI motifs (*i.e.* a cytosine linked to an inosine to form a dinucleotide), and (ii) a polycationic polymer, such as an oligopeptide (*e.g.* between 5-20 amino acids) including at least one (and preferably multiple) Lys-Arg-Lys tripeptide sequence(s). The oligonucleotide may be a deoxynucleotide comprising 26-mer sequence 5'-$(IC)_{13}$-3' (SEQ ID NO: 684). The polycationic polymer may be a peptide comprising 11-mer amino acid sequence KLKLLLLLKLK (SEQ ID NO: 685).

Bacterial ADP-ribosylating toxins and detoxified derivatives thereof may be used as adjuvants in the invention. Preferably, the protein is derived from *E.coli* (*E.coli* heat labile enterotoxin "LT"), cholera ("CT"), or pertussis ("PT"). The use of detoxified ADP-ribosylating toxins as mucosal adjuvants is described in ref. 72 and as parenteral adjuvants in ref. 73. The toxin or toxoid is preferably in the form of a holotoxin, comprising both A and B subunits. Preferably, the A subunit contains a detoxifying mutation; preferably the B subunit is not mutated. Preferably, the adjuvant is a detoxified LT mutant such as LT-K63, LT-R72, and LT-G192. The use of ADP-ribosylating toxins and detoxified derivatives thereof, particularly LT-K63 and LT-R72, as adjuvants can be found in refs. 74-75. A useful CT mutant is or CT-E29H [76]. Numerical reference for amino acid substitutions is preferably based on the alignments of the A and B subunits of ADP-ribosylating toxins set forth in ref. 77, specifically incorporated herein by reference in its entirety solely for the purpose of the alignment and amino acid numbering therein.

F. Human immunomodulators

Human immunomodulators suitable for use as adjuvants in the invention include cytokines, such as interleukins (*e.g.* IL-1, IL-2, IL-4, IL-5, IL-6, IL-7, IL-12 [78], *etc.*) [79], interferons (*e.g.* interferon-γ), macrophage colony stimulating factor, and tumor necrosis factor. A preferred immunomodulator is IL-12.

G. Bioadhesives and Mucoadhesives

Bioadhesives and mucoadhesives may also be used as adjuvants in the invention. Suitable bioadhesives include esterified hyaluronic acid microspheres [80] or mucoadhesives such as cross-linked derivatives of poly(acrylic acid), polyvinyl alcohol, polyvinyl pyrollidone, polysaccharides and carboxymethylcellulose. Chitosan and derivatives thereof may also be used as adjuvants in the invention [81].

H. Microparticles

Microparticles may also be used as adjuvants in the invention. Microparticles (*i.e.* a particle of ~100nm to ~150μm in diameter, more preferably ~200nm to ~30μm in diameter, and most preferably ~500nm to ~10μm in diameter) formed from materials that are biodegradable and non-toxic (*e.g.* a poly(α-hydroxy acid), a polyhydroxybutyric acid, a polyorthoester, a polyanhydride, a polycaprolactone, *etc.*), with poly(lactide-co-glycolide) are preferred, optionally treated to have a negatively-charged surface (*e.g.* with SDS) or a positively-charged surface (*e.g.* with a cationic detergent, such as CTAB).

I. Liposomes (Chapters 13 & 14 of ref. 27)

Examples of liposome formulations suitable for use as adjuvants are described in refs. 82-83.

J. Polyoxyethylene ether and polyoxyethylene ester formulations

Adjuvants suitable for use in the invention include polyoxyethylene ethers and polyoxyethylene esters [84]. Such formulations further include polyoxyethylene sorbitan ester surfactants in combination with an octoxynol [85] as well as polyoxyethylene alkyl ethers or ester surfactants in combination with at least one additional non-ionic surfactant such as an octoxynol [86]. Preferred polyoxyethylene ethers are selected from the following group: polyoxyethylene-9-lauryl ether (laureth 9), polyoxyethylene-9-steoryl ether, polyoxytheylene-8-steoryl ether, polyoxyethylene-4-lauryl ether, polyoxyethylene-35-lauryl ether, and polyoxyethylene-23-lauryl ether.

K. Phosphazenes

A phosphazene, such as poly[di(carboxylatophenoxy)phosphazene] ("PCPP") as described, for example, in references 87 and 88, may be used.

L. Muramyl peptides

Examples of muramyl peptides suitable for use as adjuvants in the invention include N-acetyl-muramyl-L-threonyl-D-isoglutamine (thr-MDP), N-acetyl-normuramyl-L-alanyl-D-isoglutamine (nor-MDP), and N-acetylmuramyl-L-alanyl-D-isoglutaminyl-L-alanine-2-(1'-2'-dipalmitoyl-*sn*-glycero-3-hydroxyphosphoryloxy)-ethylamine MTP-PE).

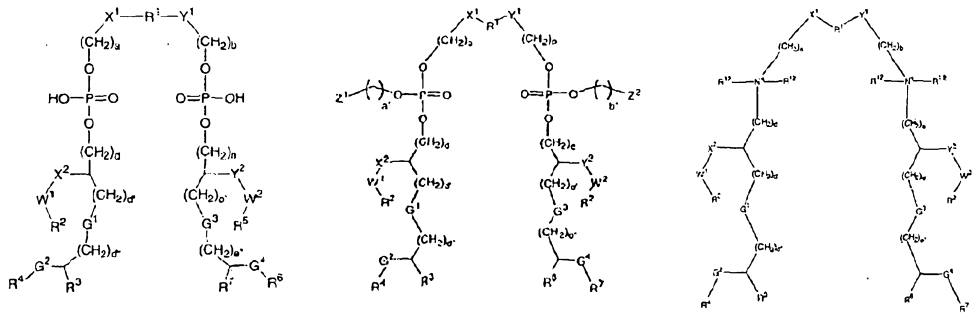
M. Imidazoquinolone Compounds.

Examples of imidazoquinolone compounds suitable for use adjuvants in the invention include Imiquimod ("R-837") [89,90], Resiquimod ("R-848") [91], and their analogs; and salts thereof (*e.g.* the hydrochloride salts). Further details about immunostimulatory imidazoquinolines can be found in references 92 to93.

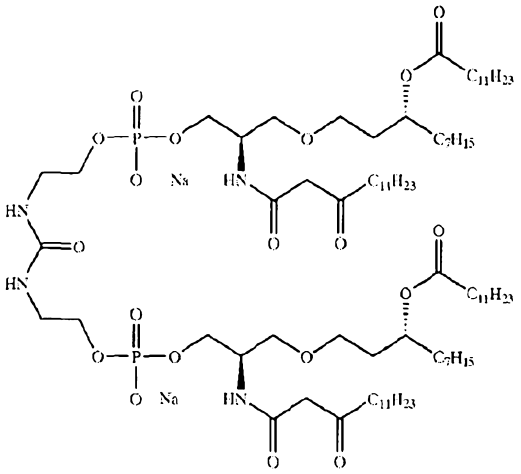
N. Substituted ureas

Substituted ureas useful as adjuvants include compounds of formula I, II or III, or salts thereof:

I II III



as defined in reference 94, such as 'ER 803058', 'ER 803732', 'ER 804053', ER 804058', 'ER 804059', 'ER 804442', 'ER 804680', 'ER 804764', ER 803022 or 'ER 804057' *e.g.*:



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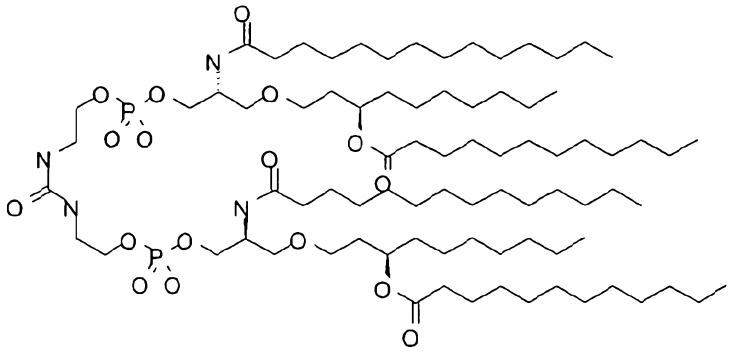

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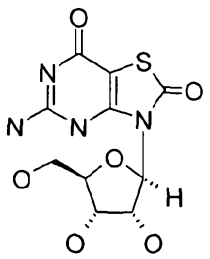
O. Further adjuvants

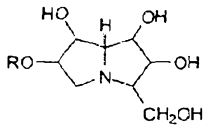
Further adjuvants that may be used with the invention include:

- An aminoalkyl glucosaminide phosphate derivative, such as RC-529 [95,96].
- A thiosemicarbazone compound, such as those disclosed in reference 97. Methods of formulating, manufacturing, and screening for active compounds are also described in reference 97. The thiosemicarbazones are particularly effective in the stimulation of human peripheral blood mononuclear cells for the production of cytokines, such as TNF-α.
- A tryptanthrin compound, such as those disclosed in reference 98. Methods of formulating, manufacturing, and screening for active compounds are also described in reference 98. The thiosemicarbazones are particularly effective in the stimulation of human peripheral blood mononuclear cells for the production of cytokines, such as TNF-α.
- A nucleoside analog, such as: (a) Isatorabine (ANA-245; 7-thia-8-oxoguanosine):



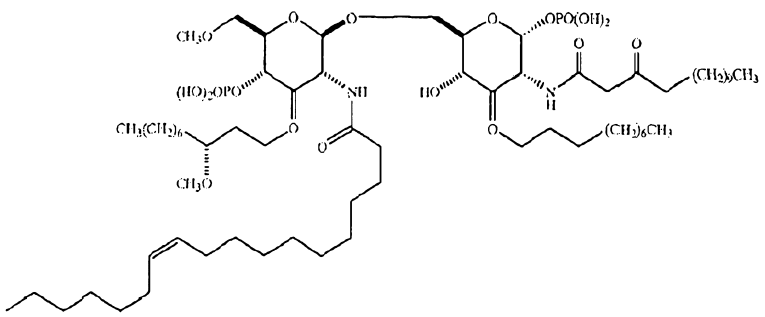
and prodrugs thereof; (b) ANA975; (c) ANA-025-1; (d) ANA380; (e) the compounds disclosed in references 99 to100Loxoribine (7-allyl-8-oxoguanosine) [101].

- Compounds disclosed in reference 102, including: Acylpiperazine compounds, Indoledione compounds, Tetrahydraisoquinoline (THIQ) compounds, Benzocyclodione compounds, Aminoazavinyl compounds, Aminobenzimidazole quinolinone (ABIQ) compounds [103,104], Hydrapthalamide compounds, Benzophenone compounds, Isoxazole compounds, Sterol compounds, Quinazilinone compounds, Pyrrole compounds [105], Anthraquinone compounds, Quinoxaline compounds, Triazine compounds, Pyrazalopyrimidine compounds, and Benzazole compounds [106].
- Compounds containing lipids linked to a phosphate-containing acyclic backbone, such as the TLR4 antagonist E5564 [107,108]:
- A polyoxidonium polymer [109,110] or other N-oxidized polyethylene-piperazine derivative.
- Methyl inosine 5'-monophosphate ("MIMP") [111].
- A polyhydroxlated pyrrolizidine compound [112], such as one having formula:



where R is selected from the group comprising hydrogen, straight or branched, unsubstituted or substituted, saturated or unsaturated acyl, alkyl (*e.g.* cycloalkyl), alkenyl, alkynyl and aryl groups, or a pharmaceutically acceptable salt or derivative thereof. Examples include, but are not limited to: casuarine, casuarine-6-α-D-glucopyranose, 3-*epi*-casuarine, 7-*epi*-casuarine, 3,7-di*epi*-casuarine, *etc.*

- A CD1d ligand, such as an α-glycosylceramide [113-114] (*e.g.* α-galactosylceramide), phytosphingosine-containing α-glycosylceramides, OCH, KRN7000 [(2S,3S,4R)-1-O-(α-D-galactopyranosyl)-2-(N-hexacosanoylamino)-1,3,4-octadecanetriol], CRONY-101, 3"-O-sulfo-galactosylceramide, *etc.*
- A gamma inulin [115] or derivative thereof, such as algammulin.



Adjuvant combinations

The invention may also comprise combinations of aspects of one or more of the adjuvants identified above. For example, the following adjuvant compositions may be used in the invention: (1) a saponin and an oil-in-water emulsion [116]; (2) a saponin (*e.g.* QS21) + a non-toxic LPS derivative (*e.g.* 3dMPL) [117]; (3) a saponin (*e.g.* QS21) + a non-toxic LPS derivative (*e.g.* 3dMPL) + a cholesterol; (4) a saponin (*e.g.* QS21) + 3dMPL + IL-12 (optionally + a sterol) [118]; (5) combinations of 3dMPL with, for example, QS21 and/or oil-in-water emulsions [119]; (6) SAF, containing 10% squalane, 0.4% Tween 80™, 5% pluronic-block polymer L121, and thr-MDP, either microfluidized into a submicron emulsion or vortexed to generate a larger particle size emulsion. (7) Ribi™ adjuvant system (RAS), (Ribi Immunochem) containing 2% squalene, 0.2% Tween 80, and one or more bacterial cell wall components from the group consisting of monophosphorylipid A (MPL), trehalose dimycolate (TDM), and cell wall skeleton (CWS), preferably MPL + CWS (Detox™); and (8) one or more mineral salts (such as an aluminum salt) + a non-toxic derivative of LPS (such as 3dMPL).

Other substances that act as immunostimulating agents are disclosed in chapter 7 of ref. 27.

The use of an aluminium hydroxide and/or aluminium phosphate adjuvant is particularly preferred, and antigens are generally adsorbed to these salts. Calcium phosphate is another preferred adjuvant. Other preferred adjuvant combinations include combinations of Th1 and Th2 adjuvants such as CpG & alum or resiquimod & alum. A combination of aluminium phosphate and 3dMPL may be used.

The compositions of the invention may elicit both a cell mediated immune response as well as a humoral immune response. This immune response will preferably induce long lasting (*e.g.* neutralising) antibodies and a cell mediated immunity that can quickly respond upon exposure to pnuemococcus.

Two types of T cells, CD4 and CD8 cells, are generally thought necessary to initiate and/or enhance cell mediated immunity and humoral immunity. CD8 T cells can express a CD8

co-receptor and are commonly referred to as Cytotoxic T lymphocytes (CTLs). CD8 T cells are able to recognized or interact with antigens displayed on MHC Class I molecules.

CD4 T cells can express a CD4 co-receptor and are commonly referred to as T helper cells. CD4 T cells are able to recognize antigenic peptides bound to MHC class II molecules. Upon interaction with a MHC class II molecule, the CD4 cells can secrete factors such as cytokines. These secreted cytokines can activate B cells, cytotoxic T cells, macrophages, and other cells that participate in an immune response. Helper T cells or CD4+ cells can be further divided into two functionally distinct subsets: TH1 phenotype and TH2 phenotypes which differ in their cytokine and effector function.

Activated TH1 cells enhance cellular immunity (including an increase in antigen-specific CTL production) and are therefore of particular value in responding to intracellular infections. Activated TH1 cells may secrete one or more of IL-2, IFN-γ, and TNF-β. A TH1 immune response may result in local inflammatory reactions by activating macrophages, NK (natural killer) cells, and CD8 cytotoxic T cells (CTLs). A TH1 immune response may also act to expand the immune response by stimulating growth of B and T cells with IL-12. TH1 stimulated B cells may secrete IgG2a.

Activated TH2 cells enhance antibody production and are therefore of value in responding to extracellular infections. Activated TH2 cells may secrete one or more of IL-4, IL-5, IL-6, and IL-10. A TH2 immune response may result in the production of IgG1, IgE, IgA and memory B cells for future protection.

An enhanced immune response may include one or more of an enhanced TH1 immune response and a TH2 immune response.

A TH1 immune response may include one or more of an increase in CTLs, an increase in one or more of the cytokines associated with a TH1 immune response (such as IL-2, IFN-γ, and TNF-β), an increase in activated macrophages, an increase in NK activity, or an increase in the production of IgG2a. Preferably, the enhanced TH1 immune response will include an increase in IgG2a production.

A TH1 immune response may be elicited using a TH1 adjuvant. A TH1 adjuvant will generally elicit increased levels of IgG2a production relative to immunization of the antigen without adjuvant. TH1 adjuvants suitable for use in the invention may include for example saponin formulations, virosomes and virus like particles, non-toxic derivatives of enterobacterial lipopolysaccharide (LPS), immunostimulatory oligonucleotides. Immunostimulatory oligonucleotides, such as oligonucleotides containing a CpG motif, are preferred TH1 adjuvants for use in the invention.

A TH2 immune response may include one or more of an increase in one or more of the cytokines associated with a TH2 immune response (such as IL-4, IL-5, IL-6 and IL-10), or an increase in the production of IgG1, IgE, IgA and memory B cells. Preferably, the enhanced TH2 immune resonse will include an increase in IgG1 production.

A TH2 immune response may be elicited using a TH2 adjuvant. A TH2 adjuvant will generally elicit increased levels of IgG1 production relative to immunization of the antigen without adjuvant. TH2 adjuvants suitable for use in the invention include, for example, mineral containing compositions, oil-emulsions, and ADP-ribosylating toxins and detoxified derivatives thereof. Mineral containing compositions, such as aluminium salts are preferred TH2 adjuvants for use in the invention.

Preferably, the invention includes a composition comprising a combination of a TH1 adjuvant and a TH2 adjuvant. Preferably, such a composition elicits an enhanced TH1 and an enhanced TH2 response, i.e., an increase in the production of both IgG1 and IgG2a production relative to immunization without an adjuvant. Still more preferably, the composition comprising a combination of a TH1 and a TH2 adjuvant elicits an increased TH1 and/or an increased TH2 immune response relative to immunization with a single adjuvant (*i.e.*, relative to immunization with a TH1 adjuvant alone or immunization with a TH2 adjuvant alone).

The immune response may be one or both of a TH1 immune response and a TH2 response. Preferably, immune response provides for one or both of an enhanced TH1 response and an enhanced TH2 response.

The enhanced immune response may be one or both of a systemic and a mucosal immune response. Preferably, the immune response provides for one or both of an enhanced systemic and an enhanced mucosal immune response. Preferably the mucosal immune response is a TH2 immune response. Preferably, the mucosal immune response includes an increase in the production of IgA.

E.coli can cause disease at a number of anatomical locations [4] and so the 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 in, or suspension in, liquid vehicles prior to injection can also be prepared (*e.g.* a lyophilised composition or a spray-freeze dried composition). 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. Such kits may comprise one or more antigens in liquid form and one or more lyophilised antigens.

Where a composition is to be prepared extemporaneously prior to use (*e.g.* where a component is presented in lyophilised form) and is presented as a kit, the kit may comprise two vials, or it may comprise one ready-filled syringe and one vial, with the contents of the syringe being used to reactivate the contents of the vial prior to injection.

Immunogenic compositions used as vaccines comprise an immunologically effective amount of antigen(s), as well as any other components, as needed. By 'immunologically effective amount', it is meant that the administration of that amount to an individual, either in a single dose or as part of a series, is effective for treatment or prevention. This amount varies depending upon the health and physical condition of the individual to be treated, age, the taxonomic group of individual to be treated (*e.g.* non-human primate, primate, *etc.*), the capacity of the individual's immune system to synthesise antibodies, the degree of protection desired, the formulation of the vaccine, the treating doctor's assessment of the medical situation, and other relevant factors. It is expected that the amount will fall in a relatively broad range that can be determined through routine trials.

Methods of treatment, and administration of the vaccine

The invention also provides a method for raising an immune response in a mammal comprising the step of administering an effective amount of a composition of the invention. The immune response is preferably protective and preferably involves antibodies and/or cell-mediated immunity. The method may raise a booster response.

The invention also provides a polypeptide of the invention for use as a medicament *e.g.* for use in raising an immune response in a mammal.

The invention also provides the use of a polypeptide of the invention in the manufacture of a medicament for raising an immune response in a mammal.

The invention also provides a delivery device pre-filled with an immunogenic composition of the invention.

By raising an immune response in the mammal by these uses and methods, the mammal can be protected against *E.coli* infection, including ExPEC and non-ExPEC strains. The invention is particularly useful for providing broad protection against pathogenic *E.coli*, including intestinal pathotypes such as EPEC, EAEC, EIEC, ETEC and DAEC pathotypes. Thus the mammal may be protected against diseases including, but not limited to peritonitis, pyelonephritis, cystitis, endocarditis, prostatitis, urinary tract infections (UTIs), meningitis (particularly neonatal

meningitis), sepsis (or SIRS), dehydration, pneumonia, diarrhea (infantile, travellers', acute, persistent, *etc.*), bacillary dysentery, hemolytic uremic syndrome (HUS), pericarditis, bacteriuria, *etc.*

The mammal is preferably a human, but may be *e.g.* a cow, a pig, a chicken, a cat or a dog, as *E.coli* disease is also problematic in these species [4]. Where the vaccine is for prophylactic use, the human is preferably a child (*e.g.* a toddler or infant) or a teenager; where the vaccine is for therapeutic use, the human is preferably a teenager or an adult. A vaccine intended for children may also be administered to adults *e.g.* to assess safety, dosage, immunogenicity, *etc.*

One way of checking efficacy of therapeutic treatment involves monitoring *E.coli* infection after administration of the compositions of the invention. One way of checking efficacy of prophylactic treatment involves monitoring immune responses, systemically (such as monitoring the level of IgG1 and IgG2a production) and/or mucosally (such as monitoring the level of IgA production), against the antigens in the compositions of the invention after administration of the composition. Typically, antigen-specific serum antibody responses are determined post-immunisation but pre-challenge whereas antigen-specific mucosal antibody responses are determined post-immunisation and post-challenge.

Another way of assessing the immunogenicity of the compositions of the present invention is to express the proteins recombinantly for screening patient sera or mucosal secretions by immunoblot and/or microarrays. A positive reaction between the protein and the patient sample indicates that the patient has mounted an immune response to the protein in question. This method may also be used to identify immunodominant antigens and/or epitopes within antigens.

The efficacy of vaccine compositions can also be determined *in vivo* by challenging animal models of *E.coli* infection, *e.g.*, guinea pigs or mice, with the vaccine compositions. A murine model of ExPEC and lethal sepsis is described in reference 120. A cotton rat model is disclosed in ref. 121

Compositions of the invention will generally be administered directly to a patient. Direct delivery may be accomplished by parenteral injection (*e.g.* subcutaneously, intraperitoneally, intravenously, intramuscularly, or to the interstitial space of a tissue), or mucosally, such as by rectal, oral (*e.g.* tablet, spray), vaginal, topical, transdermal or transcutaneous, intranasal, ocular, aural, pulmonary or other mucosal administration. Novel direct delivery forms can also include transgenic expression of the polypeptides disclosed herein in foods, e.g., transgenic expression in a potato.

The invention may be used to elicit systemic and/or mucosal immunity, preferably to elicit an enhanced systemic and/or mucosal immunity.

Preferably the enhanced systemic and/or mucosal immunity is reflected in an enhanced TH1 and/or TH2 immune response. Preferably, the enhanced immune response includes an increase in the production of IgG1 and/or IgG2a and/or IgA.

Dosage can be by a single dose schedule or a multiple dose schedule. Multiple doses may be used in a primary immunisation schedule and/or in a booster immunisation schedule. In a multiple dose schedule the various doses may be given by the same or different routes *e.g.* a parenteral prime and mucosal boost, a mucosal prime and parenteral boost, *etc.* Multiple doses will typically be administered at least 1 week apart (*e.g.* about 2 weeks, about 3 weeks, about 4 weeks, about 6 weeks, about 8 weeks, about 10 weeks, about 12 weeks, about 16 weeks, *etc.*).

Vaccines of the invention may be used to treat both children and adults. Thus a human patient may be less than 1 year old, 1-5 years old, 5-15 years old, 15-55 years old, or at least 55 years old. Preferred patients for receiving the vaccines are the elderly (*e.g.* ≥50 years old, ≥60 years old, and preferably ≥65 years), the young (*e.g.* ≤5 years old), hospitalised patients, healthcare workers, armed service and military personnel, pregnant women, the chronically ill, or immunodeficient patients. The vaccines are not suitable solely for these groups, however, and may be used more generally in a population.

Vaccines of the invention are particularly useful for patients who are expecting a surgical operation, or other hospital in-patients. They are also useful in patients who will be catheterized. They are also useful in adolescent females (*e.g.* aged 11-18) and in patients with chronic urinary tract infections.

Vaccines of the invention may be administered to patients at substantially the same time as (*e.g.* during the same medical consultation or visit to a healthcare professional or vaccination centre) other vaccines *e.g.* at substantially the same time as a measles vaccine, a mumps vaccine, a rubella vaccine, a MMR vaccine, a varicella vaccine, a MMRV vaccine, a diphtheria vaccine, a tetanus vaccine, a pertussis vaccine, a DTP vaccine, a conjugated *H.influenzae* type b vaccine, an inactivated poliovirus vaccine, a hepatitis B virus vaccine, a meningococcal conjugate vaccine (such as a tetravalent A-C-W135-Y vaccine), a respiratory syncytial virus vaccine, *etc.*

Nucleic acid immunisation

The immunogenic compositions described above include polypeptide antigens. In all cases, however, the polypeptide antigens can be replaced by nucleic acids (typically DNA) encoding those polypeptides, to give compositions, methods and uses based on nucleic acid immunisation. Nucleic acid immunisation is now a developed field (*e.g.* see references 122 to123 *etc.*).

The nucleic acid encoding the immunogen is expressed *in vivo* after delivery to a patient and the expressed immunogen then stimulates the immune system. The active ingredient will typically

take the form of a nucleic acid vector comprising: (i) a promoter; (ii) a sequence encoding the immunogen, operably linked to the promoter; and optionally (iii) a selectable marker. Preferred vectors may further comprise (iv) an origin of replication; and (v) a transcription terminator downstream of and operably linked to (ii). In general, (i) & (v) will be eukaryotic and (iii) & (iv) will be prokaryotic.

Preferred promoters are viral promoters *e.g.* from cytomegalovirus (CMV). The vector may also include transcriptional regulatory sequences (*e.g.* enhancers) in addition to the promoter and which interact functionally with the promoter. Preferred vectors include the immediate-early CMV enhancer/promoter, and more preferred vectors also include CMV intron A. The promoter is operably linked to a downstream sequence encoding an immunogen, such that expression of the immunogen-encoding sequence is under the promoter's control.

Where a marker is used, it preferably functions in a microbial host (*e.g.* in a prokaryote, in a bacteria, in a yeast). The marker is preferably a prokaryotic selectable marker (*e.g.* transcribed under the control of a prokaryotic promoter). For convenience, typical markers are antibiotic resistance genes.

The vector of the invention is preferably an autonomously replicating episomal or extrachromosomal vector, such as a plasmid.

The vector of the invention preferably comprises an origin of replication. It is preferred that the origin of replication is active in prokaryotes but not in eukaryotes.

Preferred vectors thus include a prokaryotic marker for selection of the vector, a prokaryotic origin of replication, but a *eukaryotic* promoter for driving transcription of the immunogen-encoding sequence. The vectors will therefore (a) be amplified and selected in prokaryotic hosts without polypeptide expression, but (b) be expressed in eukaryotic hosts without being amplified. This arrangement is ideal for nucleic acid immunization vectors.

The vector of the invention may comprise a eukaryotic transcriptional terminator sequence downstream of the coding sequence. This can enhance transcription levels. Where the coding sequence does not have its own, the vector of the invention preferably comprises a polyadenylation sequence. A preferred polyadenylation sequence is from bovine growth hormone.

The vector of the invention may comprise a multiple cloning site

In addition to sequences encoding the immunogen and a marker, the vector may comprise a second eukaryotic coding sequence. The vector may also comprise an IRES upstream of said second sequence in order to permit translation of a second eukaryotic polypeptide from the same

transcript as the immunogen. Alternatively, the immunogen-coding sequence may be downstream of an IRES.

The vector of the invention may comprise unmethylated CpG motifs *e.g.* unmethylated DNA sequences which have in common a cytosine preceding a guanosine, flanked by two 5' purines and two 3' pyrimidines. In their unmethylated form these DNA motifs have been demonstrated to be potent stimulators of several types of immune cell.

Vectors may be delivered in a targeted way. Receptor-mediated DNA delivery techniques are described in, for example, references 124 to125. Therapeutic compositions containing a nucleic acid are administered in a range of about 100ng to about 200mg of DNA for local administration in a gene therapy protocol. Concentration ranges of about 500 ng to about 50 mg, about 1μg to about 2 mg, about 5μg to about 500μg, and about 20μg to about 100μg of DNA can also be used during a gene therapy protocol. Factors such as method of action (*e.g.* for enhancing or inhibiting levels of the encoded gene product) and efficacy of transformation and expression are considerations which will affect the dosage required for ultimate efficacy. Where greater expression is desired over a larger area of tissue, larger amounts of vector or the same amounts re-administered in a successive protocol of administrations, or several administrations to different adjacent or close tissue portions may be required to effect a positive therapeutic outcome. In all cases, routine experimentation in clinical trials will determine specific ranges for optimal therapeutic effect.

Vectors can be delivered using gene delivery vehicles. The gene delivery vehicle can be of viral or non-viral origin (see generally references 126 to127).

Viral-based vectors for delivery of a desired nucleic acid and expression in a desired cell are well known in the art. Exemplary viral-based vehicles include, but are not limited to, recombinant retroviruses (*e.g.* references 128 to129), alphavirus-based vectors (*e.g.* Sindbis virus vectors, Semliki forest virus (ATCC VR-67; ATCC VR-1247), Ross River virus (ATCC VR-373; ATCC VR-1246) and Venezuelan equine encephalitis virus (ATCC VR-923; ATCC VR-1250; ATCC VR 1249; ATCC VR-532); hybrids or chimeras of these viruses may also be used), poxvirus vectors (*e.g.* vaccinia, fowlpox, canarypox, modified vaccinia Ankara, *etc.*), adenovirus vectors, and adeno-associated virus (AAV) vectors (*e.g.* see refs. 130 to131). Administration of DNA linked to killed adenovirus [132] can also be employed.

Non-viral delivery vehicles and methods can also be employed, including, but not limited to, polycationic condensed DNA linked or unlinked to killed adenovirus alone [*e.g.* 132], ligand-linked DNA [133], eukaryotic cell delivery vehicles cells [*e.g.* refs. 134 to135] and nucleic charge neutralization or fusion with cell membranes. Naked DNA can also be employed. Exemplary naked DNA introduction methods are described in refs. 136 and 137. Liposomes (*e.g.*

immunoliposomes) that can act as gene delivery vehicles are described in refs. 138 to139. Additional approaches are described in references 140 & 141.

Further non-viral delivery suitable for use includes mechanical delivery systems such as the approach described in ref. 141. Moreover, the coding sequence and the product of expression of such can be delivered through deposition of photopolymerized hydrogel materials or use of ionizing radiation [*e.g.* refs. 142 & 143]. Other conventional methods for gene delivery that can be used for delivery of the coding sequence include, for example, use of hand-held gene transfer particle gun [144] or use of ionizing radiation for activating transferred genes [142 & 143].

Delivery DNA using PLG {poly(lactide-co-glycolide)} microparticles is a particularly preferred method *e.g.* by adsorption to the microparticles, which are optionally treated to have a negatively-charged surface (*e.g.* treated with SDS) or a positively-charged surface (*e.g.* treated with a cationic detergent, such as CTAB).

Antibodies

Antibodies against *E.coli* antigens can be used for passive immunisation [145]. Thus the invention provides an antibody that binds to both orf353 proteins that consist of SEQ ID NOs: 1-2. In certain embodiments, the antibody will bind a fragment of orf353 selected from the group consisting of SEQ ID NOs: 211-218.

The invention also provides an antibody that binds to at least 2 (*e.g.* to 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or all 16) of the 16 bacterial Ig-like domain (group 1) proteins (orf405) that consist of SEQ ID NOs: 3-18. In certain embodiments, the antibody will bind a fragment of bacterial Ig-like domain (group 1) protein (orf405) selected from the group consisting of SEQ ID NOs: 219-307 & 683.

The invention also provides an antibody that binds to at least 2 (*e.g.* to 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or all 16) of the 22 flu antigen 43 (orf1364) proteins that consist of SEQ ID NOs: 19-40. In certain embodiments, the antibody will bind a fragment of flu antigen 43 (orf1364) selected from the group consisting of SEQ ID NOs: 308-350.

The invention also provides an antibody that binds to at least 2 (*e.g.* to 3, 4, 5, 6, or all 7) of the 7 NodT-family outer-membrane-factor-lipoprotein efflux transporters (orf1767) that consist of SEQ ID NOs: 41-47. In certain embodiments, the antibody will bind a fragment of NodT-family outer-membrane-factor-lipoprotein efflux transporter (orf1767) selected from the group consisting of SEQ ID NOs: 351-368.

The invention also provides an antibody that binds to at least 2 (*e.g.* to 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or all 13) of the 13 gspK proteins (orf3515) that consist of SEQ ID NOs: 48-60. In certain

embodiments, the antibody will bind a fragment of gspK (orf3515) selected from the group consisting of SEQ ID NOs: 369-384.

The invention also provides an antibody that binds to at least 2 (*e.g.* to 3, 4, 5, 6, 7, 8, 9, 10, or all 11) of the 11 gspJ proteins (orf3516) that consist of SEQ ID NOs: 61-71. In certain embodiments, the antibody will bind a fragment of gspJ (orf3516) selected from the group consisting of SEQ ID NOs: 385-398.

The invention also provides an antibody that binds to at least 2 (*e.g.* to 3, 4, 5, 6, 7, or all 8) of the 8 tonB-dependent siderophore receptors (orf3597) that consist of SEQ ID NOs: 72-79. In certain embodiments, the antibody will bind a fragment of tonB-dependent siderophore receptor (orf3597) selected from the group consisting of SEQ ID NOs: 399-425.

The invention also provides an antibody that binds to both the fibrial proteins (orf3613) that consist of SEQ ID NOs: 80-81. In certain embodiments, the antibody will bind a fragment of a fibrial protein (orf3613) selected from the group consisting of SEQ ID NO: 426-432.

The invention also provides an antibody that binds to at least 2 (or all 3) of the 3 upec-948 proteins that consist of SEQ ID NOs: 82-84. In certain embodiments, the antibody will bind a fragment of upec-948 selected from the group consisting of SEQ ID NOs: 493-499.

The invention also provides an antibody that binds to at least 2 (*e.g.* to 3, 4, 5, 6, or all 7) of the 7 upec-1232 proteins that consist of SEQ ID NOs: 85-91. In certain embodiments, the antibody will bind a fragment of upec-1232 selected from the group consisting of SEQ ID NOs: 500-506.

The invention also provides an antibody that binds to at least 2 (*e.g.* to 3, 4, 5, 6, or all 7) of the 7 A chain precursor of the type-1 fimbrial proteins (upec-1875) that consist of SEQ ID NOs: 92-98. In certain embodiments, the antibody will bind a fragment of A chain precursor of the type-1 fimbrial protein (upec-1875) selected from the group consisting of SEQ ID NOs: 507-515.

The invention also provides an antibody that binds to both of the yapH homolog proteins that consist of SEQ ID NOs: 99-100. In certain embodiments, the antibody will bind a fragment of yapH homolog selected from the group consisting of SEQ ID NOs: 516-638.

The invention also provides an antibody that binds to at least 2 (*e.g.* to 3, 4, or all 5) of the 5 hemolysin A (recp-3768) that consist of SEQ ID NOs: 101-105. In certain embodiments, the antibody will bind a fragment of hemolysin A (recp-3768) selected from the group consisting of SEQ ID NOs: 433-492.

The invention also provides the use of such antibodies in therapy. The invention also provides the use of such antibodies in the manufacture of a medicament. The invention also provides a method for treating a mammal comprising the step of administering an effective amount of a

antibody of the invention. As described above for immunogenic compositions, these methods and uses allow a mammal to be protected against *E.coli* infection.

The term "antibody" includes intact immunoglobulin molecules, as well as fragments thereof which are capable of binding an antigen. These include hybrid (chimeric) antibody molecules [146, 147]; F(ab')2 and F(ab) fragments and Fv molecules; non-covalent heterodimers [148, 149]; single-chain Fv molecules (sFv) [150]; dimeric and trimeric antibody fragment constructs; minibodies [151, 152]; humanized antibody molecules [153-154]; and any functional fragments obtained from such molecules, as well as antibodies obtained through non-conventional processes such as phage display. Preferably, the antibodies are monoclonal antibodies. Methods of obtaining monoclonal antibodies are well known in the art. Humanised or fully-human antibodies are preferred.

General

The practice of the present invention will employ, unless otherwise indicated, conventional methods of chemistry, biochemistry, molecular biology, immunology and pharmacology, within the skill of the art. Such techniques are explained fully in the literature. See, *e.g.*, references 155-156, *etc.*

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

"GI" numbering is used herein. A GI number, or "GenInfo Identifier", is a series of digits assigned consecutively to each sequence record processed by NCBI when sequences are added to its databases. The GI number bears no resemblance to the accession number of the sequence record. When a sequence is updated (*e.g.* for correction, or to add more annotation or information) then it receives a new GI number. Thus the sequence associated with a given GI number is never changed.

References to a percentage sequence identity between two amino acid sequences means that, when aligned, that percentage of amino acids are the same in comparing the two sequences. This alignment and the percent homology or sequence identity can be determined using software programs known in the art, for example those described in section 7.7.18 of ref. 157. A preferred alignment is determined by the Smith-Waterman homology search algorithm using an affine gap search with a gap open penalty of 12 and a gap extension penalty of 2, BLOSUM matrix of 62. The Smith-Waterman homology search algorithm is disclosed in ref. 158.

One of skill in the art would understand that "isolated" means altered "by the hand of man" from its natural state, *i.e.*, if it occurs in nature, it has been changed or removed from its original

environment, or both. For example, a polynucleotide or a polypeptide naturally present in a living organism is not "isolated" when in such living organism, but the same polynucleotide or polypeptide separated from the coexisting materials of its natural state is "isolated," as the term is used in this disclosure. Further, a polynucleotide or polypeptide that is introduced into an organism by transformation, genetic manipulation or by any other recombinant method would be understood to be "isolated" even if it is still present in said organism, which organism may be living or non-living, except where such transformation, genetic manipulation or other recombinant method produces an organism that is otherwise indistinguishable from the naturally occurring organism.

BRIEF DESCRIPTION OF DRAWINGS

Figures 1-13 show the amino acid identity for the disclosed E. coli proteins. For all figures, ## = 100% identity.

Figure 1 shows the amino acid identity between pairs of sequences of orf353 Figure 1 shows the % identity between the orf353 amino acid sequences. The labels are from left-to right and top-to-bottom: IHE3034 (an NMEC strain); RS218 (an NMEC strain); APEC01 (an APEC strain); CFT073 (an UPEC strain); 536 (an UPEC strain); UTI89 (an UPEC strain); F11 (an UPEC strain); 101-1 (an EAEC strain); O42 (an EAEC strain); 53638 (an EIEC strain); B171 (an EPEC strain); E22 (an EPEC strain); E2348/69 (an EPEC strain); E110019 (an EPEC strain); B7A (an ETEC strain); E24377A (an ETEC strain); H10407 (an ETEC strain); and SECEC (an antibiotic resistant strain).

Figure 2 shows the amino acid identity between pairs of sequences of bacterial Ig-like domain (group 1) protein (orf405). The labels are from left-to right and top-to-bottom: HS (a commensal strain); B (a Non-pathogenic strain); 8739 (a Non-pathogenic strain); C (a Non-pathogenic strain); IHE3034 (an NMEC strain); RS218 (an NMEC strain); APEC01 (an APEC strain); CFT073 (an UPEC strain); 536 (an UPEC strain); UTI89 (an UPEC strain); F11 (an UPEC strain); EDL333 (an EHEC strain); Sakai (an EHEC strain); EC508 (an EHEC strain); EC863 (an EHEC strain); EC4024 (an EHEC strain); EC4042 (an EHEC strain); EC4054 (an EHEC strain); EC4076 (an EHEC strain); EC4113 (an EHEC strain); EC4115 (an EHEC strain); EC4196 (an EHEC strain); EC4206 (an EHEC strain); EC4401 (an EHEC strain); EC4486 (an EHEC strain); EC4501 (an EHEC strain); TW14588 (an EHEC strain); 101-1 (an EAEC strain); O42 (an EAEC strain); B171 (an EPEC strain); E22 (an EPEC strain); E2348/69 (an EPEC strain); E110019 (an EPEC strain); B7A (an ETEC strain); E24377A (an ETEC strain); H10407 (an ETEC strain); and SECEC (an antibiotic resistant strain).

Figure 3 shows the amino acid identity between pairs of sequences of flu antigen 43 (orf1364). The labels are from left-to right and top-to-bottom: MG1655 (a Non-pathogenic strain); DH10B (a Non-pathogenic strain); HS (a commensal strain); B (a Non-pathogenic strain); 8739 (a Non-

pathogenic strain); C (a Non-pathogenic strain); IHE3034 (an NMEC strain); RS218 (an NMEC strain); APEC01 (an APEC strain); CFT073 (an UPEC strain); 536 (an UPEC strain); UTI89 (an UPEC strain); F11 (an UPEC strain); EDL333 (an EHEC strain); Sakai (an EHEC strain); EC508 (an EHEC strain); EC863 (an EHEC strain); EC4024 (an EHEC strain); EC4042 (an EHEC strain); EC4054 (an EHEC strain); EC4076 (an EHEC strain); EC4113 (an EHEC strain); EC4115 (an EHEC strain); EC4196 (an EHEC strain); EC4206 (an EHEC strain); EC4401 (an EHEC strain); EC4486 (an EHEC strain); EC4501 (an EHEC strain); TW14588 (an EHEC strain); 101-1 (an EAEC strain); O42 (an EAEC strain); 53638 (an EIEC strain); B171 (an EPEC strain); E22 (an EPEC strain); E2348/69 (an EPEC strain); E110019 (an EPEC strain); B7A (an ETEC strain); E24377A (an ETEC strain); H10407 (an ETEC strain); and SECEC (an antibiotic resistant strain).

Figure 4 shows the amino acid identity between pairs of sequences of NodT-family outer-membrane-factor-lipoprotein efflux transporter (orf1767). The labels are from left-to right and top-to-bottom: IHE3034 (an NMEC strain); RS218 (an NMEC strain); APEC01 (an APEC strain); CFT073 (an UPEC strain); 536 (an UPEC strain); UTI89 (an UPEC strain); F11 (an UPEC strain); EDL333 (an EHEC strain); Sakai (an EHEC strain); EC508 (an EHEC strain); EC863 (an EHEC strain); EC4024 (an EHEC strain); EC4042 (an EHEC strain); EC4054 (an EHEC strain); EC4076 (an EHEC strain); EC4113 (an EHEC strain); EC4115 (an EHEC strain); EC4196 (an EHEC strain); EC4206 (an EHEC strain); EC4401 (an EHEC strain); EC4486 (an EHEC strain); EC4501 (an EHEC strain); TW14588 (an EHEC strain); E2348/69 (an EPEC strain); and SECEC (an antibiotic resistant strain).

Figure 5 shows the amino acid identity between pairs of sequences of gspK (orf3515). The labels are from left-to right and top-to-bottom: HS (a commensal strain); B (a Non-pathogenic strain); 8739 (a Non-pathogenic strain); C (a Non-pathogenic strain); IHE3034 (an NMEC strain); RS218 (an NMEC strain); APEC01 (an APEC strain); CFT073 (an UPEC strain); 536 (an UPEC strain); UTI89 (an UPEC strain); F11 (an UPEC strain); 101-1 (an EAEC strain); O42 (an EAEC strain); 53638 (an EIEC strain); B171 (an EPEC strain); E22 (an EPEC strain); E2348/69 (an EPEC strain); E110019 (an EPEC strain); B7A (an ETEC strain); E24377A (an ETEC strain); H10407 (an ETEC strain); and SECEC (an antibiotic resistant strain).

Figure 6 shows the amino acid identity between pairs of sequences of gspJ (orf3516). The labels are from left-to right and top-to-bottom: HS (a commensal strain); IHE3034 (an NMEC strain); RS218 (an NMEC strain); APEC01 (an APEC strain); CFT073 (an UPEC strain); 536 (an UPEC strain); UTI89 (an UPEC strain); F11 (an UPEC strain); 101-1 (an EAEC strain); O42 (an EAEC strain); 53638 (an EIEC strain); B171 (an EPEC strain); E22 (an EPEC strain); E2348/69 (an EPEC strain); E110019 (an EPEC strain); B7A (an ETEC strain); E24377A (an ETEC strain); H10407 (an ETEC strain); and SECEC (an antibiotic resistant strain).

Figure 7 shows the amino acid identity between pairs of sequences of tonB-dependent siderophore receptor (orf3597). The labels are from left-to right and top-to-bottom: IHE3034 (an NMEC strain); RS218 (an NMEC strain); APEC01 (an APEC strain); CFT073 (an UPEC strain); 536 (an UPEC strain); UTI89 (an UPEC strain); F11 (an UPEC strain); EDL333 (an EHEC strain); Sakai (an EHEC strain); EC508 (an EHEC strain); EC869 (an EHEC strain); EC4024 (an EHEC strain); EC4042 (an EHEC strain); EC4045 (an EHEC strain); EC4076 (an EHEC strain); EC4113 (an EHEC strain); EC4115 (an EHEC strain); EC4196 (an EHEC strain); EC4206 (an EHEC strain); EC4401 (an EHEC strain); EC4486 (an EHEC strain); EC4501 (an EHEC strain); TW14588 (an EHEC strain); O42 (an EAEC strain); E2348/69 (an EPEC strain); and SECEC (an antibiotic resistant strain).

Figure 8 shows the amino acid identity between pairs of sequences of fibrial protein (orf3613). The labels are from left-to right and top-to-bottom: IHE3034 (an NMEC strain); RS218 (an NMEC strain); APEC01 (an APEC strain); CFT073 (an UPEC strain); 536 (an UPEC strain); and O42 (an EAEC strain).

Figure 9 shows the amino acid identity between pairs of sequences of upec-948. The labels are from left-to right and top-to-bottom: HS (a commensal strain); B (a Non-pathogenic strain); C (a Non-pathogenic strain); RS218 (an NMEC strain); CFT073 (an UPEC strain); and E2348/69 (an EPEC strain).

Figure 10 shows the amino acid identity between pairs of sequences of upec-1232. The labels are from left-to right and top-to-bottom: CFT073 (an UPEC strain); O42 (an EAEC strain); B7A (an ETEC strain); and H10407 (an ETEC strain).

Figure 11 shows the amino acid identity between pairs of sequences of A chain precursor of the type-1 fimbrial protein (upec-1875). The labels are from left-to right and top-to-bottom: IHE3034 (an NMEC strain); RS218 (an NMEC strain); APEC01 (an APEC strain); CFT073 (an UPEC strain); UTI89 (an UPEC strain); F11 (an UPEC strain); EDL333 (an EHEC strain); Sakai (an EHEC strain); EC508 (an EHEC strain); EC869 (an EHEC strain); EC4024 (an EHEC strain); EC4042 (an EHEC strain); EC4045 (an EHEC strain); EC4076 (an EHEC strain); EC4113 (an EHEC strain); EC4115 (an EHEC strain); EC4196 (an EHEC strain); EC4206 (an EHEC strain); EC4401 (an EHEC strain); EC4486 (an EHEC strain); EC4501 (an EHEC strain); TW14588 (an EHEC strain); O42 (an EAEC strain); B171 (an EPEC strain); E22 (an EPEC strain); E2348/69 (an EPEC strain); E110019 (an EPEC strain); B7A (an ETEC strain); and SECEC (an antibiotic resistant strain).

Figure 12 shows the amino acid identity between pairs of sequences of yapH homolog (upec-2820). The labels are from left-to right and top-to-bottom: CFT073 (an UPEC strain) and SECEC (an antibiotic resistant strain).

Figure 13 shows the amino acid identity between pairs of sequences of hemolysin A (recp-3768). The labels are from left-to right and top-to-bottom: RS218 (an NMEC strain); APEC01 (an

APEC strain); CFT073 (an UPEC strain); 536 (an UPEC strain); UTI89 (an UPEC strain); F11 (an UPEC strain); E110019 (an EPEC strain); B7A (an ETEC strain); E24377A (an ETEC strain); H10407 (an ETEC strain); and SECEC (an antibiotic resistant strain).

BRIEF DESCRIPTION OF SEQUENCE LISTING

SEQ ID	Description
1-2	Orf353 variants
211-216	Conserved Orf353 fragments
217-218	Conserved Orf353 linear B-cell epitopes
3-18	bacterial Ig-like domain (group 1) protein (orf405) variants
219-271	Conserved bacterial Ig-like domain (group 1) protein (orf405) fragments
272-307	Conserved bacterial Ig-like domain (group 1) protein (orf405) linear B-cell epitopes
19-40	Flu antigen 43 (orf1364) variants
308-311	Conserved flu antigen 43 (orf1364) fragments
312-350	Conserved flu antigen 43 (orf1364) linear B-cell epitopes
41-47	NodT-family outer-membrane-factor-lipoprotein efflux transporter (orf1767) variants
351-361	Conserved NodT-family outer-membrane-factor-lipoprotein efflux transporter (orf1767) fragments
362-368	Conserved NodT-family outer-membrane-factor-lipoprotein efflux transporter (orf1767) linear B-cell epitopes
48-60	gspK (orf3515) variants
369-377	Conserved gspK (orf3515) fragments
378-384	Conserved gspK (orf3515) linear B-cell epitopes
61-71	gspJ (orf3516) variants
385-389	Conserved gspJ (orf3516) fragments
390-398	Conserved gspJ (orf3516) linear B-cell epitopes
72-79	tonB-dependent siderophore receptor (orf3597) variants
399-407	Conserved tonB-dependent siderophore receptor (orf3597) fragments
408-425	Conserved tonB-dependent siderophore receptor (orf3597) linear B-cell epitopes
80-81	fibrial protein (orf3613) variants
426	Conserved fibrial protein (orf3613) fragment
427-432	Conserved fibrial protein (orf3613) linear B-cell epitopes
82-84	upec-948 variants
493-495	Conserved upec-948 fragment
496-499	Conserved upec-948 linear B-cell epitopes

85-91	upec-1232 variants
500-502	Conserved upec-1232 fragment
503-506	Conserved upec-1232 linear B-cell epitopes
92-98	A chain precursor of the type-1 fimbrial protein (upec-1875) variants
507-510	Conserved A chain precursor of the type-1 fimbrial protein (upec-1875) fragment
511-515	Conserved A chain precursor of the type-1 fimbrial protein (upec-1875) linear B-cell epitopes
99-100	yapH homolog (upec-2820) variants
516-543	Conserved yapH homolog (upec-2820) fragment
544-638	Conserved yapH homolog (upec-2820) linear B-cell epitopes
101-105	hemolysin A (recp-3768) variants
433-463	Conserved hemolysin A (recp-3768) fragment
464-492	Conserved hemolysin A (recp-3768) linear B-cell epitopes
639	Polynucleotide sequence for pUPEC-3768B4 encoding a fragment of hemolysin A (recp-3768)
640	Polypeptide sequence of the 3768B4 fragment of hemolysin A (recp-3768)
641	Polynucleotide sequence for pK1-0405B encoding a fragment of bacterial Ig-like domain (group 1) protein (orf405)
642	Polypeptide sequence of the 0405B fragment of bacterial Ig-like domain (group 1) protein (orf405)
643	Polynucleotide sequence for pCFT-2820A encoding a fragment of yapH homolog (upec-2820)
644	Polypeptide sequence of the 2820-A fragment of yapH homolog (upec-2820)
645	Polynucleotide sequence for pCFT-2820B encoding a fragment of yapH homolog (upec-2820)
646	Polypeptide sequence of the 2820-B fragment of yapH homolog (upec-2820)
647	Polynucleotide sequence for pCFT-2820C encoding a fragment of yapH homolog (upec-2820)
648	Polypeptide sequence of the 2820-C fragment of yapH homolog (upec-2820)
649	Polynucleotide sequence for pCFT-2820D encoding a fragment of yapH homolog (upec-2820)
650	Polypeptide sequence of the 2820-D fragment of yapH homolog (upec-2820)
651	Polynucleotide sequence for pK1-1364 encoding a fragment of flu antigen 43 (orf1364)
652	Polypeptide sequence of the K1-1364 fragment of bacterial Ig-like domain flu antigen 43 (orf1364)
653-655	*Escherichia* Sell repeat-containing protein (upec-5211) variants

656-664	*Escherichia* Sell repeat-containing protein (upec-5211) fragments
665-676	*Escherichia* Sell repeat-containing protein (upec-5211) linear B-cell epitopes
677	Polynucleotide sequence for pK1-0405AB encoding a fragment of bacterial Ig-like domain (group 1) protein (orf405AB)
678	Polynucleotide sequence for pK1-0405C encoding a fragment of bacterial Ig-like domain (group 1) protein (orf405C)
679	Polynucleotide sequence for pK1-0405BC encoding a fragment of bacterial Ig-like domain (group 1) protein (orf405BC)
680	Polypeptide sequence of the orf405AB of the bacterial Ig-like domain (group 1) protein (orf405)
681	Polypeptide sequence of the orf405C of the bacterial Ig-like domain (group 1) protein (orf405)
682	Polypeptide sequence of the orf405BC of the bacterial Ig-like domain (group 1) protein (orf405)
683	Conserved bacterial Ig-like domain (group 1) protein (orf405) fragment

MODES FOR CARRYING OUT THE INVENTION

orf353, bacterial Ig-like domain (group 1) protein (orf405), flu antigen 43 (orf1364), NodT-family outer-membrane-factor-lipoprotein efflux transporter (orf1767), gspK (orf3515), gspJ (orf3516), tonB-dependent siderophore receptor (orf3597), fibrial protein (orf3613), upec-948, upec-1232, A chain precursor of the type-1 fimbrial protein (upec-1875), yapH homolog (upec-2820), hemolysin A (recp-3768), and Sell repeat-containing protein (upec-5211), each as more fully described herein, have been expressed and purified, and confer protection against ExPEC strains in a sepsis animal model.

Sequences were obtained for the orthologs in various other *E.coli* strains.

Exemplary antigens for each of the protein – orf353 (SEQ ID NO:1 – amino acids 21-162), bacterial Ig-like domain (group 1) protein (orf405) (SEQ ID NO:9 – amino acids 595-1008), flu antigen 43 (orf1364) (SEQ ID NO: 27 – amino acids 53-629), NodT-family outer-membrane-factor-lipoprotein efflux transporter (orf1767) (SEQ ID NO: 41 – amino acids 15-457), gspK (orf3515) (SEQ ID NO: 56 – amino acids 32-325), gspJ (orf3516) (SEQ ID NO:65 – amino acids 16-189), tonB-dependent siderophore receptor (orf3597) (SEQ ID NO:74 – amino acids 29-713), fibrial protein (orf3613) (SEQ ID NO:80 – amino acids 28-187), upec-948 (SEQ ID NO: 82 – amino acids 24-151), upec-1232 (SEQ ID NO:89 – amino acids 26-151), A chain precursor of the type-1 fimbrial protein (upec-1875) (SEQ ID NO:97 – amino acids 25-187), yapH homolog (upec-2820) (SEQ ID NO:99), hemolysin A (recp-3768) (SEQ ID NO:103 – amino acids 24-

1024), and Sell repeat-containing protein (upec-5211) (SEQ ID NO:653) – were cloned in pET-21b vectors (Novagen) and transformed in DH5α-T1 chemically competent cells for propagation (Invitrogen). BL21 (DE3) chemically competent cells were used for expression. All candidates were cloned and expressed without the signal sequence and as his-tag fusion proteins. Candidates were purified by affinity chromatography.

Protection was evaluated in a sepsis animal model. CD1 out bred female mice (5 weeks old) from Charles River Italia were immunized by subcutaneous injections at the 1st, 21st and 35th days with 20 μg of recombinant protein in Freund's adjuvant. Positive control was immunized with 10^8 heat-inactivated bacteria (65°C for 30 minutes) in 0.15 ml of physiological solution in Freund's adjuvant (Sigma), while negative control was immunized with physiologic solution in Freund's adjuvant. Challenge was done at the 49th day with a dose of 10^7 of fresh bacterial culture/mouse (LD_{80}) by intraperitoneal (for strains IHE3034 and CFT073) or intravenous (for strain 536) injection. Heparinised-blood samples were collected from survived mice at 24 hours after challenge to determine bacteremia levels and the mortality was observed for four days after challenge.

Candidate	**Sepsis Animal Model**		
	Survival with vaccination (%)	Survival without vaccination (%)	P value
hemolysin A (recp-3768)	18/23 **(78)**	2/26 **(7)**	<0.0001
upec-1232	15/30 **(50)**	3/36 **(8)**	0.0002
gspK (orf3515)	30/110 **(27)**	11/116 **(9)**	0.0005
upec-5211	30/83 **(36)**	14/91 **(15)**	0.003
tonB-dependent siderophore receptor (orf3597)	12/40 **(32)**	5/48 **(10)**	0.03
orf353	19/76 **(25)**	7/67 **(10)**	0.03
gspJ (orf3516)	10/46 **(21)**	3/50 **(6)**	0.03
NodT-family outer-membrane-factor-lipoprotein efflux transporter (orf1767)	15/74 **(20)**	6/80 **(7)**	0.03
A chain precursor of the type-1 fimbrial protein (upec-1875)	11/23 **(47)**	5/26 **(19)**	0.06
fibrial protein (orf3613)	24/89 **(27)**	13/81 **(16)**	0.09
upec-948	12/31 **(38)**	7/38 **(18)**	0.1

Certain of the above candidates showed limited or no solubility as full length proteins (hemolysin A (recp-3768), flu antigen 43 fragment (orf1364), bacterial Ig-like domain (group 1) protein (orf405), and yapH homolog (upec-2820)). Therefore, fragments were constructed and tested for solubility.

Those that demonstrated increased solubility were further tested for their ability to provide protection in the sepsis animal model as described above.

Candidate fragment	**Sepsis Animal Model**		
	Survival with vaccination (%)	Survival without vaccination (%)	P value
2820-D (yapH homolog fragment D) (SEQ ID NO: 650)	10/34 **(29)**	3/36 **(8)**	0.03
1364 (flu antigen 43 fragment) (SEQ ID NO: 652)	21/77 **(27)**	8/84 **(9)**	0.004
405B (bacterial Ig-like domain (group 1) protein fragment) (SEQ ID NO: 642)	25/81 **(30.8)**	14/86 **(16)**	0.03
3768-B4 (with Alum) (hemolysin A fragment B4) (SEQ ID NO: 640)	13/24 **(54)**	6/24 **(25)**	0.07
2820-C (yapH homolog fragment C) (SEQ ID NO: 648)	9/32 **(28)**	4/38 **(10)**	0.07
2820-A (yapH homolog fragment A) (SEQ ID NO: 644)	8/24 **(33)**	5/28 **(17.8)**	0.2
2820-B (yapH homolog fragment B) (SEQ ID NO: 646)	10/31 **(32)**	10/38 **(26)**	0.6

To demonstrate the ability of the hemolysin A protein fragment B4 (3768-B4) to provide cross protection against other strains, mice immunized with the above hemolysin A protein fragment B4 (3768-B4) were challenged with different strains of *E. coli*, as shown in the following table.

***E. Coli* Strain**	**Protection in Sepsis Animal Model**			
	3768-B4 20µg/Alum		**3768 (insol.) 20µg/Alum**	
	Survival with vaccination (%)	Survival without vaccination (%)	Survival with vaccination (%)	Survival without vaccination (%)
536	13/24 **(54)**	6/24 **(25)**	10/16 **(62.5)**	0/16 **(0)**
CFT073	3/8 (37.5)	2/8 (25)	-	-
BK658	1/8 (12.5)	1/8 (12.5)	6/8 **(75)**	1/8 **(12.5)**

Various combinations of the three fragments of bacterial Ig-like domain (group 1) protein fragment (orf405) were tested in the mouse model of sepsis as described above. The results are provided in the following table.

Candidate fragment	Sepsis Animal Model		
	Survival with vaccination (%)	Survival without vaccination (%)	P value
405AB (SEQ ID NO: 680)	2/8 **(25)**	0/8 **(0)**	0.4
405BC (SEQ ID NO: 682)	0/8 **(27)**	0/8 **(0)**	-
405B (SEQ ID NO: 642)	25/81 **(30.8)**	14/86 **(16)**	0.03
405C (SEQ ID NO: 681)	0/10 **(0)**	1/10 **(1)**	-

It will be understood that the invention has been described by way of example only and modifications may be made whilst remaining within the scope and spirit of the invention.

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SEQ ID NO: 639

GATAAGTTTTTTGGCAGCAAATTTACAGATATCTTCCATGGCGCGGATGGTGATGACCACATAGAAGGAAATGATGGGAAT
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CTCATCATGTATAAAGCTGAAGGTAATGTTCTTTCCATTGGTCATAAAAATGGTATTACATTCAGGAACTGGTTTGAAAAA
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SEQ ID NO: 640

DKFFGSKFTDIFHGADGDDHIEGNDGNDRLYGDKGNDTLRGGNGDDQLYGGDGNDKLTGGVGNNYLNGGDGDDELQVQGNS
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LIMYKAEGNVLSIGHKNGITFRNWFEKESGDISNHQIEQIFDKDGR

SEQ ID NO: 641

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SEQ ID NO: 642

VADGQQAYTLTLTAVDSEGNPVTGEASRLRLVPQDTNGVTVGAISEIKPGVYSATVSSTRAGNVVVRAFSEQYQLGTLQQT
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SEQ ID NO: 643

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GAT

SEQ ID NO: 644

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SEQ ID NO: 645

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GCAACCATTAAGACGAATATTGCACCGGGAACTCTGCTGGATGCCAGT

SEQ ID NO: 646

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SEQ ID NO: 647

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SEQ ID NO: 648

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SEQ ID NO: 649

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SEQ ID NO: 650

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SEQ ID NO: 651

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SEQ ID NO: 652

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SEQ ID NO: 677

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GCGCAGATTTCTCTCGGCACTACGGCGGTGAATTAGACGTTATGCCGAAGCTCAATGGGCAGGACGCGGCAGCAAATGCG
GCAAAAGTAACCGTGGTGGCTGATGCATTATCTTCAAACCAGTCGAAAGTCTCTGTCGCAGAAGATCACGTAAAAGCCGGT
GAAAGCACAACCGTAACGCTGGTGGCGAAAGATGCGCATGGCAACGCTATCAGTGGTCTTTCGTTGTCGGCAAGTTTGACG
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GGAAAGACGGGCGAGCTTCGTGTCATGCCGCTCTTCAACGGCCAGCCTGCAGCCACCGAAGCCGCGCAGCTGACTGTTATT
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GAGGAGAAA

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AAGGCCACTAAATCACAGGCAAAGCCAACACTGGGTGAGTTCACCGAAACTGAAGCAGGGGTGTATCAGTCTGTCTTTACT
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GCTGAGGAGAAA

SEQ ID NO: 680

CVAWANISVQVLFPLAVTFTPVMAARAQHAVQPRLSMENTTVTADNNVEKNVASLAANAGTFLSSQPDSDATRNFITGMAT
AKANQEIQEWLGKYGTARVKLNVDKNFSLKDSSLEMLYPIYDTPTNMLFTQGAIHRTDDRTQSNIGFGWRHFSENDWMAGV
NTFIDHDLSRSHTRIGVGAEYWRDYLKLSANGYIRASGWKKSPDVEDYQERPANGWDIRAEGYLPAWPQLGASLMYEQYYG
DEVGLFGKDKRQKDPHAITAEVNYTPVPLLTLSAGHKQGKSGENDTRFGLEVNYRIGEPLEKQLDTDSIRERRMLAGSRYD
LVERNNNIVLEYRKSEVIRIALPERIEGKGGQTVSLGLVVSKATHGLKNVQWEAPSLLAAGGKITGQGNQWQVTLPAYQAG
KDNYYAISAIAYDNKGNASKRVQTEVVISGAGMSADRTALTLDGQSRIQMLANGNEQKPLVLSLRDAEGQPVTGMKDQIKT
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LGTLQQTLKFVAGPLDAAHSSITLNPDKPVVGGTVTAIWTAKDANDNPVTGLNPDAPSLSGAAAAGSTASGWTDNGDGTWT
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FTMKDAYGNPVTGLKPDAPVFSGAASTGSERPSAGNWTEKGNGVYVSTLTLGSAAGQLSVMPRVNGQNAVAQPLVLNVAGD
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SEQ ID NO: 681

LANGQSANQITLTVVDSYGNPLQGQEVTLTLPQGVTSKTGNTVTTNAAGKVDIELMSTVAGELEIEASVKNSQKTVKVKFK
ADFSTGQASLEVDAAAQKVANGKDAFTLTATVKDQYGNLLPGAVVVFNLPRGVKPLADGNIMVNADKEGKAELKVVSVTAG
TYEITASAGNDQPSNAQSVTFVADKTTATISSIEVIGNRAVADGKTKQTYKVTVTDANNNLLKDSEVTLTASPENLVLTPN
GTATTNEQGQAIFTATTTVAATYTLTAKVEQADGQESTKTAESKFVADDKNAVLAASPERVDSLVADGKTTATLTVTLMSG
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EEK

SEQ ID NO: 682

DGQSRIQMLANGNEQKPLVLSLRDAEGQPVTGMKDQIKTELTFKPAGNIVTRTLKATKSQAKPTLGEFTETEAGVYQSVFT
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TNGVTVGAISEIKPGVYSATVSSTRAGNVVVRAFSEQYQLGTLQQTLKFVAGPLDAAHSSITLNPDKPVVGGTVTAIWTAK
DANDNPVTGLNPDAPSLSGAAAAGSTASGWTDNGDGTWTAQISLGTTAGELDVMPKLNGQDAAANAAKVTVVADALSSNQS
KVSVAEDHVKAGESTTVTLVAKDAHGNAISGLSLSASLTGTASEGATVSSWTEKGDGSYVATLTTGGKTGELRVMPLFNGQ
PAATEAAQLTVIAGEMSSANSTLVADNKTPTVKTTTELTFTMKDAYGNPVTGLKPDAPVFSGAASTGSERPSAGNWTEKGN
GVYVSTLTLGSAAGQLSVMPRVNGQNAVAQPLVLNVAGDASKAEIRDMTVKVNNQLANGQSANQITLTVVDSYGNPLQGQE
VTLTLPQGVTSKTGNTVTTNAAGKVDIELMSTVAGELEIEASVKNSQKTVKVKFKADFSTGQASLEVDAAAQKVANGKDAF
TLTATVKDQYGNLLPGAVVVFNLPRGVKPLADGNIMVNADKEGKAELKVVSVTAGTYEITASAGNDQPSNAQSVTFVADKT
TATISSIEVIGNRAVADGKTKQTYKVTVTDANNNLLKDSEVTLTASPENLVLTPNGTATTNEQGQAIFTATTTVAATYTLT
AKVEQADGQESTKTAESKFVADDKNAVLAASPERVDSLVADGKTTATLTVTLMSGVNPVGGTMWVDIEAPEGVTEADYQFL
PSKNDHFASGKITRTFSTNKPGTYTFTFNSLTYGGYEMKPVTVTINAVPADTEGAEEK

CLAIMS

1. An isolated or recombinant polypeptide comprising an E. coli protein selected from the group consisting of orf353, bacterial Ig-like domain (group 1) protein (orf405), flu antigen 43 (orf1364), NodT-family outer-membrane-factor-lipoprotein efflux transporter (orf1767), gspK (orf3515), gspJ (orf3516), tonB-dependent siderophore receptor (orf3597), fibrial protein (orf3613), upec-948, upec-1232, A chain precursor of the type-1 fimbrial protein (upec-1875), yapH homolog (upec-2820), and hemolysin A (recp-3768).

2. The isolated or recombinant polypeptide of claim 1, wherein the polypeptide comprises an amino acid sequence having at least 80% identity, at least 85% identity, at least 90% identity, at least 95% identity, at least 96% identity, at least 97% identity, at least 98% identity, at least 99% identity, or 100% identity to SEQ ID NOs: 1-105.

3. The isolated or recombinant polypeptide of claim 1, wherein the polypeptide comprises an amino acid that when aligned with any of SEQ ID NOs: 1-105 using a pairwise alignment algorithm, each moving window of x amino acids from N terminus to C terminus has at least x•y identical aligned amino acids, where x is 30 and y is 0.75.

4. An isolated or recombinant polypeptide comprising at least 10 consecutive amino acids of any of SEQ ID NOs: 1-105, wherein the at least 10 consecutive amino acids is immunogenic.

5. The isolated or recombinant polypeptide of claim 4 wherein the polypeptide is orf353 and comprises less than 160, less than 150, less than 140 or less than 130 amino acids from SEQ ID NOs: 1-2.

6. The isolated or recombinant polypeptide of claim 5 wherein the at least 10 consecutive amino acids comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 211-218.

7. The isolated or recombinant polypeptide of claim 5 wherein the polypeptide comprises at least amino acids 21-162 of SEQ ID NOs: 1-2.

8. The isolated or recombinant polypeptide of claim 4 wherein the polypeptide is bacterial Ig-like domain (group 1) protein (orf405) and comprises less than 1410, less than 1400, less than 1390 or less than 1380 amino acids from SEQ ID NOs: 3-18.

9. The isolated or recombinant polypeptide of claim 8 wherein the at least 10 consecutive amino acids comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 219-307 & 683.

10. The isolated or recombinant polypeptide of claim 8 wherein the polypeptide comprises at least amino acids 595-1008 of SEQ ID NOs: 3-18.

11. The isolated or recombinant polypeptide of claim 4 wherein the polypeptide is flu antigen 43 (orf1364) and comprises less than 1040, less than 1030, less than 1020 or less than 1010 amino acids from SEQ ID NOs: 19-40.

12. The isolated or recombinant polypeptide of claim 11 wherein the at least 10 consecutive amino acids comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 308-350.

13. The isolated or recombinant polypeptide of claim 11 wherein the polypeptide comprises at least amino acids 53-620 of SEQ ID NOs: 19-40.

14. The isolated or recombinant polypeptide of claim 4 wherein the polypeptide is NodT-family outer-membrane-factor-lipoprotein efflux transporter (orf1767) and comprises less than 450, less than 440, less than 430 or less than 420 amino acids from SEQ ID NOs: 41-47.

15. The isolated or recombinant polypeptide of claim 14 wherein the at least 10 consecutive amino acids comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 351-368.

16. The isolated or recombinant polypeptide of claim 14 wherein the polypeptide comprises at least amino acids 15-457 of SEQ ID NOs: 41-47.

17. The isolated or recombinant polypeptide of claim 4 wherein the polypeptide is gspK (orf3515) and comprises less than 320, less than 310, less than 300 or less than 290 amino acids from SEQ ID NOs: 48-60.

18. The isolated or recombinant polypeptide of claim 17 wherein the at least 10 consecutive amino acids comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 369-384.

19. The isolated or recombinant polypeptide of claim 17 wherein the polypeptide comprises at least amino acids 32-325 of SEQ ID NOs: 48-60.

20. The isolated or recombinant polypeptide of claim 4 wherein the polypeptide is gspJ (orf3516) and comprises less than 180, less than 170, less than 160 or less than 150 amino acids from SEQ ID NOs: 61-71.

21. The isolated or recombinant polypeptide of claim 20 wherein the at least 10 consecutive amino acids comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 385-398.

22. The isolated or recombinant polypeptide of claim 20 wherein the polypeptide comprises at least amino acids 16-189 of SEQ ID NOs: 61-71.

23. The isolated or recombinant polypeptide of claim 4 wherein the polypeptide is tonB-dependent siderophore receptor (orf3597) and comprises less than 710, less than 700, less than 690 or less than 680 amino acids from SEQ ID NOs: 72-79.

24. The isolated or recombinant polypeptide of claim 23 wherein the at least 10 consecutive amino acids comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 399-425.

25. The isolated or recombinant polypeptide of claim 23 wherein the polypeptide comprises at least amino acids 29-713 of SEQ ID NOs: 72-79.

26. The isolated or recombinant polypeptide of claim 4 wherein the polypeptide is fibrial protein (orf3613) and comprises less than 180, less than 170, less than 160 or less than 150 amino acids from SEQ ID NOs: 80-81.

27. The isolated or recombinant polypeptide of claim 26 wherein the at least 10 consecutive amino acids comprises an amino acid sequence is SEQ ID NO: 426-432.

28. The isolated or recombinant polypeptide of claim 26 wherein the polypeptide comprises at least amino acids 25-187 of SEQ ID NOs: 80-81.

29. The isolated or recombinant polypeptide of claim 4 wherein the polypeptide is upec-948 and comprises less than 150, less than 140, less than 130 or less than 120 amino acids from SEQ ID NOs: 82-84.

30. The isolated or recombinant polypeptide of claim 29 wherein the at least 10 consecutive amino acids comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 493-499.

31. The isolated or recombinant polypeptide of claim 29 wherein the polypeptide comprises at least amino acids 24-151 of SEQ ID NOs: 82-84.

32. The isolated or recombinant polypeptide of claim 4 wherein the polypeptide is upec-1232 and comprises less than 150, less than 140, less than 130 or less than 120 amino acids from SEQ ID NOs: 85-91.

33. The isolated or recombinant polypeptide of claim 32 wherein the at least 10 consecutive amino acids comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 500-506.

34. The isolated or recombinant polypeptide of claim 32 wherein the polypeptide comprises at least amino acids 26-151 of SEQ ID NOs: 85-91.

35. The isolated or recombinant polypeptide of claim 4 wherein the polypeptide is A chain precursor of the type-1 fimbrial protein (upec-1875) and comprises less than 180, less than 170, less than 160 or less than 150 amino acids from SEQ ID NOs: 92-98.

36. The isolated or recombinant polypeptide of claim 35 wherein the at least 10 consecutive amino acids comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 507-515.

37. The isolated or recombinant polypeptide of claim 35 wherein the polypeptide comprises at least amino acids 24-187 of SEQ ID NOs: 92-98.

38. The isolated or recombinant polypeptide of claim 4 wherein the polypeptide is yapH homolog (upec-2820) and comprises less than 2640, less than 2620, less than 2600 or less than 2580 amino acids from SEQ ID NOs: 99-100.

39. The isolated or recombinant polypeptide of claim 38 wherein the at least 10 consecutive amino acids comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 516-638.

40. The isolated or recombinant polypeptide of claim 38 wherein the polypeptide comprises at least amino acids 984-1495 of SEQ ID NOs: 99-100.

41. The isolated or recombinant polypeptide of claim 38 wherein the polypeptide comprises at least amino acids 1496-1876 of SEQ ID NOs: 99-100.

42. The isolated or recombinant polypeptide of claim 4 wherein the polypeptide is hemolysin A (recp-3768) and comprises less than 1020, less than 1010, less than 1000 or less than 990 amino acids from SEQ ID NOs: 101-105.

43. The isolated or recombinant polypeptide of claim 42 wherein the at least 10 consecutive amino acids comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 433-492.

44. The isolated or recombinant polypeptide of claim 42 wherein the polypeptide comprises at least amino acids 21-1024 of SEQ ID NOs: 101-105.

45. The isolated or recombinant polypeptide of any of claims 1-4 wherein the polypeptide does not comprise a full length protein selected from the group consisting of orf353, bacterial Ig-like domain (group 1) protein (orf405), flu antigen 43 (orf1364), NodT-family outer-membrane-factor-lipoprotein efflux transporter (orf1767), gspK (orf3515), gspJ (orf3516), tonB-dependent siderophore receptor (orf3597), fibrial protein (orf3613), upec-948, upec-1232, A chain precursor of the type-1 fimbrial protein (upec-1875), yapH homolog (upec-2820), and hemolysin A (recp-3768).

46. The isolated or recombinant immunogenic polypeptide of any of claims 1-4 wherein the polypeptide does not comprise an amino acid sequence selected from the group consisting of SEQ ID NOs: 1-105.

47. The isolated or recombinant immunogenic polypeptide of any of claims 1-46 further comprising an adjuvant.

48. A polynucleotide encoding the immunogenic polypeptide of any of claims 1-46.

49. The polynucleotide of claim 48, wherein the polynucleotide has at 80% sequence identity to a nucleic acid sequence selected from the group consisting of SEQ ID NOs:106-210.

50. An *E.coli* cell, containing a plasmid that encodes the immunogenic polypeptide of any of claims 1-45.

51. An immunogenic polypeptide comprising a fragment of an orf405 protein wherein the fragment contains a deletion relative to the *E. coli* orf405 which increases solubility of the fragment as compared to the full length protein and wherein the fragment raises a substantially similar immune response in a subject as the *E. coli* orf405.

52. The immunogenic polypeptide of claim 51, wherein the deletion comprises the putative amino-terminal translocator domain.

53. The immunogenic polypeptide of claim 51, wherein the orf405 protein corresponds to the amino acid sequence of SEQ ID NO: 642.

54. The immunogenic polypeptide of any of claims 51-53, wherein the fragment comprises less than 1200 amino acids, less than 1100 amino acids, less than 1000 amino acids, less than 950 amino acids, less than 900 amino acids, less than 850 amino acids, less than 800 amino acids, less than 750 amino acids, less than 700 amino acids, less than 650 amino acids, less than 600 amino acids, less than 590 amino acids, or less than 580 amino acids of the orf405 protein.

55. The immunogenic polypeptide of any of claims 51-54 wherein the orf405 amino acid sequence comprises:

(a) the amino acid sequence selected from the group consisting of SEQ ID NOs 3-18;

(b) from 1 to 10 single amino acid alterations compared to SEQ ID NOs: 3-18;

(c) at least 85% sequence identity to any one of SEQ ID NOs: 3-18;

and/or

(d) when aligned with any of SEQ ID NOs: 3-18 using a pairwise alignment algorithm, each moving window of x amino acids from N terminus to C terminus has at least x•y identical aligned amino acids, where x is 30 and y is 0.75.

56. The immunogenic polypeptide of any of claims 51-55 wherein the immunogenic polypeptide fragment is isolated, purified, or recombinant.

57. The immunogenic polypeptide of any of claims 51-56 further comprising an adjuvant.

58. A polynucleotide encoding the immunogenic polypeptide of any of claims 51-55.

59. A host cell comprising a plasmid that encodes the immunogenic polypeptide of any of claims 51-55.

60. An immunogenic polypeptide comprising a fragment of a flu antigen 43 (orf1364) protein wherein the fragment contains a deletion relative to the *E. coli* flu antigen 43 (orf1364)which increases solubility of the fragment as compared to the full length protein and wherein the fragment raises a substantially similar immune response in a subject as the *E. coli* flu antigen 43 (orf1364).

61. The immunogenic polypeptide of claim 60, wherein the deletion comprises the carboxyl-terminal β-barrel domain.

62. The immunogenic polypeptide of claim 60, wherein the flu antigen 43 (orf1364) protein corresponds to the amino acid sequence of SEQ ID NO:652.

63. The immunogenic polypeptide of any of claims 60-62, wherein the fragment comprises less than 950 amino acids, less than 900 amino acids, less than 850 amino acids, less than 800 amino acids, less than 750 amino acids, less than 700 amino acids, less than 650 amino acids, less than 600 amino acids, less than 550 amino acids, less than 500 amino acids, less than 450 amino acids, less than 440 amino acids, or less than 430 amino acids of the flu antigen 43 (orf1364) protein.

64. The immunogenic polypeptide of any of claims 60-63 wherein the flu antigen 43 (orf1364) amino acid sequence comprises:

(a) the amino acid sequence selected from the group consisting of SEQ ID NOs 19-40;

(b) from 1 to 10 single amino acid alterations compared to SEQ ID NOs: 19-40;

(c) at least 85% sequence identity to any one of SEQ ID NOs: 19-40;

and/or

(d) when aligned with any of SEQ ID NOs: 19-40 using a pairwise alignment algorithm, each moving window of x amino acids from N terminus to C terminus has at least x•y identical aligned amino acids, where x is 30 and y is 0.75.

65. The immunogenic polypeptide of any of claims 60-64 wherein the immunogenic polypeptide fragment is isolated, purified, or recombinant.

66. The immunogenic polypeptide of any of claims 60-65 further comprising an adjuvant.

67. A polynucleotide encoding the immunogenic polypeptide of any of claims 60-64.

68. A host cell comprising a plasmid that encodes the immunogenic polypeptide of any of claims 46-64.

69. An immunogenic polypeptide comprising a fragment of an yapH homolog (upec-2820) protein wherein the fragment contains a deletion relative to the *E. coli* yapH homolog (upec-2820) which increases solubility of the fragment as compared to the full length protein and wherein the fragment raises a substantially similar immune response in a subject as the *E. coli* yapH homolog (upec-2820).

70. The immunogenic polypeptide of claim 69, wherein the yapH homolog (upec-2820) protein corresponds to the amino acid sequence of SEQ ID NO:644, SEQ ID NO:646, SEQ ID NO: 648, or SEQ ID NO: 650.

71. The immunogenic polypeptide of claim 69 or claim 70, wherein the fragment comprises less than 2500 amino acids, less than 2000 amino acids, less than 1750 amino acids, less than 1500 amino acids, less than 1400 amino acids, less than 1300 amino acids, less than 1200 amino acids, less than 1100 amino acids, less than 1000 amino acids, less than 900 amino acids, less than 850 amino acids, less than 800 amino acids, less than 750 amino acids, less than 700 amino acids, less than 650 amino acids, less than 600 amino acids, less than 550 amino acids, less than 500 amino acids, less than 450 amino acids, less than 400 amino acids, or less than 390 amino acids of the yapH homolog (upec-2820) protein.

72. The immunogenic polypeptide of any of claims 69-71 wherein the yapH homolog (upec-2820) amino acid sequence comprises:

(a) the amino acid sequence selected from the group consisting of SEQ ID NOs 99-100;

(b) from 1 to 10 single amino acid alterations compared to SEQ ID NOs: 99-100;

(c) at least 85% sequence identity to any one of SEQ ID NOs: 99-100;

and/or

(d) when aligned with any of SEQ ID NOs: 99-100 using a pairwise alignment algorithm, each moving window of x amino acids from N terminus to C terminus has at least x•y identical aligned amino acids, where x is 30 and y is 0.75.

73. The immunogenic polypeptide of any of claims 69-72 wherein the immunogenic polypeptide fragment is isolated, purified, or recombinant.

74. The immunogenic polypeptide of any of claims 69-73 further comprising an adjuvant.

75. A polynucleotide encoding the immunogenic polypeptide of any of claims 69-72.

76. A host cell comprising a plasmid that encodes the immunogenic polypeptide of any of claims 69-72.

77. An immunogenic polypeptide comprising a fragment of an hemolysin A (recp3768) protein wherein the fragment contains a deletion relative to the *E. coli* hemolysin A (recp3768) which increases solubility of the fragment as compared to the full length protein and wherein the fragment raises a substantially similar immune response in a subject as the *E. coli* hemolysin A (recp3768).

78. The isolated or recombinant polypeptide of claim 77 the deletion comprises the amino-terminal hydrophobic domain required for membrane insertion and pore formation (the hydrophobic α-helix region), the carboxyl-terminal signal sequence and the domain required for pore-forming activity after post-translational acylation.

79. The immunogenic polypeptide of claim 77, wherein the hemolysin A (recp3768) protein corresponds to the amino acid sequence of SEQ ID NO: 640.

80. The immunogenic polypeptide of any of claims 77-79, wherein the fragment comprises less than 1000 amino acids, less than 950 amino acids, less than 900 amino acids, less than 850 amino acids, less than 800 amino acids, less than 750 amino acids, less than 700 amino acids, less than 650 amino acids, less than 600 amino acids, less than 550 amino acids, less than 500 amino acids, less than 450 amino acids, less than 400 amino acids, less than 390 amino acids, less than 380 amino acids, less than 350 amino acids, less than 300 amino acids, less than 250 amino acids, less than 240 amino acids, less than 230 amino acids, or less than 220 amino acids of the hemolysin A (recp3768) protein.

81. The immunogenic polypeptide of any of claims 77-80 wherein the hemolysin A (recp3768) amino acid sequence comprises:

(a) the amino acid sequence selected from the group consisting of SEQ ID NOs 101-105;

(b) from 1 to 10 single amino acid alterations compared to SEQ ID NOs: 101-105;

(c) at least 85% sequence identity to any one of SEQ ID NOs: 101-105;

and/or

(d) when aligned with any of SEQ ID NOs: 101-105 using a pairwise alignment algorithm, each moving window of x amino acids from N terminus to C terminus has at least x•y identical aligned amino acids, where x is 30 and y is 0.75.

82. The immunogenic polypeptide of any of claims 77-81 wherein the immunogenic polypeptide fragment is isolated, purified, or recombinant.

83. The immunogenic polypeptide of any of claims 77-82 further comprising an adjuvant.

84. A polynucleotide encoding the immunogenic polypeptide of any of claims 77-81.

85. A host cell comprising a plasmid that encodes the immunogenic polypeptide of any of claims 77-81.

86. An isolated or recombinant polypeptide comprising an *Escherichia* Sell repeat-containing protein (upec-5211).

87. The isolated or recombinant polypeptide of claim 86, wherein the polypeptide comprises an amino acid sequence having at least 80% identity, at least 85% identity, at least 90% identity, at least 95% identity, at least 96% identity, at least 97% identity, at least 98% identity, at least 99% identity, or 100% identity to SEQ ID NOs: 653-655.

88. The isolated or recombinant polypeptide of claim 86, wherein the polypeptide comprises an amino acid that when aligned with any of SEQ ID NOs: 653-655 using a pairwise alignment algorithm, each moving window of x amino acids from N terminus to C terminus has at least x•y identical aligned amino acids, where x is 30 and y is 0.75.

89. An isolated or recombinant polypeptide comprising at least 10 consecutive amino acids of any of SEQ ID NOs: 653-655, wherein the at least 10 consecutive amino acids is immunogenic.

90. The isolated or recombinant polypeptide of claim 89 wherein the polypeptide comprises less than 480, less than 470, less than 460, less than 450, less than 425, less than 400, less than 350, less than 200,or less than 250 amino acids from SEQ ID NOs: 653-655.

91. The isolated or recombinant polypeptide of claim 90 wherein the at least 10 consecutive amino acids comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 656-675.

92. The isolated or recombinant polypeptide of any of claims 86-89 wherein the polypeptide does not comprise the full length *Escherichia* Sell repeat-containing protein (upec-5211).

93. The isolated or recombinant polypeptide of any of claims 86-89 wherein the polypeptide does not comprise an amino acid sequence selected from the group consisting of SEQ ID NOs: 653-655.

94. The isolated or recombinant immunogenic polypeptide of any of claims 86-93 further comprising an adjuvant.

95. A polynucleotide encoding the immunogenic polypeptide of any of claims 86-93.

96. The polynucleotide of claim 95, wherein the polynucleotide has at 80% sequence identity to a nucleic acid sequence encoding one of SEQ ID NOs:653-655.

97. An E.coli cell, containing a plasmid that encodes the immunogenic polypeptide of any of claims 86-93.

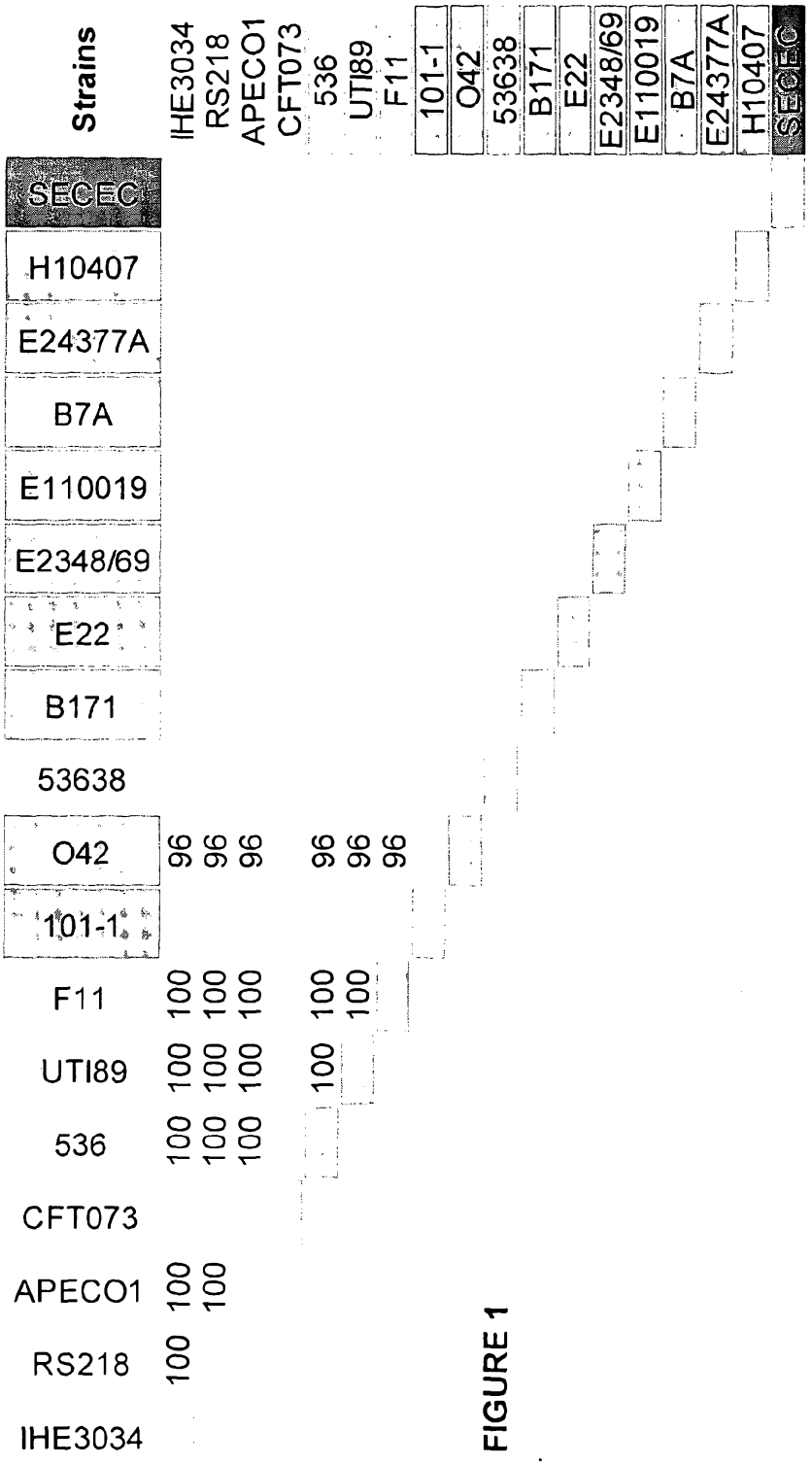


FIGURE 1

orf00353

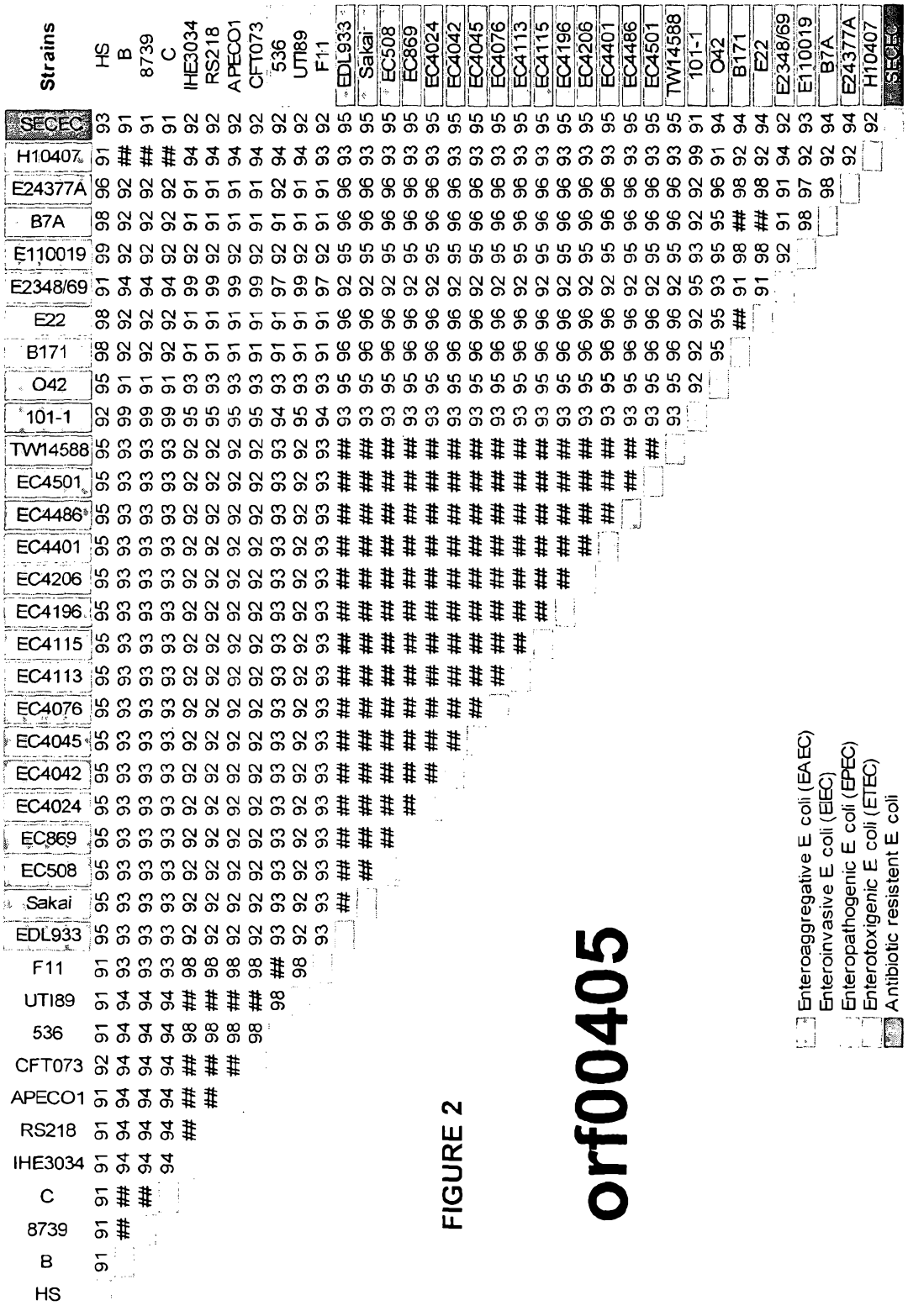
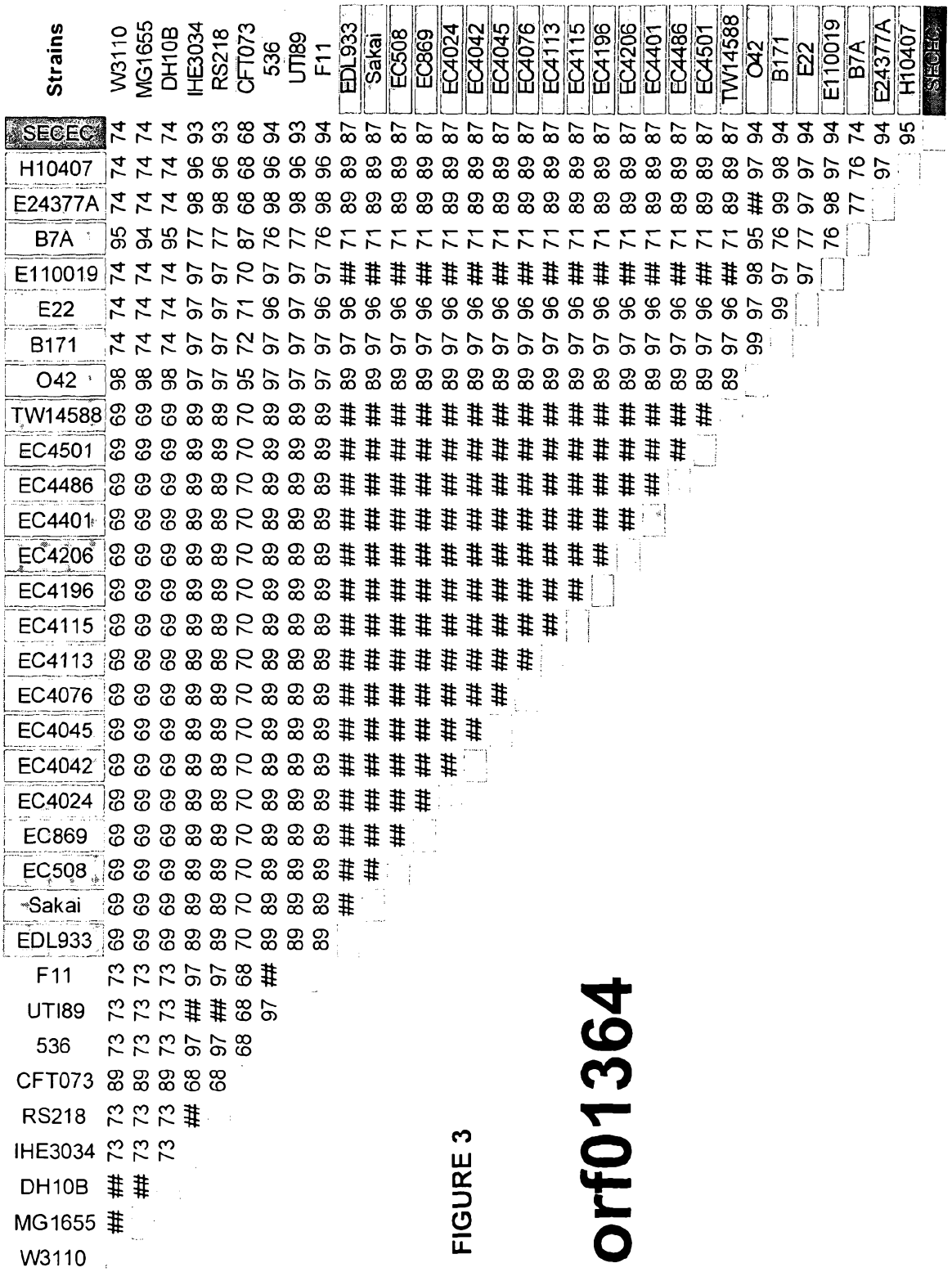

orf00405
Enteroaggregative E coli (EAEC)
Enteroinvasive E coli (EIEC)
Enteropathogenic E coli (EPEC)
Enterotoxigenic E coli (ETEC)
Antibiotic resistent E coli

FIGURE 2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IHE3034
RS218
CFT073
536
UTI89
F11
EDL933
Sakai
EC508
EC869
EC4024
EC4042
EC4045
EC4076
EC4113
EC4115
EC4196
EC4206
EC4401
EC4486
EC4501
TW14588
O42
B171
E22
E110019
B7A
E24377A
H10407
SECEC
orf01364

FIGURE 3

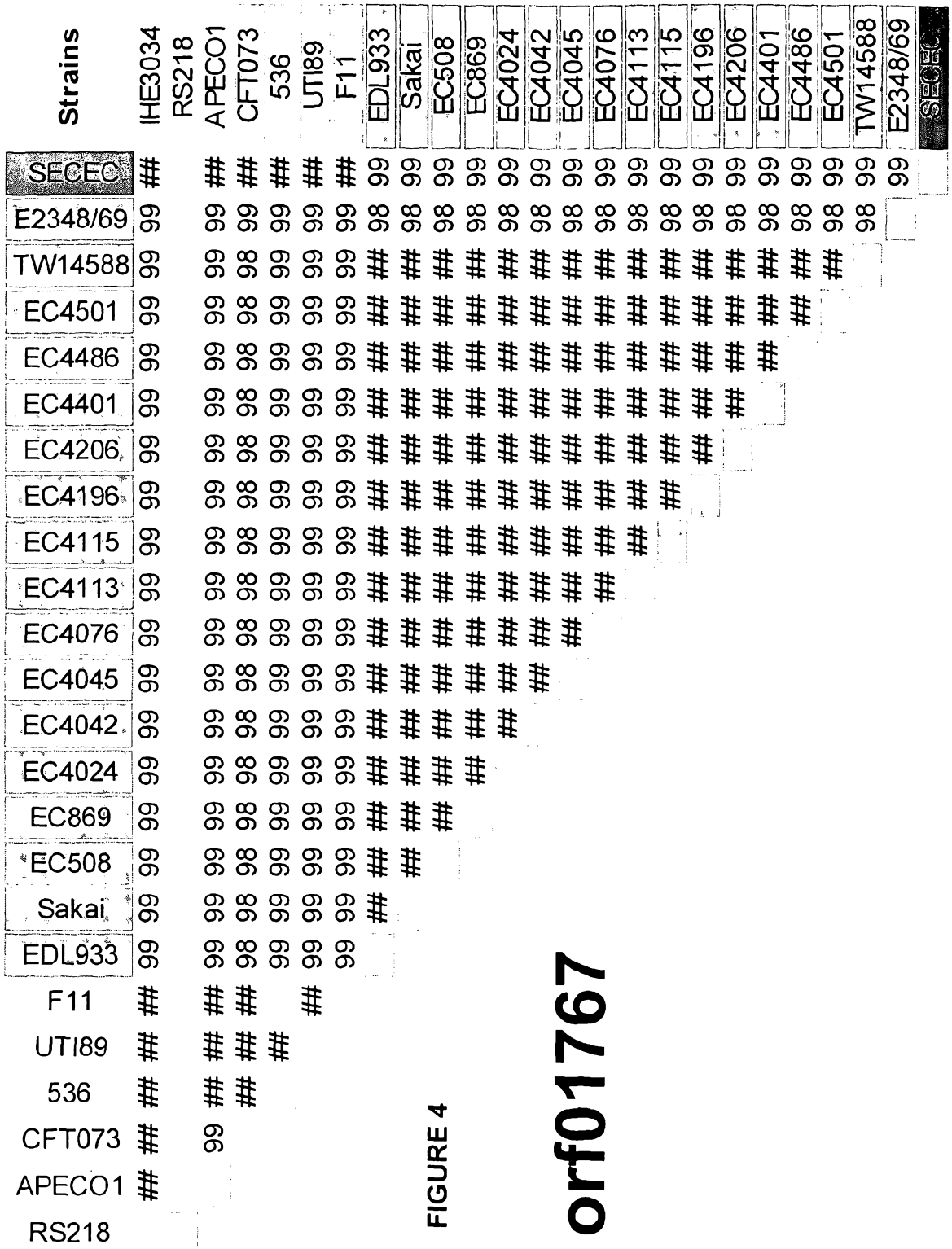
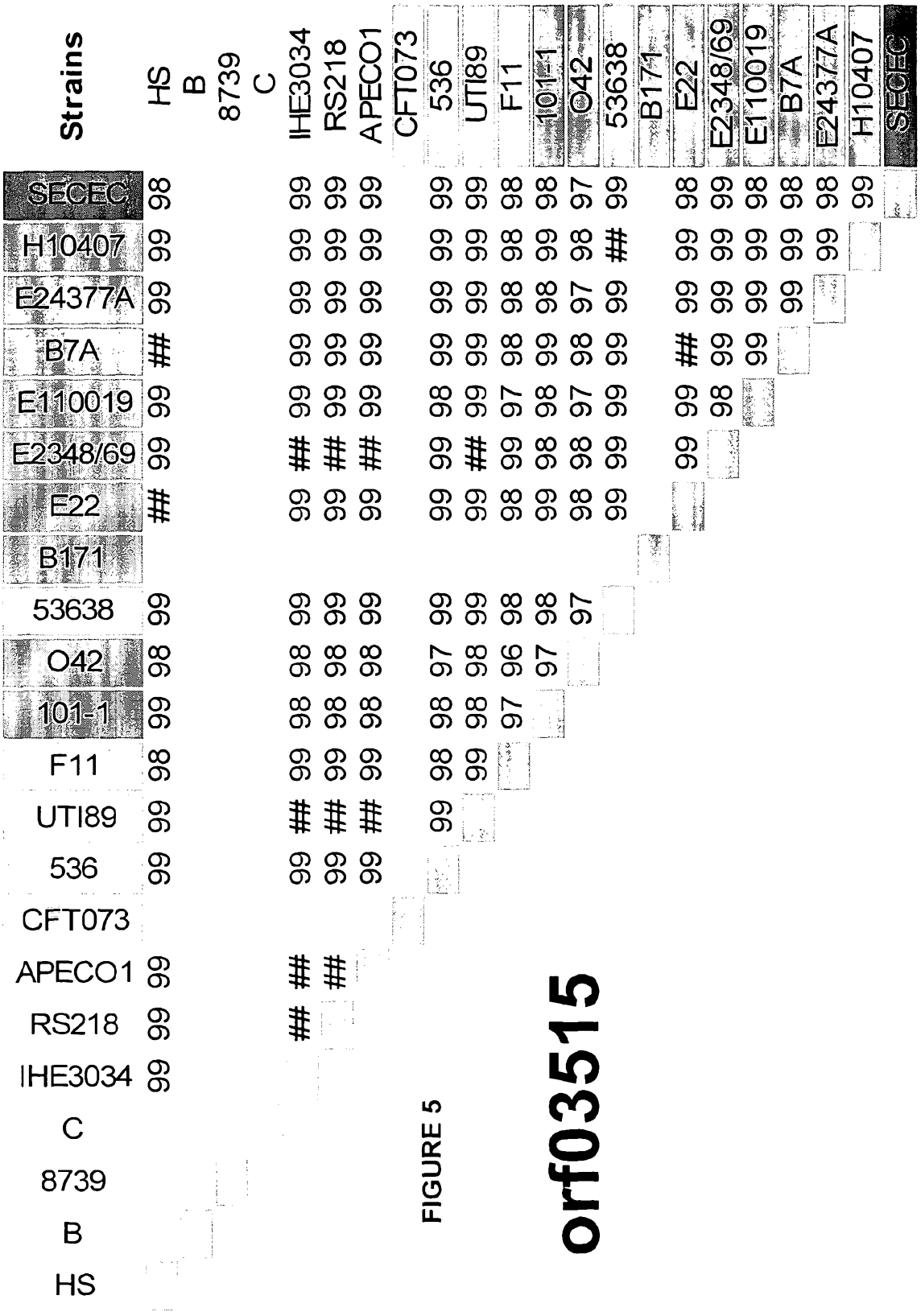


FIGURE 4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536
UTI89
F11
101-1
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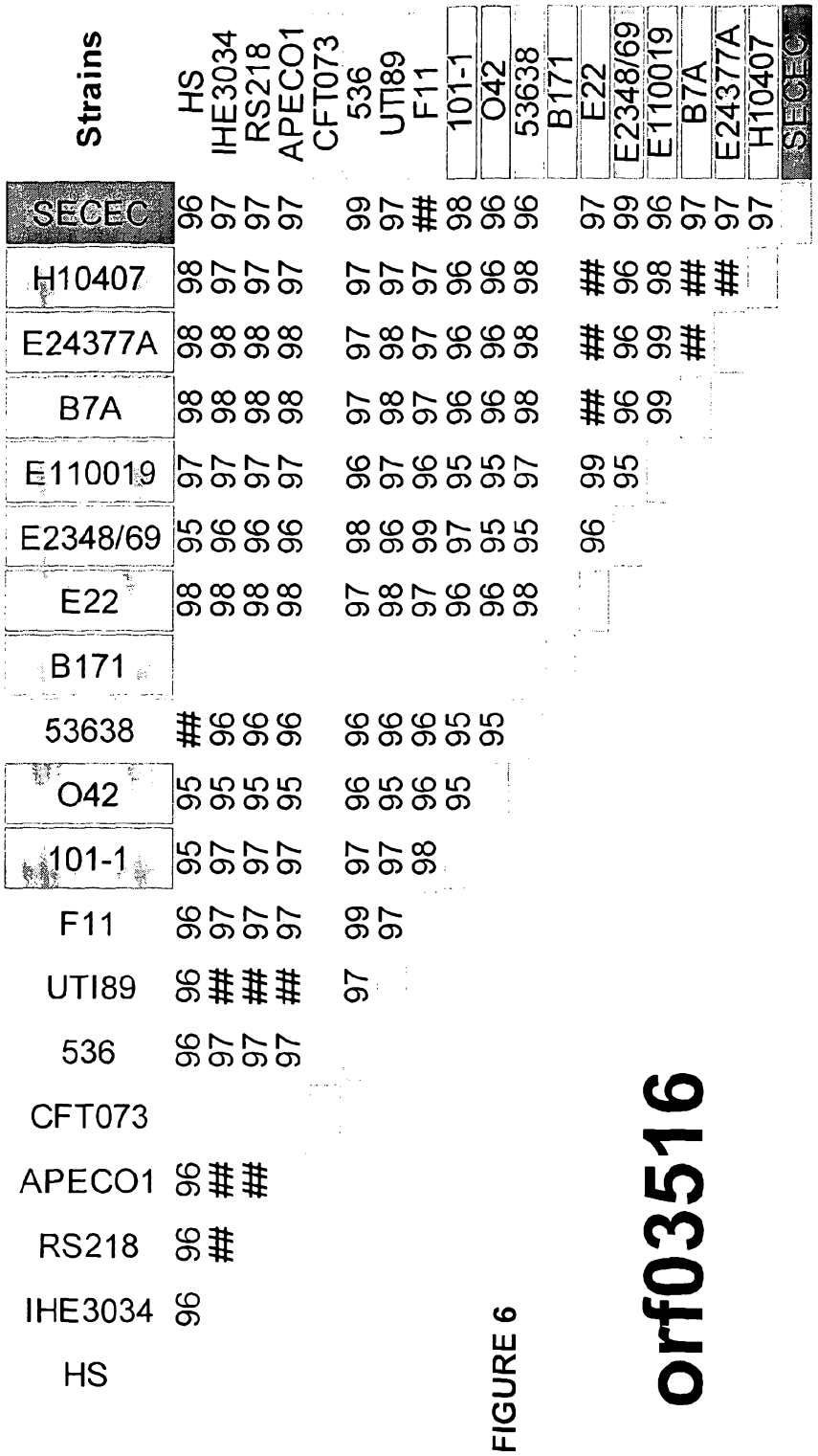
B171
E22
E2348/69
E110019
B7A
E24377A
H10407
SECEC

FIGURE 5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UTI89
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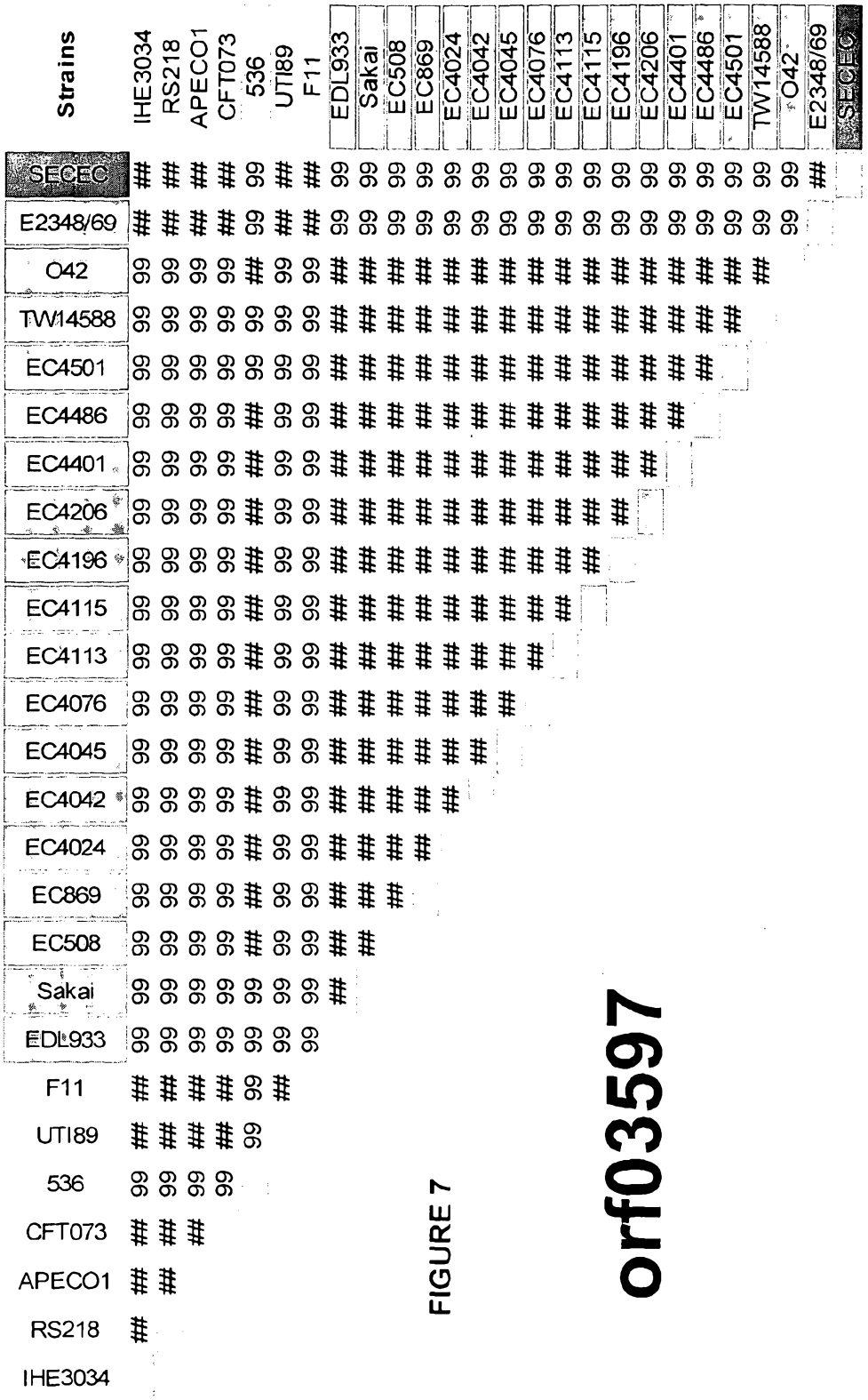
B7A
E24377A
H10407
SECEC

FIGURE 6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CFT073
536
UTI89
F11
EDL933
Sakai
EC508
EC869
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EC4045
EC4076
EC4113
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TW14588
O42
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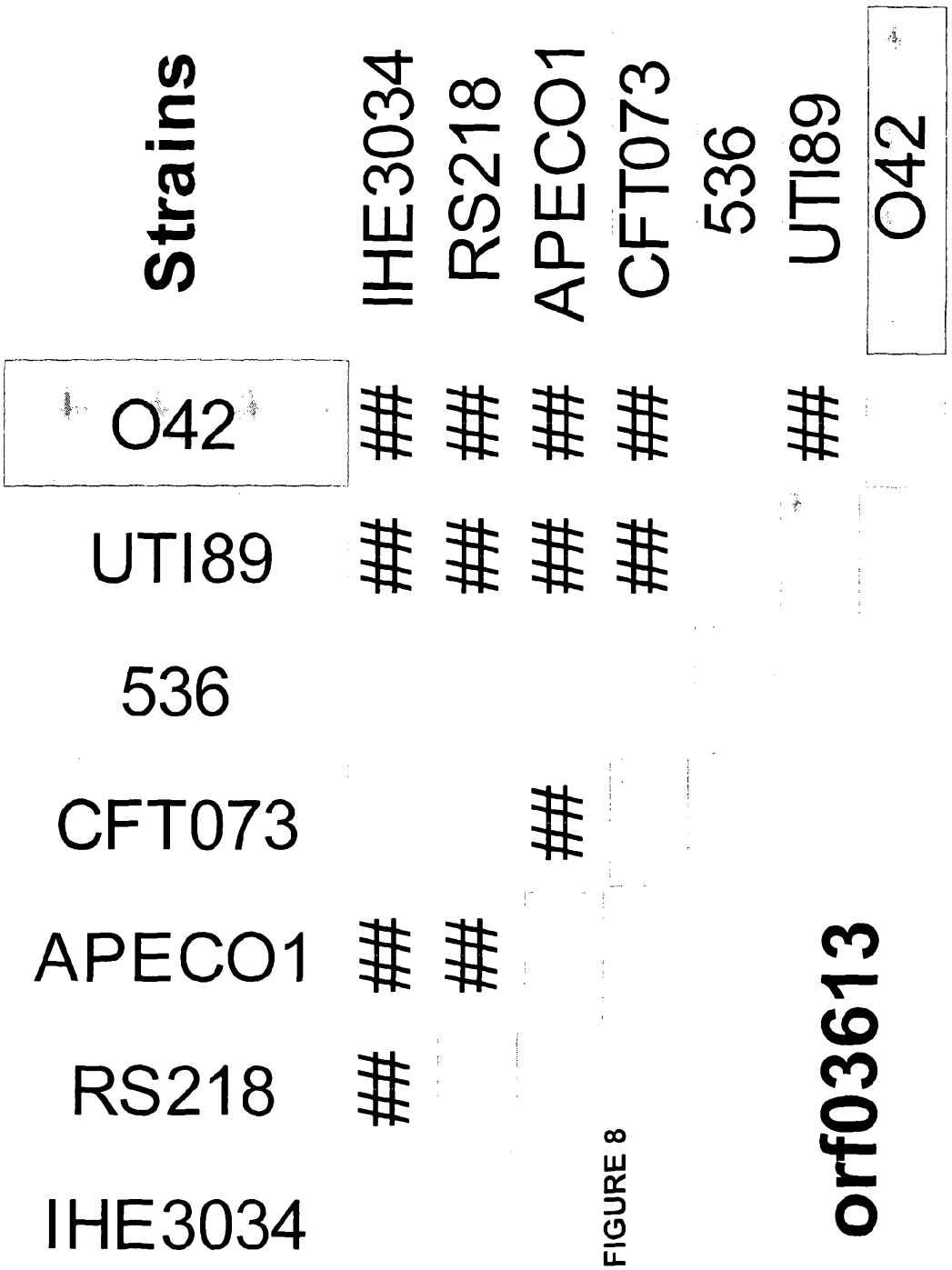
SECEC
orf03597

FIGURE 7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RS218
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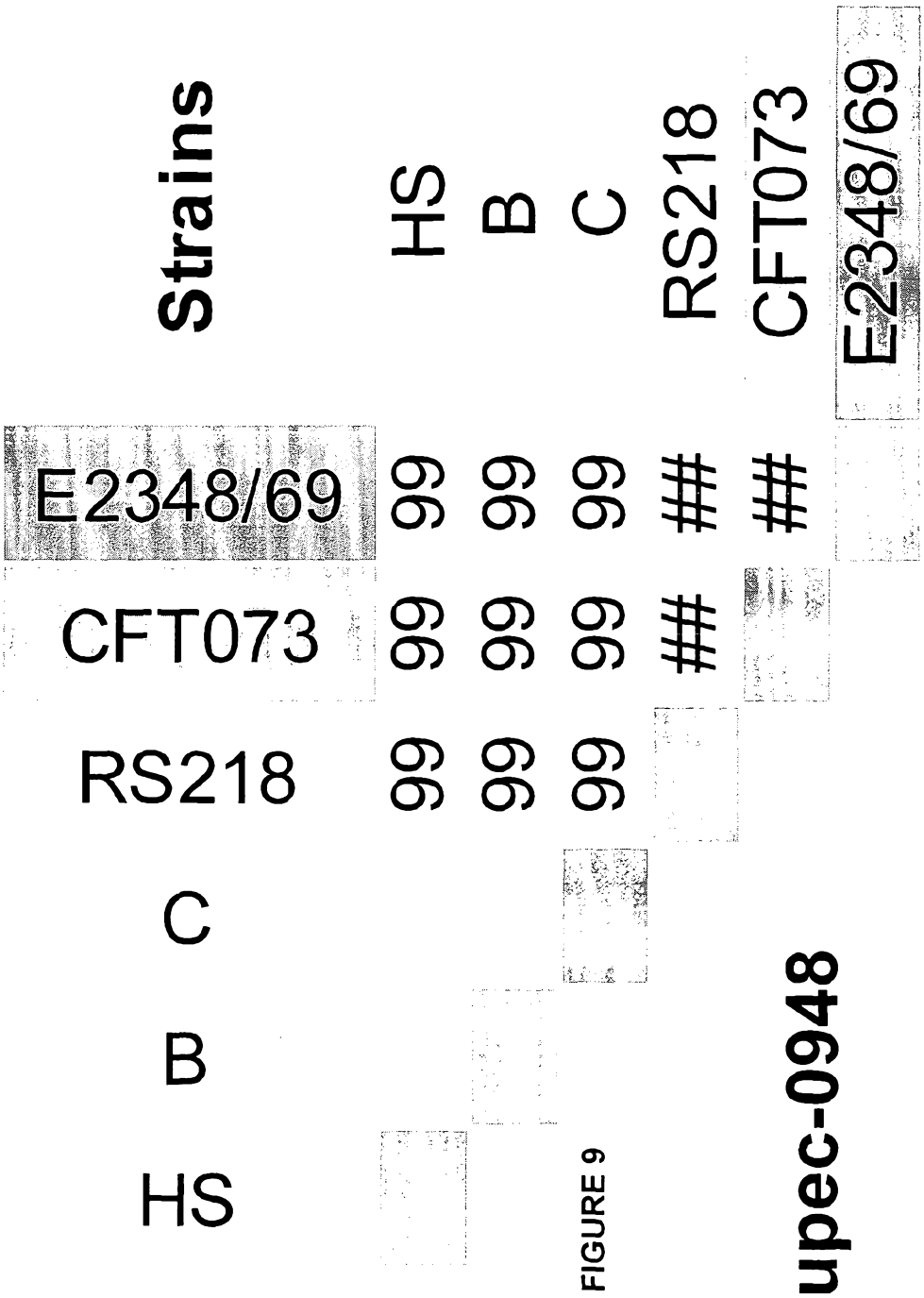
orf03613

FIGURE 8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B
C
RS218
CFT073
E2348/69
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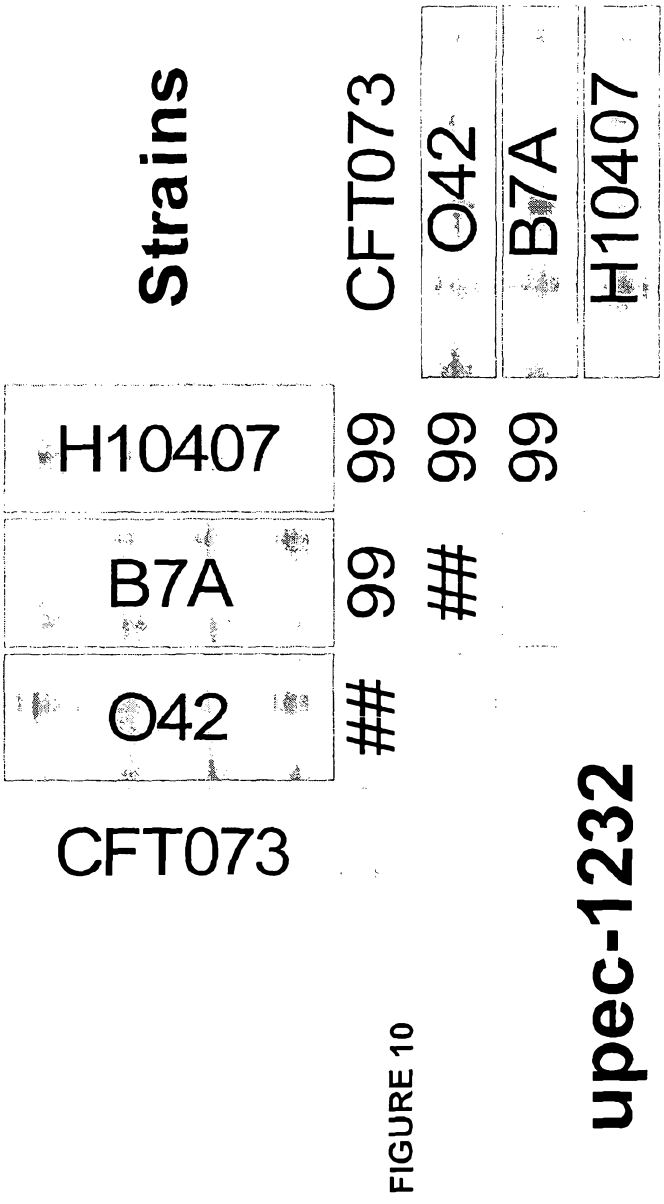
CFT073 99 99 99 ##
RS218 99 99 99
C
B
HS
upec-0948

FIGURE 9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B7A
O42
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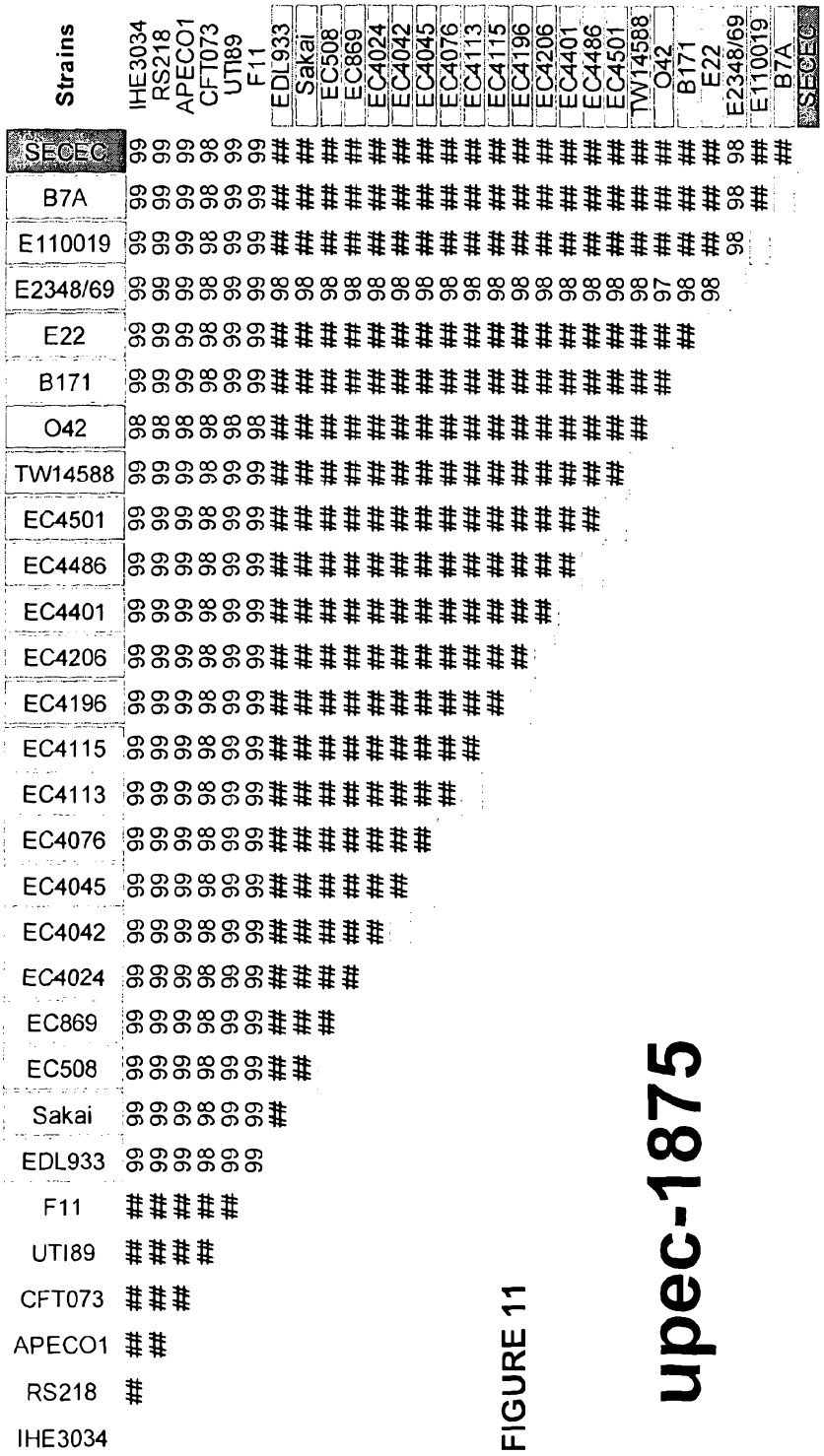
99
99
99
99
##
##

FIGURE 10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EC4115
EC4196
EC4206
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E110019
B7A
SECEC

FIGURE 11

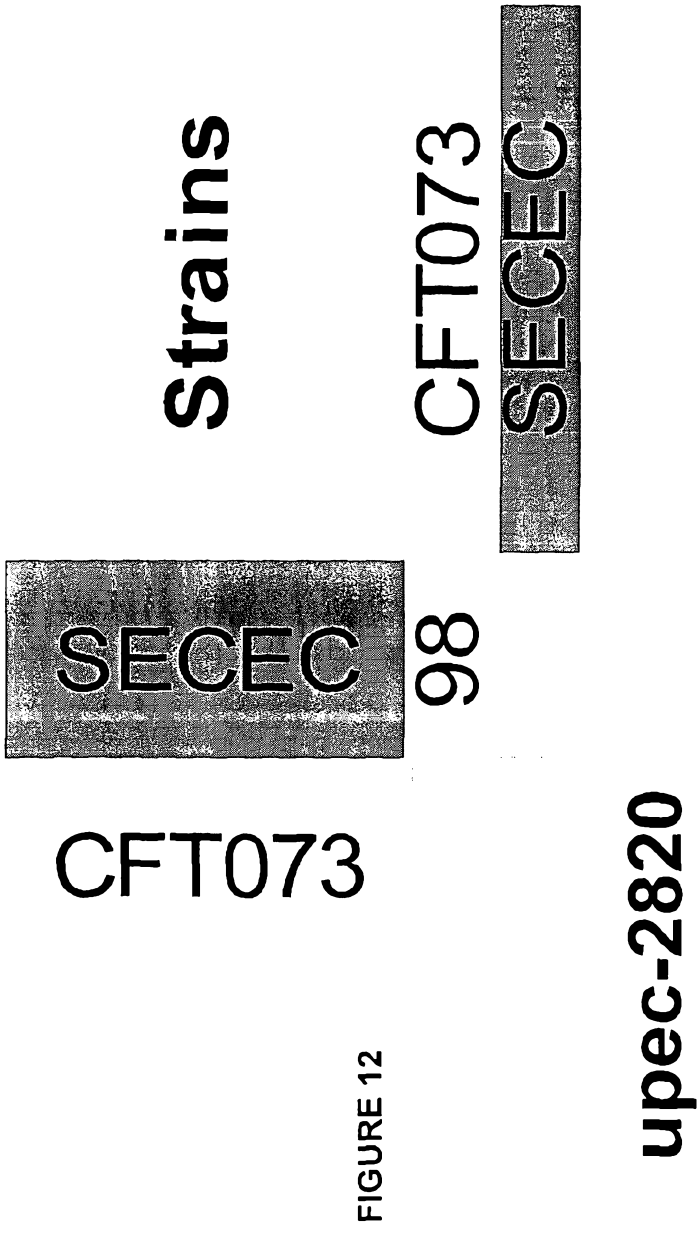
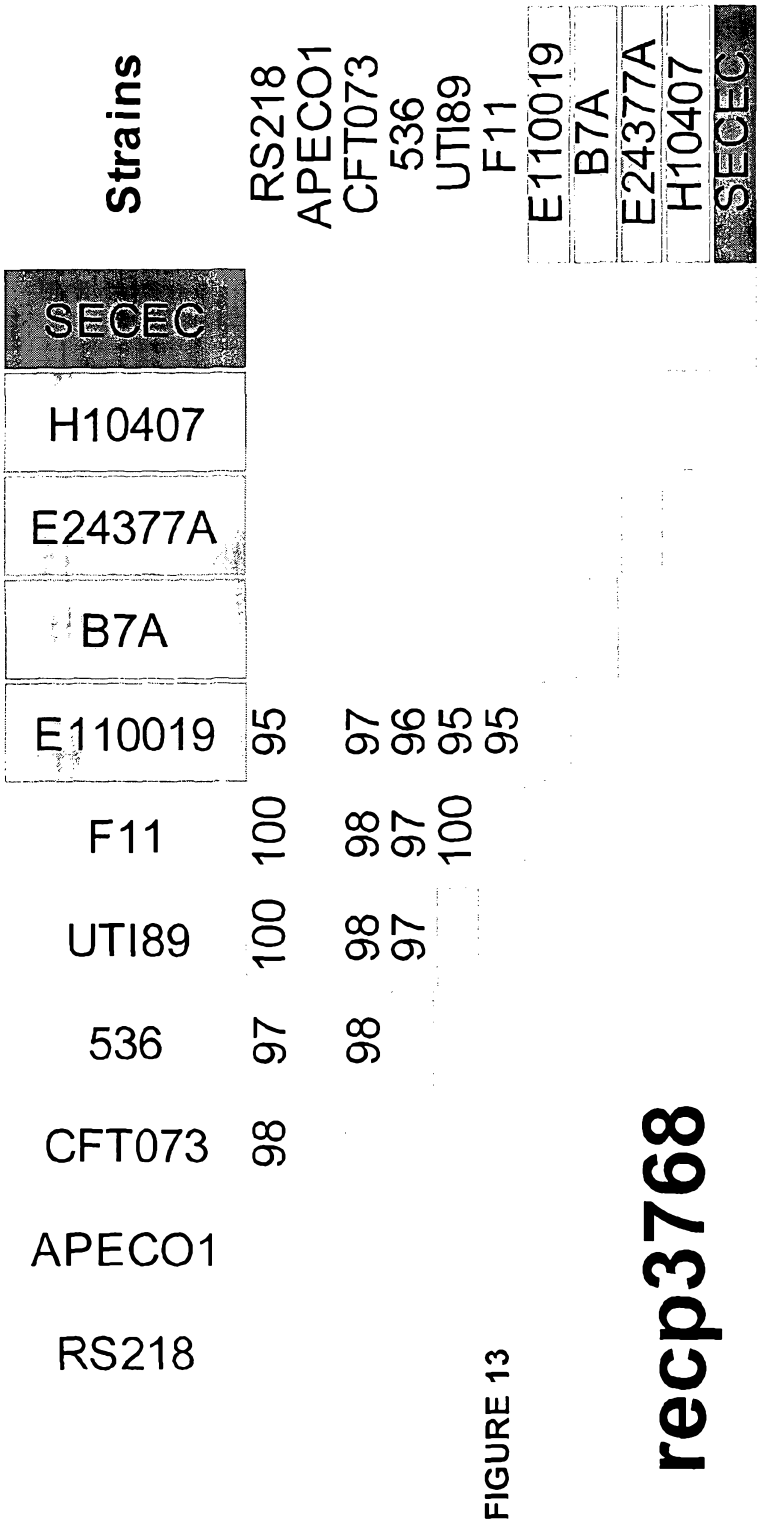


FIGURE 12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UTI89
F11
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B7A
E24377A
H10407
SECEC
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E24377A
B7A
E110019
F11
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536
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APECO1
RS218
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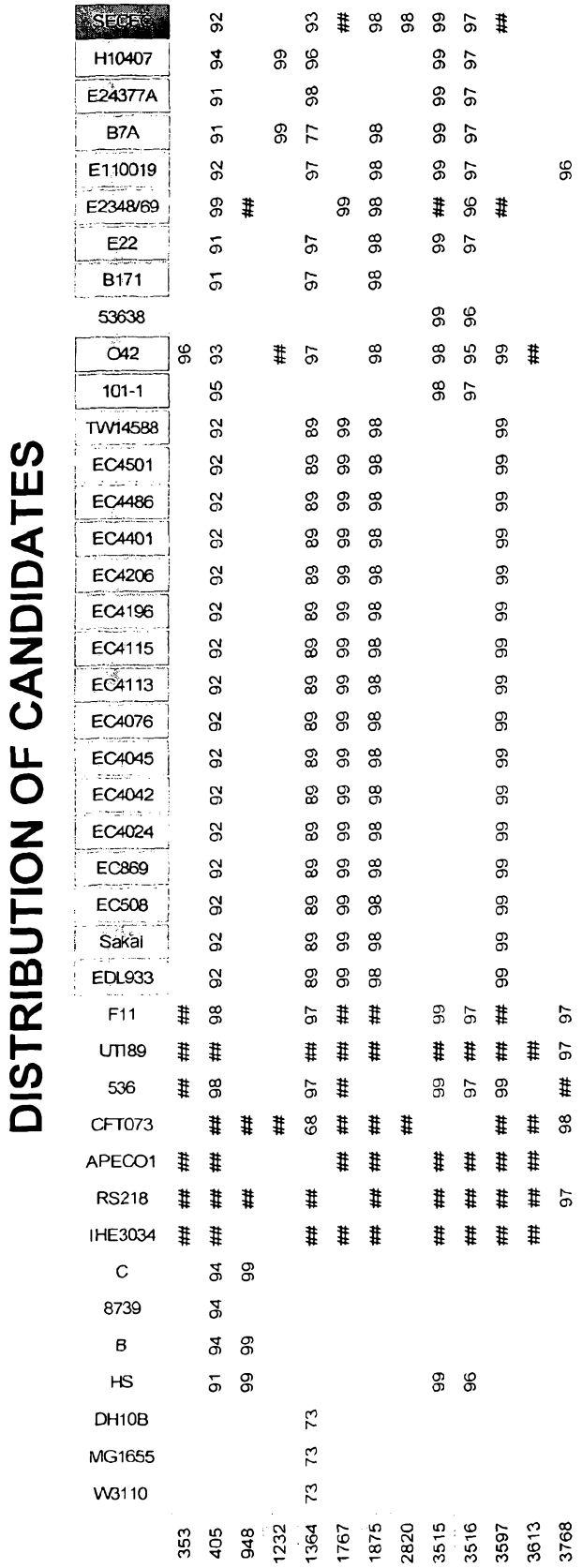
97 96 95 95
100 98 97 100
100 98 97
97 98
98
recp3768

FIGURE 13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EC4024
EC869
EC508
Sakai
EDL933
F11
UTI89
536
CFT073
APECO1
RS218
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C
8739
B
HS
DH10B
MG1655
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2820
3515
3516
3597
3613
3768

FIGURE 14