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CONSERVED ESCHERICHIA COLI IMMUNOGENS

(57) Abstract:

Homologs of the E. coli proteins 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), toriB-dependent siderophore receptor (orf597), 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 I 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 as linear B-epitopes, are provided. In addition, variants of the bacterial Ig-like 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.

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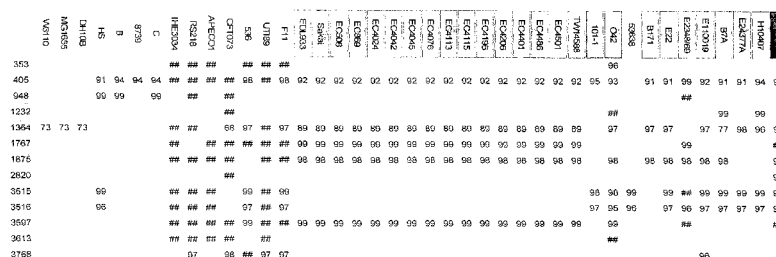


FIGURE 14

(57) Abstract: Homologs of the E. coli proteins orf353, bacterial Ig-like domain (group 1) protein (orf405), flu antigen 43 (orf364), NodT-family outer-membrane-factor-lipoprotein efflux transporter (orf1767), gspK (orf3515), gspJ (orf3516), toriB-dependent siderophore receptor (orf597), fibrin 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-5211) 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 as linear B-epitopes, are provided. In addition, variants of the bacterial Ig-like 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

5 *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
10 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
15 (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
20 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
25 *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
30 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-I 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-I 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), fimbrial protein (orf3613), upec-948, upec-1232, A chain precursor of the type-I fimbrial protein (upec-1875), yapH homolog (upec-2820), hemolysin A (recp-3768), and Sell 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), fimbrial protein (orf3613), upec-948, upec-1232, A chain precursor of the type-I 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.

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 NOs 1-2, wherein *n* is 7 or more (*e.g.* 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 NOs 1-2. Exemplary fragments are the conserved fragments SEQ ID NOs identified in the sequence alignment below.

Group A: strain IHE3034, RS218, APEC01, 536, UTI89 and F11 (SEQ ID NO: 1)
Strain 042 (SEQ ID NO: 2)

	1		50
Group A	MLKMSLYVII	LLFSLQFSAA	ITGKESEVVS PLLMDVNPSL TMENISELST
strain 042	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 042	SSEPSQQGVF	PVICTRLHPG SVMKRQLLTG	WGPVFIIGDD PFSLRWMSEH
Consensus	SSEPSQQGVF	PVICTRLHPG SVMKRQLLTG	WGPVFIIGDD PFSLRWMSEH
B-Cell Ep.	*****		

	101		150
Group A	LEILKSLNAL	GLVVNVESVE RMEVLQQRAD	GLLLLPVICD NFVQALQLNA
strain 042	LEILKSLNAL	GLVVNVESVE RMEVLQQRAD	GLLLLPVICD NFVQTLQLNA
Consensus	LEILKSLNAL	GLVVNVESVE RMEVLQQRAD	GLLLLPVICD NFVQ-LQLNA

	151	162
Group A	YPVLITEMEI	SQ
strain 042	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 SAAITGKESEVVSPLLMDVN

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

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 (e.g. 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)

30	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
35	strain CFT073	MSRYKTDNKQ	PRFRYSVLAR	CVAWANISVQ	VLFPLAVTFT	PVMAARAQHA
	Group A	MSRYKTDNKQ	PRFRYSVLAR	CVAWANISVQ	VLFPLAVTFT	PVMAARAQHA
	strain E2348-69	MSRYKTGHKQ	PRFRYSVLAR	CAWTNISVQ	VLFPLAVTFT	PVMAARAQHA
	strains B171 and E22	MSRYKTGHKQ	PLFRYSVLAR	CVAWANISVQ	VLFPLAVTFT	PVMAAQAQHA
	strain B7A	MSRYKTGHKQ	PRFRYSVLAR	CVAWANISVQ	VLFPLAVTFT	PVMAARAQHA
40	strain E110019	MSRYKTGHKQ	PRFRYSVLAR	CVAWANISVQ	VLFPLAVTFT	PVMAARAQHA
	strain HS	MSRYKTDNKQ	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
45	strain SECEC	MSRYKTGHKQ	PRFRYSVLAR	CVAWANISVQ	VLFPLAVTFT	PVMAARAQHA
	Consensus	MS-YKT--KQ	P-FRYSVLAR	CAW-NISVQ	VLFPLAVTFT	PVMAA-AQHA
			SEQ ID NO: 219	SEQ ID NO: 220		
	Frag		AAAAAAAAA	AAAAAAAAA	AAAAAAAAA	

		51				100
50	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	VQPRLSMGNT	TVTADNNVEK	NVASLAANAG	TFLSSQPDSD	ATRNFITGMA
55	strain F11	VQPRLSMGNT	TVTADNNVEK	NVASLAANAG	TFLSSQPDSD	ATRNFITGMA

	strain CFT073	VQPRLSMENT	TVTADNNVEK	NVASLAANAG	TFLSSQPDS	ATRNFITGMA
	Group A	VQPRLSMENT	TVTADNNVEK	NVASLAANAG	TFLSSQPDS	ATRNFITGMA
	strain E2348-69	VQPRLSMGNT	TVTADNNVEK	NVASFAANAG	TFLSSQPDS	ATRNFITGMA
5	strains B171 and E22	VQPRLSMENT	TVTADNNVEK	NVASFAANAG	TFLSSQPDS	ATRNFITGMA
	strain B7A	VQPRLSMGNT	TVTADNNVEK	NVASFAANAG	TFLSSQPDS	ATRNFITGMA
	strain E110019	VQPRLSMGNT	TVTADNNVEK	NVASFAANAG	TFLSSQPDS	ATRNFITGMA
	strain HS	VQPRLSMGNT	TVTADNNVEK	NVASFAANAG	TFLSSQPDS	ATRNFITGMA
	strain E24377A	VQPRLSMGNT	TVTADNNVEK	NVASFAANAG	TFLSSQPDS	ATRNFITGMA
10	strain O42	VQPRLSMENT	TVAADNNVEK	NVASFAANAG	TFLSSQPDS	ATRNFITGMA
	Group B	VQPRLSMGNT	TVTADNNVEK	NVASFAANAG	TFLSSQPDS	ATRNFITGMA
	strain SECEC	VQPRLSMGNT	TVTADSNVEK	NVASFAANAG	TFLSSQPDS	ATRNFITGMA
	Consensus	VQPRLSM-NT	TVtADnNVEK	NVAS-AANAG	TFLSSQPDS	ATRNFITGMA
	SEQ ID NO: 221	SEQ ID NOS 222-5	SEQ ID NO: 683			
	B-Cell Ep.	*****				***
15	Frag	AAAAAAAAA	AAAAAAAAA	AAAAAAAAA	AAAAAAAAA	AAAAAAAAA
		101				150
	strains B, C and 8739	TAKANQEIQE	WLGKYGTARV	KLNVDKDFSL	KDSSLEMLYP	IYDTPTNMLF
	strain H10407	TAKANQEIQE	WLGKYGTARV	KLNVDKDFSL	KDSSLEMLYP	IYDTPTNMLF
20	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
25	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
30	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
35		SEQ ID NO: 226				
	B-Cell Ep.	*****				
	Frag	AAAAAAAAA	AAAAAAAAA	AAAAAAAAA	AAAAAAAAA	AAAAAAAAA
		151				200
40	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
45	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
50	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
55	strain SECEC	TQGAIHRTDD	RTQSNIGFGW	RHFSGNDWMA	GVNTFIDHDL	SRSHTRIGVG
	Consensus	TQGAIHRTDD	RTQSNIGFGW	RHFS-NDWMA	GVNTFIDHDL	SRSHTRIGVG
		SEQ ID NO: 227				
	B-Cell Ep.	*****				
	Frag	AAAAAAAAA	AAAAAAAAA	AAAAAAAAA	AAAAAAAAA	AAAAAAAAA
60		201				250
	strains B, C and 8739	AEYWRDYLKL	SANGYIRASG	WKKSPDVEDY	QERPANGWDI	RAEGYLPAPW
	strain H10407	AEYWRDYLKL	SANGYIRASG	WKKSPDIEDY	QERPANGWDI	RAEGYLPAPW

	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
5	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
10	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
15	Consensus	AEYWRDYLKL	SANGYIRASG	WK-SPD-EDY	QERPANGWDI	RAEGYLPAWP
		SEQ ID NO: 228				
	B-Cell Ep.		**	*****	*****	* *****
	Frag	AAAAAAAAAA	AAAAAAAAAA	AAAAAAAAAA	AAAAAAAAAA	AAAAAAAAAA
20		251				300
	strains B, C and 8739	QLGASLMYEQ	YYGDEVGLFG	KDKRQKDPHA	ISAEVTTYTPV	PLLTLSAGHK
	strain H10407	QLGASLMYEQ	YYGDEVGLFG	KDKRQKDPHA	ISAEVTTYTPV	PLLTLSAGHK
	strain 101-1	QLGASLMYEQ	YYGDEVGLFG	KDKRQKDPHA	ISAEVTTYTPV	PLLTLSAGHK
	strain 536	QLGASLMYEQ	YYGDEVGLFG	KDKRQKDPHA	ITAEVNYTPV	PLLTLSAGHK
25	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	ISAEVTTYTPV	PLLTLSAGHK
30	strain B7A	QLGASLMYEQ	YYGDEVGLFG	KDKRQKDPHA	ISAEVTTYTPV	PLLTLSAGHK
	strain E110019	QLGASLMYEQ	YYGDEVGLFG	KDKRQKDPHA	ISAEVTTYTPV	PLLTLSAGHK
	strain HS	QLGASLMYEQ	YYGDEVGLFG	KDKRQKDPHA	ISAEVTTYTPV	PLLTLSAGHK
	strain E24377A	QLGASLMYEQ	YYGDEVGLFG	KDKRQKDPHA	ISAEVTTYTPV	PLLTLSAGHK
	strain O42	QLGASLMYEQ	YYGDEVGLFG	KDKRQKDPHA	ITAEVNYTPV	PLLTLSAGHK
35	Group B	QLGASLMYEQ	YYGDEVGLFG	KDKRQKDPHA	ISAEVTTYTPV	PLLTLSAGHK
	strain SECEC	QLGASLMYEQ	YYGDEVGLFG	KDKRQKDPHA	ISAEVTTYTPV	PLLTLSAGHK
	Consensus	QLGASLMYEQ	YYGDEVGLFG	KDKRQKDPHA	I-AEV-YTPV	PLLTLSAGHK
		SEQ ID NO: 229				
	B-Cell Ep.	*		*****	*	***
40	Frag	AAAAAAAAAA	AAAAAAAAAA	AAAAAAAAAA	AAAAAAAAAA	AAAAAAAAAA
		301				350
	strains B, C and 8739	QGKSGENDTR	FGLEVNYRIG	EPLAKQLDTD	SIRERRVLG	SRDYDLVERN
	strain H10407	QGKSGENDTR	FGLEVNYRIG	EPLAKQLDTD	SIRERRVLG	SRDYDLVERN
45	strain 101-1	QGKSGENDTR	FGLEVNYRIG	EPLAKQLDTD	SIRERRVLG	SRDYDLVERN
	strain 536	QGKSGENDTR	FGLEVNYRIG	EPLAKQLDTD	SIRERRVLG	SRDYDLVERN
	strain F11	QGKSGENDTR	FGLEVNYRIG	EPLAKQLDTD	SIRERRVLG	SRDYDLVERN
	strain CFT073	QGKSGENDTR	FGLEVNYRIG	EPLAKQLDTD	SIRERRVLG	SRDYDLVERN
	Group A	QGKSGENDTR	FGLEVNYRIG	EPLAKQLDTD	SIRERRVLG	SRDYDLVERN
50	strain E2348-69	QGKSGENDTR	FGLEVNYRIG	EPLAKQLDTD	SIRERRVLG	SRDYDLVERN
	strains B171 and E22	QGKSGENDTR	FGLEVNYRIG	EPLAKQLDTD	SIRERRVLG	SRDYDLVERN
	strain B7A	QGKSGENDTR	FGLEVNYRIG	EPLAKQLDTD	SIRERRVLG	SRDYDLVERN
	strain E110019	QGKSGENDTR	FGLEVNYRIG	EPLAKQLDTD	SIRERRVLG	SRDYDLVERN
	strain HS	QGKSGENDTR	FGLEVNYRIG	EPLAKQLDTD	SIRERRVLG	SRDYDLVERN
55	strain E24377A	QGKSGENDTR	FGLEVNYRIG	EPLAKQLDTD	SIRERRVLG	SRDYDLVERN
	strain O42	QGKSGENDTR	FGLEVNYRIG	EPLAKQLDTD	SIRERRVLG	SRDYDLVERN
	Group B	QGKSGENDTR	FGLEVNYRIG	EPLAKQLDTD	SIRERRVLG	SRDYDLVERN
	strain SECEC	QGKSGENDTR	FGLEVNYRIG	EPLAKQLDTD	SIRERRVLG	SRDYDLVERN
	Consensus	QGKSGENDTR	FGLEVNYRIG	EPLAKQLDTD	SIRERRVLG	SRDYDLVERN
60		SEQ ID NO: 230 SEQ ID NO: 231				
	B-Cell Ep.	*****		*****	*	
	Frag	AAAAAAAAAA	AAAAAAAAAA	AAAAAAAAAA	AAAAAAAAAA	AAAAAAAAAA

		351			400
	strains B, C and 8739	NIVLEYRKSE	VIRIALPERI	EGKGGQTL	SL GLVVS
	strain H10407	NIVLEYRKSE	VIRIALPERI	EGKGGQTL	SL GLVVS
	strain 101-1	NIVLEYRKSE	VIRIALPERI	EGKGGQTL	SL GLVVS
5	strain 536	NIVLEYRKSE	VIRIALPERI	EGKGGQTV	SL GLVVS
	strain F11	NIVLEYRKSE	VIRIALPERI	EGKGGQTV	SL GLVVS
	strain CFT073	NIVLEYRKSE	VIRIALPERI	EGKGGQTV	SL GLVVS
	Group A	NIVLEYRKSE	VIRIALPERI	EGKGGQTV	SL GLVVS
	strain E2348-69	NIVLEYRKSE	VIRIALPERI	EGKGGQTV	SL GLVVS
10	strains B171 and E22	NIVLEYRKSE	VIRIALPERI	EGKGGQTL	SL GLVVS
	strain B7A	NIVLEYRKSE	VIRIALPERI	EGKGGQTL	SL GLVVS
	strain E110019	NIVLEYRKSE	VIRIALPERI	EGKGGQTL	SL GLVVS
	strain HS	NIVLEYRKSE	VIRIALPERI	EGKGGQTL	SL GLVVS
	strain E24377A	NIVLEYRKSE	VIRIALPERI	EGKGGQTL	SL GLVVS
15	strain 042	NIVLEYRKSE	VIRIALPERI	EGKGGQTL	SL GLVVS
	Group B	NIVLEYRKSE	VIRIALPERI	EGKGGQTL	SL GLVVS
	strain SECEC	NIVLEYRKSE	VIRIALPDRI	AGKGGQTV	SL GLVVS
	Consensus	NIVLEYRKSE	VIRIALP-RI	eGKGGQ-T-SL	GLVVS
				SEQ ID NO: 232-4	SEQ ID NO: 235
20	B-Cell Ep.			* *	
	Frag	AAAAAAAAA	AAAAAAAAA	AAAAAAAAA	AAAAAAAAA
		401			450
	strains B, C and 8739	LLAEGGKITG	QGSQWQVTL	AYRPGKDN	Y AISAVAYDNK GNASKRVQTE
25	strain H10407	LLAEGGKITG	QGSQWQVTL	AYRPGKDN	Y AISAVAYDNK GNASKRVQTE
	strain 101-1	LLAEGGKITG	QGSQWQVTL	AYRPGKDN	Y AISAVAYDNK GNASKRVQTE
	strain 536	LLAAGGKITG	QGNQWQVTL	AYQAGKDN	Y AISAIAYDNK GNASKRVQTE
	strain F11	LLAAGGKITG	QGNQWQVTL	AYQAGKDN	Y AISAIAYDNK GNASKRVQTE
	strain CFT073	LLAAGGKITG	QGNQWQVTL	AYQAGKDN	Y AISAIAYDNK GNASKRVQTE
30	Group A	LLAAGGKITG	QGNQWQVTL	AYQAGKDN	Y AISAIAYDNK GNASKRVQTE
	strain E2348-69	LLAAGGKITG	QGNQWQVTL	AYQAGKDN	Y AISAIAYDNK GNASKRVQTE
	strains B171 and E22	LLAEGGKITG	QGSQWQVTL	AYRPGKDN	Y AISAVAYDNK GNASKRVQTE
	strain B7A	LLAEGGKITG	QGSQWQVTL	AYRPGKDN	Y AISAVAYDNK GNASKRVQTE
	strain E110019	LLAEGGKITG	QGSQWQVTL	AYRPGKDN	Y AISAVANDNK GNASKRVQTE
35	strain HS	LLAEGGKITG	QGSQWQVTL	AYRPGKDN	Y AISAVAYDNK GNASKRVQTE
	strain E24377A	LLAEGGKITG	QGSQWQVTL	AYRPGKDN	Y AISAVAYDNK GNASKRVQTE
	strain 042	LLAEGGKITG	QGSQWQVTL	AYRPGKDN	Y AVSAIAYDNK GNASKRVQTE
	Group B	LLAEGGKITG	QGSQWQVTL	AYRPGKDN	Y AISAVAYDNK GNTSKRVQTE
	strain SECEC	LLAAGGKITG	QGNQWQVTL	AYQAGKDN	Y AISAVAYDNK GNASKRVQTE
40	Consensus	LLA-GGKITG	QG-QWQVTL	AY--GKDN	Y A-SA-A-DNK GNASKRVQTE
				SEQ ID NO: 236	
	B-Cell Ep.			*** *	
	Frag	AAAAAAAAA	AAAAAAAAA	AAAAAAAAA	AAAAAAAAA
45		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
50	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
55	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 042	VVISGAGMSA	DRTALTLDGQ	SRIQMLANGN	EQKPLVLSLR DAEGQPVTGM
60	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

B-Cell Ep. Frag		*****				
		AAAAAAAAAA	AAAAAAAAAA	AAAAAAAAAA	AAAAAAAAAA	AAAAAAAAAA
		501				550
5	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
10	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
15	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
20	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
25	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
30	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
35	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
40	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	AAAAAAAAAA	AAABBBBBBB
		601				650
50	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
55	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
60	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	IKPGVYSAV

strain SECEC		SHTLTTLTAVD	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.		*****		*****		
5	Frag	BBBBBBBBBB	BBBBBBBBBB	BBBBBBBBBB	BBBBBBBBBB	BBBBBBBBBB
		651		700		
10	strains B, C and 8739	SSTRAGNVVV	RAFSEQYQLG	TLQOTLK FVA	GPLDAAHSSI	TLNPDKPVVG
	strain H10407	SSTRAGNVVV	RAFSEQYQLG	TLQOTLK FVA	GPLDAAHSSI	PLNPDKPVVG
	strain 101-1	SSTRAGNVVV	RAFSEQYQLG	TLQOTLK FVA	GPLDAAHSSI	TLNPDKPVVG
	strain 536	SSTRAGNVVV	RAFSEQYQLG	TLQOTLK FVA	GPLDAAHSSI	TLNPDKPVVG
	strain F11	SSTRAGNVVV	RAFSEQYQLG	TLQOTLK FVA	GPLDAAHSSI	TLNPDKPVVG
15	strain CFT073	SSTRAGNVVV	RAFSEQYQLG	TLQOTLK FVA	GPLDAAHSSI	TLNPDKPVVG
	Group A	SSTRAGNVVV	RAFSEQYQLG	TLQOTLK FVA	GPLDAAHSSI	TLNPDKPVVG
	strain E2348-69	SSTRAGNVVV	RVFSEQYQLG	TLQOTLK FVA	GPLDAAHSSI	TLNPDKPVVG
	strains B171 and E22	SSTRAGNVVV	RAFSEQYQLG	TLQOTLK FVA	GPLDAAHSSI	TLNPDKPVVG
	strain B7A	SSTRAGNVVV	RAFSEQYQLG	TLQOTLK FVA	GPLDAAHSSI	TLNPDKPVVG
20	strain E110019	SSTRAGNVVV	RAFSEQYQLG	TLQOTLK FVA	GPLDAAHSSI	TLNPDKPVVG
	strain HS	SSTRAGNVVV	RAFSEQYQLG	TLQOTLK FVA	GPLDAAHSSI	TLNPDKPVVG
	strain E24377A	SSTRAGNVVV	RAFSEQYQLG	TLQOTLK FVA	GPLDAAHSSI	TLNPDKPVVG
	strain O42	SSTRAGNVVV	RAFSEQYQLG	TLQOTLK FVA	GPLDAAHSSI	TLNPDKPVVG
	Group B	SSTRAGNVVV	RAFSEQYQLG	TLQOTLK FVA	GPLDAAHSSI	TLNPDKPVVG
25	strain SECEC	SSTRAGNVVV	RAFSEQYQLG	TLQOTLK FVA	GPLDAAHSSI	TLNPDKPVVG
	Consensus	SSTRAGNVVV	R-FSEQYQLG	TLQOTLK FVA	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		
30	strains B, C and 8739	GTVTAIWTAK	DAYDNPVTS	TPEAPSLAGA	AAVGSTASGW	TNNGDGTWTA
	strain H10407	GTVTAIWTAK	DAYDNPVTS	TPEAPSLAGA	AAVGSTASGW	TNNGDGTWTA
	strain 101-1	GTVTAIWTAK	DANDNPVTGL	NPDAAPSLSGA	AAVGSTASGW	TDNGDGTWTA
	strain 536	GTVTAIWTAK	DANDNPVTGL	NPDAAPSLSGA	AAAGSTASGW	TDNGDGTWTA
	strain F11	GTVTAIWTAK	DANDNPVTGL	NPDAAPSLSGA	AAAGSTASGW	TDNGDGTWTA
35	strain CFT073	GTVTAIWTAK	DANDNPVTGL	NPDAAPSLSGA	AAAGSTASGW	TDNGDGTWTA
	Group A	GTVTAIWTAK	DANDNPVTGL	NPDAAPSLSGA	AAAGSTASGW	TDNGDGTWTA
	strain E2348-69	GTVTAIWTAK	DANDNPVTGL	NPDAAPSLSGA	AAAGSTASGW	TDNGDGTWTA
	strains B171 and E22	GTVTAIWTVK	DAYDNPVTS	TPEAPSLAGA	AAVGSTASGW	TNNGDGTWTA
	strain B7A	GTVTAIWTVK	DAYDNPVTS	TPEAPSLAGA	AAVGSTASGW	TNNGDGTWTA
40	strain E110019	GTVTAIWTAK	DANDNPVTGL	NPDAAPSLSGA	AAAGSTASGW	TDNGDGTWTA
	strain HS	GTVTAIWTAK	DANDNPVTGL	NPDAAPSLSGA	AAAGSTASGW	TDNGDGTWTA
	strain E24377A	GTVTAIWTVK	DAYDNPVTS	TPEAPSLAGA	AAVGSTASGW	TNNGDGTWTA
	strain O42	GTVTAIWTAK	DANDNPVTGL	NPDAAPSLSGA	AAAGSTASGW	TNNGDGTWTA
	Group B	GTVTAIWTVK	DAYDNPVTS	TPEAPSLAGA	AAAGSTASGW	TNNGDGTWTA
45	strain SECEC	GTVTAIWTAK	DAYDNPVTS	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		
55	strains B, C and 8739	QITLGSTAGE	LEVMPKLNQ	DAAANA AKVT	VVADALSSNQ	SKVSV AEDHV
	strain H10407	QITLGSTAGE	LEVMPKLNQ	DAAANA AKVT	VVADALSSNQ	SKVSV AEDHV
	strain 101-1	QISLGTTAGE	LEVMPKLNQ	DAAANA AKVT	VVADALSSNQ	SKVSV AEDHV
	strain 536	QISLGTTAGE	LDVMPKLNQ	DAAANA AKVT	VVADALSSNQ	SKVSV AEDHV
	strain F11	QISLGTTAGE	LDVMPKLNQ	DAAANA AKVT	VVADALSSNQ	SKVSV AEDHV
60	strain CFT073	QISLGTTAGE	LDVMPKLNQ	DAAANA AKVT	VVADALSSNQ	SKVSV AEDHV
	Group A	QISLGTTAGE	LDVMPKLNQ	DAAANA AKVT	VVADALSSNQ	SKVSV AEDHV
	strain E2348-69	QISLGTTAGE	LDVMPKLNQ	DAAANA AKVT	VVADALSSNQ	SKVSV AEDHV
	strains B171 and E22	QITLGSTAGE	LEVMPKLNQ	DAAANA AKVT	VVADALSSNQ	SKVSV AEDHV
	strain B7A	QITLGSTAGE	LEVMPKLNQ	DAAANA AKVT	VVADALSSNQ	SKVSV AEDHV
	strain E110019	QISLGTTAGE	LEVIPKLNQ	DAAANA AKVT	VVADALSSNQ	SKVSV AEDHV
	strain HS	QISLGTTAGE	LEVIPKLNQ	DAAANA AKVT	VVADALSSNQ	SKVSV AEDHV

5	strain E24377A	QITLGSTAGE	LEVMPKLNQ	DAAANAAKVT	VVADALSSNQ	SKVSV AEDHV
	strain 042	QITLGSTAGE	LEVMPKLNQ	DAAANAAKVT	VVADALSSNQ	SKVSV AEDHV
	Group B	QITLGSTAGE	LEVMPKLNQ	NAAANAAKVT	VVADALSSNQ	SKVSV AEDHV
	strain SECEC	QITLGSTAGE	LDVMPKLNQ	DAAANAAKVT	VVADALSSNQ	SKVSV AEDHV
	Consensus	<u>QI-LG-TAGE</u>	<u>L-V-PKLNQ</u>	<u>-AAANAAKVT</u>	<u>VVADALSSNQ</u>	<u>SKVSV AEDHV</u>
SEQ ID NO: 249						

B-Cell Ep.						
Frag						
BBBBBBBBBBB BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB						
10		801				850
	strains B, C and 8739	KAGESTTVTL	IAKDAHGNTI	SGLSLSASLT	GTASEGATVS	SWTEKGDGSY
	strain H10407	KAGESTTVTL	IAKDAHGNTI	SGLSLSASLT	GTASEGATVS	SWTEKGDGSY
	strain 101-1	KAGESTTVTL	VAKDAHGNAI	SGLSLSASLT	GTASEGATVS	SWTEKGDGSY
	strain 536	KAGESTTVTL	VAKDAHGNAI	SGLSLSASLT	GTASEGATVS	SWTEKGDGSY
15	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
20	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 042	KAGESTTVTL	IAKDAHGNAI	SGLSLSASLT	GTASEGATVS	SWTEKGDGSY
25	Group B	KAGESTTVTL	VAKDAHGNAI	SGLALSASLT	GTASEGATVS	SWTEKGNDSY
	strain SECEC	KAGESTTVTL	IAKDAHGNAI	SGLSLSASLT	GAASEGATVS	SWTEKGDGSY
	Consensus	<u>KAGESTTVTL</u>	<u>-AKDAHGN-I</u>	<u>-GL-LSASLT</u>	<u>G-ASEGATVS</u>	<u>sWTEKG--SY</u>
SEQ ID NO: 250-253						

B-Cell Ep.						
Frag						
BBBBBBBBBBB BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB						
30		851				900
	strains B, C and 8739	VATLTTGGKT	GELRVMPFN	GQPAATEAAQ	LTVIAGEMSS	ANSTLVAANK
	strain H10407	VATLTTGGKT	GELRVMPFN	GQPAATEAAQ	LTVIAGEMSS	ANSTLVADNK
	strain 101-1	VATLTTGGKT	GELRVMPFN	GQPAATEAAQ	LTVIAGEMSS	ANSTLVADNK
	strain 536	VATLTTGGKT	GELRVMPFN	GQPAATEAAQ	LTVIAGEMSS	ANSTLVADNK
35	strain F11	VATLTTGGKT	GELRVMPFN	GQPAATEAAQ	LTVIAGEMSS	ANSTLVADNK
	strain CFT073	VATLTTGGKT	GELRVMPFN	GQPAATEAAQ	LTVIAGEMSS	ANSTLVADNK
	Group A	VATLTTGGKT	GELRVMPFN	GQPAATEAAQ	LTVIAGEMSS	ANSTLVADNK
	strain E2348-69	VATLTTGGKT	GELRVMPFN	GQPAATEAAQ	LTVIAGEMSS	ANSTLVADNK
	strains B171 and E22	VATLTTGGKT	GELRVMPFN	GQPAATEAAQ	LTVIAGEMSS	ANSTLVADNK
40	strain B7A	VATLTTGGKT	GELRVMPFN	GQPAATEAAQ	LTVIAGEMSS	ANSTLVADNK
	strain E110019	VATLTTGGKT	GELRVMPFN	GQPAATEAAQ	LTVIAGEMSS	ANSTLVADNK
	strain HS	VATLTTGGKT	GELRVMPFN	GQPAATEAAQ	LTVIAGEMSS	ANSTLVADNK
	strain E24377A	VATLTTGGKT	GELRVMPFN	GQPAATEAAQ	LTVIAGEMSS	ANSTLVADNK
	strain 042	VATLTTGGKT	GELRVMPFN	GQPAATEAAQ	LTVIAGEMSS	ANSTLVADNK
45	Group B	VATLTTGGKT	GELRVMPFN	GQPAATEAAQ	LTVIAGEMSS	ANSTLVADNK
	strain SECEC	VATLTTGGKT	GELRVMPFN	GQPAATEAAQ	LTVIAGEMSS	ANSTLVADNK
	Consensus	<u>VATLTTGGKT</u>	<u>GEL-VMPLFN</u>	<u>GQPAATEAAQ</u>	<u>LTVIAGEMSS</u>	<u>ANSTLVA-N-</u>
SEQ ID NO: 254						

B-Cell Ep.						
Frag						
BBBBBBBBBBB BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB BBBBBBBBBB						
50		901				950
	strains B, C and 8739	APTVMKTTTEL	TFTVKDAYGN	PVTGLKPDAP	VFSGAASTGS	ERPSAGNWTE
	strain H10407	APTVMKTTTEL	TFTVKDAYGN	PVTGLKPDAP	VFSGAASTGS	ERPSAGNWTE
	strain 101-1	APTVMKTTTEL	TFTVKDAYGN	PVTGMKPDAP	VFSGAANTGS	ERPSAGNWTE
	strain 536	TPTVKTTTEL	TFTVKDAYGN	PVTGLKPDAP	VFSGAASTGS	ERPSAGNWTE
55	strain F11	TPTVKTTTEL	TFTVKDAYGN	PVTGLKPDAP	VFSGAASTGS	ERPSAGNWTE
	strain CFT073	TPTVKTTTEL	TFTVKDAYGN	PVTGLKPDAP	VFSGAASTGS	ERPSAGNWTE
	Group A	TPTVKTTTEL	TFTVKDAYGN	PVTGLKPDAP	VFSGAASTGS	ERPSAGNWTE
	strain E2348-69	TPTVKTTTEL	TFTVKDAYGN	PVTGLKPDAP	VFSGAASTGS	ERPSAGNWTE
	strains B171 and E22	APTVMKTTTEL	TFTVKDAYGN	PVTGMKPDAP	VFSGAASTGT	ERPSTGDWTE

5	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 042	TPTVKTTTEL	TFTVKDAYGN	PVTGLKPDAP	VFSGAASTGS	ARPSAGSWTE
	Group B	APTVKTTTEL	TFTVKDAYGN	PVTGLKPDAP	VFSGAASTGS	ERPSAGNWTE
	strain SECEC	APTVKATTEL	TFTAKDAYGN	PVSGLKLDAP	VFSGAASTGS	ERPSAGSWTE
10	Consensus	-PTVK-TT-L	TFT-KDAYGN	-V-G-K-DAP	-FSGAASTG-	-RPS-G-WTE
	Frag	BBBBBBBBBB	BBBBBBBBBB	BBBBBBBBBB	BBBBBBBBBB	BBBBBBBBBB
15		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
20	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
25	strain 042	QSNQVYVATL	TLGSAAGQLS	VMPRVNGQNA	VAQPLVLNVA	GDASRAVISED
	Group B	KGNGVYVSTL	TLGSAAGQLS	VMPRVNGQNA	VAQPLVLNVA	GDASKAEIRD
	strain SECEC	QSNQVYVATL	TLGSAAGQLS	VMPRVNGQNA	VAQPLVLNVA	GDASKAEIRD
	Consensus	--NGVYV-TL	TLGSAAGQLS	VMPRVNGQNA	VAQPLVLNVA	GDAS-A-I-D
		SEQ ID NO: 256				
		***** *				
		BBBBBBBBBB	BBBBBBBBBB	BBBBBBBBBB	BBBBBBBBBB	BBBBBBBBBB
30	B-Cell Ep.					
	Frag	BBBBBBBBBB	BBBBBBBBBB	BBBBBBBBBB	BBBBBBBBBB	BBBBBBBBBB
35		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
40	Group A	MTVKVNNQLA	NGQSANQITL	TVVDSYGNPL	QGQEVTLTLP	QGVTSKTGNT
	strain E2348-69	MTVKVNNQLA	NGQSANQITL	TVVDSYGNPL	QGQEVTLTLP	QGVTSKTGNT
	strains B171 and E22	MTVKVDNQLA	NGQSTNQVTL	TVVDITYGNPL	QGQNVTLTLP	KGVTSTKTGNT
	strain B7A	MTVKVDNQLA	NGQSTNQVTL	TVVDITYGNPL	QGQNVTLTLP	KGVTSTKTGNT
	strain E110019	MTVKVDNQLA	NGQSTNQVTL	TVVDITYGNPL	QGQNVTLTLP	KGVTSTKTGNT
	strain HS	MTVKVDNQLA	NGQSTNQVTL	TVVDITYGNPL	QGQNVTLTLP	KGVTSTKTGNT
	strain E24377A	MTVKVDNQLA	NGQSTNLVTL	TVVDITYGNPL	QGQEVTLNLP	QGVTSKTGNT
45	strain 042	MAVKVNNQLA	NGQSANQVTL	TVVDSYGNPL	QGQEVTLTLP	QGVTSKTGNT
	Group B	MTVKVNNQLA	NGQSANQITL	TVVDITYGNPL	QGQEVTLTLP	QGVTSKTGNT
	strain SECEC	MTVKVDNQLA	NGQSTNQVTL	TVVDITYGNPL	QGQEVTLTLP	QGVTSKTGNT
	Consensus	M-VKV-NQLA	NGQSTN--TL	TVVDSYGNPL	QGQ-VTL-LP	-GVTSKTGNT
		SEQ ID NO: 257-9				
		*** *****				
		BBBBBBBBBCC	CCCCCCCCCCC	CCCCCCCCCCC	CCCCCCCCCCC	CCCCCCCCCCC
50	B-Cell Ep.					
	Frag	BBBBBBBBBCC	CCCCCCCCCCC	CCCCCCCCCCC	CCCCCCCCCCC	CCCCCCCCCCC
55		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
60	Group A	VTTNAAGKVD	IELMSTVAGE	LEIEASVKNS	QKTVKVKFKA	DFSTGQASLE
	strain E2348-69	VTTNAAGKVD	IELMSTVAGE	LEIEASVKNS	QKTVKVKFKA	DFSTGQASLE

5	strains B171 and E22	VTDAAGKAD	IELMSTVAGE	HSITASVNNA	QKTVTVKFKA	DFSTGQASLE
	strain B7A	VTDAAGKAD	IELMSTVAGE	HSITASVNNA	QKTVTVKFKA	DFSTGQASLE
	strain E110019	VTDAAGKAD	IELMSTVAGE	HSITASVNNA	QKTVTVKFKA	DFSTGQASLE
	strain HS	VTDAAGKAD	IELMSTVAGE	HSITASVNNA	QKTVTVKFKA	DFSTGQASLE
	strain E24377A	VTNAAGKAD	IELISTVAGE	LEIAAAVKNS	QKTVTVKFNA	DASTGQANLQ
10	strain O42	VTNAAGKAD	IELISTVAGE	LEIAAAVKNS	QKTVTVKFNA	DASTGQANLQ
	Group B	VTNAAGKAD	IELMSTVAGE	HNISASVNGA	QKTVTVKFNA	DASTGQANLQ
	strain SECEC	VTNAAGKAD	IELISTVAGE	LEIAAAVKNS	QKTVTVKFNA	DASTGQANLQ
	Consensus	VT--AAGK-D	IEL-STVAGE	--I-A-V---	QKTV-VKF-A	D-STGQA-L-
	B-Cell Ep.	***	*****			
	Frag	CCCCCCCCC	CCCCCCCCC	CCCCCCCCC	CCCCCCCCC	CCCCCCCCC
		1101				
15	strains B, C and 8739	VDGSTPKVAN	DNDAFTLTAT	VKDQYGNLLP	GAVVVFNLPW	GVKPLADGNI
	strain H10407	VDGSTPKVAN	DNDAFTLTAT	VKDQYGNLLP	GAVVVFNLPW	GVKPLADGNI
	strain 101-1	VDGSTPKVAN	DNDAFTLTAT	VKDQYGNLLP	GAVVVFNLPW	GVKPLADGNI
	strain 536	VDTAVQKVAN	GKDAFTLTAT	VKDQYGNLLP	GAVVVFNLPW	GVKPLADGNI
	strain F11	VDTAVQKVAN	GKDAFTLTAT	VKDQYGNLLP	GAVVVFNLPW	GVKPLADGNI
20	strain CFT073	VDAAAQKVAN	GKDAFTLTAT	VKDQYGNLLP	GAVVVFNLPW	GVKPLADGNI
	Group A	VDAAAQKVAN	GKDAFTLTAT	VKDQYGNLLP	GAVVVFNLPW	GVKPLADGNI
	strain E2348-69	VDAAAQKVAN	GKDAFTLTAT	VKDQYGNLLP	GAVVVFNLPW	GVKPLADGNI
	strains B171 and E22	VDSAAPKVAN	GKDAFTLTAT	VEDKNGNPVP	GSLVTFNLPW	GVKPLTGDNV
	strain B7A	VDSAAPKVAN	GKDAFTLTAT	VEDKNGNPVP	GSLVTFNLPW	GVKPLTGDNV
25	strain E110019	VDSAAPKVAN	GKDAFTLTAT	VEDKNGNPVP	GSLVTFNLPW	GVKPLTGDNV
	strain HS	VDSAAPKVAN	GKDAFTLTAT	VEDKNGNPVP	GSLVTFNLPW	GVKPLTGDNV
	strain E24377A	VDTAVQKVAN	GKDAFTLTAT	VEDKNGNPVP	GSLVTFNLPW	GVKPLTGDNV
	strain O42	VDTAVQKVAN	GKDAFTLTAT	VEDKNGNPVP	GSLVTFNLPW	GVKPLTGDNV
	Group B	VDAAAQKVAN	GKDAFTLTAN	VEDKNGNPVP	GSLVTFNLPW	GVKPLTGDNV
30	strain SECEC	VDAAAQKVAN	GKDAFTLTAN	VEDKNGNPVP	GSLVTFNLPW	GVKPLTGDNV
	Consensus	VD---KVAN	--DAFTLTAT	V-D--GN--P	G--V-FNLP-	GVKPL---N-
	Frag	CCCCCCCCC	CCCCCCCCC	CCCCCCCCC	CCCCCCCCC	CCCCCCCCC
		1151				
35	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
40	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	WVKANDEGKA	ELQVVSVTAG	TYEITASAGN	SQPSDTQTIT	FVADKATATV
	strain B7A	WVKANDEGKA	ELQVVSVTAG	TYEITASAGN	SQPSDTQTIT	FVADKATATV
45	strain E110019	WVKANDEGKA	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
50	strain SECEC	WVKANDEGKA	ELQVVSVTAG	TYEITASAGN	DQPSDAQTIT	FVADKATATV
	Consensus	-V-A--EGKA	EL-V-SVTAG	TYEITaSAGN	-QPS--Q--T	FVADK-TAT-
	B-Cell Ep.			SEQ ID NO: 264-6		
	Frag	CCCCCCCCC	CCCCCCCCC	CCCCCCCCC	CCCCCCCCC	CCCCCCCCC
		1201				
55	strains B, C and 8739	SSIEVIGNRA	VADGKTKQTY	KVTVTDANNN	LLKDSOVLTL	ASSENVLVLP
	strain H10407	SSIEVIGNRA	VADGKTKQTY	KVTVTDANNN	LLKDSOVLTL	ASSENVLVLP
	strain 101-1	SSIEVIGNRA	VADGKTKQTY	KVTVTDANNN	LLKDSOVLTL	ASSENVLVLP
	strain 536	SSIEVIGNRA	VADGKTKQTY	KVTVTDANNN	LLKDSEVTLT	ASPENVLVLP
	strain F11	SSIEVIGNRA	VADGKTKQTY	KVTVTDANNN	LLKDSEVTLT	ASPENVLVLP
60	strain CFT073	SSIEVIGNRA	VADGKTKQTY	KVTVTDANNN	LLKDSEVTLT	ASPENVLVLP
	Group A	SSIEVIGNRA	VADGKTKQTY	KVTVTDANNN	LLKDSEVTLT	ASPENVLVLP
	strain E2348-69	SSIEVIGNRA	VADGKTKQTY	KVTVTDANNN	LLKDSEVTLT	ASPENVLVLP

5	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
10	strain O42	SGIEVIGNYA	LADGKAKQTY	KVTVTDANNN	LLKDSDVTLT	ASPASLNLEP
	Group B	SGIEVIGNYA	LADGNAKQTY	KVTVTDANNN	LLKDSEVTLT	ASPANLVLT
	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				
15	B-Cell Ep.	**** *				
	Frag	CCCCCCCC	CCCCCCCC	CCCCCCCC	CCCCCCCC	CCCCCCCC
		1251				
	strains B, C and 8739	KGTAKTNEQG	QAVFTGSTTI	AATYTLTAKV	EQANGQVSTK	TAESKFVADD
	strain H10407	KGTAKTNEQG	QAVFTGSTTI	AATYTLTAKV	EQANGQVSTK	TAESKFVADD
20	strain 101-1	KGTAKTNEQG	QAVFTGSTTI	AATYTLTAKV	EQANGQVSTK	TAESKFVADD
	strain 536	NGTATTNEQG	QAIFTATTTT	AATYTLTAKV	EQADGQESTK	TAESKFVADD
	strain F11	NGTATTNEQG	QAIFTATTTT	AATYTLTAKV	EQADGQESTK	TAESKFVADD
	strain CFT073	NGTATTNEQG	QAIFTATTTT	AATYTLTAKV	EQADGQESTK	TAESKFVADD
	Group A	NGTATTNEQG	QAIFTATTTT	AATYTLTAKV	EQADGQESTK	TAESKFVADD
25	strain E2348-69	NGTATTNEQG	QAIFTATTTT	AATYTLTAKV	EQADGQESTK	TAESKFVADD
	strains B171 and E22	NGTATTNEQG	QAIFTATTTT	AATYTLKAQV	SQTNGQVSTK	TAESKFVADD
	strain B7A	NGTATTNEQG	QAIFTATTTT	AATYTLKAQV	SQTNGQVSTK	TAESKFVADD
	strain E110019	NGTATTNEQG	QAIFTATTTT	AATYTLKAQV	SQTNGQVSTK	TAESKFVADD
	strain HS	NGTATTNEQG	QAIFTATTTT	AATYTLKAQV	SQTNGQVSTK	TAESKFVADD
30	strain E24377A	NGTATTNEQG	QAIFTATTTT	AATYTLKAQV	SQTNGQVSTK	TAESKFVADD
	strain O42	NGTATTNEQG	QAIFTATTTT	AATYTLKAQV	SQTNGQVSTK	TAESKFVADD
	Group B	NGTAKTNEQG	QAIFTATTTT	AAKYTLTAKV	SQADGQESTK	TAESKFVADD
	strain SECEC	DGTAKTNEQG	QAIFTATTTT	AAKYTLTAKV	EQANGQESTK	TAESKFVADD
	Consensus	-GTA-TNEQG	QA-FT--TT-	AA-YTL-A-V	-Q--GQ-STK	TAESKFVADD
35		SEQ ID NO: 268				
	B-Cell Ep.	*** *				
	Frag	CCCCCCCC	CCCCCCCC	CCCCCCCC	CCCCCCCC	CCCCCCCC
		1301				
	strains B, C and 8739	KNAVLAASPE	RVDSLVDGK	TTATMTVTLM	AGVNPVGGSM	WVDIEAPEGV
40	strain H10407	KNAVLAASPE	RVDSLVDGK	TTATMTVTLM	AGVNPVGGSM	WVDIEAPEGV
	strain 101-1	KNAVLAASPE	RVDSLVDGK	TTATMTVTLM	AGVNPVGGSM	WVDIEAPEGV
	strain 536	KNAELAATSD	.VHSLVDGV	TTATLTVTLF	SANNPVGGTM	WVDIEAPEGV
	strain F11	KNAELAATSD	.VHSLVDGV	TTATLTVTLF	SANNPVGGTM	WVDIEAPEGV
	strain CFT073	KNAVLAASPE	RVDSLVDGK	TTATLTVTLM	SGVNPVGGTM	WVDIEAPEGV
45	Group A	KNAVLAASPE	RVDSLVDGK	TTATLTVTLM	SGVNPVGGTM	WVDIEAPEGV
	strain E2348-69	KNAVLAASPE	RVDSLVDGK	TTATLTVTLM	SGVNPVGGTM	WVDIEAPEGV
	strains B171 and E22	KNAVLTAASSD	.MQSLVDGK	STAKLEVTLM	SANNPVGGNM	WVDIQTPEGV
	strain B7A	KNAVLTAASSD	.MQSLVDGK	STAKLEVTLM	SANNPVGGNM	WVDIQTPEGV
	strain E110019	KNAVLTAASSD	.MQSLVDGK	STAKLEVTLM	SANNPVGGNM	WVDIQTPEGV
50	strain HS	KNAVLTAASSD	.MQSLVDGK	STAKLEVTLM	SANNPVGGNM	WVDIQTPEGV
	strain E24377A	KNAVLTAASSD	.MQSLVDGK	STAKLEVTLM	SANNPVGGNM	WVDIQTPEGV
	strain O42	KNAELTAASSD	.VQSLVDGK	STAKLEVTLF	SANNPVGGNV	WVDIEAPEGV
	Group B	TNAVLTAASSD	.VTSLVADGI	STAKLEVTLM	SANNPVGGNM	WVDIKTPEGV
	strain SECEC	KNAVLAASSD	.VTSLVADGV	QTATMTVTLF	SANNPVGGNV	WVDIEAPEGV
55	Consensus	-NA-L-A---	---SLVADG-	-TA---VTL-	---NPVGG--	WVDI--PEGV
	B-Cell Ep.	****				
	Frag	CCCCCCCC	CCCCCCCC	CCCCCCCC	CCCCCCCC	CCCCCCCC
		1351				
	strains B, C and 8739	TEKDYQFLPS	KADHFSGGKI	TRTFSTSKPG	VYTFTFNALT	YGGYEMTPVK
60	strain H10407	TEKDYQFLPS	KADHFSGGKI	TRTFSTSKPG	VYTFTFNALT	YGGYEMTPVK
	strain 101-1	TEKDYQFLPS	KADHFSGGKI	TRTFSTSKPG	VYTFTFNALT	YGGYEMTPVK
	strain 536	TEADYQFLPS	KNDHFASGKI	TRTFSTNKPG	TYTFTFNSLT	YGGYEMKPV
	strain F11	TEADYQFLPS	KNDHFASGKI	TRTFSTNKPG	TYTFTFNSLT	YGGYEMKPV
	strain CFT073	TEADYQFLPS	KNDHFASGKI	TRTFSTNKPG	TYTFTFNSLT	YGGYEMKPV

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Group A          TEADYQFLPS KNDHFASGKI TRTFSTNKP G TYTFTFNSLT YGGYEMKPVT
strain E2348-69  TEADYQFLPS KNDHFASGKI TRTFSTNKP G TYTFTFNSLT YGGYEMKPVT
strains B171 and E22  TEKDYQFLPS KNDHFVSGKI TRKFSTSKPG VYTFTFNALT YGGYEMKPVT
strain B7A      TEKDYQFLSS KNDHFVSGKI TRKFSTSKPG VYTFTFNALT YGGYEMKPVT
5 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
10 strain SECEC  TEKDYQFLPS KNDHFVSGKI TRTFSTNKP G 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
15
      1401          1418
strains B, C and 8739 VTINAVAAET ENGEEEEMP
strain H10407        VTINAVAAET ENGEEEEMP
strain 101-1         VTINAVAAET ENGEEEEMP
20 strain 536         VTINAVPADT EGAE EK~~
strain F11           VTINAVPADT EGAE EK~~
strain CFT073        VTINAVPADT EGAE EK~~
Group A             VTINAVPADT EGAE EK~~
strain E2348-69     VTINAVPADT EGAE EK~~
25 strains B171 and E22 VTITAVDADT AKDEEAMK
strain B7A          VTITAVDADT AKDEEAMK
strain E110019      VTITAVDADT AKDEEAMK
strain HS           VTITAVDADT AKDEEAMK
strain E24377A      VTITAVDADT AKDEEAMK
30 strain O42        VTITAVDADT AKGEEAMK
Group B            VTITAVDADT AKGEEAMN
strain SECEC        VTITAVDANT ATGEEAMK
      Consensus  VTI-AV-A-T ---EE---
Frag              CCCCCCCCCC CCCCCCCC
35
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
40 SEQ ID NO: 232  RI(E/A)GKGGQT
SEQ ID NO: 233  RIEGKGGQT
SEQ ID NO: 234  RIACKGGQT
SEQ ID NO: 250  ASEGAT(V/I)S(S/G)WTEKG
SEQ ID NO: 251  ASEGATISSWTEKG
45 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
50 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
55 SEQ ID NO: 266  SVTAGTYEITVSAGN
SEQ ID NO: 269  PEGVTE(K/A)DYQFL
SEQ ID NO: 270  PEGVTEKDYQFL
SEQ ID NO: 271  PEGVTEADYQFL
60 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 SGWKSPDVEDYQERPANGWDIR
 SEQ ID NO: 277 YLPAPWQ
 SEQ ID NO: 278 KDKRQKDPHAI
 5 SEQ ID NO: 279 GHKQGKSGENDTR
 SEQ ID NO: 280 KQLDTSI
 SEQ ID NO: 281 IEGKGGQT
 SEQ ID NO: 282 DNKGNASKRV
 SEQ ID NO: 283 DAEGQPVTGMKDQ
 10 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
 15 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
 20 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
 25 SEQ ID NO: 299 RVNGQNAV
 SEQ ID NO: 300 QLANGQSTN
 SEQ ID NO: 301 SYGNPLQGQ
 SEQ ID NO: 302 GVTSTGTGNTVTT
 SEQ ID NO: 303 LMSTVAGE
 30 SEQ ID NO: 304 TYEITASAGN
 SEQ ID NO: 305 KQTYKVTVTDA
 SEQ ID NO: 306 STKTAESKFVAD
 SEQ ID NO: 307 PEGVTE

35 **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
 40 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,
 45 150, 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)

- 5 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)
 10 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)
 15 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)
 20 strain B7A (SEQ ID NO: 37)
 strain CFT073 (SEQ ID NO: 38)
 strain O42 (SEQ ID NO: 39)
 strain CFT073 (SEQ ID NO: 40)

25		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
30	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
35	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
40	strain H10407	MKRHLNTSYR	LVWNHITGTL	VVASELARSR	GKRTGVAVAL	SLATATSVPA
	strain W3110 and DH10B	MKRHLNTCYR	LVWNHMTGAF	VVASELARAR	GKRGGVAVAL	SLAAVTSPLV
	strain MG1655	MKRHLNTCYR	LVWNHMTGAF	VVASELARAR	GKRGGVAVAL	SLAAVTSPLV
	strain O42	MKRHLNTCYR	LVWNHITGAF	VVASELARAR	GKRGGVAVAL	SLAAVTSPLV
	strain B7A	MKRHLNTSYR	LVWNHITGTL	VVASELARSR	GKRAGVAVAL	SLAAVTSVPA
45	strain CFT073	MKRHLNTSYR	LVWNHITGAF	VVASELARAR	GKRAGVAVAL	SLAAATSLPA
	strain O42	MKRHLNTCYR	LVWNHITGAF	VVASELARAR	GKRGGVAVAL	SLAAVTSPLV
	strain CFT073	MKRHLNTCYR	LVWNHITGAF	VVASELARAR	GKRGGVAVAL	SLAAVTPLPV
	Consensus	MKRHLNT-YR	LVWNH-TG--	VVASELAR-R	GK--GVA-AL	SLA--T--P-
	B-Cell Ep.			***	*****	

50		51				100
	strain E110019	LAADKVVQAG	ETVNDGTLTN	HDNQIVFGTA	NGMTISTGLE	LGPDSEENTG
	Group A	LAADKVVQAG	ETVNDGTLTN	HDNQIVFGTA	NGMTISTGLE	LGPDSEENTG
	strain B171	LAADTVVQAG	ETVNGGTLTN	HDNQIVLGTA	NGMTISTGLE	LGPDSEENTG
55	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
60	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

5	strain F11 and 536	LAADTVVQAG	ETVNDGTLTN	HDNQIVLGTA	NGMTISTGLE	YGPDNEANTG
	strain SECEC	LAADTVVEAG	ETVNGGTLTN	HDNQIVFGTT	NGMTISTGLE	YGTDNEANTG
	strain H10407	LAADSVMQAG	ETVSGGTLEN	HDNQIVFGTT	NGITISTGLE	YGPDNEANTG
	strain W3110 and DH10B	LAADIVVHPG	ETVNGGTLAN	HDNQIVFGTT	NGMTISTGLE	YGPDNEANTG
	strain MG1655	LAADIVVHPG	ETVNGGTLAN	HDNQIVFGTT	NGMTISTGLE	YGPDNEANTG
10	strain O42	LAADIVVHPG	ETVNGGTLAN	HDNQIVFGTT	NGMTISTGLE	YGPDNEANTG
	strain B7A	LAADKVVQAG	ETVNDGTLTN	HDNQIVLGTA	NGMTISTGLE	YGPDNEANTG
	strain CFT073	LAADSVPAG	ETVNGGTLIN	HDRQFVSGTA	DGMTVSTGLE	LGADSDNNTG
	strain O42	LAADIVVHPG	ETVNGGTLVN	HDNQFVSGTA	DGVTVSTGLE	LGPDSDNNTG
	strain CFT073	LSADIVVHPG	ETVNGGTLVN	HDNQFVSGTA	NGVTVSTGLE	LGPDSDNNTG
	Consensus	L-AD-VV--G	ETV--GTL-N	HD-Q-V-GT-	-G-T-S-GLE	-G-D---NTG
	B-Cell Ep.	*	*****		***	*****
		101				
15	strain E110019	GQWIQNGGIA	GNTTVTNNGR	QVVLEGGTAS	DTVIRDGGGQ	SLNGLAVNTT
	Group A	GQWIQNGGIA	GNTTVTNNGR	QVVLEGGTAS	DTVIRDGGGQ	SLNGLAVNTT
	strain B171	GQWIQNGGIA	GNTTVTNNGR	QVVLEGGTAS	DTVIRDGGGQ	SLNGLAVNTT
	strain E22	GQWIQNGGIA	GNTTVTNNGR	QVVLEGGTAS	DTVIRDGGGQ	SLNGLAVNTT
	strain B171	GQWIQNGGIA	NNTTVTGGGL	QRVNAGGSVS	DTVISAGGGQ	SLQGQAVNTT
20	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
25	strain E22	GQWIQNGGTA	NNTTVTGGGL	QRVNAGGSVS	DTVISAGGGQ	SLQGQAVNTT
	strain H10407	GQWIQNGGIA	NNTTVTGGGL	QRVNAGGSVS	DTVISAGGGQ	SLQGQAVNTT
	strain F11 and 536	GQWIQNGGIA	NNTTVTGGGL	QRVNAGGSVS	DTVISAGGGQ	SLQGQAVNTT
	strain SECEC	GQWVQDGGTA	SNTTISGGGL	QFVGAGGKAT	DTIINEGGGQ	SLKGLALNTT
	strain H10407	GQWVQDGGTA	SNTTISGGGL	QFVGAGGKAT	DTIINEGGGQ	SLKGLALNTT
30	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
35	strain O42	GQQIARGGTA	RNTRVTANGL	QDVMAGGSAT	DTVISAGGGQ	NLRGQAYGTV
	strain CFT073	GQWIKAGGTG	RNTRVTANGL	QIVQAGGTAS	DTVIRDGGGQ	SLNGLAVNTT
	Consensus	GQ----GG--	--T-----G-	Q-V--GG---	DT-I---GGGQ	-L-G-A--T-
	B-Cell Ep.	*****	*****	*****	*****	*****
		151				
40	strain E110019	LNNRGEQWVH	EGGVATGTII	NRDGYQSVKS	GGLATGTIIN	TGAEGGPDS
	Group A	LNNRGEQWVH	EGGVATGTII	NRDGYQSVKS	GGLATGTIIN	TGAEGGPDS
	strain B171	LNNRGEQWVH	EGGVATGTII	NRDGYQSVKS	GGLATGTIIN	TGAEGGPDS
	strain E22	LNNRGEQWVH	EGGVATGTII	NRDGYQSVKS	GGLATGTIIN	TGAEGGPDS
	strain B171	LNG.GEQWVH	EGGIATGTVI	NEKGWQAVKS	GAMATDTVVN	TGAEGGPDAE
45	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	EGGIATGTVI	NEKGWQAVKS	GAMATDTVVN	TGAEGGPDAE
50	strain E22	LNG.GEQWVH	EGGIATGTVI	NEKGWQAVKS	GAMATDTVVN	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
55	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	NEKGWQAVKS	GAVATDTVVN	TGAEGGPDAE
	strain CFT073	L.NGGEQWVH	AGGRASGTVI	NQDGYQTIKH	GGLVTGTIVN	TGAEGGPDS
60	strain O42	L.NGGEQWVH	AGGSASGTVI	NQSGYQTIKH	GGQATGTIVN	TGAEGGPDS
	strain CFT073	LDNRGEQWVH	GKGKAAGTII	NQDGYQTIKH	GGLATGTIVN	TGAEGGPDS
	Consensus	L---G-QW-H	-G--A--T-I	N--G-Q--K-	G---T-T--N	TGAEGGP---

B-Cell Ep.

		201				250
5	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
10	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
15	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
20	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	NVSTGQMVG	IAESTTINKN	GRQVIWSSGI	ARDTLIYTG	DQTVHGEAHN
25	strain O42	NVSSGQMVG	TAESTTINKN	GRQVIWSSGM	ARDTLIYAGG	DQTVHGEAHN
	strain CFT073	NVSSGQMVG	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
30	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
35	strain B171	TTLNGGYQYV	HNGGTASGTV	VNSDGWQIIK	EGGLADFTTV	NQKGLQVNA
	strain B171	TTLNGGYQYV	HNGGTASGTV	VNSDGWQIIK	EGGLADFTTV	NQKGLQVNA
	strain E24377A and O42	TTLNGGYQYV	HNGGTASDTV	VNSDGWQIVK	EGGLADFTTV	NQKGLQVNA
	strain E24377A	TTLNGGYQYV	HNGGTASGTV	VNSDGWQIIK	EGGLADFTTV	NQKGLQVNA
40	Group B	TTLNGGYQYV	HNGGTASDTV	VNSDGWQIIK	EGGLADFTTV	NQKGLQVNA
	strain E110019	TTLNGGYQYV	HNGGTASDTV	VNSDGWQIVK	EGGLADFTTV	NQKGLQVNA
	strain E22	TTLNGGYQYV	HNGGTASGTV	VNSDGWQIIK	EGGLADFTTV	NQKGLQVNA
	strain H10407	TTLNGGYQYV	HNGGTASGTV	VNSDGWQIIK	EGGLADFTTV	NQKGLQVNA
	strain F11 and 536	TTLNGGNQYV	HNGGTASGTV	VNSDGWQIVK	EGGLADFTIV	NQKGLQVNA
	strain SECEC	TTLNGGNQYV	HNGGTTSDTV	VNSDGWQIIK	EGGLADFTTV	NQKGLQVNA
	strain H10407	TTLNGGNQYV	HNGGTASDTV	VNSDGWQIIK	EGGLADFTTV	NQKGLQVNA
45	strain W3110 and DH10B	TTLNGGYQYV	HNGGTASDTV	VNSDGWQIVK	NGGVAGNTTV	NQKGRLOVDA
	strain MG1655	TTLNGGYQYV	HNGGTASDTV	VNSDGWQIVK	NGGVAGNTTV	NQKGRLOVDA
	strain O42	TTLNGGYQYV	HNGGTASDTV	VNSDGWQIVK	NGGVAGNTTV	NQKGRLOVDA
	strain B7A	TTLNGGYQYV	HNGGTASGTV	VNSDGWQIVK	NGGVAGNTTV	NQKGRLOVDA
	strain CFT073	TRLEGGNQYV	HKYGLALNTV	INEGGWQVVK	AGGTAGNTTI	NQNGELRVHA
50	strain O42	TRLEGGNQYV	HKYGLALNTV	INEGGWQVIK	EGGTTAHTTI	NQKGLQVNA
	strain CFT073	TRLEGGNQYV	HNGGTATETL	INRDGWQVIK	EGGTAAHTTI	NQKGLQVNA
	Consensus	T-L-GG-QYV	H--G----T-	-N--GWQ--K	-GG----T--	NQ-G-L-V-A
B-Cell Ep.		***	*****	***	*****	***

55		301				350
	strain E110019	GGEATAVTQN	TGGALVTSTA	ATVIGTNRLG	NFTVENGKAD	GVVLESGGRL
	Group A	GGEATAVTQN	TGGALVTSTA	ATVIGTNRLG	NFTVENGKAD	GVVLESGGRL
	strain B171	GGEATAVTQN	TGGALVTSTA	ATVTGANRLG	HFSVGNMGAD	NVVLENGGRL
	strain E22	GGEATAVTQN	TGGALVTSTA	ATVTGANRLG	HFSVGNMGAD	NVVLENGGRL
60	strain B171	GGTATHVTLK	QGGALVTSTA	ATVLGSNRLG	NFTVENGKAD	GVVLESGGRL
	strain B171	GGTATHVTLK	QGGALVTSTA	ATVLGSNRLG	NFTVENGKAD	GVVLESGGRL
	strain E24377A and O42	GGTATNVTLK	QGGALVTSTA	ATVTGSNRLG	NFTVENGKAD	GVVLESGGRL
	strain E24377A	GGTATNVTLK	QGGALVTSTA	ATVTGSNRLG	NFTVENGKAD	GVVLESGGRL

Group B		GGTATNVTLT	QGGALVTSTA	ATVTGSNRLG	NFTVENGNAD	GVVLESGGRL
strain E110019		GGTATNVTLK	QGGALVTSTA	ATVTGSNRLG	NFTVENGNAD	GVVLESGGRL
strain E22		GGTATNVTLK	QGGALVTSTA	ATVLGSNRLG	NFTVENGNAD	GVVLESGGRL
strain H10407		GGTATHVTLK	QGGALVTSTA	ATVLGSNRLG	NFTVENGNAD	GVVLESGGRL
5	strain F11 and 536	GGTATNVTLK	QGGALVTSTA	ATVTGSNRLG	NFTVENGNAD	GVVLESGGRL
strain SECEC		GGTATNVTLK	QGGALVTSTA	ATVTGSNRLG	NFAVENGNAD	GVVLESGGRL
strain H10407		GGTATNVTLK	QGGALVTSTA	ATVLGSNRLG	NFTVENGNAD	GVVLESGGRL
strain W3110 and DH10B		GGTATNVTLK	QGGALVTSTA	ATVTGINRLG	AFSVVEGKAD	NVVLENGGRL
strain MG1655		GGTATNVTLK	QGGALVTSTA	ATVTGINRLG	AFSVVEGKAD	NVVLENGGRL
10	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
15	Consensus	GG-A--VT--	-GGALVTSTA	ATV-G-NRLG	-F-V--G-AD	-VVLE-GGRL
B-Cell Ep.		SEQ ID NO: 308				

		351				400
20	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
25	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
30	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
35	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
40	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
45	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
50	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
55	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
60	strain H10407	ASGK.FSIDG	ISGQASGLLL	ENGGSFTVNA	GGQAGNTTVG	HRGTLTLAAG
strain W3110 and DH10B		SDGKAFSIGG	..GQADALML	EKGSSFTLNA	GDTATDITV.	.NGGLFTARG
strain MG1655		SDGKAFSIGG	..GQADALML	EKGSSFTLNA	GDTATDITV.	.NGGLFTARG
strain O42		SDGKAFSIGG	..GQADALML	EKGSSFTLNA	GDTATDITV.	.NGGLFTARG

5	strain B7A	SDGKAFSIGG	..GQADALML	EKGSSFTLNA	GDATDTTV.	.NGGLFTARG
	strain CFT073	SDGTAFRIGG	..GQADALML	EKGSSFTLNA	GDATDTTV.	.NGGLFTARG
	strain O42	SDGTAFRIGG	..GQADALML	EKGSSFTLNA	GDATDTTV.	.NGGLFTARG
	strain CFT073	SDGKAFSIGG	..GQADALML	EKGSSFTLNA	GDATDTTV.	.NGGLFTARG
	B-Cell Ep.	Consensus	--G--F-I-G	--GQA--L-L	E-G-SFT-NA	G--A--TTV--G-L--A-G
		*****		****	*****	
		451				
10	strain E110019	GSLSGRTQLS	KGASMLVNGD	VVST.....	.GDIV.....	
	Group A	GSLSGRTQLS	KGASMLVNGD	VVST.....	.GDIV.....	
	strain B171	GSLSGRTQLS	KGASMLVNGD	VVST.....	.GDIV.....	
	strain E22	GSLSGRTQLS	KGASMLVNGD	VVST.....	.GDIV.....	
	strain B171	GSLSGRTQLS	KGASMLVNGD	VVST.....	.GDIV.....	
15	strain B171	GSLSGRTQLS	KGASMLVNGD	VVST.....	.GDIV.....	
	strain E24377A and O42	GSLSGRTQLS	KGASMLVNGD	VVST.....	.GDIV.....	
	strain E24377A	GSLSGRTQLS	KGASMLVNGD	VVST.....	.GDIV.....	
	Group B	GSLSGRTQLS	KGASMLVNGD	VVST.....	.GDIV.....	
	strain E110019	GSLSGRTQLS	KGASMLVNGD	VVST.....	.GDIV.....	
20	strain E22	GSLSGRTQLS	KGASMLVNGD	VVST.....	.GDIV.....	
	strain H10407	GSLSGRTQLS	KGASMLVNGD	VVST.....	.GDIV.....	
	strain F11 and 536	GSLSGRTQLS	KGASMLVNGD	VVST.....	.GDIV.....	
	strain SECEC	GSLSGRTQLS	KGASMLVNGD	VVST.....	.GDIV.....	
	strain H10407	GSLSGRTQLS	KGASMLVNGD	VVST.....	.GDIV.....	
25	strain W3110 and DH10B	GTLAGTTTLN	NGAILTSLGK	TVNNDTLTIR	EGDALLQGGG	LTGNGSVEKS
	strain MG1655	GTLAGTTTLN	NGAILTSLGK	TVNNDTLTIR	EGDALLQGGG	LTGNGSVEKS
	strain O42	GTLAGTTTLN	NGAILTSLGK	TVNNDTLTIR	EGDALLQGGG	LTGNGSVEKS
	strain B7A	GTLAGTTTLN	NGAILTSLGK	TVNNDTLTIR	EGDALLQGGG	LTGNGSVEKS
	strain CFT073	GSLAGTTTLN	NGATFTLAGK	TVNNDTLTIR	EGDALLQGGG	LTGNGRVEKS
30	strain O42	GSLAGTTTLN	NGATFTLAGK	TVNNDTLTIR	EGDALLQGGG	LTGNGRVEKS
	strain CFT073	GTLAGTTTLN	NGAILTSLGK	TVNNDTLTIR	EGDALLQGGG	LTGNGSVEKS
	B-Cell Ep.	Consensus	G-L-G-T-L-	-GA---L-G-	-V-----	-GD-----
		*****				*****
		501				
35	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.....	...KLTTN..
40	strain B171	NAGEIRFDNQ	T.TQDAV.LS	R.AVAKGDSP	VTFH.....	...KLTTN..
	strain E24377A and O42	NAGEIRFDNQ	T.TPDAA.LS	R.AVAKGDSP	VTFH.....	...KLTTN..
	strain E24377A	NAGEIRFDNQ	T.TPDAA.LS	R.AVAKGDSP	VTFH.....	...KLTTN..
	Group B	NAGEIRFDNQ	T.TPDAA.LS	R.AVAKGDSP	VTFH.....	...KLTTN..
	strain E110019	NAGEIRFDNQ	T.TPDAA.LS	R.AVAKGDSP	VTFH.....	...KLTTN..
45	strain E22	NAGEIRFDNQ	T.TPDAA.LS	R.AVAKGDSP	VTFH.....	...KLTTN..
	strain H10407	NAGEIRFDNQ	T.TPDAA.LS	R.AVAKGDSP	VTFH.....	...KLTTN..
	strain F11 and 536	NAGEIRFDNQ	T.TPDAA.LS	R.AVAKGDSP	VTFH.....	...KLTTN..
	strain SECEC	NAGEIRFDNQ	T.TPDAA.LS	R.AVAKGDSP	VTFH.....	...KLTTN..
	strain H10407	NAGEIRFDNQ	T.TPDAA.LS	R.AVAKGDSP	VTFH.....	...KLTTN..
50	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	VTTDVIAQRG	TALKLTGSTV
55	strain O42	GSGTLTVSNT	TLTQKAVNLN	EGTLTLNDST	VTTDVIAQRG	TALKLTGSTV
	strain CFT073	GSGTLTVSNT	TLTQKAVNLN	EGTLTLNDST	VTTDVIAQRG	TALKLTGSTV
	B-Cell Ep.	Consensus	--G-----N-	T-T-----L-	-----VT-	---KLT---

		551				
60	strain E110019					
	Group A					
	strain B171					

	strain E22					
	strain B171					
	strain B171					
	strain E24377A and O42					
5	strain E24377A					
	Group B					
	strain E110019					
	strain E22					
	strain H10407					
10	strain F11 and 536					
	strain SECEC					
	strain H10407					
	strain W3110 and DH10B	LNGAIDPTNV	TLASGATWNI	PDNATVQSVV	DDLSHAGQIH	FTSTRTGKFF
	strain MG1655	LNGAIDPTNV	TLASGATWNI	PDNATVQSVV	DDLSHAGQIH	FTSTRTGKFF
15	strain O42	LNGAIDPTNV	TLASGATWNI	PDNATVQSVV	DDLSHAGQIH	FTSTRTGKFF
	strain B7A	LNGAIDPTNV	TLASGATWNI	PDNATVQSVV	DDLSHAGQIH	FTSTRTGKFF
	strain CFT073	LNGAIDPTNV	TLTSGATWNI	PDNATVQSVV	DDLSHAGQIH	FTSARTGKFF
	strain O42	LNGAIDPTNV	TLTSGATWNI	PDNATVQSVV	DDLSHAGQIH	FTSTRTGKFF
	strain CFT073	LNGAIDPTNV	TLASDATWNI	PDNATVQSVV	DDLSHAGQIH	FTSRTGTFF
20	Consensus	-----	-----	-----	-----	-----
	B-Cell Ep.	*****	**	****	*****	*****

		601				650
	strain E110019	NLT	GQGGTINMRV	RLD.GSNASD	QLVINGGQAT	GKTWLAFTNV
25	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
30	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
35	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
40	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
45	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
50	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
55	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
60	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

	strain H10407	GNSNLGVATS	GQGIRVVDQA	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	FNyTLNRDSD
5	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
10	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
15	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
20	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
25	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
30	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	ESWYLSEER	YRAEVPLYAS	MLTQAMDYDR	ILAGSRSHQT	GVNGENNSVR
	strain O42	ESWYLSEER	YRAEVPLYAS	MLTQAMDYDR	ILAGSRSHQT	GVNGENNSVR
	strain CFT073	ESWYLRSENA	YRAEVPLYAS	MLTQAMDYDR	ILAGSRSHQT	GVNGENNSVR
35	Consensus	E-WYLSE--	YRAEVPLY-S	MLTQAMDYDR	I-AGSRSHQT	GVnGENNS-R
	B-Cell Ep.	****		SEQ ID NO: 309	SEQ ID NO: 310-313	*****
		751				800
40	strain E110019	LSIQGGHLGH	DNNGGIARGA	TPESSGSYGF	VRLEGDLLRT	EVAGMSLTG
	Group A	LSIQGGHLGH	DNNGGIARGA	TPESSGSYGF	VRLEGDLLRT	EVAGMSLTG
	strain B171	LSIQGGHLGH	DNNGGIARGA	TPESSGSYGL	VRLEGDLLRT	EVAGMSLTG
	strain E22	LSIQGGHLGH	DNNGGIARGA	TPESNGSYGF	VRLEGDLLRT	EVAGMSLTG
	strain B171	LSIQGGHLGH	DNNGGIARGA	TPESNGSYGF	VRLEGDLLRT	EVAGMSLTG
45	strain B171	LSIQGGHLGH	DNNGGIARGA	TPESNGSYGF	VRLEGDLLRT	EVAGMSLTG
	strain E24377A and O42	LSIQGGHLGH	DNNGGIARGA	TPESSGSYGF	VRLEGDLLRT	EVAGMSLTG
	strain E24377A	LSIQGGHLGH	DNNGGIARGA	TPESSGSYGF	VRLEGDLLRT	EVAGMSLTG
	Group B	LSIQGGHLGH	DNNGGIARGA	TPESNGSYGF	VRLEGDLLRT	EVAGMSLTG
	strain E110019	LSIQGGHLGH	DNNGGIARGA	TPESSGSYGF	VRLEGDLLRT	EVAGMSLTG
50	strain E22	LSIQGGHLGH	DNNGGIARGA	TPESNGSYGF	VRLEGDLLRT	EVAGMSLTG
	strain H10407	LSIQGGHLGH	DNNGGIARGA	TPESSGSYGF	VRLEGDLLRT	EVAGMSLTG
	strain F11 and 536	LSIQGGHLGH	VNNGGIARGA	TPESSGSYGL	VRLEGDLLRT	EVAGMSLTG
	strain SECEC	LSIQGGHLGH	DNNGGIARGA	TPESSGSYGF	VRLESDLLRT	EVAGMSVTAG
	strain H10407	LSIQGGHLGH	DNNGGIARGA	TPESSGSYGF	VRLEGDLLRT	EVAGMSVTAG
55	strain W3110 and DH10B	LSIQGGHLGH	DNNGGIARGA	TPESSGSYGF	VRLEGDMRT	EVAGMSVTAG
	strain MG1655	LSIQGGHLGH	DNNGGIARGA	TPESSGSYGF	VRLEGDMRT	EVAGMSVTAG
	strain O42	LSIQGGHLGH	DNNGGIARGA	TPESSGSYGF	VRLEGDLLRT	EVAGMSLTG
	strain B7A	LSIQGGHLGH	DNNGGIARGA	TPESSGSYGF	VRLEGDLLRT	EVAGMSVTAG
	strain CFT073	LSIQGGHLGH	DNNGGIARGA	TPESSGSYGF	VRLEGDLLRT	EVAGMSLTG
60	strain O42	LSIQGGHLGH	DNNGGIARGA	TPESSGSYGF	VRLEGDLLRT	EVAGMSLTG
	strain CFT073	LSIQGGHLGH	DNNGGIARGA	TPESSGSYGF	VRLEGDLLRT	DVAGMSVTAG
	Consensus	LSIQGGHLGH	-NNNGIARGA	TPES-GSYG-	VRLE-DL-RT	-VAGMS-T-G
		SEQ ID NO: 314	SEQ ID NO: 315			

B-Cell Ep.

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		801		850		
5	strain E110019	VYGAAGHSSV	DVKDDDDGSRA	GTVRDDAGSL	GGYLNLVHTS	SGLWADIVAQ
	Group A	VYGAAGHSSV	DVKDDDDGSRA	GTVRDDAGSL	GGYLNLVHTS	SGLWADIVAQ
	strain B171	VYGAAGHSSV	DVKDDDDGSRA	GTVRDDAGSL	GGYLNLTHTS	SGLWADIVAQ
	strain E22	VYGAAGHSSV	DVKNDGDSRA	GTVRDDAGSL	GGYLNLVHTS	SGLWADIVAQ
	strain B171	VYGAAGHSSV	DVKDDDDGSRA	GTVRDDAGSL	GGYLNLTHTS	SGLWADIVAQ
10	strain B171	VYGAAGHSSV	DVKDDDDGSRA	GTVRDDAGSL	GGYLNLTHTS	SGLWADIVAQ
	strain E24377A and O42	VHGAAGHSSV	DVKDDDDGSRA	GTVRDDAGSL	GGYLNLTHTS	SGLWADIVAQ
	strain E24377A	VYGAAGHSSV	DVKDDDDGSRA	GTARDAGSL	GGYLNLVHTS	SGLWADIVAQ
	Group B	VYGAAGHSSV	DVKDDDDGSRA	GTVRDDAGSL	GGYLHLVHTS	SGLWADIVAQ
	strain E110019	VYGAAGHSSV	DVKDDDDGSRA	GTVRDDAGSL	GGYLNLVHTS	SGLWADIVAQ
15	strain E22	VYGAAGHSSV	DVKDDDDGSRA	GTVRDDAGSL	GGYLNLTHTS	SGLWADIVAQ
	strain H10407	VYGAAGHSSV	DVKDDDDGSRA	GTVRDDAGSL	GGYLNLTHTS	SGLWADIVAQ
	strain F11 and 536	VYGAAGHSSV	DVKDDDDGSRA	GTVRDDAGSL	GGYLNLVHTS	SGLWADIVAQ
	strain SECEC	VYSAAGHSSV	DVKDDDDGSRA	GTVRDDAGSL	GGYLNLVHTS	SGLWADIMAQ
	strain H10407	VYGAAGHSSV	DVKDDDDGSRA	GTVRDDAGSL	GGYLNLVHTS	SGLWADIVAQ
20	strain W3110 and DH10B	VYGAAGHSSV	DVKDDDDGSRA	GTVRDDAGSL	GGYLNLVHTS	SGLWADIVAQ
	strain MG1655	VYGAAGHSSV	DVKDDDDGSRA	GTVRDDAGCL	GGYLNLVHTS	SGLWADIVAQ
	strain O42	VYGAAGHSSV	DVKDDDDGSRA	GTVRDDAGSL	GGYLNLTHTS	SGLWADIVAQ
	strain B7A	VYGAAGHSSV	DVKDDDDGSRA	GTVRDDAGSL	GGYLNLIHNA	SGLWADIVAQ
	strain CFT073	VYGAAGHSSV	DVKDDDDGSRA	GTVRDDAGSL	GGYMNLTHTS	SGLWADIVAQ
25	strain O42	VYGAAGHSSV	DVKDDDDGSRA	GTVRDDAGSL	GGYMNLTHTS	SGLWADIVAQ
	strain CFT073	IYGAAGHSSV	DVKDDDDGSRA	GTVRDDAGSL	GGYMNLTHTS	SGLWADIVAQ
	Consensus	---AAGHSSV	DVK--DDGSRA	GT-RDDAG-L	GGY--L-H--	SGLWADI-AQ
		SEQ ID NO: 316				

B-Cell Ep.

30		851		900		
	strain E110019	GTRHSMKASS	DNNDFRARGW	GWLGSLETGL	PFSITDNLM	EPQLQYTWQG
	Group A	GTRHSMKASS	DNNDFRARGW	GWLGSLETGL	PFSITDNLM	EPQLQYTWQG
	strain B171	GTRHSMKASS	DNNDFRARGW	GWLGSLETGL	PFSITDNLM	EPQLQYTWQG
	strain E22	GTHSMKASS	DNNDFRARGW	GWLGSLETGL	PFSITDNLM	EPQLQYTWQG
35	strain B171	GTRHSMKASS	DNNDFRARGW	GWLGSLETGL	PFSITDNV	EPQLQYTWQG
	strain B171	GTRHSMKASS	DNNDFRARGW	GWLGSLETGL	PFSITDNLM	EPQLQYTWQG
	strain E24377A and O42	GTRHSMKASS	DNNDFRARGW	GWLGSLETGL	PFSITDNLM	EPQLQYTWQG
	strain E24377A	GTRHSMKASS	DNNDFRARGW	GWLGSLETGL	PFSITDNLM	EPQLQYTWQG
	Group B	GTRHSMKASS	DNNDFRARGW	GWLGSLETGL	PFSITDNLM	EPQLQYTWQG
40	strain E110019	GTRHSMKASS	DNNDFRARGW	GWLGSLETGL	PFSITDNLM	EPQLQYTWQG
	strain E22	GTRHSMKASS	DNNDFRARGW	GWLGSLETGL	PFSITDNLM	EPQLQYTWQG
	strain H10407	GTRHSMKASS	DNNDFRARGW	GWLGSLETGL	PFSITDNLM	EPQLHYTWQG
	strain F11 and 536	GTRHSMKASS	DNNDFRARGW	GWLGSLETGL	PFSITDNLM	EPQLQYTWQG
	strain SECEC	GTRHSMKASS	DNNDFRARGW	GWLGSLETGL	PFSITDNLM	EPQLQYTWQG
45	strain H10407	GTRHSMKAST	DNNDFRARGW	GWLGSLETGL	PFSITDNLM	EPQLQYTWQG
	strain W3110 and DH10B	GTRHSMKASS	DNNDFRARGW	GWLGSLETGL	PFSITDNLM	EPQLQYTWQG
	strain MG1655	GTRHSMKASS	DNNDFRARGW	GWLGSLETGL	PFSITDNLM	EPQLQYTWQG
	strain O42	GTRHSMKASS	DNNDFRARGW	GWLGSLETGL	PFSITDNLM	EPQLHYTWQG
	strain B7A	GTRHSMKASS	DNNDFRVRGW	GWLGSLETGL	PFSITDNLM	EPQLQYTWQG
50	strain CFT073	GTRHSMKASS	DNNDFRARGR	GWLGSLETGL	PFSITDNLM	EPRLQYTWQG
	strain O42	GTRHSMKASS	GNNDFRARGW	GWLGSLETGL	PFSITDNLM	EPRLQYTWQG
	strain CFT073	GTRHSMKASS	GNNDFRARGR	GWLGSLETGL	PFSITDNLM	EPRLQYTWQG
	Consensus	GT-HSMKAS-	-NNDFR-RG-	GWLGSLETGL	PFSITDN-ML	EP-L-YTWQG
		SEQ ID NO: 317				
		SEQ ID NO:				

55 318

B-Cell Ep.

		901				950
60	strain E110019	LSLDDGQDNA	GYVKFGHGSA	QHVRAGFRLG	SHNDMTFEGE	TSSRDTLRDS
	Group A	LSLDDGQDNA	GYVKFGHGSA	QHVRAGFRLG	SHNDMTFEGE	TSSRDTLRDS
	strain B171	LSLDDGQDNA	GYVKFGHGSA	QHVRAGFRLG	SHNDMTFEGE	TSSRDTLRDS
	strain E22	LSLDDGQDNA	GYVKFGHGSA	QHVRAGFRLG	SHNDMTFEGE	TSSRDTLRDS
	strain B171	LSLDDGQDNA	GYVKFGHGSA	QHVRAGFRLG	SHNDMSFEGE	TSSRDTLRDS

	strain B171	LSLDDGQDNA	GYVKFGHGSA	QHVRAGFRLG	SHNDMSFGE	TSSRDTLRDS
	strain E24377A and O42	LSLDDGQDNA	GYVKFGHGSA	QHVRAGFRLG	SHNDMSFGE	TSSRDTLRDS
	strain E24377A	LSLDDGQDNA	GYVKFGHGSA	QHVRAGFRLG	SHNDMNFGE	TSSRDTLRDS
	Group B	LSLDDGQDNA	GYVKFGHGSA	QHVRAGFRLG	SHNDMNFGE	TSSRDTLRDS
5	strain E110019	LSLDDGQDNA	GYVKFGHGSA	QHVRAGFRLG	SHNDMTFGE	TSSRDTLRDS
	strain E22	LSLDDGQDNA	GYVKFGHGSA	QHVRAGFRLG	SHNDMSFGE	TSSRDTLRDS
	strain H10407	LSLDDGQDNA	GYVKFGHGSA	QHVRAGFRLG	SHNDMTFGE	TSSRDTLRDS
	strain F11 and 536	LSLDDGQDNA	GYVKFGHGSA	QHVRAGFRLG	SHNDMNFGE	TSSRDTLRDS
	strain SECEC	LSLDDGQDNA	GYVKFGHGSA	QHVRAGFRLG	SHNDMSFGE	TSSRDTLRDS
10	strain H10407	LSLDDGKDNA	GYVKFGHGSA	QHVRAGFRLG	SHNDMTFGE	TSSRAPLRDS
	strain W3110 and DH10B	LSLDDGKDNA	GYVKFGHGSA	QHVRAGFRLG	SHNDMTFGE	TSSRAPLRDS
	strain MGL655	LSLDDGKDNA	GYVKFGHGSA	QHVRAGFRLG	SHNDMTFGE	TSSRAPLRDS
	strain O42	LSLDDGQDNA	GYVKFGHGSA	QHVRAGFRLG	SHNDMTFGE	TSSRDTLRDS
	strain B7A	LSLDDGQDNA	GYVKFGHGSA	QHVRAGFRLG	SHNDMNFGE	TSSRDTLRDS
15	strain CFT073	LSLDDGKDNA	GYVKFGHGSA	QHVRAGFRLG	SHNDMTFGE	TSSRAPLRDS
	strain O42	LSLDDGKDNA	GYVKFGHGSA	QHVRAGFRLG	SHNDMTFGE	TSSRAPLRDS
	strain CFT073	LSLDDGKDNA	GYVKFGHGSA	QHVRAGFRLG	SHNDMTFGE	TSSRAPLRDS
	Consensus	LSLDDG-DNA	-YVKFGHGS-	QH-RAGFRLG	SH-DM-FG-G	TSSR--L--S
20	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
25	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
30	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
35	strain SECEC	AKHRVRELPV	NWWVQPSVIR	TFSSRGDMSM	GTAAAGSNMT	FSPSQNGTSL
	strain H10407	AKHSMRELPV	NWWVQPSVIR	TFSSRGDMSM	GTAAAGSNMT	FSPSRNGTSL
	strain W3110 and DH10B	AKHSVSELPV	NWWVQPSVIR	TFSSRGDMRV	GTSTAGSGMT	FSPSQNGTSL
	strain MGL655	AKHSVSELPV	NWWVQPSVIR	TFSSRGDMRV	GTSTAGSGMT	FSPSQNGTSL
	strain O42	TKHGVSELPV	NWWVQPSVIR	TFSSRGDMSM	GTAAAGSNMT	FSPSQNGTSL
40	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
45		SEQ ID NO: 319				
	B-Cell Ep.	****		****	*****	*****
		1001				1044
50	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	NMTF
55	strain B171	DLQAGLEARV	RENITLGVQA	GYAHSVSGSS	AEGYNGQATL	NMTF
	strain E24377A and O42	DLQAGLEARV	RENITLGVQA	GYAHSVSGSS	AEGYNGQATL	NMTF
	strain E24377A	DLQAGLEARV	RENITLGVQA	GYAHSVSGSS	AEGYNGQATL	NMTF
	Group B	DLQAGLEARV	RENITLGVQA	GYAHSVSGSS	AEGYNGQATL	NMTF
	strain E110019	DLQAGLEARV	RENITLGVQA	GYAHSVSGSS	AEGYNGQATL	NMTF
60	strain E22	DLQAGLEARV	RENITLGVQA	GYAHSVSGSS	AEGYNGQATL	NMTF
	strain H10407	DLQAGLEARV	RENITLGVQA	GYAHSVSGNS	AEGYNGQATL	NMTF
	strain F11 and 536	DLQAGLEARV	RENITLGVQA	GYAHSVSGSS	AEGYNGQATL	NMTF
	strain SECEC	DLQAGLEARV	RENITLGVQA	GYAHSVSGSS	AEGYNGQATL	NMTF

strain H10407 DLQAGLEARV RENITLGVQA GYAHSVIGSS AEGYNGQATL NVTF
 strain W3110 and DH10B DLQAGLEARV RENITLGVQA GYAHSVSGSS AEGYNGQATL NVTF
 strain MG1655 DLQAGLEARV RENITLGVQA GYAHSVSGSS AEGYNGQATL NVTF
 strain 042 DLQAGLEARV RENITLGVQA GYAHSVSGSS AEGYNGQATL NVTF
 5 strain B7A DLQAGLEARV RENITLGVQA GYVHSVSGSS AEGYNGQATL NVTF
 strain CFT073 DLQAGLEARV RENITLGVQA GYAHSSINGSS AEGYNSQATL NVTF
 strain 042 DLQAGLEARV RENITLGVQA GYAHSVSGSS AEGYNSQATL NVTF
 strain CFT073 DLQAGLEARV RENITLGVQA GYAHSVSGSS AEGYNGQATL NVTF
 10 Consensus DLQAGLEAR- RENITLGVQA GY-HS--G-S AEGYN-QATL N-TF
 SEQ ID NO: 320 SEQ ID NO: 321
 B-Cell Ep. *****

 SEQ ID NO: 310 SRSHQ(T/S)GV(N/S)GENNS
 SEQ ID NO: 311 SRSHQTGVNGENNS
 15 SEQ ID NO: 312 SRSHQSGVSGENNS
 SEQ ID NO: 313 SRSHQTGVSGENNS

 B-Cell Epitopes
 SEQ ID NO: 322 RARGKRGG
 20 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
 25 SEQ ID NO: 328 YAGGDQTVHG
 SEQ ID NO: 329 QYVHNGGTASDTVVNS
 SEQ ID NO: 330 GGVAGNTTVNQKRLQVDAGGTATNVTLK
 SEQ ID NO: 331 HTATNTRVDDGGTLDVRNGGTATTVSMG
 SEQ ID NO: 332 GAAVSGTRSDGKAFFSIGG
 30 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
 35 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
 40 SEQ ID NO: 343 NRDSDESWY
 SEQ ID NO: 344 HLGHDNNGGIARGATPSSGSY
 SEQ ID NO: 345 YGAAGHSSVDVKDDGSRAGTVRD
 SEQ ID NO: 346 TRHSMKASSDNDFRA
 SEQ ID NO: 347 SLDDGKDNAGY
 45 SEQ ID NO: 348 DMTFGEGTSSRAPLRDSAKHS
 SEQ ID NO: 349 DMRVGTSTAGSGMTFSPSQNGTSL
 SEQ ID NO: 350 YAHSVSGSSAEGYNGQAT

Orf1767 protein

50 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
 55 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 APEC01 (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 PATLPGAQGG GKAISHDWQQ
	strain 536 and F11	MLRRSLIFLV	LLSAGCVSLD	PHYSTPESPI PATLPGAQGG GKAISHDWQQ
20	strain SECEC	MLRRSLIFLV	LLSAGCVSLD	PHYSTPESPI PATLPGAQGG GKAISHDWQQ
	strain APEC01	MLRRSLIFLV	LLSAGCVSLD	PHYSTPESPI PATLPGAQGG GKAISHDWQQ
	strain CFT073	MLRRSLIFLV	LLSAGCVSLD	PHYSTPESPI PATLPGAQGG GKAISHDWQQ
	strain E2348-69	MLRRSLIFLV	LLSAGCVSLD	PHYSTPESPI PATLPGAQGG GKAISHDWQQ
	Group A	MLRRSLIFLV	LLSAGCVSLD	PHYSTPESPI PATLPGAQGG GKAISHDWQQ
25	Consensus	MLRRSLIFLV	LLSAGCVSLD	PHYSTPESPI PATLPGAQGG 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 APEC01	VIHDPRLQQV	VTIALNSNRD	VQKAIADIDS ARALYGQTNA SLFPTVNAAL
	strain CFT073	VIHDPRLQQV	VTIALNSNRD	VQKAIADIDS ARALYGQTNA SLFPTVNAAL
35	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	TVSSYTDLDF GRNQSLSRAA RETWLASEFT
	strain 536 and F11	SSTRSRSLAN	GTGTTAEADG	TVSSYTDLDF GRNQSLSRAA RETWLASEFT
	strain SECEC	SSTRSRSLAN	GTGTTAEADG	TVSSYTDLDF GRNQSLSRAA RETWLASEFT
	strain APEC01	SSTRSRSLAN	GTVTAEADG	TVSSYTDLDF GRNQSLSRAA RETWLASEFT
45	strain CFT073	SSTRSRSLAN	GTGTTAEADG	TVSSYTDLDF GRNQSLSRAA RETWLASEFT
	strain E2348-69	SSTRSRSLAN	GTGTTAEADG	TVSSYTDLDF GRNQSLSRAA RETWLASEFT
	Group A	SSTRSRSLAN	GTETAEADG	TVSSFTDLDF GRNQSLSRAA RETWLASEFT
	Consensus	SSTRSRSLAN	GT-TTAEADG	TVSS-TLDF GRNQSLSRAA RETWLASEFT

SEQ ID NO: 353

SEQ ID NO: 354

50 B-Cell Ep. * * * * *

		151		200
	strain UTI89 and IHE3034	AQNTRLTLIA	EISTAWLTLA	ADNSNLALAK ETMASAENSL KIIQRQQQVG
	strain 536 and F11	AQNTRLTLIA	EISTAWLTLA	ADNSNLALAK ETMASAENSL KIIQRQQQVG
55	strain SECEC	AQNTRLTLIA	EISTAWLTLA	ADNSNLALAK ETMASAENSL KIIQRQQQVG
	strain APEC01	AQNTRLTLIA	EISTAWLTLA	ADNSNLALAK ETMASAENSL KIIQRQQQVG
	strain CFT073	AQNTRLTLIA	EISTAWLTLA	ADNSNLALAK ETMASAENSL KIIQRQQQVG
	strain E2348-69	AQSTRTLIA	EISTAWLTLA	ADNSNLALAK ETMASAENSL KIIQRQQQVG
	Group A	AQNTRLTLIA	EISTAWLTLA	ADNSNLALAK ETMTSAENSL KIIQRQQQVG

		Consensus	<u>AQ-TRLTLIA EISTAWLTLA ADNSNLALAK ETM-SAENSL KIIQROQQVG</u>			
			SEQ ID NO: 355		SEQ ID NO: 356	
B-Cell Ep.			*****			
5		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 APEC01	TAAATDVSEA	MSVYQQARAS	VASYQTQVMQ	DKNALNLLAG	TTLAENLLPG
10	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.		*****	***	***		
15		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
20	strain APEC01	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
25			SEQ ID NO: 357			
B-Cell Ep.			**** *****			
		301				350
	strain UTI89 and IHE3034	PTISLTASAG	VGSDALSSLF	SHGMQIWSFA	PSVTLPPLFTG	GSNLAQLRYA
30	strain 536 and F11	PTISLTASAG	VGSDALSSLF	SHGMQIWSFA	PSVTLPPLFTG	GSNLAQLRYA
	strain SECEC	PTISLTASAG	VGSDALSSLF	SHGMQIWSFA	PSVTLPPLFTG	GSNLAQLRYA
	strain APEC01	PTISLTASAG	VGSDALSSLF	SHGMQIWSFA	PSVTLPPLFTG	GSNLAQLRYA
	strain CFT073	PTISLTASAG	VGSDALSSLF	SHGMQIWSFA	PSVTLPPLFTG	GSNLAQLRYA
	strain E2348-69	PTISLTASAG	VGSDALSSLF	SHGMQIWSFA	PSVTLPPLFTG	GSNLAQLRYA
35	Group A	PTISLTASAG	VGSDALSSLF	SHGMQIWSFT	PSVTLPPLFTG	GSNLAQLRYA
	Consensus	PTISLTASAG	VGSDALSSLF	SHGMQIWSF-	PSVTLPPLFTG	GSNLAQLRYA
B-Cell Ep.			*** *****			
		351				400
40	strain UTI89 and IHE3034	EAQKRGLIAT	YEKTVQSAFK	DVANALARRT	TLEEQLDAQR	QYVKAQQQTV
	strain 536 and F11	EAQKRGLIAT	YEKTVQSAFK	DVANALARRT	TLEEQLDAQR	QYVKAQQQTV
	strain SECEC	EAQKRGLIAT	YEKTVQSAFK	DVANALARRT	TLEEQLDAQR	QYVKAQQQTV
	strain APEC01	EAQKRGLIAT	YEKTVQSAFK	DVANALARRT	TLEEQLDAQR	QYVKAQQQTV
45	strain CFT073	EAQKRGLIAT	YEKNVQSAFK	DVANALARRT	TLEEQLDAQR	QYVKAQQQTV
	strain E2348-69	EAQKRGLIAT	YEKTVQSAFK	EVANALARRT	TLEEQLDAQS	QYVKAQQQTV
	Group A	EAQKRGLIAT	YEKTVQRAFK	DVANALARRT	TLEEQLDAQR	QYVKAQQQTV
	Consensus	EAQKRGLIAT	YEK-VQ-AFK	-VANALARRT	TLEEQLDAQ-	QYVKAQQQTV
B-Cell Ep.			SEQ ID NO: 359 SEQ ID NO: 360			
50			*****			
		401				450
	strain UTI89 and IHE3034	DVGLRRYQAG	VG DYLTVLTA	QRSLWSAQQE	LLALQLTDFT	NRITLWQSLG
	strain 536 and F11	DVGLRRYQAG	VG DYLTVLTA	QRSLWSAQQE	LLALQLTDFT	NRITLWQSLG
55	strain SECEC	DVGLRRYQAG	VG DYLTVLTA	QRSLWSAQQE	LLALQLTDFT	NRITLWQSLG
	strain APEC01	DVGLRRYQAG	VG DYLTVLTA	QRSLWSAQQE	LLALQLTDFT	NRITLWQSLG
	strain CFT073	DVGLRRYQAG	VG DYLTVLTA	QRSLWSAQQE	LLALQLTDFT	NRITLWQSLG
	strain E2348-69	DVGLRRYQAG	VG DYLTVLTA	QRSLWSAQQE	LLALQLTDFT	NRITLWQSLG
	Group A	DVGLRRYQAG	VG DYLTVLTA	QRSLWSAQQE	LLALQLTDFT	NRITLWQSLG
60	Consensus	DVGLRRYQ-G	VG DYLTVLTA	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
5 strain CFT073         GGMSSLK
strain E2348-69        GGMSSLK
Group A               GGMSSLK
                    Consensus GGMSSLK

10 B-Cell Epitopes
SEQ ID NO: 362 DPHYSTPESPIPATLPGAQGQGAIS
SEQ ID NO: 363 SRSLANGTGTTAEADGTVS
SEQ ID NO: 364 QQVGTAAATDVSE
SEQ ID NO: 365 RASVAS
15 SEQ ID NO: 366 DIQEAEHNLKSANADIGA
SEQ ID NO: 367 SAGVGSD
SEQ ID NO: 368 QYVKAEQQTV

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Orf3515 protein

20 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%,
25 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
30 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.

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strain 536 (SEQ ID NO: 48)
strain SECEC (SEQ ID NO: 49)
35 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)
40 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)
45 strain O42 (SEQ ID NO: 60)

1
strain 536 MITLPPKRG ALVVVLVLLA VMMLVTITLS GRMQQQLGRT RSQQEYQQAL
strain SECEC MITLPPKRG ALVVVLVLLA VMMLVTITLS GRMQQQLGRT RSQQEYQQAL
50 strain E22 and B7A MITSPPKRG ALVVVLVLLA VMMLVTITLS GRMQQQLGRT RSQQEYQQAL
strain HS MITSPPKRG ALVVVLVLLA VMMLVTITLS GRMQQQLGRT RSQQEYQQAL
strain E24377A MITSPPKRG ALVVVLVLLA VMMLVTITLS GRMQQQLGRT RSQQEYQQAL
50

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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
5	strain E110019	MITSPPKRGM	ALVVVLVLLA	VMMLVTITLS	GRMQQQLGRT	RSQQEYQQAL
	strain F11	MITSPPKRGM	ALVVVLVLLA	VIMLVITITLS	GRMQQQLGRT	RSQQEYQLAL
	strain 101-1	MITLPPKRG	ALVVVLVLLA	VMMLVTITLS	GRMQQQLGRT	RSQQEYQQAL
	strain 042	MIISPPKRG	ALAVVLVLLA	VMMLVTITLS	ARMQQQLGRT	RSQQEYQQAL
10	Consensus	MI--PPKRG	AL-VVLVLLA	V-MLV-ITLS	-RMQQQLGRT	RSQQEYQ-AL
	B-Cell Ep.				SEQ ID NO: 369	*****
		51				100
	strain 536	WYSASAESLA	LSALSLSLKN	EKRVHLAQPW	ASGPRFFPLP	QGQIAVTLRD
15	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	TSGRFFPLP	QGQIAVTLRD
20	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
25	strain 101-1	WYSASAESLA	LSALSLSLKN	EKRVHLAQPW	ASGPRFFPLP	QGQIAVTLRD
	strain 042	WYSASAESLA	LSALSLSLKN	EKRVHLAQPW	ASGPRFFPLP	QGQIAVTLRD
	Consensus	WYSASAESLA	LSALSLSLKN	EKRVHL-QPW	-SGPRFFPLP	QGQIAVTLRD
	B-Cell Ep.				SEQ ID NO: 370	SEQ ID NO: 371
						** *****
30						
		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
35	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
40	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
45	Consensus	AQACFNLNAL	AQPTT--RP-	AVQQLI-LI-	RL-VPAYRAE	LIAESLWEFI
	B-Cell Ep.				SEQ ID NO: 372	

		151				200
50	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
55	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	QGMDAGLYQK
60	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

SEQ ID NO: 373

B-Cell Ep.

** ***** **

		201		250
5	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
10	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 DVTQSVILEA LFDPWLSPVQ	ARALLQQRPA
15	strain F11	LKPLVCALPM	ARQQININTL DVTQSVILEA LFDPWLSPVQ	ARALLQQRPA
	strain 101-1	LKPLVCALPM	TRQQININTL DVTQSVILEA LFDPWLSPVQ	ARALLQQRPA
	strain 042	LKPLVCALPM	ARQQININTL DVTQSVILEA LFDPWLSPVQ	ARALLQQRPA
	Consensus	<u>LKPLVCALPM</u>	<u>-RQQININTL DVTQSV-LEA</u>	<u>LFDPWLSPVQ ARALLQQRPA</u>

SEQ ID NO: 374 SEQ ID NO: 375 SEQ ID NO: 376

20 B-Cell Ep.

		251		300
	strain 536	KGWEDVDQFL	AQPLLADVDE RTKKQLKTVL SVDSNYFWLR	SDITVNEIEL
	strain SECEC	KGWEDVDQFL	AQPLLADVDE RTKKQLKTVL SVDSNYFWLR	SDITVNEIEL
25	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
30	strain E2348-69	KGWEDVDQFL	AQPLLADVDE RTKKQLKTVL SVDSNYFWLR	SDITVNEIEL
	Group A	KGWEDVDQFL	AQPLLADVDE RTKKQLKTVL SVDSNYFWLR	SDITVNEIEL
	strain E110019	KGWEDVDQFL	AQPLLADVDE RTKKQLKTVL SVDSNYFWLR	SDITVNEIEL
	strain F11	KGWEDVDQFL	AQPLLADVDE RTKKQLKTVL SVDSNYFWLR	SDITVNEIEL
	strain 101-1	KGWEDVDQFL	AQPLLADVDE RTKKQLKTVL SVDSNYFWLR	SDITVNEIEL
35	strain 042	KGWEDVDQFL	AQPLLADVDD RTKKQLKTVL SVDSNYFWLR	SDITVNEIEL
	Consensus	<u>KGWEDVDQFL</u>	<u>AQPLLADVDD-</u>	<u>RTKKQLKTVL SVDSNYFWLR SDITVNEIEL</u>

SEQ ID NO: 377

B-Cell Ep.

***** ** *****

		301		325
40	strain 536	TMNSLIVRMG	PQHFSVLWHQ TGESE	
	strain SECEC	TMNSLIVRMG	PQHFSVLWHQ TGESE	
	strain E22 and B7A	TMNSLIVRMG	PQHFSVLWHQ TGESE	
	strain HS	TMNSLIVRMG	PQHFSVLWHQ TGESE	
45	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	
50	strain E110019	TMNSLIVRMG	PQHFSVLWHQ TGESE	
	strain F11	TMNSLIIRMG	PQHFSVLWHQ TGESE	
	strain 101-1	TMNSLIVRMG	SQHFSVIWHQ TGESE	
	strain 042	TMNSLIVRMG	PQHFSVLWHQ TGESE	
	Consensus	<u>TMNSLI</u> -RMG	<u>-QHFSV-WHQ</u>	<u>TGESE</u>

55

B-Cell Epitopes

SEQ ID NO: 378 QLGRTRSQQEY

SEQ ID NO: 379 PWASGPRFFPL

SEQ ID NO: 380 AQPTTASRP

60 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
30 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	QTMSFLNHDH
35 strain SECEC		MLVAIAIFAS	LALMAQQVTN	GVTRVNSAVA	GHDQKLNLMQ	QTMSFLNHDH
strain 536		MLVAIAIFAS	LALMAQQVTN	GVTRVNSAVA	GHDQKLNLMQ	QTMSFLNHDH
strain E2348-69		MLVAIAIFAS	LALMAQQVTN	GVTRVNSAVA	GHDQKLNLMQ	QTMSFLNHDH
strain 101-1		MLVAIAIFAL	LALMAQQVTN	GVTRVNSAVA	GHDQKLNLMQ	QTMSFLTHDL
strain O42		MLVAIAIFAS	LALMAQQVTN	GVTRVNSAIG	EHDQKLNLMQ	QTMSFLTHDL
40	Consensus	MLVAIAIFA-	LALMAQQVTN	GVTRVN-A--	-HDQKLNLMQ	QTMSFL-HDL
			SEQ ID NO: 385		SEQ ID NO: 386	
B-Cell Ep.			** ****	*** **		

		51				100
45 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	AGAGVLSEES	GGMRFVRGGV	VNPLMRLPRS
50 strain F11		TQMMPRPVRG	DQGQREPALL	AGAGVLASES	EGMRFVRGGV	VNPLMRLPRS
strain SECEC		TQMMPRPVRG	DQGQREPALL	AGAGVLASES	EGMRFVRGGV	VNPLMRLPRS
strain 536		TQMMPRPVRG	DQGQREPALL	AGAGVLASES	EGMRFVRGGV	VNPLMRLPRS

	strain E2348-69	TQMMPRPV RG	DQGQREPA LL	AGAGVLA SES	EGIRFVRGG V	VNPLMRLPR S
	strain 101-1	TQMMPRPV RG	DQGQREPA LL	AGAGVLA SES	GGMRFVRGG V	VNLLMRLPR S
	strain 042	TQMMPRPV RG	DQGQREPA LL	AGPGVLA SES	EGMRFVRGG V	VNPLMRLPR S
5	Consensus	<u>TQMMPRPV RG</u>	<u>-QGQREPA LL</u>	<u>AG-GVL-SES</u>	<u>-G-RFVRGG V</u>	<u>VN-LMR-PR S</u>
	B-Cell Ep.	SEQ ID NO: 387	SEQ ID NO: 388	*****	*****	
		101				150
10	Group A	NLLTVGYRI H	DGYLERLAW P	LTDAAGSVK P	TMQKLIPAD S	LRLQFYDGTR
	strain E110019	NLLTVGYRI H	DGYLERLAW P	LTDAAGSVK P	TMQKLIPAD S	LRLQFYDGTR
	strain H10407	NLLTVGYRI H	DGYLERLAW P	LTDAAGSVK P	TMQKLIPAD S	LRLQFYDGTR
	strain HS and 53638	NLLTVGYRI H	DGYLERLSW P	LTDAAGSVK P	TMQKLIPAD S	LHLQFYDGTR
	Group B	NLLTVGYRI H	DGYLERLAW P	LTDAAGSVK P	TTQKLIPAD S	LRLQFYDGTR
	strain F11	NLLTVGYRI H	GGYLERLAW P	LTDAAGSVK P	TTQKLIPAD S	LRLQFHDGTR
15	strain SECEC	NLLTVGYRI H	GGYLERLAW P	LTDAAGSVK P	TTQKLIPAD S	LRLQFHDGTR
	strain 536	NLLTVGYRI H	GGYLERLAW P	LTDAAGSVK P	TTQKLIPAD S	LRLQFYDGTR
	strain E2348-69	NLLTVGYRI H	GGYLERLAW P	LTDAAGSVK P	TTQKLIPAD S	LRLQFHDGTC
	strain 101-1	NLLTVGYRI H	GGYLERLAW P	LTDAAGSVK P	TTQKLIPAD S	LRLQFHDGTR
	strain 042	NLLTVGYRI H	GGYLERLAW P	LTDAADSVK P	TTQKLIPAD S	LRLQFYDGTR
20	Consensus	<u>NLLTVGYRI H</u>	<u>-GYLERL-WP</u>	<u>LTDAAGSVK P</u>	<u>T-QKLIPAD S</u>	<u>L-LQF-DGT-</u>
	B-Cell Ep.	SEQ ID NO: 389	SEQ ID NO: 390-391	*****	*	**
		151				189
25	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	
30	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	
35	strain 042	WQESWSSVQA	IPVAVRMTLH	SPQWGEIERI	WLLRGPQLS	
	Consensus	<u>WQESWSSVQA</u>	<u>-PVA VR-TLH</u>	<u>SPQWGEIERI</u>	<u>WLLRGPQ~~</u>	
	B-cell Ep.	SEQ ID NO: 393	SEQ ID NO: 394	*****		
40	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				
45	SEQ ID NO: 396	AVAGHD				
	SEQ ID NO: 397	PRPVRGDQGQREPA				
	SEQ ID NO: 398	TRWQESWSS				

50 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 APEC01, 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 042 (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	LKGRALFSL	FAAPMIHATD	SVTTKDGETI TVTADANTAT
	strain F11	MAMFTPSFSG	LKGRALFSL	FAAPMIHATD	SVTTKDGETI TVTADANTAT
20	Group A	MAMFTPSFSG	LKGRALFSL	FAAPMIHATD	SVTTKDGETI TVTADANTAT
	strain SECEC	MAMFTPSFSG	LKGRALFSL	FAAPMIHATD	SVTTKDGETI TVTADANTAT
	Group B	MAKFTPSFSG	IKGRALFSL	FAAPMIHATD	TATTKDGETI TVTADANTAT
	strain 042	MAKFTPSFSG	IKGRALFSL	FAAPMIHATD	TATTKDGETI TVTADANTAT
	Group C	MAKFTPSFSG	IKGRALFSL	FAAPMIHATD	TATTKDGETI TVTADANTAT
25	strain 536	MAKFTPSFSG	IKGRALFSL	FAAPMIHATD	TATTKDGETI TVTADANTAT
	Consensus	MA-FTPSFSG	<u>-KGRALFSL</u>	<u>FAAPMIHATD</u>	<u>--TTKDGETI</u> TVTADANTAT
				SEQ ID NO: 399	SEQ ID NO: 400
	B-Cell Ep.			*****	*****
		51			100
	strain E2348-69	EATDGYQPLS	TSTATLTDM	MLDIPQVVNT	VSDQVLENQN ATTLDEALYN
	strain F11	EATDGYQPLS	TSTATLTDM	MLDIPQVVNT	VSDQVLENQN ATTLDEALYN
	Group A	EATDGYQPLS	TSTATLTDM	MLDIPQVVNT	VSDQVLENQN ATTLDEALYN
	strain SECEC	EATDGYQPLS	TSTATLTDM	MLDIPQVVNT	VSDQVLENQN ATTLDEALYN
35	Group B	EATDGYQPLS	TSTATLTDM	MLDIPQVVNT	VSDQVLENQN ATTLDEALYN
	strain 042	EATDGYQPLS	TSTATLTDM	MLDIPQVVNT	VSDQVLENQN ATTLDEALYN
	Group C	EATDGYQPLS	TSTATLTDM	MLDIPQVVNT	VSDQVLENQN ATTLDEALYN
	strain 536	EATDGYQPLS	TSTATLTDM	MLDIPQVVNT	VSDQVLENQN ATTLDEALYN
	Consensus	<u>EATDGYQPLS</u>	<u>TSTATLTDM</u>	<u>MLDIPQVVNT</u>	<u>VSDQVLENQN</u> ATTLDEALYN
40	B-Cell Ep.	*****	*****	*****	*****
		101			150
	strain E2348-69	VSNVVQTNTL	GGTQDAFVRR	GFGANRDGSI	MTNGLRTVLP RSFNAATERV
	strain F11	VSNVVQTNTL	GGTQDAFVRR	GFGANRDGSI	MTNGLRTVLP RSFNAATERV
45	Group A	VSNVVQTNTL	GGTQDAFVRR	GFGANRDGSI	MTNGLRTVLP RSFNAATERV
	strain SECEC	VSNVVQTNTL	GGTQDAFVRR	GFGANRDGSI	MTNGLRTVLP RSFNAATERV
	Group B	VSNVVQTNTL	GGTQDAFVRR	GFGANRDGSI	MTNGLRTVLP RSFNAATERV
	strain 042	VSNVVQTNTL	GGTQDAFVRR	GFGANRDGSI	MTNGLRTVLP RSFNAATERV
	Group C	VSNVVQTNTL	GGTQDAFVRR	GFGANRDGSI	MTNGLRTVLP RSFNAATERV
50	strain 536	VSNVVQTNTL	GGTQDAFVRR	GFGANRDGSI	MTNGLRTVLP RSFNAATERV
	Consensus	<u>VSNVVQTNTL</u>	<u>GGTQDAFVRR</u>	<u>GFGANRDGSI</u>	<u>MTNGLRTVLP</u> RSFNAATERV
	B-Cell Ep.	***	*****	*****	
		151			200
55	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

5	Group B	EVLKGPASTL	YGILDPGGGLI	NVVTKRPEKT	FHGSVSATSS	SFGGGTGQLD
	strain 042	EVLKGPASTL	YGILDPGGGLI	NVVTKRPEKT	FHGSVSATSS	SFGGGTGQLD
	Group C	EVLKGPASTL	YGILDPGGGLI	NVVTKRPEKT	FHGSVSATSS	SFGGGTGQLD
	strain 536	EVLKGPASTL	YGILDPGGGLI	NVVTKRPEKT	FHGSVSATSS	SFGGGTGQLD
	B-Cell Ep.	Consensus	<u>EVLKGPASTL</u>	<u>YGILDPGGGLI</u>	<u>NVVTKRPEKT</u>	<u>FHGSVSATSS</u>
			*****	*****	*****	*****
			201			250
10	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
15	strain 042	ITGPIEGTQL	AYRLTGEVQD	EDYWRNFGKE	RSTFIAPSLT	WFGDNATVTM
	Group C	ITGPIEGTQL	AYRLTGEVQD	EDYWRNFGKE	RSTFIAPSLT	WFGDNATVTM
	strain 536	ITGPIEGTQL	AYRLTGEVQD	EDYWRNFGKE	RSTFIAPSLT	WFGDNATVTM
	B-Cell Ep.	Consensus	<u>ITGPIEGTQL</u>	<u>AYRLTGEVQD</u>	<u>EDYWRNFGKE</u>	<u>RSTFIAPSLT</u>
			*****	*****	*****	*****
			251			300
20	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	DGQSDLAQLN
	Group B	LYSHRDYKTP	FDRGTIFDLT	TKQPVNVDRK	IRFDEPFNIT	DGQSDLAQLN
25	strain 042	LYSHRDYKTP	FDRGTIFDLT	TKQPVNVDRK	IRFDEPFNIT	DGQSDLAQLN
	Group C	LYSHRDYKTP	FDRGTIFDLT	TKQPVNVDRK	IRFDEPFNIT	DGQSDLAQLN
	strain 536	LYSHRDYKTP	FDRGTIFDLT	TKQPVNVDRK	IRFDEPFNIT	DGQSDLAQLN
	B-Cell Ep.	Consensus	<u>LYSHRDYKTP</u>	<u>FDRGTIFDLT</u>	<u>TKQPVNVDRK</u>	<u>IRFDEPFNIT</u>
			*****	*****	*****	*****
			301			350
35	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
40	strain 042	AEYHLNSQWT	ARFDYSYSQD	KYSDNQARVT	AYDATTGTLT	RRVDATQGST
	Group C	AEYHLNSQWT	ARFDYSYSQD	KYSDNQARVT	AYDATTGTLT	RRVDATQGST
	strain 536	AEYHLNSQWT	ARFDYSYSQD	KYSDNQARVT	AYDATTGTLT	RRVDATQGST
	B-Cell Ep.	Consensus	<u>AEYHLNSQWT</u>	<u>ARFDYSYSQD</u>	<u>KYSDNQARVT</u>	<u>AYDATTGTLT</u>
			SEQ ID NO: 401	*****	*****	*****
			351			400
45	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
50	strain 042	QRMHSTRADL	QGNVDIAGFY	NEILGGVSYE	YYDLLRTDMI	RCKNAKDFNI
	Group C	QRMHSTRADL	QGNVDIAGFY	NEILGGVSYE	YYDLLRTDMI	RCKNAKDFNI
	strain 536	QRMHSTRADL	QGNVDIAGFY	NEILGGVSYE	YYDLLRTDMI	RCKNAKDFNI
	B-Cell Ep.	Consensus	<u>QRMH-TRADL</u>	<u>QGNVDIAGFY</u>	<u>NEILGGVSYE</u>	<u>YYDLLRTDMI</u>
			SEQ ID NO: 402	***		
			401			450
60	strain E2348-69	YNPVYGNTSK	CTTVSASDSD	QTIKQESYSA	YAQDALYLT	NWIAVAGIRY
	strain F11	YNPVYGNTSK	CTTVSASDSD	QTIKQESYSA	YAQDALYLT	NWIAVAGIRY
	Group A	YNPVYGNTSK	CTTVSASDSD	QTIKQENYSA	YAQDALYLT	NWIAVAGIRY
	strain SECEC	YNPVYGNTSK	CTTVSASDSD	QTIKQESYSA	YAQDALYLT	NWIAVAGIRY
	Group B	YNPVYGNTSK	CTTVSASDSD	QTIKQESYSA	YAQDALYLT	NWIAVAGIRY

	strain 042	YNPVYGNSTK	CTTVSASDSD	QTIKQESYSA	YAQDALYLT	NWIAVAGIRY
	Group C	YNPVYGNSTK	CTTVSASDSD	QTIKQESYSA	YAQDALYLT	NWIAVAGIRY
	strain 536	YNPVYGNSTK	CTTVSASDSD	QTIKQESYSA	YAQDALYLT	NWIAVAGIRY
5	Consensus	YNPVYGNSTK	CTTVSASDSD	QTIKQE-YSA	YAQDALYLT	NWIAVAGIRY
		SEQ ID NO: 403		SEQ ID NO: 404		
	B-Cell Ep.	*****	*****	*****	*	
		451				500
10	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
15	strain 042	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
20	strain E2348-69	QSSIASYIGD	LPPESSNAYE	VGAKFELFDG	ITADIALFDI	HKRNVLVTES
	strain F11	QSSIASYIGD	LPPESSNAYE	VGAKFELFDG	ITADIALFDI	HKRNVLVTES
	Group A	QSSIASYIGD	LPPESSNAYE	VGAKFELFDG	ITADIALFDI	HKRNVLVTES
	strain SECEC	QSSIASYIGD	LPPESSNAYE	VGAKFELFDG	ITADIALFDI	HKRNVLVTES
25	Group B	QSSIASYIGD	LPPESSNAYE	VGAKFELFDG	ITADIALFDI	HKRNVLVTES
	strain 042	QSSIASYIGD	LPPESSNAYE	VGAKFELFDG	ITADIALFDI	HKRNVLVTES
	Group C	QSSIASYIGD	LPPESSNAYE	VGAKFELFDG	ITADIALFDI	HKRNVLVTES
	strain 536	QSSIASYIGD	LPPESSNAYE	VGAKFELFDG	ITADIALFDI	HKRNVLVTES
	Consensus	QSSIASYIGD	LPPESSNAYE	VGAKFELFDG	ITADIALFDI	HKRNVLVTES
30	B-Cell Ep.	**	*****			*
		551				600
35	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
40	strain 042	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
	B-Cell Ep.	*****				*****
		601				650
45	strain E2348-69	GKPLPNVPRH	TGSLFLTYDI	HNMPGNNTLT	FGGGGHGVS	RSATNGADYY
	strain F11	GKPLPNVPRH	TGSLFLTYDI	HNMPGNNTLT	FGGGGHGVS	RSATNGADYY
	Group A	GKPLPNVPRH	TGSLFLTYDI	HNMPGNNTLT	FGGGGHGVS	RSATNGADYY
	strain SECEC	GKPLPNVPRH	TGSLFLTYDI	HNMPGNNTLT	FGGGGHGVS	RSATNGADYY
50	Group B	GKPLPNVPRH	TGSLFLTYDI	HNMPGNNTLT	FGGGGHGVS	RSATNGADYY
	strain 042	GKPLPNVPRH	TGSLFLTYDI	HNMPGNNTLT	FGGGGHGVS	RSATNGADYY
	Group C	GKPLPNVPRH	TGSLFLTYDI	HNMPGNNTLT	FGGGGHGVS	RSATNGADYY
	strain 536	GKPLPNVPRH	TGSLFLTYDI	HNMPGNNTLT	FGGGGHGVS	RSATNGADYY
	Consensus	GKPLPN-PRH	TGSLFLTYDI	HNMPGNNTLT	FGGGGH-VSR	RSATNGADYY
55	B-Cell Ep.	*****		*****	*****	*****
		651				700
60	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

	strain O42	LPGYFVADAF	AAYKMKLQYP	VTQLNVKNL	FDKTYYTSSI	ATNNLGNQIG
	Group C	LPGYFVADAF	AAYKMKLQYP	VTQLNVKNL	FDKTYYTSSI	ATNNLGNQIG
	strain 536	LPGYFVADAF	AAYKMKLQYP	VTQLNVKNL	FDKTYYTSSI	ATNNLGNQIG
	Consensus	LPGYFVADAF	AAYKMKLQYP	VTQLNVKNL	FDKTYYTSSI	ATNNLGNQIG
5	B-Cell Ep.					* *****
		701	713			
	strain E2348-69	DPREVQFTVK	MEF			
	strain F11	DPREVQFTVK	MEF			
10	Group A	DPREVQFTVK	MEF			
	strain SECEC	DPREVQFTVK	MEF			
	Group B	DPREVQFTVK	MEF			
	strain O42	DPREVQFTVK	MEF			
	Group C	DPREVQFTVK	MEF			
15	strain 536	DPREVQFTVK	MEF			
	Consensus	DPREVQFTVK	MEF			
	B-Cell Ep.	*****				
	B-Cell Epitopes					
20	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				
25	SEQ ID NO: 413	GEVQDEYWRN				
	SEQ ID NO: 414	DYKTPFD				
	SEQ ID NO: 415	KQPVNV				
	SEQ ID NO: 416	FNITDGQSDL				
	SEQ ID NO: 417	SYSQDKYSDNQARVTAYDATTGTLT				
30	SEQ ID NO: 418	VDATQGSTQRM				
	SEQ ID NO: 419	PVYGNTSKCTTVSASDSDQTIKQESYSAY				
	SEQ ID NO: 420	QYAGKGRPFENVNTDSRDEQWT				
	SEQ ID NO: 421	GDLPPESSNAYE				
	SEQ ID NO: 422	SVGDETIAKT				
35	SEQ ID NO: 423	AKVLEDPDYAGKPLPNVPRH				
	SEQ ID NO: 424	NMPGNNTLTFGGGGHGVSRRSATNGADYY				
	SEQ ID NO: 425	IATNNLGNQIGDPREV				

Orf3613 protein

- 40 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%,
 45 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
 50 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, APEC01, RS218 and IHE3034 (SEQ ID NO: 80)
Strain O42 (SEQ ID NO: 81)

5		1	50
	Group A	MLKKTLLSMF ATALLSGVAF NALADDANQG SGKITFKGEV IDAPCSIAPG	
	strain O42	MEKKTLLSMF ATALLSGVAF NALADDANQG SGKITFKGEV IDAPCSIAPG	
10		Consensus M-KKTLLSMF ATALLSGVAF NALADDANQG SGKITFKGEV IDAPCSIAPG	
		SEQ ID NO: 426	
	B-Cell Ep.	*****	*****
		51	100
	Group A	DEDQTINLGE VADTVLKSGQ KSLPVDVTIH LQDCILSDGT NTVDKVKITF	
15	strain O42	DEDQTINLGE VADTVLKSGQ KSLPVDVTIH LQDCILSDGT NTVDKVKITF	
		Consensus DEDQTINLGE VADTVLKSGQ KSLPVDVTIH LQDCILSDGT NTVDKVKITF	
	B-Cell Ep.	*****	
		101	150
20	Group A	SSASVDATDS NLLKNTLEGN IGGATDVGVV LVKSDNTNVT LGTPITINFP	
	strain O42	SSASVDATDS NLLKNTLEGN IGGATDVGVV LVKSDNTNVT LGTPITINFP	
		Consensus SSASVDATDS NLLKNTLEGN IGGATDVGVV LVKSDNTNVT LGTPITINFP	
	B-Cell Ep.	*****	***
		151	187
25	Group A	TTNSYQELNF KARMESLGRT ATPGNVQAQA NYVLDYK	
	strain O42	TTNSYQELNF KARMESLGRT ATPGNVQAQA NYVLDYK	
		Consensus TTNSYQELNF KARMESLGRT ATPGNVQAQA NYVLDYK	
	B-Cell Ep.	*****	***
30	B-Cell Epitopes		
	SEQ ID NO: 427	ADDANQGSKGIT	
	SEQ ID NO: 428	CSIAPGDEDQTIN	
	SEQ ID NO: 429	ASVDATDS	
35	SEQ ID NO: 430	EGNIGGATD	
	SEQ ID NO: 431	NEFTTNSY	
	SEQ ID NO: 432	LGRTATPGNVQAQ	

Recp3768 protein

40 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%,
45 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
50 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)						
5	Strain CFT073 (SEQ ID NO: 103)					
Group A: strain RS218, UT189 and F11 (SEQ ID NO: 104)						
Strain E110019 (SEQ ID NO: 105)						
		1				50
10	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
15	Consensus	<u>MPTITTAQIK</u>	<u>STLQSAKQS-</u>	<u>-NKLHSAGQS</u>	<u>TKDALKKAAE</u>	<u>-TRNAGNRLI</u>
		SEQ ID NO: 433		SEQ ID NO: 434		
B-Cell Ep.		*****	*****	*****	*****	*****
		51				100
20	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
25	Consensus	<u>LLIPKDYKGQ</u>	<u>GSSLNDLVRT</u>	<u>ADELGIEVQY</u>	<u>DEKNGTAITK</u>	<u>QVFGTAEKLI</u>
		SEQ ID NO: 435				
B-Cell Ep.		*****	***	**	*****	.
		101				150
30	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
35	Consensus	<u>GLTERGVTIF</u>	<u>AP-LDKLLQK</u>	<u>YQKAGNKLGG</u>	<u>SAENIGDNLG</u>	<u>KAG--LSTFQ</u>
		SEQ ID NO: 436				
B-Cell Ep.		*****				
		151				200
40	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
45	Consensus	<u>NFLGTALSSM</u>	<u>KIDELIK-QK</u>	<u>SG-NVSSSE-</u>	<u>A-ASIELINQ</u>	<u>LVDTAAS-NN</u>
		SEQ ID NO: 437		SEQ ID NO: 438		
B-Cell Ep.		*****				
		201				250
50	strain 536	NVNSFSQQLN	KLGSVLSNTK	HLNGVGKQLQ	NLPNLDNIGA	GLDTVSGILS
	strain 536	NVNSFSQQLN	KLGSVLSNTK	HLNGVGKQLQ	NLPNLDNIGA	GLDTVSGILS
	strain CFT073	NVNSFSQQLN	KLGSVLSNTK	HLTGVGKQLQ	NLPNLDNIGA	GLDTVSGILS
	Group A	NVNSFSQQLN	KLGSVLSNTK	HLNGVGKQLQ	NLPNLDNIGA	GLDTVSGILS
	strain E110019	NVNSFSQQLN	TLGSVLSNTK	HLNGVGKQLQ	NLPNLDNIGA	GLDTVSGILS
55	Consensus	<u>NVNSFSQQLN</u>	<u>-LGSVLSNTK</u>	<u>HL-GVGKQLQ</u>	<u>NLPNLDNIGA</u>	<u>GLDTVSGILS</u>
		SEQ ID NO: 439	SEQ ID NO: 440	SEQ ID NO: 441		
		251				300
60	strain 536	VISASFILSN	ADADTGTKAA	AGVELTTKVL	GNVGKGISQY	IIAQRAAQGL
	strain 536	AISASFILSN	ADADTGTKAA	AGVELTTKVL	GNVGKGISQY	IIAQRAAQGL
	strain CFT073	AISASFILSN	ADADTGTKAA	AGVELTTKVL	GNVGKGISQY	IIAQRAAQGL

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		
5	B-Cell Ep.	*****		**	****	
		301				350
strain 536		STSAAGGLI	ASAVTLAISP	LSFLSIADKF	KRANKIEEYS	QRFKKLGYDG
strain 536		STSAAGGLI	ASVVTLAISP	LSFLSIADKF	KRANKIEEYS	QRFKKLGYDG
10	strain CFT073	STSAAGGLI	ASVVTLAISP	LSFLSIADKF	KRANKIEEYS	QRFKKLGYDG
Group A		STSAAGGLI	ASVVTLAISP	LSFLSIADKF	KRANKIEEYS	QRFKKLGYDG
strain E110019		STSAAGGLI	ASAVILAISP	LSFLSIADKF	KRANKIEEYS	QRFKKLGYDG
Consensus		STSAAGGLI	AS-V-LAISP	LSFLSIADKF	KRANKIEEYS	QRFKKLGYDG
		SEQ ID NO: 444				
15	B-Cell Ep.	*****				
		351				400
strain 536		DSLLAAFHKE	TGAIDASLTT	ISTVLASVSS	GISAAATTSL	VGAPVSALVG
strain 536		DSLLAAFHKE	TGAIDASLTT	ISTVLASVSS	GISAAATTSL	VGAPVSALVG
20	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: 444				
25	B-Cell Ep.	* *****				
		401				450
strain 536		AVTGIISGIL	EASKQAMFEH	VASKMADVIA	EWEKKHGKNY	FENGYDARHA
strain 536		AVTGIISGIL	EASKQAMFEH	VASKMADVIA	EWEKKHGKNY	FENGYDARHA
30	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.		*****				
35		451				500
strain 536		AFLEDNFKIL	SQYNKEYSVE	RSVLITQQHW	DTLIGELAGV	TRNGDKTLTG
strain 536		AFLEDNFEIL	SQYNKEYSVE	RSVLITQQHW	DTLIGELAGV	TRNGDKTLTG
strain CFT073		AFLEDNFKIL	SQYNKEYSVE	RSVLITQQHW	DTLIGELAGV	TRNGDKTLTG
40	Group A	AFLEDNFKIL	SQYNKEYSVE	RSVLITQQHW	DMLIGELASV	TRNGDKTLTG
strain E110019		AFLEDNFKIL	SQYNKKYSVE	RSVLITQQHW	DTLIGELAGV	TRNGDKTLTG
Consensus		AFLEDNF-IL	SQYNK-YSVE	RSVLITQQHW	D-LIGELA-V	TRNGDKTLTG
		SEQ ID NO: 446			SEQ ID NO: 447	
B-Cell Ep.		** *****				
45		501				550
strain 536		KSYIDYYEEG	KRLEKKPDEF	QKQVFDPLKG	NIDLSDSKSS	TLLKFVTPLL
strain 536		KSYIDYYEEG	KRLEKEPDEF	QKQVFDPLKG	NIDLSVIKSS	TLLKFITPLL
strain CFT073		KSYIDYYEEG	KRLEKKPDEF	QKQVFDPLKG	NIDLSDSKSS	TLLKFVTPLL
50	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.		*****		*****	*	
55		551				600
strain 536		TPGEEIRERR	QSGKYEYITE	LLVKGVDKWT	VKGVQDKGSV	YDYSNLIQHA
strain 536		TPGKEIRERR	QSGKYEYITE	LLVKGVDKWT	VKGVQDKGSV	YDYSNLIQHA
strain CFT073		TPGEEIRERR	QSGKYEYITE	LLVKGVDKWT	VKGVQDKGSV	YDYSNLIQHA
60	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
5	strain CFT073	SVGNNQYREI	RIESHLGDGD	DKVFLSAGSA	NIYAGKGHDV	VYYDKTDTGY
	Group A	SVGNNQYREI	RIESHLGDGD	DKVFLSAGSA	NIYAGKGHDV	VYYDKTDTGY
	strain E110019	SVGNNQYRGI	RIESHLGDGD	DKVFLSAGSA	NIYAGKGHDV	VYYDKTDTGY
	Consensus	<u>SVGNNQYR-I</u>	<u>RIESHLGDGD</u>	<u>DKVFL-AGSA</u>	<u>NIYAGKGHDV</u>	<u>VYYDKTDTGY</u>
		SEQ ID NO: 451		SEQ ID NO: 452		
10	B-Cell Ep.	*****	*****	*	*****	*****
		651				700
	strain 536	LTIDGTKATE	AGNYTVTRVL	GGDVKVLQEV	VKEQEVSVGK	RTEKTQYRSY
	strain 536	LTIDGTKATE	AGNYTVTRVL	GGDVKVLQEV	VKEQEVSVGK	RTEKTQYRSY
15	strain CFT073	LTIDGTKATE	AGNYTVTRVL	GGDVKILQEV	VKEQEVSVGK	RTEKTQYRSY
	Group A	LTIDGTKATE	AGNYTVTRVL	GGDVKVLQEV	VKEQEVSVGK	RTEKTQYRSY
	strain E110019	LTIDGTKATE	AGNYTVTRVL	GGDVKVLQEV	AKEQEVSVGK	RTEKTQYRSY
	Consensus	<u>LTIDGTKATE</u>	<u>AGNYTVTRVL</u>	<u>GGDVK-LQEV</u>	<u>-KEQEVSVGK</u>	<u>RTEKTQYRSY</u>
		SEQ ID NO: 453				
20	B-Cell Ep.	*	*****	****	*****	*****
		701				750
	strain 536	EFTHINGTDL	TETDNLYSVE	ELIGTNRADK	FFGSKFTDIF	HGADGDDHIE
	strain 536	EFTHINGTDL	TETDNLYSVE	ELIGTNRADK	FFGSKFTDIF	HGADGDDHIE
25	strain CFT073	EFTHINGKNL	TETDNLYSVE	ELIGTTRADK	FFGSKFTDIF	HGADGDDHIE
	Group A	EFTHINGKNL	TETDNLYSVE	ELIGTTRADK	FFGSKFTDIF	HGADGDDHIE
	strain E110019	EFTHINGKNL	TETDNLYSVE	ELIGTTRADK	FFGSKFTDIF	HGADGDDHIE
	Consensus	<u>EFTHING--L</u>	<u>TETDNLYSVE</u>	<u>ELIGT-RADK</u>	<u>FFGSKFTDIF</u>	<u>HGADGDD-IE</u>
		SEQ ID NO: 454		SEQ ID NO: 455		
30	B-Cell Ep.	****	***		*****	*****
		751				800
	strain 536	GNDGNDRLYG	DKGNDTLRGG	NGDDQLYGGD	GNDKLTGGVG	NNYLNGGDGD
	strain 536	GNDGNDRLYG	DKGNDTLRGG	NGDDQLYGGD	GNDKLTGGVG	NNYLNGGDGD
35	strain CFT073	GNDGNDRLYG	DKGNDTLRGG	NGDDQLYGGD	GNDKLIGGTG	NNYLNGGDGD
	Group A	GNDGNDRLYG	DKGNDTLRGG	NGDDQLYGGD	GNDKLIGGTG	NNYLNGGDGD
	strain E110019	GNDGNDRLYG	DKGNDTLRGG	NGDDQLYGGD	GNDKLIGGTG	NNYLNGGDGD
	Consensus	<u>GNDGNDRLYG</u>	<u>DKGNDTLRGG</u>	<u>NGDDQLYGGD</u>	<u>GNDKLIGGTG</u>	<u>NNYLNGGDGD</u>
		SEQ ID NO: 456		SEQ ID NO: 457	SEQ ID NO: 458	
40	B-Cell Ep.	*****	*****	*****	*****	*****
		801				850
	strain 536	DELQVQGNL	AKNVLSGGKG	NDKLYGSEGA	DLLDGEGGND	LLKGGYGNDI
	strain 536	DELQVQGNL	AKNVLSGGKG	NDKLYGSEGA	DLLDGEGGND	LLKGGYGNDI
45	strain CFT073	DELQVQGNL	AKNVLSGGKG	NDKLYGSEGA	DLLDGEGGND	LLKGGYGNDI
	Group A	DELQVQGNL	AKNVLSGGKG	NDKLYGSEGA	DLLDGEGGND	LLKGGYGNDI
	strain E110019	DELQVQGNL	AKNVLSGGKG	NDKLYGSEGA	DLLDGEGGND	LLKGGYGNDI
	Consensus	<u>DELQVQGNL</u>	<u>AKNVLSGGKG</u>	<u>NDKLYGSEGA</u>	<u>DLLDGEGGND</u>	<u>LLKGGYGNDI</u>
	B-Cell Ep.	*****	*****	*****	*****	*****
50		851				900
	strain 536	YRYLSGYGHH	IIDDDGGKDD	KLSLADIDFR	DVAFKREGND	LIMYKAEGNV
	strain 536	YRYLSGYGHH	IIDDDGGKDD	KLSLADIDFR	DVAFKREGND	LIMYKAEGNV
	strain CFT073	YRYLSGYGHH	IIDDDGGKDD	KLSLADIDFR	DVAFRREGND	LIMYKAEGNV
55	Group A	YRYLSGYGHH	IIDDEGGKDD	KLSLADIDFR	DVAFKREGND	LIMYKAEGNV
	strain E110019	YRYLSGYGHH	IIDDDGGKED	KLSLADIDFR	DVAFKREGND	LIMYKAEGNV
	Consensus	<u>YRYLSGYGHH</u>	<u>IIDD-GGK-D</u>	<u>KLSLADIDFR</u>	<u>DVAF-REGND</u>	<u>LIMYKAEGNV</u>
		SEQ ID NO: 459		SEQ ID NO: 460		
	B-Cell Ep.	*****	*****	**	*****	*****
60		901				950
	strain 536	LSIGHKNGIT	FRNWFEEKESG	DISNHQIEQI	FDKDGRVITP	DSLKKAFEYQ
	strain 536	LSIGHKNGIT	FRNWFEEKESG	DISNHQIEQI	FDKDGRVITP	DSLKKAFEYQ

strain CFT073 LSIGHKNGIT FRNWFEKESG DISNHQIEQI FDKDGRVITP DSLKKALEYQ
 Group A LSIGHKNGIT FRNWFEKESG 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 QSNNKVSIVY 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 HLGDDDD
 SEQ ID NO: 480 YDKTDTGYL
 SEQ ID NO: 481 GTKATEAGNY
 SEQ ID NO: 482 EVSVGKRTEKTQY
 SEQ ID NO: 483 GTDLTET
 SEQ ID NO: 484 HGADGDDHIEGNDGNDRLYGDKGNDTLRGGNGDDQLYGGDGNDKLTGGVGNNYLNGGDGDDDELQV
 SEQ ID NO: 485 LSGGKGNDKLYGSEGADLLDGGEENDLLKGGYGN
 SEQ ID NO: 486 IDDDGGKDDKL
 SEQ ID NO: 487 EKESGDISH
 SEQ ID NO: 488 GRVITPDSLK
 SEQ ID NO: 489 EYQQSNNQANYV
 SEQ ID NO: 490 YASTYADL
 SEQ ID NO: 491 NFDVKEERS
 SEQ ID NO: 492 GNASDFS

Upec948 protein

60 '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.*).

- 5 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
10 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)

15
Group A 1 50
strain HS VSLSTALRMT CRRRLSLIV GPASLNRFIP PFQHFQQRHN VSNGWRPVKN
strain B and C VSLSTALRMT CRRRLSLIV GPASLNRFIP PFQHFQQRHN VSNGWRPVKD
Consensus VSLSTALRMT CRRRLSLIV GPASLNRFIP P-QHFQQRHN VSNGWRPVK-
20 SEQ ID NO: 493 SEQ ID NO: 494
B-Cell Ep. ** *****

25
Group A 51 100
strain HS GGDICHQIVN RQAVGKPAST DFFNKKVTTS TDMAVRSAGS ISAISCAVSA
strain B and C GGDICHQIVN RQAVGKPAST DFFNKKVTTS TDMAVRSAGS ISAISCAVSA
Consensus GGDICHQIVN RQAVGKPAST DFFNKKVTTS TDMAVRSAGS ISAISCAVSA
30 SEQ ID NO: 495
B-Cell Ep. *** ***** ** *****

35
Group A 101 150
strain HS GLEMRGITVI IAFTSISIMA CRRVPRSAPD CGLRSTISVI SVLPRLMGVS
strain B and C GLEMRGITVI IAFTSISIMA CRRVPRSAPD CGLRSTISVI SVLPRMMGVS
Consensus GLEMRGITVI IAFTSISIMA CRRVPRSAPD CGLRSTISVI SVLPR-MGVS
40 B-Cell Ep. ***** **

40
Group A 151
strain HS S
strain B and C S
Consensus S

45
B-Cell Epitopes
SEQ ID NO: 496 HNVSNNGWRPVKNGGD
SEQ ID NO: 497 AVGKFASTDF
SEQ ID NO: 498 VTTSTDMAVR
SEQ ID NO: 499 VPRSAPDCG

50 *Upec1232 protein*

'upec1232' protein from *E. coli* UPEC is disclosed in reference 6 (SEQ ID 138) is also known as: 'cl275 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.*).

- 5 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
- 10 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)
 15 strain CFT073 (SEQ ID NO: 89)
 strain O42 (SEQ ID NO: 90)
 strain CFT073 (SEQ ID NO: 91)

		1				50
20	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
25	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
30	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
35	Consensus	MIHLFKTCMI	T-FILGL-WS	APLRAQDQRY	ISIRNTDTIW	LPGNICAYQF
		SEQ ID NO: 500		SEQ ID NO: 501		
		51				100
40	strain H10407	RLDNNGNDEG	FGPLTITLQL	KDKYGQTLVT	RKMETEAFGD	SNATRTTDAF
	strain H10407	RLDNNGNDEG	FGPLTITLQL	KDKYGQTLVT	RKMETEAFGD	SNATRTTDAF
	strain B7A	RLDNNGNDEG	FGPLTITLQL	KDKYGQTLVT	RKMETEAFGD	SNATRTTDAF
	strain O42	RLDNNGNDEG	FGPLTITLQL	KDKYGQTLVT	RKMETEAFGD	SNATRTTDAF
	strain CFT073	RLDNNGNDEG	FGPLTITLQL	KDKYGQTLVT	RKMETEAFGD	SNATRTTDAF
	strain O42	RLDNNGNDEG	FGPLTITLQL	KDKYGQTLVT	RKMETEAFGD	SNATRTTDAF
45	strain CFT073	RLDNNGNDEG	FGPLTITLQL	KDKYGQTLVT	RKMETEAFGD	SNATRTTDAF
	Consensus	RLDNNGNDEG	FGPLTITLQL	KDKYGQTLVT	RKMETEAFGD	SNATRTTDAF
	B-Cell Ep.	*****	**	*****	*****	
		101				150
50	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
55	strain O42	LETECVENVA	TTEIIKATEE	SNGHRVSLPL	SVFDPQDYHP	LLITVSGKNV

strain CFT073		LETECVENVA TTEIIKATEE SNGHRVSLPL SVFDPQDYHP LLITVSGKNV
Consensus		<u>LETECVENVA TTEIIKATEE SNGHRVSLPL SVF-PQDYHP LLITVSGKNV</u>
		SEQ ID NO: 502
5	B-Cell Ep.	*****
		151
	strain H10407	N
	strain H10407	N
	strain B7A	N
10	strain O42	N
	strain CFT073	N
	strain O42	N
	strain CFT073	N
	Consensus	<u>N</u>
15	B-Cell Epitopes	
	SEQ ID NO: 503	DNGGNDEGFG
	SEQ ID NO: 504	TEAFGDSNATRT
	SEQ ID NO: 505	KATEESNGHR
20	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 (e.g. 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)	
40	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)	
45	
	1
	50
	Group A
	Group B
	strain SECEC
50	strain O42
	Group C
	strain CFT073

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MKLKHVGMIV VSVLAMSSAA VSAAEGDESV TTTVNGGVIH FKGEVVNAAC
MKLKHVGMIV VSVLAMSSAA VSAAEGDESV TTTVNGGVIH FKGEVVNAAC
MKLKHVGMIV VSVLAMSSAA VSAAEGDESV TTTVNGGVIH FKGEVVNAAC
MKLKHVGMIV VSVLAMSSAA VSAAEGDESV TTTVNGGVIH FKGEVVNAAC
MKLKHVGIIIV VSVLAMSSAA VSAAEGDESV TTTVNGGVIH FKGEVVNAAC
MKLKHVGIIIV VSVLAMSSAA VSAAEGDESV TTTVNGGVIH FKGEVVNAAC

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	strain E2348-69	MKLKHVGIIIV	VSVLAMSSAA	VSAAEGDES	MTTVNGGVIH	FKGEVVNAAC
	Consensus	MKLKHVG-IV	VSVLAMSSAA	VSAAEGDES	-TTVNGGVIH	FKGEVVNAAC
		SEQ ID NO: 507			SEQ ID NO: 508	
	B-Cell Ep.	*****			****	
5		51				100
	Group A	AIDSESMNQT	VELGQVRSSR	LAKAGDLSSA	VGFNIKLND	DTNVSSNAAV
	Group B	AIDSESMNQT	VELGQVRSSR	LAKAGDLSSA	VGFNIKLND	DTNVSSNAAV
	strain SECEC	AIDSESMNQT	VELGQVRSSR	LAKAGDLSSA	VGFNIKLND	DTNVSSNAAV
10	strain 042	AIDSESMNQT	VELGQVRSSR	LAKAGDLSSA	VGFNIKLND	DTNVSSNAAV
	Group C	AIDSESMNQT	VELGQVRSSR	LAKAGDLSSA	VGFNIKLND	DTNVSSNAAV
	strain CFT073	AIDSESMNQT	VELGQVRSSR	LAKAGDLSSA	VGFNIKLND	DTNVSSNAAV
	strain E2348-69	AIDSESMNQT	VELGQVRSSR	LAKAGDLSSA	VGFNIKLND	DTNVSSNAAV
	Consensus	AIDSESMNQT	VELGQVRSSR	LAKAGDLSSA	VGFNIKLND	DTNVSSNAAV
15	B-Cell Ep.				*****	
		101				150
	Group A	AFLGTTVTSN	DDTLALQSSA	AGSAQNVGIQ	ILDRTGEVLI	LDGATFSAKT
	Group B	AFLGTTVTSN	DDTLALQSSA	AGSAQNVGIQ	ILDRTGEVLI	LDGATFSAKT
20	strain SECEC	AFLGTTVTSN	DDTLALQSSA	AGSAQNVGIQ	ILDRTGEVLI	LDGATFSAKT
	strain 042	AFLGTTVTSN	DDTLALQSSA	AGSAQNVGIQ	ILDRTGEVLI	LDGGTFS
	Group C	AFLGTTVTSN	DDTLALQSSA	AGSAQNVGIQ	ILDRTGEVLV	LDGATFSAKT
	strain CFT073	AFLGTTVTSN	DDTLALQSSA	AGSAQNVGIQ	ILDSTGEVLV	LDGATFSAKT
	strain E2348-69	AFLGTTVTSN	DDTLALQSSA	AGSAQNVGIQ	ILDRTGEVLV	LDGATFSAKT
25	Consensus	AFLGTTVTSN	DDTLALQSSA	AGSAQNVGIQ	ILD-TGEVL-	LDG-TFSAKT
	B-Cell Ep.	*****	*****	**	*****	
		151				187
	Group A	DLIDGTNILP	FQARYIALGQ	SVAGTANADA	TFKVQYL	
30	Group B	DLIDGTNILP	FQARYIALGQ	SVAGTANADA	TFKVQYL	
	strain SECEC	DLIDGTNILP	FQARYIALGQ	SVAGTANADA	TFKVQYL	
	strain 042	DLIDGTNILP	FQARYIALGQ	SVAGTANADA	TFKVQYL	
	Group C	DLIDGTNILP	FQARYIALGQ	SVAGTANADA	TFKVQYL	
	strain CFT073	DLIDGTNILP	FQARYIALGQ	SVAGTANADA	TFKVQYL	
35	strain E2348-69	DLIDGTNILS	FQARYIALGQ	SVAGTANADA	TFKVQYL	
	Consensus	DLIDGTNIL-	FQARYIALGQ	SVAGTANADA	TFKVQYL	
		SEQ ID NO: 509		SEQ ID NO: 510		
	B-Cell Ep.	*****				
40	B-Cell Epitopes					
	SEQ ID NO: 511	VSAAEGDES				
	SEQ ID NO: 512	DTNVSSN				
	SEQ ID NO: 513	TVTSNDDTLA				
	SEQ ID NO: 514	SAAGSAQN				
45	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,

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

		401		450
	strain CFT073	DKYALQAEGM	VAGSNGSSAI	NNGVINIRPF KNAFAPEGIN TAIVVSNNGGM
	strain SECEC	DKYALQAEGM	VAGSNGSSAI	NNGVINIRPF KNAFAPEGIN TAIVVSNNGGM
	Consensus	<u>DKYALQAEGM</u>	<u>VAGSNGSSAI</u>	<u>NNGVINIRPF KNAFAPEGIN TAIVVSNNGGM</u>
60	B-Cell Ep.	*****	* *****	***** **

5	strain CFT073 strain SECEC B-Cell Ep.	Consensus	451						500
			ATNKGTINIT	ADASTNDNNG	KTRGVNVGAG	GSFINSAFGS	INVGIAEDKT		
			ATNKGTINIT	ADASTNDNNG	KTRGVNVGAG	GSFINSAFGS	INVGIAEDKT		
			ATNKGTINIT	ADASTNDNNG	KTRGVNVGAG	GSFINSAFGS	INVGIAEDKT		
10	strain CFT073 strain SECEC B-Cell Ep.	Consensus	501						550
			ATHSAVGSVA	IEVQNGANKV	VNEGTFILGR	GAQGNYGILA	KDAGTVDDVN		
			ATHSAVGSVA	IEVQNGANKV	VNEGTFILGR	GAQGNYGILA	KDAGSVDDVN		
			ATHSAVGSVA	IEVQNGANKV	VNEGTFILGR	GAQGNYGILA	KDAG-VDVN		
15	strain CFT073 strain SECEC B-Cell Ep.	Consensus	551						600
			KGTITIDGHD	SDAPALNVGM	LANNSSGMKN	SGIINVNGLN	STGLQVINAG		
			KGTITIDGYD	SDAPALNVGM	LANNSSGMKN	SGIINVNGLN	STGLQVINAG		
			KGTITIDG-D	SDAPALNVGM	LANNSSGMKN	SGIINVNGLN	STGLQVINAG		
20	strain CFT073 strain SECEC B-Cell Ep.	Consensus	601						650
			QLNSDGTINV	GGKGISGFR	NYGAWVEGAG	SNVNVSGKIS	LAGTGAVGVF		
			QLNSDGTINV	GGEIGSSGFR	NYGAWVEGAR	SNVNVSGKIN	LSGTGAVGVF		
			QLNSDGTINV	GG-GISSGFR	NYGAWVEGA-	SNVNVSGKI-	L-GTGAVGVF		
25	strain CFT073 strain SECEC B-Cell Ep.	Consensus	651						700
			AKDGGSLTSL	GNGAVLFGSS	DQIGFYVYGK	DSAIHNTGSG	VMDVSTENST		
			AKDGGSLTSL	GNGAVLFGSS	DQIGFYVYGK	DSAIHNTGSG	VMDVSTENST		
			AKDGGSLTSL	GNGAVLFGSS	DQIGFYVYGK	DSAIHNTGSG	VMDVSTENST		
30	strain CFT073 strain SECEC B-Cell Ep.	Consensus	701						750
			LFRIASGATF	QGTADASSAL	TASGKNSYAL	IATGKSDGGV	ASTVTSSGGM		
			LFRIASGATF	QGTADASSAL	TASGKNSYAL	IATGKSDGGV	ASTVTSSGGM		
			LFRIASGATF	QGTADASSAL	TASGKNSYAL	IATGKSDGGV	ASTVTSSGGM		
35	strain CFT073 strain SECEC B-Cell Ep.	Consensus	751						800
			INLTGEGATA	TLIEGGAQGT	IESNAIINMD	NASAIAGIAD	GNGYDISGKL		
			INLTGEGATA	TLIEGGAQGT	IESNAIINMD	NASAIAGIAD	GNGYDISGKL		
			INLTGEGATA	TLIEGGAQGT	IESNAIINMD	NASAIAGIAD	GNGYDISGKL		
40	strain CFT073 strain SECEC B-Cell Ep.	Consensus	801						850
			INPKDKTLL	TAGAQLSSTQ	DKVTGYIARN	GATLNNTGNI	IFTGKNTVG		
			INPKDKTLL	TAGAQLSSTQ	DKVTGYIARN	GATLNNTGNI	IFTGKNTVG		
			INPKDKTLL	TAGAQLSSTQ	DKVTGYIARN	GATLNNTGNI	IFTGKNTVG		
45	strain CFT073 strain SECEC B-Cell Ep.	Consensus	851						900
			RVEEGAVGTN	SGNITVQDGG	VGLIANATQD	VTTINNSGNL	VLKGGDNANR		
			RVEEGAVGTN	SGNITVQDGG	VGLIANATQD	VTTINNSGNL	VLKGGDNANR		
			RVEEGAVGTN	SGNITVQDGG	VGLIANATQD	VTTINNSGNL	VLKGGDNANR		
50	strain CFT073 strain SECEC B-Cell Ep.	Consensus	901						950
			TTGIKASGTT	TTVNMTAGTI	SLQGQGAIGV	EASNKGTVNL	DGSAVPNFAS		
			TTGIKASGTT	TTVNMTAGTI	SLQGQGAIGV	EASNKGTVNL	DGSAVPNFAS		
			TTGIKASGTT	TTVNMTAGTI	SLQGQGAIGV	EASNKGTVNL	DGSAVPNFAS		

5	strain CFT073 strain SECEC Consensus	951	DGSGITDQIA FRIIGDGATI KTNIAPGTLL DASGERSVLF RIEDGAKQAG	1000
			DGSGITDQIA FRIIGDGATI KTNIAPGTLL DASGERSVLF RIEDGAKQAG	
			DGSGITDQIA FRIIGDGATI KTNIAPGTLL DASGERSVLF RIEDGAKQAG	
			SEQ ID NO: 522	
	B-Cell Ep.	*****	*** ***** ** *****	
10	strain CFT073 strain SECEC Consensus	1001	SLLMKTS GTG SRGIWATGKG SNVLADAGSD FQILGAQAQG LYVTGGATAT	1050
			SLLMKTS GTG SRGIWATGKG SNVLADAGSD FQILGAQAQG LYVTGGATAT	
			SLLMKTS GTG SRGIWATGKG SNVLADAGSD FQILGAQAQG LYVTGGATAT	
			*****	*****
15	strain CFT073 strain SECEC Consensus	1051	LKQGASVNLV GDGAVVAEVD GNEYALDGSI TQTNTGSVIT NEADISSPLN	1100
			LKQGASVNLV GDGAVVAEVD GNEYALDGSI TQTNTGSVIT NEADISSPLN	
			LKQGASVNLV GDGAVVAEVD GNEYALDGSI TQTNTGSVIT NEADISSPLN	
			****	*****
20	B-Cell Ep.		*****	*****
			*****	*****
			*****	*****
			*****	*****
25	strain CFT073 strain SECEC Consensus	1101	NAKGFITRNQ GLLINNGNID FTTGTDNIGV WVDNGRFENT GSRIAVNGVA	1150
			NAKGFITRNQ GLLINSGNID FTTGTDNIGV WVDNGRFENT GSRIAVNGVA	
			NAKGFITRNQ GLLIN-GNID FTTGTDNIGV WVDNGRFENT GSRIAVNGVA	
			SEQ ID NO: 523	
	B-Cell Ep.	*	** *****	*****
30	strain CFT073 strain SECEC Consensus	1151	LFVEGAQSQI TSTGGDIVAV DGEAAIKLGA GASLNLGSG LGTIEGQKNA	1200
			LFVEGEHAQI TSTGGDIVAV DGEAAIKLGA GASLNLGSG LGTIEGQKNA	
			LFVEG---QI TSTGGDIVAV DGEAAIKLGA GASLNLGSG LGTIEGQKNA	
			SEQ ID NO: 524	
	B-Cell Ep.	****	*****	*****
35	strain CFT073 strain SECEC Consensus	1201	HGILLDTGAV GLVIDGAKIN VNAAGAVGHG IENRAEIEGI QLTNTTEINV	1250
			HGILLDTGAV GLVIDGAKIN VNAAGAVGHG IENRAEIEGI QLTNTTEINV	
			HGILLDTGAV GLVIDGAKIN VNAAGAVGHG IENRAEIEGI QLTNTTEINV	
			*****	*****
40	B-Cell Ep.		*****	*****
			*****	*****
			*****	*****
			*****	*****
45	strain CFT073 strain SECEC Consensus	1251	ADGIGVRTSA SLAKTNSGTI NVDGSGIALA FQKADGSETD NNLDMSDSAG	1300
			ADGIGVRTSA SLAKTNSGTI NVDGSGIALA FQKADGSETD NNLDMSDSGG	
			ADGIGVRTSA SLAKTNSGTI NVDGSGIALA FQKADGSETD NNLDMSDS-G	
			*****	*****
50	strain CFT073 strain SECEC Consensus	1301	LVINLKGT DG TGIFANTKDG AVVKSGASVN VIQADGGSAL VVNNAASEVV	1350
			LVINLKGTGG TGIFANTKDG AVVKSGASVN VTQADGGSAL VVNNAASEVV	
			LVINLKGT-G TGIFANTKDG AVVKSGASVN V-QADGGSAL VVNNAASEVV	
			SEQ ID NO: 525	SEQ ID NO: 526
	B-Cell Ep.	****	*****	*****
55	strain CFT073 strain SECEC Consensus	1351	QSGNLISASL SHAVVDASKA QSFTNKGQIK AASTTGTAMA FDDAVNTTVL	1400
			QSGNLISASL SHAVVDASKA QSFTNKGQIK AASATGTAMA FDDAVNTTVL	
			QSGNLISASL SHAVVDASKA QSFTNKGQIK AAS-TGTAMA FDDAVNTTVL	
			SEQ ID NO: 527	
	B-Cell Ep.	****	*****	**
60	strain CFT073	1401	NDSGAEIQGV VALNGGDNTF TNKGSITGTV SAKEGNNTFL FDDGSTLTGE	1450

strain SECEC		NDSGAEIQGV VALNGGDNTF TNKGSITGTV SAKEGNNTFL FDDGSILTGE	
B-Cell Ep.		Consensus NDSGAEIQGV VALNGGDNTF TNKGSITGTV SAKEGNNTFL FDDGS-LTGE	
		*****	*****
5		1451	1500
strain CFT073		VTAGNGNNNV TLNGKTHVDQ VTAGTGKNTF TIKGEGATWN LLDGGQGDS	
strain SECEC		VAAGNGNNNV TLNGKAHVDK VTAGTGKNTF TIKGEGATWN LLDGGQGDS	
		Consensus V-AGNGNNNV TLNGK-HVD- VTAGTGKNTF TIKGEGATWN LLDGGQGDS	
		SEQ ID NO: 528	SEQ ID NO: 529
10	B-Cell Ep.	*****	*****
		1501	1550
strain CFT073		SLIFDNAIHT LDSVVKLQNF EHVGLKNSSL VTLKEALVLT DGGNGPGSVD	
strain SECEC		SLIFDNAIHT LDSAVKLRF EHVGLKNSSL VTLKEALVLT DGGTGPSVD	
		Consensus SLIFDNAIHT LDS-VKL-NF EHVGLKNSSL VTLKEALVLT DGG-GPGSVD	
		SEQ ID NO: 530	
B-Cell Ep.		*	*****
		1551	1600
strain CFT073		IESGSELAI PAVAGNFTFD PLLTGKGTLS ARLDADTSF EFSHNVGDQF	
strain SECEC		IESGSELAI PAVAGNFTFD PLLTGKGTLS ARLDADTSF EFSHNVGDQF	
		Consensus IESGSELAI PAVAGNFTFD PLLTGKGTLS ARLDADTSF EFSHNVGDQF	
		SEQ ID NO: 531	
25	B-Cell Ep.	****	*****
		1601	1650
strain CFT073		AGTLKLGTS FALEGLNTSG LTHAMLMSET GNITTVGSGV QQIGGLGFNG	
strain SECEC		AGTLKLGTS FALEGLNTSG LTHAMLMSET GNITTVGSGV QQIGGLGFNG	
		Consensus AGTLKLGTS FALEGLNTSG LTHAMLMSET GNITTVGSGV QQIGGLGFNG	
		*****	**
		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 QLQVDENGQ AISHSQTEDV	
strain SECEC		DTRKNLLEQD DAQTLVTLVN AAGTVTGTGG QLQVDENGQ AISHSQTEDV	
		Consensus DTRKNLLEQD DAQTLVTLVN AAGTVTGTGG QLQVDENGQ AISHSQTEDV	
		**** **	*****
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 AHQLDLSGSV	
strain SECEC		LQMANDNVLG ATGSLNVASN AVFRTDYSQ TVGALQTETG AHQLDLSGSV	
		Consensus LQMANDNVLG ATG-LNVASN AVFRT-GYSQ TVGALQTETG AHQLDLSGSV	
		SEQ ID NO: 533	SEQ ID NO: 534

B-Cell Ep. ****

5 strain CFT073 1901 1950
strain SECEC LTVSGTQRQP GDDNGGIEN NVLSGEGTLA VTGSNLTVHG TNIGFTGNAS
Consensus LTVSGTQRQP GDDNGGIEN NVLTGDGTLA VTGSNLTVHG TNIGFTGNVS
LTVSGTQRQP GDDNGGIEN NVL-G-GTLA VTGSNLTVHG TNIGFTGN-S
SEQ ID NO: 535

B-Cell Ep. *****

10 strain CFT073 1951 2000
strain SECEC LTQGALVEMN GAQGLGSQGS ISFESLNDRL AIDIADGSGV SSNLSKSLSG
Consensus LT-G-LVEMN GAQGLGSQGS ISFESLNDRL AIDIADGSGV SSNLSKSLSG
LT-G-LVEMN GAQGLGSQGS ISFESLNDRL AIDIADGSGV SSNLSKSLSG
SEQ ID NO: 536

15 B-Cell Ep. ***** *

20 strain CFT073 2001 2050
strain SECEC EGSVGILNTT DLTLSGDN SN FSGEFRVQKD AALRASDEKH LGTGLIDSDG
Consensus KGSVGILNTT DLTLSGDN SN FSGEFRVQKD AALRASDEKH LGTGLIDSDG
-GSVGILNTT DLTLSGDN-N FSGEFRVQKD AALRASDEKH LGTGLIDSDG
SEQ ID NO: 537 SEQ ID NO: 538

B-Cell Ep. *** ***** **

25 strain CFT073 2051 2100
strain SECEC VTWLTASGNW LLKNDITGSG ALVKQGAGNL IINHELTYTG DTTVESGVLI
Consensus VTWLTASGNW LLKNDITGSG ALVKQGAGNL IINHELTYTG DTTVENGVLI
VTWLTASGNW LLKNDITGSG ALVKQGAGNL IINHELTYTG DTTVE-GVLI

30 B-Cell Ep. ****

35 strain CFT073 2101 2150
strain SECEC VGDDSVTRAA GATLSGSKNI HVLNGGTL SG LGTVSGQVNN QGTLASLNAL
Consensus VGDDSVTRAA GATLSGSKNI HVLNGGTL SG LGTVSGQVNN QGTLASLNAL
VGDDSVTRAA GATLSGSKNI HVLNGGTL SG LGTVSGQVNN QGTLASLNAL
SEQ ID NO: 539

B-Cell Ep. ***** *

40 strain CFT073 2151 2200
strain SECEC SGYETAEVGN FTVGSLTNTG VIRLAGGKTG NTLTVNGDYT GGGTLIINTV
Consensus SGYETAAGN FTVGSLTNTG VIRLAGGKTG NTLTVNGDYT GGGTLIINTV
SGYETAE-GN FTVGSLTNTG VIRLAGGKTG NTLTVNGDYT GGGTLIINTV
SEQ ID NO: 540

B-Cell Ep. ***** *

45 strain CFT073 2201 2250
strain SECEC LGDDTSTTDK LIVTGNTSGD TGVVVNNVRG QGAQTADGIE IVHVGGQSDG
Consensus LGDDTS-TDK LIVTGNTSGD TGVVVNNVRG QGAQTADGIE IVHVGGQSDG
LGDDTS-TDK LIVTGNTSGD TGVVVNNVRG QGAQTADGIE IVHVGGQSDG
SEQ ID NO: 541

50 B-Cell Ep. ***** *

55 strain CFT073 2251 2300
strain SECEC NFRLQNRAVA GAWEYFLHKG NAGGTDGNWY LRSELPPEPQ PQPQPQPQPQ
Consensus NFRLQNRAVA GAWEYFLHKG NAGGTDGNWY LRSELPPE.. .
NFRLQNRAVA GAWEYFLHKG NAGGTDGNWY LRSELPPE-- ----
** * ***** *

B-Cell Ep. **

60 strain CFT073 2301 2350
strain SECEC PQPQPQPQPQ PQPHPTDPKP VQKVYRPEAG SYIANIAAAN TLENIRMHDR
Consensus PQPQPQPQPQ PQPHPTDPKP VQKVYRPEAG SYIANIAAAN TLENIRMHDR
PQPQPQPQPQ PQPHPTDPKP VQKVYRPEAG SYIANIAAAN TLENIRMHDR
SEQ ID NO: 542

B-Cell Ep. ***** *

5	strain CFT073 strain SECEC B-Cell Ep.	Consensus	2351	2400
			EGETYYTDVF TGEKKATSMW MRHIGGHNW KDSSSQLNTQ SNRYVVQLGG	
			EGETYYTDVF TGEKKATSMW MRHIGGHNW KDSSSQLNTQ SNRYVVQLGG	
			EGETYYTDVF TGEKKATSMW MRHIGGHNW KDSSSQLNTQ SNRYVVQLGG	
10	strain CFT073 strain SECEC B-Cell Ep.	Consensus	2401	2450
			SIAQWTDGQD RLQQGIMAGY GNEKSSTTSS LSGYKSKGAI NGYSTGLYGT	
			SIAQWTDGQD RLQLGIMAGY GNEKSSTTSS LSGYKSKGAI NGYSTGLYGT	
			SIAQWTDGQD RLQ-GIMAGY GNEKSSTTSS LSGYKSKGAI NGYSTGLYGT	
15	strain CFT073 strain SECEC B-Cell Ep.	Consensus	2451	2500
			WQQNDGNDNG AYVDTWIIQY GWFNNTVNGEK LAAESWKS RG FTGSVEAGYT	
			WQQNDGNDNG AYVDTWIIQY GWFNNTVNGEK LAAESWKS RG FTGSVEAGYT	
			WQQNDGNDNG AYVDTWIIQY GWFNNTVNGEK LAAESWKS RG FTGSVEAGYT	
20	strain CFT073 strain SECEC B-Cell Ep.	Consensus	2501	2550
			FKAGEFTGSQ GSHYDWYIQP QSQITWMNVR ASEHTEKNGT KVQLSGDGN I	
			FKAGEFTGSQ GSHYDWYIQP QSQITWMNVR ASEHTEKNGT KVQLSGDGN I	
			FKAGEFTGSQ GSHYDWYIQP QSQITWMNVR ASEHTEKNGT KVQLSGDGN I	
25	strain CFT073 strain SECEC B-Cell Ep.	Consensus	2551	2600
			QSRLGVRTYL KGKSASDDNK AHQFEPFVEV NWIHNTRSWG VKMDNTALSQ	
			QSRLGVRTYL KGKSASDDNK AHQFEPFVEV NWIHNTRSWG VKMDNTALSQ	
			QSRLGVRTYL KGKSASDDNK AHQFEPFVEV NWIHNTRSWG VKMDNTALSQ	
30	strain CFT073 strain SECEC B-Cell Ep.	Consensus	2601	2649
			DGATNIAEVK TGVQGKLS DN LNVWGNVG VQ AGDKGYSDAQ AMLGIKYIF	
			DGATNIAEVK TGVQGKLS DN LNVWGNVG VQ AGDKGYSDAQ AMLGIKYIF	
			DGATNIAEVK TGVQGKLS DN LNVWGNVG VQ AGDKGYSDAQ AMLGIKYIF	
35	strain CFT073 strain SECEC B-Cell Ep.	Consensus	2601	2649
			DGATNIAEVK TGVQGKLS DN LNVWGNVG VQ AGDKGYSDAQ AMLGIKYIF	
			DGATNIAEVK TGVQGKLS DN LNVWGNVG VQ AGDKGYSDAQ AMLGIKYIF	
			DGATNIAEVK TGVQGKLS DN LNVWGNVG VQ AGDKGYSDAQ AMLGIKYIF	
40	strain CFT073 strain SECEC B-Cell Ep.	Consensus	2601	2649
			DGATNIAEVK TGVQGKLS DN LNVWGNVG VQ AGDKGYSDAQ AMLGIKYIF	
			DGATNIAEVK TGVQGKLS DN LNVWGNVG VQ AGDKGYSDAQ AMLGIKYIF	
			DGATNIAEVK TGVQGKLS DN LNVWGNVG VQ AGDKGYSDAQ AMLGIKYIF	
45	strain CFT073 strain SECEC B-Cell Ep.	Consensus	2601	2649
			DGATNIAEVK TGVQGKLS DN LNVWGNVG VQ AGDKGYSDAQ AMLGIKYIF	
			DGATNIAEVK TGVQGKLS DN LNVWGNVG VQ AGDKGYSDAQ AMLGIKYIF	
			DGATNIAEVK TGVQGKLS DN LNVWGNVG VQ AGDKGYSDAQ AMLGIKYIF	
50	strain CFT073 strain SECEC B-Cell Ep.	Consensus	2601	2649
			DGATNIAEVK TGVQGKLS DN LNVWGNVG VQ AGDKGYSDAQ AMLGIKYIF	
			DGATNIAEVK TGVQGKLS DN LNVWGNVG VQ AGDKGYSDAQ AMLGIKYIF	
			DGATNIAEVK TGVQGKLS DN LNVWGNVG VQ AGDKGYSDAQ AMLGIKYIF	
55	strain CFT073 strain SECEC B-Cell Ep.	Consensus	2601	2649
			DGATNIAEVK TGVQGKLS DN LNVWGNVG VQ AGDKGYSDAQ AMLGIKYIF	
			DGATNIAEVK TGVQGKLS DN LNVWGNVG VQ AGDKGYSDAQ AMLGIKYIF	
			DGATNIAEVK TGVQGKLS DN LNVWGNVG VQ AGDKGYSDAQ AMLGIKYIF	
60	strain CFT073 strain SECEC B-Cell Ep.	Consensus	2601	2649
			DGATNIAEVK TGVQGKLS DN LNVWGNVG VQ AGDKGYSDAQ AMLGIKYIF	
			DGATNIAEVK TGVQGKLS DN LNVWGNVG VQ AGDKGYSDAQ AMLGIKYIF	
			DGATNIAEVK TGVQGKLS DN LNVWGNVG VQ AGDKGYSDAQ AMLGIKYIF	

	SEQ ID NO: 568	GIADGNNGYDI
	SEQ ID NO: 569	INPKDKTT
	SEQ ID NO: 570	QLSSTQDKVT
	SEQ ID NO: 571	TVGVRVEEGAVGTNSGNITVQDG
5	SEQ ID NO: 572	TQDVTINN
	SEQ ID NO: 573	GDNANRTTGIKASGTTTTVNM
	SEQ ID NO: 574	AIGVEASNKGTVNLDGSAVPNFAADGSGIT
	SEQ ID NO: 575	ATIKTNIA
	SEQ ID NO: 576	LLDASGE
10	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
15	SEQ ID NO: 582	GRFENTGSRI
	SEQ ID NO: 583	QSQITSTGGDIVAV
	SEQ ID NO: 584	LGTIEGQKN
	SEQ ID NO: 585	AGAVGHGIIENRAE
	SEQ ID NO: 586	SLAKTNSGTINVDG
20	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
25	SEQ ID NO: 592	LNGGDNTFTNKGSI GTVSAKEGN
	SEQ ID NO: 593	STLTGEVTAGNGNNNVTLN
	SEQ ID NO: 594	KTHVDQVTAGTGKNTFTIKGEGA
	SEQ ID NO: 595	LDGGQGDSDS
	SEQ ID NO: 596	DGGNGPGSVDI ESG
30	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
35	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
40	SEQ ID NO: 607	GAQLTGA
	SEQ ID NO: 608	SNGGNNTGDTLV
	SEQ ID NO: 609	GYSQTVGALQTETG
	SEQ ID NO: 610	SGTQRQPGDDNNGGI
	SEQ ID NO: 611	AQGLGSQGSI
45	SEQ ID NO: 612	ADGSGVSSN
	SEQ ID NO: 613	SKSLSGEGS
	SEQ ID NO: 614	TLSGDNSNFS
	SEQ ID NO: 615	TYTGDITVE
	SEQ ID NO: 616	DSVTRAAGATLSG
50	SEQ ID NO: 617	TVSGQVNNQGT
	SEQ ID NO: 618	GYETA EV
	SEQ ID NO: 619	GGKTGNTLT VNGDYTGG
	SEQ ID NO: 620	GDDTSTT
	SEQ ID NO: 621	NTSGDTGV
55	SEQ ID NO: 622	VRGQGAQTAD
	SEQ ID NO: 623	GGQSDGNF
	SEQ ID NO: 624	GNAGGTDGNWY
	SEQ ID NO: 625	ELPPEPQPQPQPQPQPQPQPQPQPQPQPQP
	SEQ ID NO: 626	DREGETYY
60	SEQ ID NO: 627	FTGEKKA
	SEQ ID NO: 628	NRWKDSSSQ LNTQ
	SEQ ID NO: 629	AQWTDGQDRL
	SEQ ID NO: 630	GYGNEKSSTTSSLSGYKSKGAINGY

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

10 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.

15 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, 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.

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

30	strain CFT073 and 83972	MKKSLLAVML	TGLFALVSLP	ALGNVNLEQL	KQKAESGEAK	AQLELGYRYF
	strain ED1a	MKKSLLAVML	TGLFALVSLP	ALGNVNLEQL	KQKAESGEAK	AQLELGYRYF
	<i>E. fergusonii</i>	MKKSLLAALL	TGLFALVSLP	ALGNVNFEL	KQKAERGEAK	AQLELGYRYF
	Consensus	MKKSLLA +L	<u>TGLFALVSLP</u>	<u>ALGNVN</u>	<u>EQL</u>	<u>KQKAE</u> <u>GEAK</u> <u>AQLELGYRYF</u>
			SEQ ID NO: 656			SEQ ID NO: 657

B-Cell Ep. *

35	strain CFT073 and 83972	QGNETTCDLT	QAMDWFERRA	EQGYTPAEYV	LGLRYMNGEG	VPQDYAQA
	strain ED1a	QGNETTCDLT	LAMDWFERRA	EQGYTPAEYV	LGLRYMNGEG	VPQDYAQA
	<i>E. fergusonii</i>	QGNETTCDLT	QAIDWFERRA	EQGYTPAEFV	LGLRYMNGEG	VPKDYAQA
	Consensus	<u>QGNETTCDLT</u>	<u>A+DWFERRA</u>	<u>EQGYTPAE+V</u>	<u>LGLRYMNGEG</u>	<u>VP+DYAQA</u>
40	B-Cell Ep.	*****		* *****	*** *****	

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

50	strain CFT073 and 83972	QSMGDAYFEG	DGVTRDYVMA	REWYSKAAEQ	GNVWSCNQLG	YMYSRGLGVE
	strain ED1a	QSMGDAYFEG	DGVTRDYVMA	REWYSKAAEQ	GNVWSCNQLG	YMYSRGLGVE

5	E. fergusonii	QSMGDAYFEG DGVTRDYVMA REWYSKAAEQ GNVWSCNQLG YIYSKGLGVE
	Consensus	<u>QSMGDAYFEG DGVTRDYVMA REWYSKAAEQ GNVWSCNQLG</u> Y+YS+GLGVE
		SEQ ID NO: 659
	B-Cell Ep.	***** ****
		***** ***
10	strain CFT073 and 83972	RNDAISAQWY RKSATSGDEL GQLHLADMYF FGIGVTQDYT QSRVLFSSQA
	strain ED1a	RNDAISAQWY RKSATSGDEL GQLHLADMYF FGIGVTQDYT QSRVLFSSQA
	E. fergusonii	KNDAISAQWY RKSATSGDEL GQLHLADMYF FGIGVTQDYT QSRILFTQSA
	Consensus	<u>+NDAISAQWY RKSATSGDEL GQLHLADMYF FGIGVTQDYT</u> QSR+LF+QSA
		SEQ ID NO: 660
15	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
20	Consensus	<u>EQGN+IAQ+R LGYILE+GLA GAKEPLKALE WYRKSAEQGN</u> + GQYYLA +
		SEQ ID NO: 661
	B-Cell Ep.	** *****
25	strain CFT073 and 83972	YDKGAEGVAK NREQAISWYT KSAEQGDATA QANLGAIYFR LGSEEEHKKK
	strain ED1a	YDKGAEGVAK NREQAISWYT KSAEQGDATA QANLGAIYFR LGSEEEHKKK
	E. fergusonii	YIRRAEGIPY NREQAIWYT KSAEQGDTDA QVNLGALLYR HGSEEEQRRR
	Consensus	Y + AEG+ NREQAI WYT KSAEQGD A Q NLGA+ +R GSEEE ++A
30	strain CFT073 and 83972	VEWFRKAAAK GEKAAQFNLG NALLQGKGVK KDEQQAAIWM RKAAEQGLSA
	strain ED1a	VEWFRKAAAK GEKAAQFNLG NALLQGKGVK KDEQQAAIWM RKAAEQGLSA
	E. fergusonii	VDWYRKAAEE GVAMAQFNLG NALLQGKGVK KDEQQAAIWM RKAAEQGFSS
	Consensus	<u>V+W+RKAA + G AQFNLG NALLQGKGVK KDEQQAAIWM RKAAEQG</u> S+
		SEQ ID NO: 662
35	B-Cell Ep.	*** *****
	strain CFT073 and 83972	AQVQLGEIYY YGLGVERDYV QAWAWFDTAS TNDMNLFSTE NRNITEKKLT
	strain ED1a	AQVQLGEIYY YGLGVERDYV QAWAWFDTAS TNDMNLFSTE NRNITEKKLT
	E. fergusonii	AQVQLGEIYY YGLGVERDYV QAWAWFDTAS TNDMNLFSTE NRNITEKKLT
40	Consensus	<u>AQVQLGEIYY YGLGVERDYV QAWAWFDTAS TNDMNLFSTE</u> NRNITEKKLT
		SEQ ID NO: 663
	B-Cell Ep.	*** ** *****
45	strain CFT073 and 83972	AKQLQQAELL SQQYIEKYAP EAWARMQKLK AQSAVKTGNK
	strain ED1a	TKQLQQAELL SQQYIEKYAT EAWARMQKLK AQSAVKTGNK
	E. fergusonii	AKQLQQAELL SQQYIEKYAP EAWARMQKLN ARSTVTTGNK
	Consensus	<u>KQLQQAELL SQQYIEKYA</u> EAWARMQKL A+S V TGNK
		SEQ ID NO: 664
50	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
55	SEQ ID NO: 669	EQGRDSGQQSMGDAYFEGDGV
	SEQ ID NO: 670	SKAAEQGNV
	SEQ ID NO: 671	YRKATSGDEL
	SEQ ID NO: 672	TQDYT
	SEQ ID NO: 673	LAGAKEPL
55	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 $x \cdot y$ 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 fibrin 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 $x \cdot y$ 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: 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 $x \cdot y$ 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 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 $x \cdot y$ 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 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.

5 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
10 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
15 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
20 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 $\alpha\%$ 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 $x \cdot y$ identical aligned amino acids, where: x is selected from 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90,
25 100, 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
30 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
35 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. coli* 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 $x \cdot y$ 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, paralog, 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.

- 5 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
10 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
15 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
20 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.
25 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
30 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
35 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 OD₆₀₀ 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.

- 5 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), fimbrial 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.

- 25 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

- 30 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.

- 5 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.

- 10 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.*

- 15 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.
- 20

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.
- 25

- 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.
- 30

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:

5 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, 10 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 15 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 20 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 25 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 30 amorphous aluminium hydroxyphosphate with PO_4/Al molar ratio between 0.84 and 0.92, included at $0.6 \text{ mg Al}^{3+}/\text{ml}$. 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 $0.5\text{-}20 \mu\text{m}$ (*e.g.* about $5\text{-}10 \mu\text{m}$) after any antigen adsorption. Adsorptive capacities of between $0.7\text{-}1.5 \text{ mg protein per mg Al}^{+++}$ at pH 7.4 have been reported for aluminium phosphate 35 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.* $\geq 5:1$, $\geq 6:1$, $\geq 7:1$, $\geq 8:1$, $\geq 9:1$, *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 5 μ m 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 $<1\mu\text{m}$ *e.g.* $\leq 750\text{nm}$, $\leq 500\text{nm}$, $\leq 400\text{nm}$, $\leq 300\text{nm}$, $\leq 250\text{nm}$, $\leq 220\text{nm}$, $\leq 200\text{nm}$, 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:

- 10 • 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.
- 15 • 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.
- 20 • 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.
- 25 • 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.* 750 $\mu\text{g}/\text{ml}$ polysorbate 80, 110 $\mu\text{g}/\text{ml}$ Triton X-100 and 100 $\mu\text{g}/\text{ml}$ 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.
- 30
- 35

- 5 • 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.
- 10 • 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.
- 15 • 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).
- 20 • 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.
- 25 • 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), dimethyldioctadecylammonium bromide and/or

30 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].

35

- 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 *Quillaja saponaria* Molina tree have been widely studied as adjuvants. Saponin can also be commercially obtained from *Smilax ornata* (sarsapilla), *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 cholesterol can be used to form unique particles called immunostimulating complexes (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.

5 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
10 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
15 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, Q β -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

20 *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.

25 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 0.22 μ m membrane [55]. Other non-toxic LPS derivatives include monophosphoryl
30 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/analogues 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 as 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) Cpl 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: 96). The polycationic polymer may be a peptide comprising 11-mer amino acid sequence KKLKLLLLK (SEQ ID NO: 97).

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 pyrrolidone, 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 ~150 μ m in diameter, more preferably ~200nm to ~30 μ m in diameter, and most preferably ~500nm to ~10 μ m 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-stearyl ether, polyoxyethylene-8-stearyl 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

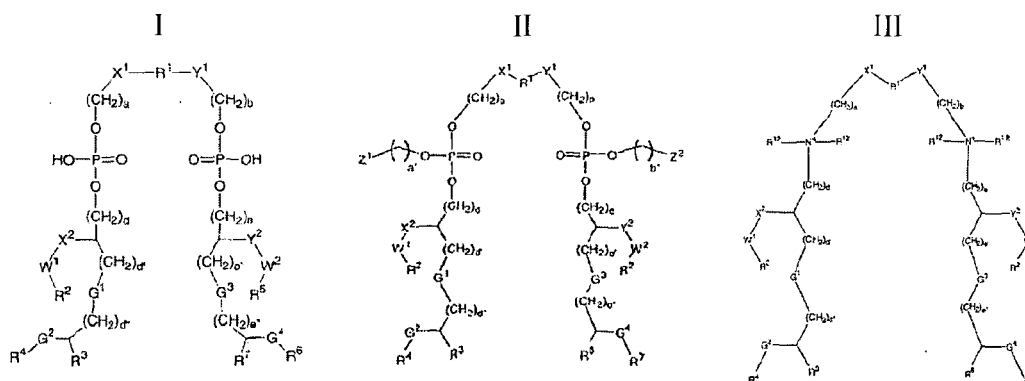
Examples of muramyl peptides suitable for use as adjuvants in the invention include N-acetylmuramyl-L-threonyl-D-isoglutamine (thr-MDP), N-acetyl-normuramyl-L-alanyl-D-isoglutamine (nor-MDP), and N-acetylmuramyl-L-alanyl-D-isoglutaminyl-L-alanine-2-(1'-2'-dipalmitoyl-*sn*-glycero-3-hydroxyphosphoryloxy)-ethylamine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

M. Imidazoquinolone Compounds.

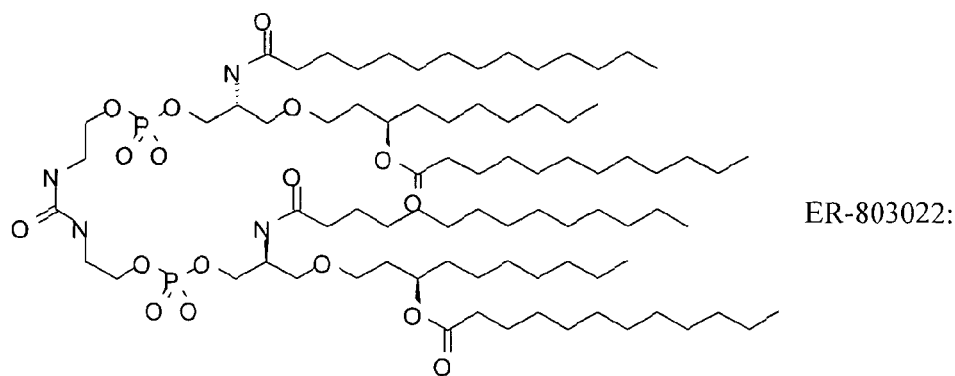
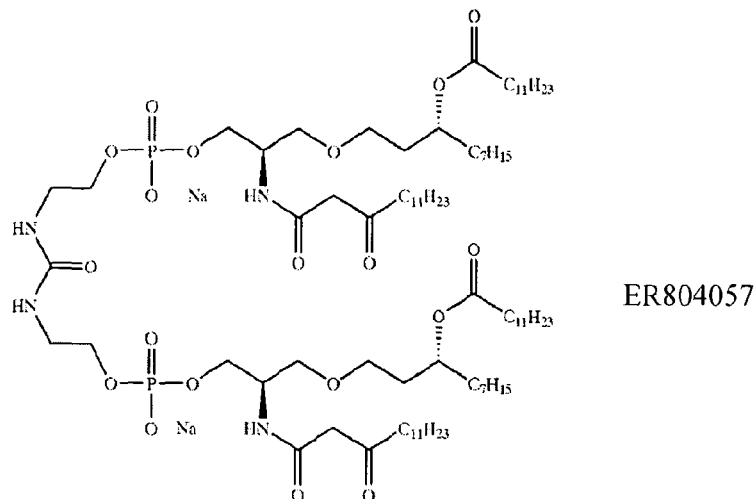
Examples of imidazoquinolone compounds suitable for use as adjuvants in the invention include Imiquimod ("R-837") [89,90], Resiquimod ("R-848") [91], and their analogs; and salts thereof (*e.g.* the hydrochloride salts). Further details about immunostimulatory imidazoquinolones can be found in references 92 to 93.

N. Substituted ureas

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



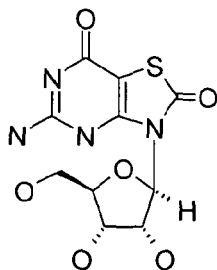
as defined in reference 94, such as 'ER 803058', 'ER 803732', 'ER 804053', 'ER 804058', 'ER 804059', 'ER 804442', 'ER 804680', 'ER 804764', 'ER 803022' or 'ER 804057' *e.g.*:



O. Further adjuvants

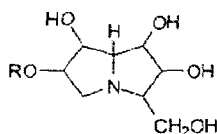
Further adjuvants that may be used with the invention include:

- 5 • An aminoalkyl glucosaminide phosphate derivative, such as RC-529 [95,96].
- A thiosemicarbazone compound, such as those disclosed in reference 97. Methods of
 10 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
 15 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):



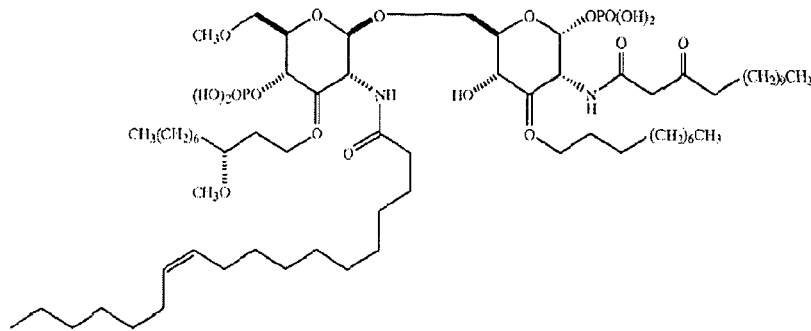
and prodrugs thereof; (b) ANA975; (c) ANA-025-1; (d) ANA380; (e) the compounds disclosed in references 99 to 100 Loxoribine (7-allyl-8-oxoguanosine) [101].

- Compounds disclosed in reference 102, including: Acylpiperazine compounds, Indole-dione compounds, Tetrahydroisoquinoline (THIQ) compounds, Benzocyclodione compounds, Aminoazavinyl compounds, Aminobenzimidazole quinolinone (ABIQ) compounds [103,104], Hydrapthalamide compounds, Benzophenone compounds, Isoxazole compounds, Sterol compounds, Quinazolinone 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 polyoxodonium polymer [109,110] or other N-oxidized polyethylene-piperazine derivative.
- Methyl inosine 5'-monophosphate ("MIMP") [111].
- A polyhydroxylated 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 pneumococcus.

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 recognize 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 response will include an increase in IgG1 production.

- 5 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
10 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
15 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
20 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
25 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
30 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
35 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
5 *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
10 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-
15 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
20 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
25 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,
30 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 to 123 *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 to 125. 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 to 127).

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 to 129), 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 to 131). 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 to 135] 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 to 139. 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
5 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
10 (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
15 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.

20 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
25 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
30 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.

10 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 fimbrial 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); EI10019 (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	fibril protein (orf3613) variants
426	Conserved fibril protein (orf3613) fragment
427-432	Conserved fibril 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-I fimbrial protein (upec-1875) variants
507-510	Conserved A chain precursor of the type-I fimbrial protein (upec-1875) fragment
511-515	Conserved A chain precursor of the type-I 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 I) protein (orf405)
642	Polypeptide sequence of the 0405B fragment of bacterial Ig-like domain (group I) 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	<i>Escherichia</i> Sell repeat-containing protein (upec-5211) variants

656-664	<i>Escherichia</i> Sell repeat-containing protein (upec-5211) fragments
665-676	<i>Escherichia</i> 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), fibril 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), fibril 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 Sel1 repeat-containing protein (upec-5211) (SEQ ID NO:653) – were cloned in pET-21b vectors (Novagen) and transformed in DH5 α -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.

5 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 μ g of recombinant protein in Freund's adjuvant. Positive control was immunized with 10⁸ 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 10⁷ of fresh bacterial culture/mouse (LD₈₀) 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
fimbrial protein (orf3613)	24/89 (27)	13/81 (16)	0.09
upec-948	12/31 (38)	7/38 (18)	0.1

15 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.

<i>E. Coli</i> 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.

REFERENCES

- [1] Kaper *et al.* (2004) *Nat Rev Microbiol.* 2(2):123-40.
- [2] Anjum *et al.* (2007) *Appl Environ Microbiol* 73 :5692-7.
- [3] Russo & Johnson (2000) *J Infect Dis* 181:1753-1754.
- [4] Smith *et al.* (2007) *Foodborne Pathogens And Disease* 4:134-63.
- [5] WO2006/089264.
- [6] WO2006/091517.
- [7] Needleman & Wunsch (1970) *J. Mol. Biol.* 48, 443-453.
- [8] Rice *et al.* (2000) *Trends Genet* 16:276-277.
- [9] Geysen *et al.* (1984) *PNAS USA* 81:3998-4002.
- [10] Carter (1994) *Methods Mol Biol* 36:207-23.
- [11] Jameson, BA *et al.* 1988, *CABIOS* 4(1):181-186.
- [12] Raddrizzani & Hammer (2000) *Brief Bioinform* 1(2):179-89.
- [13] Bublil *et al.* (2007) *Proteins* 68(1):294-304.
- [14] De Lalla *et al.* (1999) *J. Immunol.* 163:1725-29.
- [15] Kwok *et al.* (2001) *Trends Immunol* 22:583-88.
- [16] Brusica *et al.* (1998) *Bioinformatics* 14(2):121-30
- [17] Meister *et al.* (1995) *Vaccine* 13(6):581-91.
- [18] Roberts *et al.* (1996) *AIDS Res Hum Retroviruses* 12(7):593-610.
- [19] Maksyutov & Zagrebelnaya (1993) *Comput Appl Biosci* 9(3):291-7.
- [20] Feller & de la Cruz (1991) *Nature* 349(6311):720-1.
- [21] Hopp (1993) *Peptide Research* 6:183-190.
- [22] Welling *et al.* (1985) *FEBS Lett.* 188:215-218.
- [23] Davenport *et al.* (1995) *Immunogenetics* 42:392-297.
- [24] Chen *et al.* (2007) *Amino Acids* 33(3):423-8.
- [25] US patent 5,707,829
- [26] *Current Protocols in Molecular Biology* (F.M. Ausubel *et al.* eds., 1987) Supplement 30.
- [27] *Vaccine Design: The Subunit and Adjuvant Approach* (eds. Powell & Newman) Plenum Press 1995 (ISBN 0-306-44867-X).

- [28] *Vaccine Adjuvants: Preparation Methods and Research Protocols* (Volume 42 of *Methods in Molecular Medicine* series). ISBN: 1-59259-083-7. Ed. O'Hagan.
- [29] US patent 6355271.
- [30] WO00/23105.
- [31] WO90/14837.
- [32] WO90/14837.
- [33] Podda (2001) *Vaccine* 19: 2673-2680.
- [34] *Vaccine Design: The Subunit and Adjuvant Approach* (eds. Powell & Newman) Plenum Press 1995 (ISBN 0-306-44867-X).
- [35] *Vaccine Adjuvants: Preparation Methods and Research Protocols* (Volume 42 of *Methods in Molecular Medicine* series). ISBN: 1-59259-083-7. Ed. O'Hagan.
- [36] Allison & Byars (1992) *Res Immunol* 143:519-25.
- [37] Hariharan *et al.* (1995) *Cancer Res* 55:3486-9.
- [38] US-2007/014805.
- [39] Suli *et al.* (2004) *Vaccine* 22(25-26):3464-9.
- [40] WO95/11700.
- [41] US patent 6,080,725.
- [42] WO2005/097181.
- [43] WO2006/113373.
- [44] Han *et al.* (2005) *Impact of Vitamin E on Immune Function and Infectious Diseases in the Aged at Nutrition, Immune functions and Health EuroConference*, Paris, 9-10 June 2005.
- [45] US- 6630161.
- [46] US 5,057,540.
- [47] WO96/33739.
- [48] WO96/11711.
- [49] WO00/07621.
- [50] Barr *et al.* (1998) *Advanced Drug Delivery Reviews* 32:247-271.
- [51] Sjolanderet *et al.* (1998) *Advanced Drug Delivery Reviews* 32:321-338.
- [52] Niikura *et al.* (2002) *Virology* 293:273-280.
- [53] WO03/024481.
- [54] Gluck *et al.* (2002) *Vaccine* 20:B10-B16.
- [55] EP-A-0689454.
- [56] Johnson *et al.* (1999) *Bioorg Med Chem Lett* 9:2273-2278.
- [57] Evans *et al.* (2003) *Expert Rev Vaccines* 2:219-229.
- [58] Meraldi *et al.* (2003) *Vaccine* 21:2485-2491.
- [59] Pajak *et al.* (2003) *Vaccine* 21:836-842.
- [60] Kandimalla *et al.* (2003) *Nucleic Acids Research* 31:2393-2400.
- [61] WO02/26757.
- [62] WO99/62923.
- [63] Krieg (2003) *Nature Medicine* 9:831-835.
- [64] US 6,429,199.
- [65] Kandimalla *et al.* (2003) *Biochemical Society Transactions* 31 (part 3):654-658.
- [66] Blackwell *et al.* (2003) *J Immunol* 170:4061-4068.
- [67] WO01/95935.
- [68] Kandimalla *et al.* (2003) *BBRC* 306:948-953.
- [69] WO03/035836.
- [70] WO01/22972.

- [71] Schellack *et al.* (2006) *Vaccine* 24:5461-72.
- [72] WO95/17211.
- [73] WO98/42375.
- [74] Beignon *et al.* (2002) *Infect Immun* 70:3012-3019.
- [75] Pine *et al.* (2002) *J Control Release* 85:263-270.
- [76] Tebbey *et al.* (2000) *Vaccine* 18:2723-34.
- [77] Domenighini *et al.* (1995) *Mol Microbiol* 15:1165-1167.
- [78] WO99/40936.
- [79] WO99/44636.
- [80] Singh *et al.* (2001) *J Cont Release* 70:267-276.
- [81] WO99/27960.
- [82] US 6,090,406.
- [83] EP-A-0626169.
- [84] WO99/52549.
- [85] WO01/21207.
- [86] WO01/21152.
- [87] Andrianov *et al.* (1998) *Biomaterials* 19:109-115.
- [88] Payne *et al.* (1998) *Adv Drug Delivery Review* 31:185-196.
- [89] US 4,680,338.
- [90] US 4,988,815.
- [91] WO92/15582.
- [92] Stanley (2002) *Clin Exp Dermatol* 27:571-577.
- [93] Jones (2003) *Curr Opin Investig Drugs* 4:214-218.
- [94] WO03/011223.
- [95] Johnson *et al.* (1999) *Bioorg Med Chem Lett* 9:2273-2278.
- [96] Evans *et al.* (2003) *Expert Rev Vaccines* 2:219-229.
- [97] WO2004/060308.
- [98] WO2004/064759.
- [99] US 6,924,271.
- [100] US 5,658,731.
- [101] US patent 5,011,828.
- [102] WO2004/87153.
- [103] US 6,605,617.
- [104] WO02/18383.
- [105] WO2004/018455.
- [106] WO03/082272.
- [107] Wong *et al.* (2003) *J Clin Pharmacol* 43(7):735-42.
- [108] US2005/0215517.
- [109] Dyakonova *et al.* (2004) *Int Immunopharmacol* 4(13):1615-23.
- [110] FR-2859633.
- [111] Signorelli & Hadden (2003) *Int Immunopharmacol* 3(8):1177-86.
- [112] WO2004/064715.
- [113] De Libero *et al.*, *Nature Reviews Immunology*, 2005, 5: 485-496
- [114] WO03/105769
- [115] Cooper (1995) *Pharm Biotechnol* 6:559-80.
- [116] WO99/11241.
- [117] WO94/00153.

- [118] WO98/57659.
- [119] European patent applications 0835318, 0735898 and 0761231.
- [120] Durant *et al.* (2007) *Infect Immun* 75:1916-25.
- [121] WO02/081653.
- [122] Donnelly *et al.* (1997) *Annu Rev Immunol* 15:617-648.
- [123] *Gene Vaccination : Theory and Practice* (1998) ed. Raz (ISBN 3540644288).
- [124] Findeis *et al.*, *Trends Biotechnol.* (1993) 11:202
- [125] Wu *et al.*, *J. Biol. Chem.* (1991) 266:338
- [126] Jolly, *Cancer Gene Therapy* (1994) 1:51
- [127] Kaplitt, *Nature Genetics* (1994) 6:148
- [128] WO 90/07936.
- [129] WO 91/02805.
- [130] WO 94/12649.
- [131] WO 95/00655.
- [132] Curiel, *Hum. Gene Ther.* (1992) 3:147
- [133] Wu, *J. Biol. Chem.* (1989) 264:16985
- [134] US patent 5,814,482.
- [135] WO 97/42338.
- [136] WO 90/11092.
- [137] US patent 5,580,859
- [138] US patent 5,422,120
- [139] EP-0524968.
- [140] Philip, *Mol. Cell Biol.* (1994) 14:2411
- [141] Woffendin, *Proc. Natl. Acad. Sci.* (1994) 91:11581
- [142] US patent 5,206,152.
- [143] WO 92/11033.
- [144] US patent 5,149,655.
- [145] Brandt *et al.* (2006) *J Antimicrob Chemother.* 58(6):1291-4. Epub 2006 Oct 26
- [146] Winter *et al.*, (1991) *Nature* 349:293-99
- [147] US 4,816,567.
- [148] Inbar *et al.*, (1972) *Proc. Natl. Acad. Sci. U.S.A.* 69:2659-62.
- [149] Ehrlich *et al.*, (1980) *Biochem* 19:4091-96.
- [150] Huston *et al.*, (1988) *Proc. Natl. Acad. Sci. U.S.A.* 85:5897-83.
- [151] Pack *et al.*, (1992) *Biochem* 31, 1579-84.
- [152] Cumber *et al.*, (1992) *J. Immunology* 149B, 120-26.
- [153] Riechmann *et al.*, (1988) *Nature* 332, 323-27.
- [154] GB 2,276,169.
- [155] Gennaro (2000) *Remington: The Science and Practice of Pharmacy*. 20th edition, ISBN: 0683306472.
- [156] *PCR (Introduction to Biotechniques Series)*, 2nd ed. (Newton & Graham eds., 1997, Springer Verlag)
- [157] *Current Protocols in Molecular Biology* (F.M. Ausubel *et al.*, eds., 1987) Supplement 30
- [158] Smith & Waterman (1981) *Adv. Appl. Math.* 2: 482-489.
- [159] Welch *et al.* (2002) *Proc. Natl. Acad. Sci. U.S.A.* 99(26) 17020-17024.

SEQ ID NO: 639

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 5 GATAAGCTAACCGGAGGTGTGGTAATAACTACCTTAATGGCGGAGACGGGGATGATGAGCTTCAGGTTCAAGGTAATTCT
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 GAAGGGAATGATCTCCTGAAGGGGGGGTATGGTAATGATATTTATCGTTATCTTTCAGGATATGGCCATCATATTATTGAC
 GATGATGGGGGAAAAGACGATAAACTCAGTTTGGCTGATATTGATTTCCGGGACGTTGCCTTTAAGCGAGAAGGAAATGAC
 CTCATCATGTATAAAGCTGAAGGTAATGTTCTTTCCATTGGTCATAAAAAATGGTATTACATTACAGAACTGGTTTGAAAAA
 10 GAGTCAGGTGATATCTCTAATCACCAGATAGAGCAGATTTTTGATAAAGATGGCCG

SEQ ID NO: 640

DKFFGSKFTDIFHGADGDDHIEGNDGNDRLYGDKNNDTLRGGNGDDQLYGGDGNDKLTGGVGNNYLNGGDGDDELQVQNS
 LAKNVLSGGKGNKLYGSEADLLDGGEGNDLLKGGYGNDIYRYLSGYGHHIIDDGGKDDKLSLADIDFRDVAFKREGND
 15 LIMYKAEGNVLSIGHKNGITFRNWFEKESGDISNHQIEQIFDKDGR

SEQ ID NO: 641

GTTGCTGATGGTCAGCAAGCCTACACGCTGACACTGACAGCGGTGGACTCCGAGGGTAATCCGGTGACGGGAGAAGCCAGC
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 20 ACGGTTTCTTCGACCCGTGCCGAAACGTTGTTGTGCGTGCCCTCAGCGAGCAGTATCAGCTGGGCACATTACAACAAACG
 CTGAAGTTTGTGCGGGGCCGCTTGATGCAGCACATTCTCCATCACAATCCTGATAAACCGGTGGTTGGCGGTACA
 GTTACGGCAATCTGGACGGCAAAAGATGCTAATGACAACCTGTAACCTGGCCTCAATCCGGATGCACCGTCATTATCGGGC
 GCAGCTGCTGCTGGTTCTACGGCATCAGGCTGGACGGATAATGGCGACGGGACCTGGACTGCGCAGATTTCTCTCGGCACT
 ACGGCGGGTGAATTAGACGTTATGCCGAAGCTCAATGGGACAGGACGGCGAGCAAAATGCGGCAAAAGTAACCGTGGTGGCT
 25 GATGCATTATCTTCAAACAGTCGAAAGTCTCTGTGCGAGAAGATCACGTAAAAGCCGGTGAAGCACAACCGTAACGCTG
 GTGGCGAAAGATGCGCATGGCAACGCTATCAGTGGTCTTTCTGTTGTCGGCAAGTTTGACGGGGACCGCTCTGAAGGGGCG
 ACCGTTTCCAGTTGGACCGGAAAAAGGTGACGGTTCCTATGTTGCTACGTTAACTACAGGCGGAAAGACGGGCGAGCTTCGT
 GTCATGCCGCTCTTCAACGGCCAGCCTGCAGCCACCGAAGCCGCGCAGCTGACTGTTATTGCCGGAGAGATGTCATCAGCG
 AACTCTACGCTTGTGCGGACAATAAACTCCAACGGTTAAAACGACGACGGAACCTCACCTTACCATGAAGGATGCGTAC
 30 GGAATCCGGTCACCGGGCTGAAGCCAGATGCACAGTGTTTAGTGGTGCCGCCAGCACGGGGAGTGAGCGTCTCTTCAGCA
 GGAACTGGACAGAGAAAGGTAATGGGGTCTACGTGTGACCTTAACGCTGGGATCTGCCGCGGGTCAGTTGTCTGTGATG
 CCGCGAGTGAACGGCCAAAATGCCGTTGCTCAGCCACTGGTGCTGAATGTTGCAGGTGACGCATCTAAGGCTGAGATTCTG
 GATATGACAGTGAAGGTTAATAACCA

SEQ ID NO: 642

VADGQQAYTLTLTAVDSEGNPVTGEASRLRLVPQDTNGVTVGAISEIKPGVYSATVSSTRAGNVVVRAFSEQYQLGTLQQT
 LKFVAGPLDAAHSSITLNPDKPVVGGTVTAIWTAKDANDNPVTGLNPDAPSLSGAAAAGSTASGWTNNGDGTWTAQISLGT
 TAGELDVMPKLNQDAAANAAKVTVVADALSSNQSKVSVAEDHVKAGESTTVTLVAKDAHGNAISGLSLSASLTGTASEGA
 TVSSWTEKGDGSYVATLTTGGKTGELRVMPLEFNGQPAATEAAQLTVIAGEMSSANSTLVADNKPTPVKTTTELFTMTKDAY
 40 GNPVTGLKPDAPVFESGAASTGSRPSAGNWTEKNGVYVSTLTLGSAAGQLSVMPRVNGQNAVAQPLVLNVAGDASKAEIR
 DMTVKVNNQ

SEQ ID NO: 643

ATTAATTGCAATAACGCAATGGCAGATGTCATATGTCACCAGACTGGCGTCCGGGTACGAATAACTCGGGTGTGGGGCT
 45 GCAACAGTAAGTGTTAAAACCGAATACATCACTGGTCCAAATGTCGTCCAGTCTGGTGGGTGAGTCTTATCTGGATGACT
 GTAGAACAGGCAATTTTAAATGGCTACACCACTGGAGATAATTTATCCGGATTGATTTACGTCAATACCGGAGAAAAACA
 AAAACCATTACAGTGAAGGATGAGGTTACTGGCGCTTCTCAAACACTTCAAGTGTTTGATACTGACTCTTTCTCACACGC
 GATGCGGGGACTGGGGGAAATGAAACCATTCCTGGTTTTAGTGGCACTGCGGATTTTTCAATGCGACACGTTTTGTAAAC
 50 GCCAATAATGGCGGTACAGCTATTTTGGATGTGGGTTACCAGCAATCGGTAATTTTTTAAAAATACACAGCTTGCTGTA
 GCTGATGGAGAAGGTTCTCTGTGTATGGAACCTGGTCAATGATTTTTATTTTACGCTGGTGCAACCATGCAGGGGGGC
 GCGGTTACTCAAAAAATCATTGACTCAATGAAATATGCTGGAACAATTACTGATTGGGCGGGAAAAGTACACCATATTAAC
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 GCTGAATTTAATAAGGCCCTTATTGTACCAAGCATAATTACAATGTGGATATGACCGCTGGGGGACGTATAGACTCAACT
 CCTTACAAAGAAAAATGTAGGGCTGCTTGCTGTTCTCCATGCAACCAATAACGCACGAGCAATATTAGGTAAAACGGGTAAA
 55 TTAAGTGGAGTCTTCTGCTATGGGAATGGAGGAGGATCGTTGCAACTAATGGTGGGACCGGTGTTAATGAAGGGGTC
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 AATGATAAATATGCTCTCCAGGCAGAGGGGATGGTTGCCGGTAGTAATGGTTCTTCAGCCATTAATAATGGTGTATTAAAT
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AAAGGCACAATAAATATTACTGCCGATGCATCAACTAATGATAATAATGGCAAACACGAGGTGTAAATGTTGGAGCTGGA
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GAT

SEQ ID NO: 644

INCNNAMADVILSPDWRPGTNNSGVGAATVSGKTEYITGPNVVQSGGSLIWMTEQAILNGYTTGDNLSGLIYVNTGEKT
KITITVKDEVTGASQTLQVFDTSFSQRDAGTGNETIPGFSGTADFFNATRFVTANNGGTAILDVGSPAIGNFFKNTQLAV
ADGEGSSVVWNSVNDIFYFQPGATMQGGGVTKIIDSMTKYAGTITDWAGKVHHINSLDDLKQYNQYLIKSLDKTLSYKQYD
AEFNKALIVTKHNYNVDMTAGGRIDSTPYKENVGLLAVLHATNNARAILGKTGKLTGVLPAVNGGGIVATNGGTGVNEGV
IDAIGTEMIAYQDSTIVNDGTLFVWDNNDKYALQAEGMVAGSNGSSAINNGVINIRPFKNAPFAPEGINTAIVVSNGGMATN
KGTINITADASTNDNNGKTRGVNVGAGGSFINSAFGSINVGIAEDKTATHSAVGSVAIEVQNGANKVVNEGTIFLGRGAQG
NYGILAKDAGTVDVVNKGTITIDGHDSD

SEQ ID NO: 645

GCACCTGCACTGAATGTTGGCATGCTGGCAAATAATAGCTCCGGGATGAAAACTCCGGGATTATCAATGTTAATGGTCTG
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AGTGGTTTTCCGTAACATGTTGGCTGGGTGGAAGGTGCCGGAAGCAATGTTAATGTATCCGGAAAAATCAGTCTTGCCGGT
ACGGGGGCTGTGGGGTTTTTGCTAAAGATGGCGGCAGTCTGACCCGTGTCAGGCAATGGTGCACTGCTATTTGGCAGCAGC
GATCAGATAGGCTTTTATGTCTATGGAAGGACTCTGCCATTCAATAACCGGAAGCGGTGTTATGGATGTGTCCACTGAA
AACTCAACATTATTCGGTATTGCCAGTGGTGCGACATTCAGGGAAGTGCAGATGCTTCTTCTGCACTTACGGCGTCTGGT
AAGAACTCTTATGCACTTATTGCCACGGGGAATCGGATGGCGGTGTGGCTCGACAGTAACGTCTGGAGGAATGACCATC
AACCTGACGGGTGAGGGGGCTACAGCGACTTTAATTGAAGGGGAGCGCAGGGCACAATTGAAAGTAATGCCATTATCAAT
ATGGATAATGCCAGTGCAGTAGCCGGTATTGCGGATGGCAATGGCTATGATATTTCCGGCAAACATCAATCCGAAGGAC
AAGACCACACTATTAACGGCGGGGGCTCAGTTAAGTTCACCCAGGATAAAGTGACCGGGTATATCGCCCGTAATGGGGCC
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AACAGCGGAAATATTACAGTTCAGGATGGTGGTGTGGGACTAATTGCTAATGCCACACAAGATGTTACAACGATTAATAAC
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AATATGACCGCGGGTACTATATCTTTGTCAGGGACAGGGGGCGATTGGCGCTGAGGCCAGCAATAAAGGGGACTGTTAACCTT
GATGGTTCGGCAGTACCGAACTTTGCTGCTGACGGCTCTGGTATTACCGATCAGATTGCTTTTCGTATTATCGGAGATGGT
GCAACCATTAAAGACGAATATTGCACCGGGAAGTCTGCTGGATGCCAGT

SEQ ID NO: 646

APALNVGMLANNSSGMKNSGIINVNGLNSTGLQVINAGQLNSDGTINVGGKGISSGFRNYGAWVEGAGSNVNVSGKISLAG
TGAVGVFAKDGGSLLTSLNGAVLFGSSDQIGFYVYKDSAIHNTGSGVMDVSTENSTLFRIASGATFQGTADASSALTASG
KNSYALIAATGKSDGGVASTVTSGGMTINLTGEGATATLIEGGAQGTIESNAIINMDNASAIAGIADNGYDISGKLINPKD
KTTLLTAGAQLSSTQDKVTGYIARNGATLNNTGNIIFTGKNTVGVVVEGAVGTNSGNIITVDGGVGLIANATQDVTTINN
SGNLVLKGGDNANRTTGIKASGTTTTVNMTAGTISLQGGGAIGVEASNKGTVNLDGSAVNPFAADGSGITDQIAFRIIGDG
ATIKTNIAPGTLDDAS

SEQ ID NO: 647

GGGGAACGTTCTGTACTTTTCCGTATTGAAGATGGGGCAAACAGGCCGGCTCTCTGCTGATGAAAACCTCCGGGACAGGC
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GTTGTGCGGGAAGTTGACGGAATGAATACGCTCTGGATGGCAGTATTACACAAACGAATACTGGCTCGGTTATTACCAAT
GAGGCAGATATCTCTCGCCGCTGAATAATGCCAAGGGCTTTATTACGCGTAATCAGGGACTGTTGATTAACAACGGCAAC
ATTGATTTCACTACCGGTACAGATAATATCGGCGTCTGGGTGATAACGGCCGCTTTGAAAATACAGGAAGCCGTATTGCG
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ATGGCGTTTGTATGACGCCGTGAATACCACCGTACTGAATGACAGCGGTGCTGAAATTCAGGGGGTGTGGCTCTGAACGGC
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GATGGCAGCACACTGACAGGAGAAGTGAAGTGCAGGAAATGGCAATAATAATGTAACACTCAATGGTAAGACTCATGTTGAT
CAGGTTACTGCCGTACCGGGAAGAACACCTTCACCATTAAAGGTGAAGGGGCAACCTGGAACCTGCTGGATGGCGGG

SEQ ID NO: 648

5 GERSVLFRIEDGAKQAGSLLMKTSCTGSRGIWATGKGSNVLADAGSDFQILGAQAQGLYVTGGATATLKQASVNLVGDGA
VVAEVDGNEYALDGSITQNTGTVITNEADISSPLNNAKGFITRNQGLLINNGNIDFTTGTNDIGVWVDNDRFENTGSRIA
VNGVALFVEGAQSQITSTGGDIVAVDGEAAIKLGAGASLNLAGSGLGTIEGQKNAHGILLDTGAVGLVIDGAKINVNAAGA
VGHGIENRAEIEGIQLTNTTEINVADGIGVRTSASLAKTNSGTINVDGSGIALAFQKADGSETDNNLMDSDSAGLVINLKG
10 TDGTGIFANTKDGAVVKSASVNVIQADGGSALVNNAASEVVQSGNLI SASLSHAVVDASKAQSFTNKGQIKAASTTGTA
MAFDDAVNTTVLNDSGAEIQGVVALNGGDNTFTNKGSI GTVSAKEGNNTFLFDDGSTLTGEVTAGNGNNVTLNGKTHVD
QVTAGTGKNTFTIKGEGATWNLDDGG

SEQ ID NO: 649

15 CAGGGAGATTCTGATTCCCTGATTTTTGATAACGCCATTTCATACGCTGGATTCTGTTGTAAACTACAGAATTTTGAACAT
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GGAACACTGTCTGCCCCGTCTTGATGCCGACACATCTGCTTTGAATTCAGCCATAACGTCGGGGATCAATTTGCCGGAAC
CTGAAGCTGGGTACTAGTAGCTTTGCTCTGGAAGGGCTGAATACGAGCGGGTTAACCCATGCAATGCTGATGTCTGAAACC
20 GTTAATACACAAACGGTTGGCTCCGGTGTTCAGCAGATTGGCGGTCTTGGGTTCAATGGCGGAACGCTGATTTTTGGTTCC
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ATTCAGGTCACCATGCCAGATGAAGTGATTAATGATATTCGGCTGTTGATACCCGTAAGAATTTGCTGGAGCAGGATGAT
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25 CTGCTGGGAAGCTCCGACGCTATTAAAGGTGACGAGCTGTACATAGGCTATGGGCTGAAGTCGCTGGATTTACAGGGAACC
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CGCAGCGGCACATTACAGATGGCAAATGATAATGTACTTGGCGCAACAGGTAATCTGAACGTCGCCAGCAATGCCGTCTTC
AGAACAAAC

SEQ ID NO: 650

30 QGDSDSLIFDNAIHTLDSVVKLQNFHVGLKNSSLVTLKEALVLTDDGNGPGSVSDIESGSELAIIPAVAGNFTFDPLLTGK
GTLSARLDADTSFAFEFSHNVDQFAGTLKLGTSFALEGLNTSGLTHAMLMSETGNITTVGSGVQQIGGLGFNGGTLIFGS
VMPGDTIASNSIETSAAGTLDIRGKGTIQVTMPDEVINDIPAVDTRKNLLEQDDAQTLLVTLVNAAGTVTGTGGQLQLVDEN
GQAISSHSQTFDVTQGGEVVAQGNIDYKLLGSSDGIKGDGLYIGYGLKSLDLQGTGDKALVLTPRANAQGLQTLGAQLTGA
35 GDLAIEAAGQVTVLSNGGNNTGDTLVRSGTLQMANDNVLGATGNLNVASNAVFRTN

SEQ ID NO: 651

GCTGACACGGTTGTACAGGCGGGAGAAACCGTGAACGGCGGAACACTGACAAATCATGACAACCAGATTGTCCTCGGTACG
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40 GGCGGTATCGCCAACAACACTACTGTACCGGTGGTGGTCTTCAGAGAGTGAATGCCGGAGGAAGCGTTTCAGACACGGTT
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45 ACTGTACATGGTTCACGCACTGGATACCACGCTGAATGGGGGTACCAGTATGTGCACAACGGAGGTACAGCATCTGACACT
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50 ACAGATGTCACCATGACATCCGGTGGTGGCTGATTGCGACAGTGGTGCCACTGTTGAGGGGACCAATGCCAGCGGTAAG
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55 AGTAACCTCACCGGTACAGGTGGCACCATCAATATGCGTGTTCGCCTTGATGGCAGCAATGCCCTCTGACCAGCTGGTGATT
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CAGGGTATCCGGTGTGGATGCACAGAATGGTGGCACCACAGAAGAAGGTGCGTTTGCCTGAGTCGCCCGCTTCAGGCC
GGCGCCTTTAACTACACCTGAACCGTGACAGCGATGAAGACTGGTACCTGCGCAGTGAAAATGCTTATCGTGCTGAAGTC
CCC

SEQ ID NO: 652

ADTVVQAGETVNGGTLTNHDNQIVLGTANGMTISTGLEYPDNEANTGGQWIONGGIANNTTVTGGGLQRVNAGGSVS DTV
 ISAGGGQSLQGQAVNTTLNGGEQWVHEGGIATGTVINEKGWQAVKSGAMATDTVVNTGAEGGPDAENGDTGQTVYGDVVRT
 5 TINKNGRQIVAAEGTANTTVVYAGGDQTVHGHALD T T L N G G Y Q Y V H N G G T A S D T V V N S D G W Q I I K E G G L A D F T T V N Q K G K L
 QVNAGGTATNVTLTQGGALVTSTAATVTGSNRLGNFTVENGNADGVVLES GGRLDVLEGHSAWKTLVDDGGTLAVSAGGKA
 TDVTMTSGGALIADSGATVEGTNASGKFSIDGISGQASGLLLENGGSFTVNAGGLASNTTVGHRGTLTLAAGGSLSGRTQL
 SKGASMLVNGDVVSTGDIVNAGEIRFDNQTTTPDAALSRVAKGDSFVTFHKLTTSNLTGQGGTINMRVRLDGSNASDQLVI
 10 N G G Q A T G K T W L A F T N V G N S N L G V A T S G Q G I R V V D A Q N G A T T E E G A F A L S R P L Q A G A F N Y T L N R D S D E D W Y L R S E N A Y R A E V
 P

SEQ ID NO: 677

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 15 GCTAAAGCTAACCAGGAAATTCAGGAGTGGCTCGGGAATACGGTACTGCGCGCGTCAAACCTGAATGTGATAAAAAATTTTC
 TCGCTGAAGGACTCTTCGCTGGAAATGCTTTATCCGATTTATGATACACCGACAAATATGTTGTTCACTCAGGGGGCAATA
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 20 GGCTGGGATATTTCGTGCTGAGGGCTATTTACCTGCCTGGCCGAGCTTGCGCAAGCCTGATGTATGAACAGTATTATGGC
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 25 GGCAAGGGCGGCCAGACGGTTTCCCTGGGGCTTGTGGTCAGCAAAGCAACTCACGGTCTGAAAAATGTGCAATGGGAAGCG
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 30 GAACTAACCTTCAAACCGGCTGGAAATATTGTGACTCGTACCCTGAAGGCCACTAAATCACAGGC AAAAGCCAAACACTGGGT
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 35 AAACCAGGGGTTTACAGCGCCACGGTTTCTTCGACCCGTGCCGGAAACGTTGTTGTGCGTGCCCTTCAGCGAGCAGTATCAG
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 40 GCAAAAGTAACCGTGGTGGCTGATGCATTATCTTCAAACAGTCGAAAGTCTCTGTGCGAGAAGATCAGTAAAAGCCGGT
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 45 TTCACCATGAAGGATGCGTACGGGAATCCGGTCACCGGGCTGAAGCCAGATGCACCAAGTGTTTAGTGGTGCCGCCAGCACG
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SEQ ID NO: 678

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 55 GCGATTTCAGTACCGGTCAGGCGAGCCTGGAGGTAGACGCCGCTGCTCAAAAAGTGGCAAACGGCAAAGATGCCTTTACG
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 60 GGGACGGCGACAACGAATGAGCAAGGGCAGGCTATTTTACCGCCACGACCACTGTGCGAGCGACATATACACTCACGGCG

AAAGTGGACAGGCCGACGGTCAGGAATCGACGAAAACCTGCCGAATCTAAATTCGTGCGGGATGATAAAACGCGGTGCTC
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5 AACTCTTTGACATATGGAGGGTATGAAATGAAACCAGTGACTGTGACAATTAACGCCGTTCTCTGCAGATACTGAAGGCGCT
GAGGAGAAA

SEQ ID NO: 679

GACGGTCAGAGCCGTATTCAAATGCTTGCTAACGGTAATGAGCAAAAGCCGCTGGTGCTGTCTCTGCGCGACGCCGAGGGC
10 CAGCCAGTCACGGGCATGAAAGATCAGATCAAGACTGAACTAACCTTCAAACCGGCTGGAATATTTGTGACTCGTACCCTG
AAGGCCACTAAATCACAGGCAAGCCAACACTGGGTGAGTTCACCGAACTGAAGCAGGGGTGTATCAGTCTGTCTTTACT
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15 ACTAATGGTGTAAACGGTTGGTGCCATTTTCGAAATAAAACCAGGGGTTTACAGCGCCACGGTTTCTTCGACCCGTGCCGA
AACGTTGTTGTGCGTGCCTTCAGCGAGCAGTATCAGCTGGGCACATTACAACAAACGCTGAAGTTTGTTCGCGGGCCGCTT
GATGCAGCACATTCGTCCATCAGCTGAATCCTGATAAACCAGGTGGTGGCGGTACAGTTACGGCAATCTGGACGGCAAAA
GATGCTAATGACAACCTGTAACCTGGCCTCAATCCGGATGCACCGTCATTATCGGGCGCAGCTGCTGCTGGTTCTACGGCA
TCAGGCTGGACGGATAATGGCGACGGGACCTGGACTGCGCAGATTCTCTCGGCACTACGGCGGGTGAATTAGACGTTATG
20 CCGAAGCTCAATGGGCAGGACGCGGCAGCAAAATGCGGCAAAAGTAACCGTGGTGGCTGATGCATTATCTTCAAACCACTCG
AAAGTCTCTGTGCGAGAAGATCAGCTAAAAGCCGGTGAAAGCACAAACCGTAACGCTGGTGGCGAAAGATGCGCATGGCAAC
GCTATCAGTTGGTCTTTTCGTTGTCGGCAAGTTTGACGGGGACCGCCTCTGAAGGGGCGACCGTTTCCAGTTGGACCGGAAAA
GGTGACGGTTCTTATGTTGCTACGTTAACTACAGGCGGAAAGACGGGCGAGCTTCGTGTGATGCCGCTCTTCAAACGGCCAG
CCTGCAGCCACCGAAGCCGCGCAGCTGACTGTTATTGCGGAGAGATGTCATCAGCGAACTCTACGCTTGTTCGCGACAAT
25 AAAACTCCAACGGTTAAACGACGACGGAACCTCACCTTCACCATGAAGGATGCGTACGGGAATCCGGTCACCGGGCTGAAG
CCAGATGCACCACTGTTTAGTGGTGCCGCCAGCACGGGGAGTGAGCGTCTTCAGCAGGAACTGGACAGAGAAAGGTAAT
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GTTGCTCAGCCACTGGTGTGAATGTTGCAGGTGACGCATCTAAGGCTGAGATTTCGTGATATGACAGTGAAGGTTAATAAC
CAACTGGCTAATGGACAGTCTGCTAACCCAGATCACCTGACCGTCGTGGACAGCTATGGTAACCCGTTGCAGGGGCAAGAA
30 GTTACGCTGACTTTACCGCAGGGTGTGACCAAGACGGGGAATACAGTAACAACCAATGCGGCAGGGAAGTGGACATT
GAGCTTATGTCAACGGTTGACGGGAACCTGAGATCGAGGCCCTCGGTGAAAAACTCTCAGAAGACGGTCAAGGTGAAATTC
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35 GGAACCTATGAGATCACGGCTCAGCAGGAAATGACCAGCCTTCAATGCGCAGTCTGTAACGTTTGTGGCTGATAAGACT
ACGGCGACCATCTCCAGTATTGAGGTGATTGGCAACCGTGCAGTGGCGGACGGCAAAACCAACAGACGTATAAAGTTACG
GTGACTGATGCCAATAACAACCTGCTGAAAGATAGCGAAGTGACGCTGACTGCCAGCCCGGAAAAATTTAGTTCTGACTCCC
AATGGGACGGCGACAACGAATGAGCAAGGGCAGGCTATTTTACCGCCACGACCACTGTGCGCAGCGACATATACACTCACG
CGGAAAGTGAACAGGCCGACGGTCAGGAATCGACGAAAACCTGCCGAATCTAAATTCGTGCGGATGATAAAACGCGGTG
40 CTCGCTGCATCTCCAGAGCGTGTAGATTCTCTGGTGGCGGACGGGAAGACTACTGCAACACTGACGGTTACTCTGATGTCG
GGTGTCAACCCCGTAGGAGGAACCATGTGGGTGACATTGAGGCTCCGGAAGGGGTGACAGAGGCGGATTATCAGTTCCTG
CCGTGCAAAAATGACCATTTCGCGAGCGGGAAAAATCACGCGTACATTAGTACCAACAAGCCAGGTACATACACATTACACA
TTCAACTCTTTGACATATGGAGGGTATGAAATGAAACCAGTGACTGTGACAATTAACGCCGTTCTCTGCAGATACTGAAGGC
GCTGAGGAGAAA

SEQ ID NO: 680

CVAWANISVQVLFPLAVTFPTVMAARAQHAVQPRLSMENNTVTADNNVEKNVASLAANAGTFLSSQPDSDATRNFI TGMAT
AKANQEIQEWLGKYGTARVKLVNDKNFSLKDSSLEMLYPIYDTPTNMLFTQGAHRTDDRTQSNIGFWRHFSENDWMAGV
NTFIDHDLRSSTRIGVGAIEYWRDYLKLSANGYIRASGWKSPDVEDYQERPANGWDIRAEGYLPAPWQLGASLMYEQYYG
50 DEVLFGKDKRQKDPHAITAENVYTPVPLLTLSAGHKQKSGENDTRFGLVNYRIGEPLEKQLDTSIRERRMLAGSRD
LVERNNNIVLEYRKSEVIRIALPERIEGKGGQTVSLGLVSVKATHGLKNVQWEAPSLAAGGKITGQGNQWQVTLPAYQAG
KDNYYAISAIAYDNKGNASKRVQTEVVISGAGMSADRTALTLDGQSRIQMLANGNEQKPLVLSLRDAEGQPVTGMKDQIKT
ELTFKPAGNIVRTLKATKSQAKPTLGEFTETETAGVYQSVFTTGTQSGEATITVSVDDMSKTVTAELRATMMDVSNSTLSA
NEPSGDVVDAGQAYTLTLTAVDSEGNPVTGEASRLRLVPQDTNGVTVGAISEIKPGVYSATVSSTRAGNVVVRVFSEQYQ
55 LGTLQQTTLKFVAGPLDAAHSSITLNPDPKPVVGGTGTAIWTAKDANDNPVTGLNPDAPSLSGAAAAGSTASGWTNDNGDGTWT
AQISLGTTAGELDVMPKLNQDAAANAAKVTVVADALSSNQSKVSVAEDHVKAGESTTVTLVAKDAHGNAISGLSLSASLT
GTASEGATVSSWTEKGDGSYVATLTGKGTGELRVMPLFNGQPAATEAAQLTVIAGEMSSANSTLVADNKTPTVKTTTELT
FTMKDAYGNPVTGLKPDAPVFSAASTGSERPSAGNWTGKNGVYVSTLTLSAAGQLSVMPRVNGQNAVAQPLVLNVAGD
ASKAEIRDMTVKVNNQ

SEQ ID NO: 681

LANGQSANQITLTVVDSYGNPLQGQEVTLTLPQGVTSKTGNTVTTNAAGKVDIELMSTVAGELEIEASVKNSQKTVKVKFK
 ADFSTGQASLEVDAQAQKVANGKDAFTLTATVKDQYGNLLPGAVVFNLPBGVKPLADGNIMVNADKEGKAEKVVSVTAG
 TYEITASAGNDQPSNAQSVTFVADKTTATISSIEVIGNRAVADGKTKQTYKVTVDANNLLKDSEVTLTASPENLVLT
 5 GTATTNEQGQAI FTATTTVAATYTLTAKVEQADGQESTKTAESKFVADDKNAVLAASPERVDSLADGKTTATLTVTLM
 VNPVGGTMWVDIEAPEGVTEADYQFLPSKNDHFASGKITRTFSTNKPCTYTFTFNSLTYYGGYEMKPVTVTINAVPADTEGA
 EEK

SEQ ID NO: 682

DGQSRIQMLANGNEQKPLVLSLRDAEGQPVTGMKDQIKTELTFKPAGNIVTRTLKATKSQAKPTLGEFTETEAGVYQSVFT
 TGTQSGEATITVSVDDMSKTVTAE LRATMMDVSNSTLSANEP SGDVVADGQQAYTLTLTAVDSEGNPVTGEASRLRLVPQD
 TNGVTVGAI SEIKPGVYSATVSSSTRAGNVVVR AFSEQYQLGTLQQTLK FVAGPLDAAHSSITLNPDKPVVGGTVTAIWTA
 DANDNPVTGLNPDAPSLSGAAAAGSTASGWT DNGDGTWTAQISLGT TAGELDVMPKLNQDAAANA AKVTVVADALSSNQ
 KVSVAEDHVKAGESTTVTLVAKDAHGNAISGLSLSASLTGTASEGATVSSWTEKGDGSYVATLTGGKTGELRVMPLENGQ
 10 PAATEAAQLTVIAGEMSSANSTLVADNKTPTVKTTTELFTMKDAYGNPVTGLKPDAPVFSGAASTGSEKPSAGNWTEKGN
 GVVVSTLTLSAAGQLSVMPRVNGQNAVAQPLVLNVAGDASKAEIRDMTVKVNNQLANGQSANQITLTVVDSYGNPLQGQ
 VTLTLPQGVTSKTGNTVTTNAAGKVDIELMSTVAGELEIEASVKNSQKTVKVKFKAD FSTGQASLEVDAQAQKVANGKDAF
 TLTATVKDQYGNLLPGAVVFNLPBGVKPLADGNIMVNADKEGKAEKVVSVTAGTYEITASAGNDQPSNAQSVTFVADKT
 15 TATISSIEVIGNRAVADGKTKQTYKVTVDANNLLKDSEVTLTASPENLVLT PNGTATTNEQGQAI FTATTTVAATYTLT
 AKVEQADGQESTKTAESKFVADDKNAVLAASPERVDSLADGKTTATLTVTLMGVNPNVGGTMWVDIEAPEGVTEADYQFL
 20 PSKNDHFASGKITRTFSTNKPCTYTFTFNSLTYYGGYEMKPVTVTINAVPADTEGAEEK

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),
5 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,
10 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
15 $x \cdot y$ 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
20 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
25 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
30 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
5 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
10 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.
- 15 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.
- 20 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.
- 25 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
30 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 fibrin 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), fimbrial 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.
- 5 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
10 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
15 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
20 450 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;
- 25 (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
30 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.