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(54) **VACCINE AND ANTIBODY AGAINST CLOSTRIDIOIDES DIFFICILE TOXIN**

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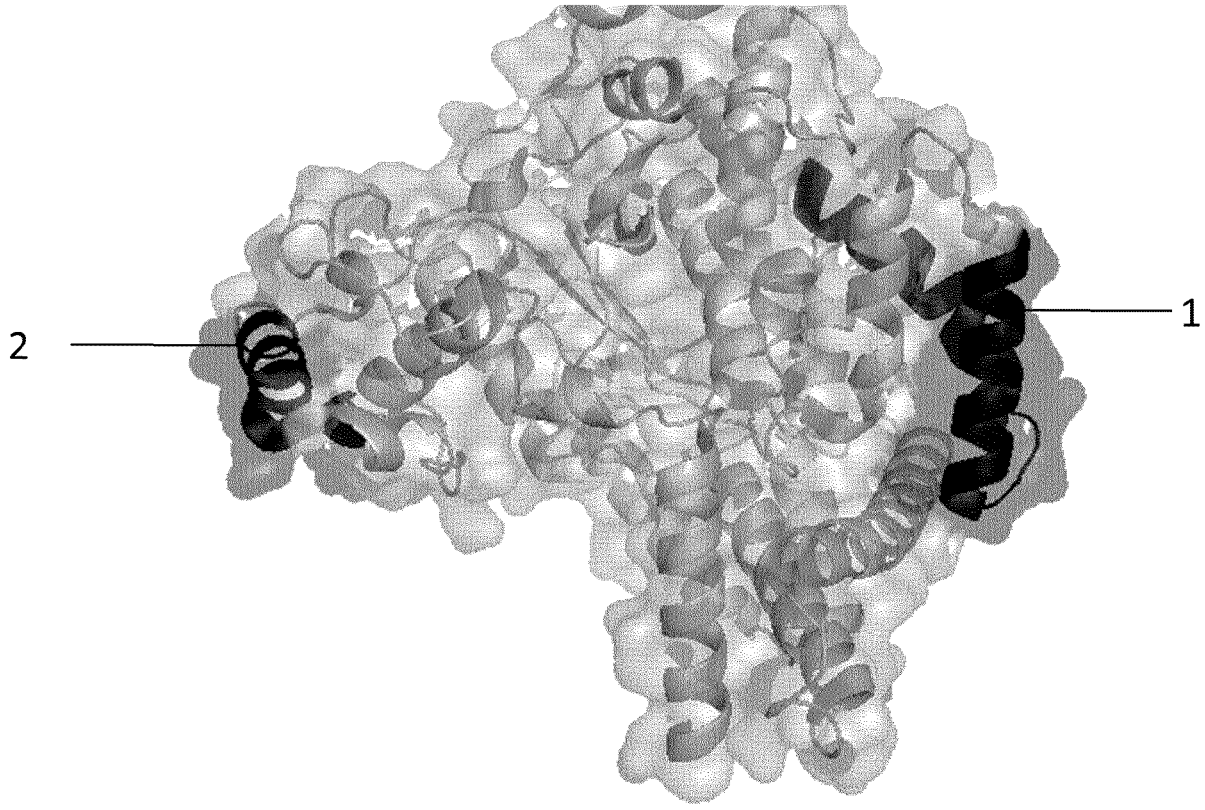
(57) **ABSTRACT**

The invention provides an antigenic peptide comprising an epitope for use in the prevention and/or treatment of an infection by *C. difficile*, e.g. for use as a vaccine in the prevention and/or treatment of an infection by *C. difficile*, and protective antibodies directed against the epitope.

Specification includes a Sequence Listing.



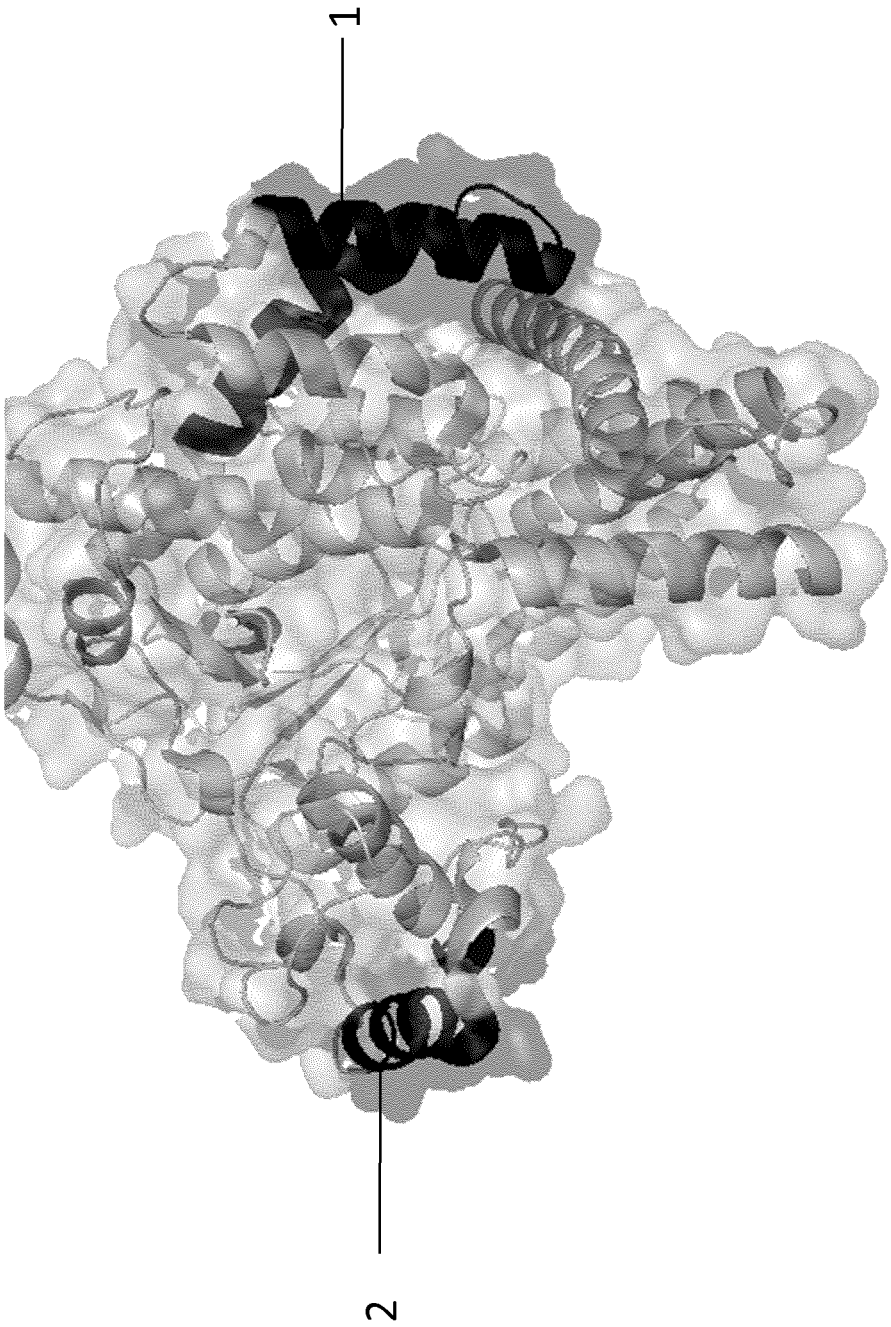


Fig. 1

VACCINE AND ANTIBODY AGAINST CLOSTRIDIOIDES DIFFICILE TOXIN

[0001] The present invention relates to a peptide containing a novel peptide epitope for use as antigen, preferably contained in an antigenic peptide, e.g. in the prevention and/or treatment of an infection by *Clostridioides difficile* (former name: *Clostridium difficile*). Further, the invention relates to a process for producing and/or selecting at least one antibody directed against the novel peptide epitope and to binding peptides having affinity for the novel peptide epitope, and to the use of such binding peptides in the prevention and/or treatment of an infection by *Clostridioides difficile* (*C. difficile*). *C. difficile* secretes *C. difficile* Toxin A (TcdA) and *C. difficile* Toxin B, both of which are peptides, TcdA has 308 kDa, TcdB has 270 kDa. The peptide epitope is a portion of peptide toxin TcdB, and the binding peptide is specific for this portion of TcdB.

STATE OF THE ART

[0002] WO 2016/131157 A1 describes peptides comprising portions of *Clostridium difficile* toxins A and B, which portions contain epitopes, as well as the generation of antibody directed against the peptides, both for use in the treatment of *Clostridium difficile* infections.

OBJECT OF THE INVENTION

[0003] It is an object of the invention to provide a peptide containing an alternative epitope suitable for raising an immune response in the prevention or treatment of infections by *C. difficile* and/or for selecting binding peptides for use of the peptide and for use of the binding peptides in the prevention or treatment of infections by *C. difficile*.

DESCRIPTION OF THE INVENTION

[0004] The invention achieves the object by the features of the claims, especially by providing an antigenic peptide comprising or consisting of the epitope of SEQ ID NO: 13 for use in the prevention and/or treatment of an infection by *C. difficile*, e.g. for use as a vaccine in the prevention and/or treatment of an infection by *C. difficile*. Accordingly, the antigenic epitope can be administered to a mammal, e.g. to a human, for the prevention and/or treatment of an infection by *C. difficile*, e.g. by injection into the mammal. For use of the antigenic peptide as a vaccine, the antigenic peptide can be formulated in a pharmaceutical composition, e.g. in a mixture with an adjuvant.

[0005] The epitope of SEQ ID NO: 13 has been identified as a target of antibody binding, which results in the neutralization of the *C. difficile* toxin B. The epitope of SEQ ID NO: 13 is based on SEQ ID NO: 1, which is comprised of amino acids No. 402 to 437 of SEQ ID NO: 2, which is the amino acid sequence of TcdB of the reference strain (clade 1) VPI10463, as well as on the epitopes of variants of TcdB, which are SEQ ID NO: 11 for toxin B of hypervirulent strain 820291 (clade 2) containing the epitope at amino acids No. 402 to 437, and SEQ ID NO: 12 1470 (clade 4) containing the epitope at amino acids No. 403 to 438.

[0006] Accordingly, SEQ ID NO: 2, SEQ ID NO: 11 and SEQ ID NO: 12 also represent the amino acid sequences of TcdB variants having essentially the same length and functional elements, e.g. peptides having a homology of at least 90%, preferably of at least 95%, more preferably of at least 98% or at least 99%, to SEQ ID NO: 2, SEQ ID NO: 11 and/or to SEQ ID NO: 12.

[0007] It has been found that the SEQ ID NO: 13, e.g. SEQ ID NO: 1, amino acids No. 402 to 437 of SEQ ID NO: 11 and/or amino acids No. 403 to 438 of SEQ ID NO: 12, forms a unique epitope, especially a unique antigenic epitope of *C. difficile* toxin B (TcdB), and that a binding peptide with affinity to this epitope can effectively neutralize TcdB, especially wild-type TcdB containing this epitope. SEQ ID NO: 13 (three letter code) has the following amino acids and one of the amino acids (single letter code) in the place of the amino acid No. for Xaa as indicated below:

amino acid No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14
SEQ ID NO: 13	Gln	Ile	Xaa	Asn	Arg	Tyr	Lys	Ile	Leu	Asn	Xaa	Xaa	Leu	Asn
possible amino acids			EQDN								NDEQ	ST		

amino acid No.	15	16	17	18	19	20		21	22	23	24	25	26	27
SEQ ID NO: 13	Pro	Xaa	Ile	Ser	Xaa	Xaa		Asn	Asp	Phe	Asn	Thr	Thr	Xaa
possible amino acids		AIVL			EQDN	DGAVIL								TMS

amino acid No.	28	29	30	31	32	33	34	35	36
SEQ ID NO: 13	Asn	Xaa	Phe	Xaa	Xaa	Ser	Xaa	Xaa	Ala
possible amino acids		TANSTLVID		IGLVA	DENQ		ILVA	MGAVIL	

[0008] The antigenic peptide comprising the epitope of SEQ ID NO: 13 is especially for use in the prevention or treatment of infections by *C. difficile*, especially for raising an immune response directed against TcdB, e.g. for neutral-

izing TcdB. Preferably, the antigenic peptide contains at least two copies of SEQ ID NO: 13.

[0009] The complete TcdB peptide contains an N-terminal glucosyltransferase domain (GTD) at amino acids No. 1 to 543 of SEQ ID NO: 2, a cysteine protease domain (CPD) at amino acids No. 544 to 767 of SEQ ID NO: 2. The CPD catalyses proteolytic auto-processing of TcdB to release the GTD into the cytosol of an infected cell upon translocation. Amino acids No. 768 to 1852 of SEQ ID NO: 2 are currently designated a translocation domain (TLD) and contain three cell surface binding regions. At the C-terminus, TcdB contains so-called combined repetitive oligo peptides (CROPs) which are currently assumed to have a cell-binding and stabilizing role.

[0010] The antigenic peptide comprising the epitope of SEQ ID NO: 13 is not the complete TcdB peptide, and it preferably does not comprise an E3 domain and/or no E4 domain, e.g. no CROPs. Optionally, in addition or in the alternative, the antigenic peptide does not contain a functional GTD and/or does not comprise a functional TLD and/or does not comprise a functional CPD and/or does not comprise CROPs, preferably the antigenic peptide does not comprise a functional GTD, no functional CPD and no functional CROPs, e.g. in order to prevent a toxic effect of the antigenic peptide.

[0011] The E3 domain is comprised of amino acids No. 2138 to 2271 of SEQ ID NO: 2, the E4 domain is comprised of amino acids No. 2272 to 2366 of SEQ ID NO: 2. The CROPs comprises domains E1, E2, E3 and E4, wherein the E1 domain is comprised of amino acids No. 1875 to 2005 of SEQ ID NO: 2, the E2 domain is comprised of amino acids No. 2006 to 2137 of SEQ ID NO: 2. The domains E1 to E4 of SEQ ID NO: 11 and SEQ ID NO: 12, respectively, are comprised of the same amino acid Nos. The CROPs is comprised of amino acid Nos. 1853 to 2366 of SEQ ID NO: 2, of SEQ ID NO: 11 and of SEQ ID NO: 12

[0012] For the purpose of the present invention, the term peptide is not limited to a certain length of the amino acid chain.

[0013] The antigenic peptide comprising the epitope of SEQ ID NO: 13 can e.g. contain only the portion of the GTD consisting of amino acids No. 361 to 543 of SEQ ID NO: 2, which portion is given as SEQ ID NO: 3, or a fraction thereof, or can contain only the portion of the GTD including the CPD, the fraction consisting of amino acids No. 361 to 767 of SEQ ID NO: 2, which portion is given as SEQ ID NO: 4, or a fraction thereof, and optionally can contain additional amino acids, or consist of one of these portions. These portions exclude the catalytically active centre of the GTD and therefore avoid a toxic effect of the GTD. The antigenic peptide comprising the epitope of SEQ ID NO: 13 preferably does not comprise amino acids No. 322 to 325 and/or does not comprise amino acids No. 340 to 351, e.g. does not comprise amino acids No. 290 to 360 or amino acids No. 322 to 351 of SEQ ID NO: 2, resp. of SEQ ID NO: 11 or of SEQ ID NO: 12.

[0014] Further, the antigenic peptide comprising the epitope of SEQ ID NO: 13 preferably does not comprise the amino acid sequence of the CPD, and/or not the amino acid sequence for the TLD and/or not the amino acid sequence of the CROPs.

[0015] On the basis of the epitope of SEQ ID NO: 13, the invention also relates to a process for eliciting binding peptides, e.g. antibody, and/or for generating and/or isolating binding peptides having affinity for the epitope of SEQ ID NO: 13. A process for eliciting and/or generating binding peptides, e.g. antibodies, in an animal, preferably in a mammal, e.g. a human, comprises the steps of administering an antigenic peptide containing the epitope of SEQ ID NO: 13, e.g. in a peptide which in addition to SEQ ID NO: 13 contains amino acid sections which are not antigenic to the animal or which peptide consists of SEQ ID NO: 13, preferably in a pharmaceutical composition containing an adjuvant, preferably followed by at least one booster administration of the antigenic peptide containing the epitope of SEQ ID NO: 13 to the animal.

[0016] Subsequently, antibody-producing cells can be isolated from the animal, e.g. isolating B-cells from blood, or isolating spleen cells, for generating antibody-producing cells, e.g. using the hybridoma technique. For example, B-cell sorting from a biopsy, e.g. whole blood, obtained from a human, e.g. who is diagnosed to have an infection by *C. difficile*, and identification of antibody or cells producing antibody binding to a peptide containing the epitope of SEQ ID NO: 13 can be used.

[0017] As a further alternative, phage display, e.g. as described herein, using a library e.g. of antibodies or of arbitrary peptides on an antigenic peptide comprising the epitope of SEQ ID NO: 13 can be used for selection of binding peptides. Optionally, antibody can be isolated from the serum of the animal to which the peptide containing the epitope of SEQ ID NO: 13 was administered, e.g. by immobilizing a peptide containing the epitope of SEQ ID NO: 13 and contacting this with the serum, washing the immobilized peptide and eluting antibody from the immobilized peptide to generate an isolated fraction of antibody having affinity for the epitope of SEQ ID NO: 13. As a representative epitope, SEQ ID NO: 1 can be used.

[0018] Administration of an antigenic peptide comprising the epitope SEQ ID NO: 13, e.g. as the only antigenic epitope with N-terminal and/or C-terminal additional amino acid sections that can be devoid of antigenic epitopes, to an experimental animal leads to the generation of antibody which recognize the epitope of SEQ ID NO: 13.

[0019] A binding peptide that has affinity for the epitope SEQ ID NO: 13 neutralizes the effect of the TcdB peptide, showing that a binding peptide recognizing the epitope SEQ ID NO: 13 confers at least partial prevention and/or at least partial treatment or cure of an infection by *C. difficile*. This neutralizing effect of binding peptides directed against the epitope of SEQ ID NO: 13 is shown e.g. by cell assays detecting reduction of cell rounding in the presence of TcdB.

[0020] The epitope of SEQ ID NO: 13 was identified on fragments of the TcdB peptide by two scFv-Fc molecules selected from a naïve human phage display library as scFv. From the phage library, two binding peptides were identified that have a high binding affinity for the epitope SEQ ID NO: 1, which was used as a representative of SEQ ID NO: 13.

[0021] Generally, the binding peptides of the invention have affinity for the epitope of SEQ ID NO: 1 and the binding peptides can have a format of natural or synthetic binding peptides, e.g. of antibodies, especially IgG, IgM, IgA or IgE, scFv, scFv-Fc, minibodies, diabodies or other antibody derived formats.

[0022] In detail, the binding peptide of the invention has a paratope of framework regions (FR) and of complemen-

tarity determining regions (CDR) in an arrangement of FR1-CDR1-FR2-CDR2-FR3-CDR3, preferably additionally FR4,

in a first embodiment preferably with the following heavy chain complementarity determining regions (CDRH):

CDRH1 consisting of amino acids 26 to 33 of SEQ ID NO: 5,

CDRH2 consisting of amino acids 51 to 58 of SEQ ID NO: 5, and

CDRH3 consisting of amino acids 97 to 112 of SEQ ID NO: 5,

preferably with FR1 consisting of amino acids 1 to 25 of SEQ ID NO: 5,

FR2 consisting of amino acids 34 to 50 of SEQ ID NO: 5,

FR3 consisting of amino acids 59 to 96 of SEQ ID NO: 5,

and optional FR4 consisting of amino acids 113 to 123 of SEQ ID NO: 5,

preferably in combination with the following light chain complementarity determining regions (CDRL):

CDRL1 consisting of amino acids 26 to 34 of SEQ ID NO: 6,

CDRL2 consisting of amino acids 52 to 54 of SEQ ID NO: 6,

CDRL3 consisting of amino acids 91 to 101 of SEQ ID NO: 6,

preferably with FR1 consisting of amino acids 1 to 25 of SEQ ID NO: 6,

FR2 consisting of amino acids 35 to 51 of SEQ ID NO: 6,

FR3 consisting of amino acids 55 to 90 of SEQ ID NO: 6,

and optional FR4 consisting of amino acids 102 to 111 of SEQ ID NO: 6.

[0023] It has been found that the heavy chain can form a paratope also with another light chain, e.g. the heavy chain of the first embodiment can associate with the light chain of the second embodiment, and the heavy chain of the second embodiment can associate with the light chain of the first embodiment. Optionally, the heavy chain can be present in combination with another light chain, as the specificity for the antigen is mainly determined by the heavy chain.

[0024] In the first embodiment, the binding peptide can comprise the heavy chain of SEQ ID NO: 5 and the light chain of SEQ ID NO: 6, e.g. with a linker between the heavy chain and the light chain. SEQ ID NO: 9 is a binding peptide containing the heavy chain-linker-light chain of the first embodiment, wherein the linker is comprised of amino acids 124 to 141 as an exemplary scFv.

[0025] In a second embodiment, the binding peptide, which preferably is an antibody, preferably has the following heavy chain complementarity determining regions (CDRH):

CDRH1 consisting of amino acids 26 to 33 of SEQ ID NO: 7,

CDRH2 consisting of amino acids 51 to 58 of SEQ ID NO: 7, and

CDRH3 consisting of amino acids 97 to 117 of SEQ ID NO: 7,

preferably with FR1 consisting of amino acids 1 to 25 of SEQ ID NO: 7,

FR2 consisting of amino acids 34 to 50 of SEQ ID NO: 7,

FR3 consisting of amino acids 59 to 96 of SEQ ID NO: 7,

and optional FR4 consisting of amino acids 118 to 128 of SEQ ID NO: 7,

preferably in combination with the following light chain complementarity determining regions (CDRL):

CDRL1 consisting of amino acids 25 to 33 of SEQ ID NO: 8,

CDRL2 consisting of amino acids 51 to 53 of SEQ ID NO: 8,

CDRL3 consisting of amino acids 90 to 100 of SEQ ID NO: 8,

preferably with FR1 consisting of amino acids 1 to 24 of SEQ ID NO: 8,

FR2 consisting of amino acids 34 to 50 of SEQ ID NO: 8,

FR3 consisting of amino acids 54 to 89 of SEQ ID NO: 8,

and optional FR4 consisting of amino acids 101 to 110 of SEQ ID NO: 8.

[0026] In the second embodiment, the binding peptide can comprise the heavy chain of SEQ ID NO: 7 and the light chain of SEQ ID NO: 8, e.g. with a linker between the heavy chain and the light chain. SEQ ID NO: 10 is a binding peptide containing the heavy chain-linker-light chain of the first embodiment, wherein the heavy chain is comprised of amino acids 1-128, the light chain is comprised of amino acids 147-256, and the linker is comprised of amino acids 129 to 146 as an exemplary scFv.

[0027] In detail, the epitope of SEQ ID NO: 13, e.g. represented by SEQ ID NO: 1, and the binding peptide of the first and second embodiments were selected by a phage display library using the naïve human antibody gene libraries HAL9 and HAL10, against immobilized peptides which was full-length TcdB peptide (SEQ ID NO: 2) or fragments thereof (amino acids 1-1852, amino acids 1-1128, respectively of SEQ ID NO: 2), each with an additional C-terminal His_6 tag, expressed in *Bacillus megaterium*. Fusion peptides that were His-tagged TcdB or fragments thereof were isolated by Ni^{2+} affinity chromatography (Ni-IDA columns, Macherey-Nagel, Germany). The phage display library containing the antibody gene libraries, which can also be described as binding peptide libraries, herein is also termed antibody phage library.

[0028] The antibody phage display library contained the binding peptides in scFv format. The library was used for selection by incubation on full-length TcdB and/or on the fragments, immobilized on Costar High binding microtiter plates at room temperature. Negative selection on immobilized peptide of amino acids No. 1-1128 of SEQ ID NO: 2 was used to isolate peptides binding to the TLD. After three rounds of panning, monoclonal scFv were produced and screened for binding to TcdB by an antigen-ELISA. DNA of binding phage was isolated and sequenced, unique scFv sequences of binding peptides were recloned (pCSE2.6-hIgG1-Fc-XP, accessible at PMID:23802841) for production in mammalian cells (HEK293-6E cells) as scFv-Fc, which is an IgG-like bivalent format. Binding peptides were purified using protein A.

[0029] For epitope mapping, a phage display library of fragments of the TcdB gene was constructed using Phusion DNA polymerase with tcdb gene specific primers on genomic DNA of *C. difficile* in PCR and fragmenting the amplificate by ultrasound, filling cohesive ends to blunt ends and phosphorylation by the Fast DNA Repair Kit, obtainable from Thermo Scientific, and cloning the fragments into a dephosphorylated pHORF3 library vector (Kügler et al., Applied Microbiology and Biotechnology, 447-458 (2008)). The vector was used to transform TOP10F' *E. coli*, from which the phage library was produced using Hyperphage. Phage displaying toxin fragments were selected on antibody using SEQ ID NO: 9, respectively SEQ ID No: 10. Sequenc-

ing of the selected phagemids resulted in identification of TcdB-fragments that were bound by the antibodies.

[0030] Further, the epitope was mapped using a 15-mer peptide array with an offset of 2 amino acids for neighbouring peptides.

[0031] These assays indicate affinity of the binding peptides, especially of the binding peptides of the first and second embodiments, for the epitope of SEQ ID NO: 13, as exemplified by SEQ ID NO: 1.

[0032] The protective effect of antibody having affinity for the epitope of SEQ ID NO: 1 was analysed in an in vitro TcdB neutralization assay using Vero cells (African green monkey kidney cells). Vero cells were cultivated in RPMI medium supplemented with 2 g/L $NaHCO_3$, 2 mM stable glutamine (FG1215, obtainable from Biochrom) and 10% fetal calf serum at 37° C. in a 5% CO_2 atmosphere, with passaging two to three times per week when confluency exceeded 90%. Presence of the toxin TcdB leads to a breakdown of the actin cytoskeleton, which is easily visible as rounding of the cells using bright field microscopy. Accordingly, activity of the toxin, and the neutralization of the toxin by binding peptide was observed using the microscopic determination of cell rounding. Cells were seeded to 10 000 cells per well of a 96-well cell culture plate (Cellstar, Greiner bio-one, Germany) and cultivated in the medium for 16 h prior to adding TcdB. TcdB was added in an amount to obtain a concentration of 0.1 pM in the cell culture. Before adding the toxin to the cultivated cells, TcdB was diluted in cell culture medium. For positive intoxication assays, the TcdB in medium was added to the cultivated cells. As a negative comparison without intoxication, only medium was added to cultivated cells. For neutralization assays, the binding peptide was added to the TcdB in the medium to a final concentration of 100 nM, incubated for 30 min at room temperature, and then added to the cultivated cells. Cell rounding was analyzed when in the positive intoxication assay 70-80% of cells were rounded, indicating intoxication. For evaluation, the percentage of rounded cells in the neutralization assays was determined and normalized to the percentage of rounded cells determined in the negative and positive comparative intoxication assays.

[0033] On the example of the binding peptides of the first and second embodiments, the TcdB neutralization assay showed that the binding peptides of the invention result in an effective neutralization of the full-length toxin TcdB. In this in vitro assay, these exemplary binding peptides were found to neutralize TcdB to more than 75% as indicated by a reduction of rounded cells by more than 75%.

[0034] Generally optionally, the peptide comprising the epitope of SEQ ID NO: 13, e.g. of SEQ ID NO: 1, especially when for use as an antigenic peptide, it can comprise additional antigenic epitopes of TcdB and/or of TcdA, e.g. the epitopes of amino acid Nos. 322 to 325 and/or of amino acid Nos. 340 to 351, and/or the domain of amino acid Nos. 290 to 360, resp., of SEQ ID NO: 2 or of SEQ ID NO: 11. Optionally, the antigenic peptide can consist of at least one copy or at least two copies of the epitope of SEQ ID NO: 13 in combination with one or at least two of the epitopes of amino acid Nos. 322 to 325 and/or of amino acid Nos. 340 to 351, and/or the domain of amino acid Nos. 290 to 360 of SEQ ID NO: 2 or of SEQ ID NO: 11.

[0035] For illustration, FIG. **1** shows a section of a crystal structure of the GT domain of TcdB, modified from a PDB file (accession No 2bvm), indicating at 1 the epitope of SEQ ID NO: 1 emphasized in black, and at 2 indicating amino acids 322-325 and 340-351 also emphasized in black. This shows that the epitope of the invention, and hence the binding site for binding peptides of the invention, are located at a great distance from an epitope indicated at 2 of amino acids 322-325 and 340-351.

SEQUENCE LISTING

<160> NUMBER OF SEQ ID NOS: 13

<210> SEQ ID NO 1
<211> LENGTH: 36
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: immunogenic epitope of TcdB

<400> SEQUENCE: 1

```
Gln Ile Glu Asn Arg Tyr Lys Ile Leu Asn Asn Ser Leu Asn Pro Ala
1               5                  10                  15

Ile Ser Glu Asp Asn Asp Phe Asn Thr Thr Thr Asn Thr Phe Ile Asp
            20                  25                  30

Ser Ile Met Ala
        35
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<210> SEQ ID NO 2
<211> LENGTH: 2366
<212> TYPE: PRT
<213> ORGANISM: Clostridioides difficile
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 1..543
<223> OTHER INFORMATION: GTD domain
<220> FEATURE:

-continued

<223> OTHER INFORMATION: Toxin B of VPI10463 (clade 1)
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 402..437
<223> OTHER INFORMATION: epitope
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 544..767
<223> OTHER INFORMATION: CPD domain
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<221> NAME/KEY: CHAIN
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<223> OTHER INFORMATION: E4 domain

<400> SEQUENCE: 2

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

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

Glu Tyr His Asn Met Ser Glu Asn Thr Val Val Glu Lys Tyr Leu Lys
        35                  40                  45

Leu Lys Asp Ile Asn Ser Leu Thr Asp Ile Tyr Ile Asp Thr Tyr Lys
    50                  55                  60

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

Thr Glu Val Leu Glu Leu Lys Asn Asn Asn Leu Thr Pro Val Glu Lys
                85                  90                  95

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

Asn Tyr Ile Asn Gln Trp Lys Asp Val Asn Ser Asp Tyr Asn Val Asn
        115                 120                 125

Val Phe Tyr Asp Ser Asn Ala Phe Leu Ile Asn Thr Leu Lys Lys Thr
    130                 135                 140

Val Val Glu Ser Ala Ile Asn Asp Thr Leu Glu Ser Phe Arg Glu Asn
145                 150                 155                 160

Leu Asn Asp Pro Arg Phe Asp Tyr Asn Lys Phe Phe Arg Lys Arg Met
                165                 170                 175

Glu Ile Ile Tyr Asp Lys Gln Lys Asn Phe Ile Asn Tyr Tyr Lys Ala
            180                 185                 190

Gln Arg Glu Glu Asn Pro Glu Leu Ile Ile Asp Asp Ile Val Lys Thr
        195                 200                 205

Tyr Leu Ser Asn Glu Tyr Ser Lys Glu Ile Asp Glu Leu Asn Thr Tyr
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-continued

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    210                 215                 220

Ile Glu Glu Ser Leu Asn Lys Ile Thr Gln Asn Ser Gly Asn Asp Val
225                 230                 235                 240

Arg Asn Phe Glu Glu Phe Lys Asn Gly Glu Ser Phe Asn Leu Tyr Glu
                245                 250                 255

Gln Glu Leu Val Glu Arg Trp Asn Leu Ala Ala Ala Ser Asp Ile Leu
            260                 265                 270

Arg Ile Ser Ala Leu Lys Glu Ile Gly Gly Met Tyr Leu Asp Val Asp
        275                 280                 285

Met Leu Pro Gly Ile Gln Pro Asp Leu Phe Glu Ser Ile Glu Lys Pro
    290                 295                 300

Ser Ser Val Thr Val Asp Phe Trp Glu Met Thr Lys Leu Glu Ala Ile
305                 310                 315                 320

Met Lys Tyr Lys Glu Tyr Ile Pro Glu Tyr Thr Ser Glu His Phe Asp
                325                 330                 335

Met Leu Asp Glu Glu Val Gln Ser Ser Phe Glu Ser Val Leu Ala Ser
            340                 345                 350

Lys Ser Asp Lys Ser Glu Ile Phe Ser Ser Leu Gly Asp Met Glu Ala
        355                 360                 365

Ser Pro Leu Glu Val Lys Ile Ala Phe Asn Ser Lys Gly Ile Ile Asn
    370                 375                 380

Gln Gly Leu Ile Ser Val Lys Asp Ser Tyr Cys Ser Asn Leu Ile Val
385                 390                 395                 400

Lys Gln Ile Glu Asn Arg Tyr Lys Ile Leu Asn Asn Ser Leu Asn Pro
                405                 410                 415

Ala Ile Ser Glu Asp Asn Asp Phe Asn Thr Thr Thr Asn Thr Phe Ile
            420                 425                 430

Asp Ser Ile Met Ala Glu Ala Asn Ala Asp Asn Gly Arg Phe Met Met
        435                 440                 445

Glu Leu Gly Lys Tyr Leu Arg Val Gly Phe Phe Pro Asp Val Lys Thr
    450                 455                 460

Thr Ile Asn Leu Ser Gly Pro Glu Ala Tyr Ala Ala Ala Tyr Gln Asp
465                 470                 475                 480

Leu Leu Met Phe Lys Glu Gly Ser Met Asn Ile His Leu Ile Glu Ala
                485                 490                 495

Asp Leu Arg Asn Phe Glu Ile Ser Lys Thr Asn Ile Ser Gln Ser Thr
            500                 505                 510

Glu Gln Glu Met Ala Ser Leu Trp Ser Phe Asp Asp Ala Arg Ala Lys
        515                 520                 525

Ala Gln Phe Glu Glu Tyr Lys Arg Asn Tyr Phe Glu Gly Ser Leu Gly
    530                 535                 540

Glu Asp Asp Asn Leu Asp Phe Ser Gln Asn Ile Val Val Asp Lys Glu
545                 550                 555                 560

Tyr Leu Leu Glu Lys Ile Ser Ser Leu Ala Arg Ser Ser Glu Arg Gly
                565                 570                 575

Tyr Ile His Tyr Ile Val Gln Leu Gln Gly Asp Lys Ile Ser Tyr Glu
            580                 585                 590

Ala Ala Cys Asn Leu Phe Ala Lys Thr Pro Tyr Asp Ser Val Leu Phe
        595                 600                 605

Gln Lys Asn Ile Glu Asp Ser Glu Ile Ala Tyr Tyr Tyr Asn Pro Gly
    610                 615                 620
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Asp Gly Glu Ile Gln Glu Ile Asp Lys Tyr Lys Ile Pro Ser Ile Ile
625                 630                 635                 640

Ser Asp Arg Pro Lys Ile Lys Leu Thr Phe Ile Gly His Gly Lys Asp
                645                 650                 655

Glu Phe Asn Thr Asp Ile Phe Ala Gly Phe Asp Val Asp Ser Leu Ser
            660                 665                 670

Thr Glu Ile Glu Ala Ala Ile Asp Leu Ala Lys Glu Asp Ile Ser Pro
        675                 680                 685

Lys Ser Ile Glu Ile Asn Leu Leu Gly Cys Asn Met Phe Ser Tyr Ser
    690                 695                 700

Ile Asn Val Glu Glu Thr Tyr Pro Gly Lys Leu Leu Leu Lys Val Lys
705                 710                 715                 720

Asp Lys Ile Ser Glu Leu Met Pro Ser Ile Ser Gln Asp Ser Ile Ile
                725                 730                 735

Val Ser Ala Asn Gln Tyr Glu Val Arg Ile Asn Ser Glu Gly Arg Arg
            740                 745                 750

Glu Leu Leu Asp His Ser Gly Glu Trp Ile Asn Lys Glu Glu Ser Ile
        755                 760                 765

Ile Lys Asp Ile Ser Ser Lys Glu Tyr Ile Ser Phe Asn Pro Lys Glu
    770                 775                 780

Asn Lys Ile Thr Val Lys Ser Lys Asn Leu Pro Glu Leu Ser Thr Leu
785                 790                 795                 800

Leu Gln Glu Ile Arg Asn Asn Ser Asn Ser Ser Asp Ile Glu Leu Glu
                805                 810                 815

Glu Lys Val Met Leu Thr Glu Cys Glu Ile Asn Val Ile Ser Asn Ile
            820                 825                 830

Asp Thr Gln Ile Val Glu Glu Arg Ile Glu Glu Ala Lys Asn Leu Thr
        835                 840                 845

Ser Asp Ser Ile Asn Tyr Ile Lys Asp Glu Phe Lys Leu Ile Glu Ser
    850                 855                 860

Ile Ser Asp Ala Leu Cys Asp Leu Lys Gln Gln Asn Glu Leu Glu Asp
865                 870                 875                 880

Ser His Phe Ile Ser Phe Glu Asp Ile Ser Glu Thr Asp Glu Gly Phe
                885                 890                 895

Ser Ile Arg Phe Ile Asn Lys Glu Thr Gly Glu Ser Ile Phe Val Glu
            900                 905                 910

Thr Glu Lys Thr Ile Phe Ser Glu Tyr Ala Asn His Ile Thr Glu Glu
        915                 920                 925

Ile Ser Lys Ile Lys Gly Thr Ile Phe Asp Thr Val Asn Gly Lys Leu
    930                 935                 940

Val Lys Lys Val Asn Leu Asp Thr Thr His Glu Val Asn Thr Leu Asn
945                 950                 955                 960

Ala Ala Phe Phe Ile Gln Ser Leu Ile Glu Tyr Asn Ser Ser Lys Glu
                965                 970                 975

Ser Leu Ser Asn Leu Ser Val Ala Met Lys Val Gln Val Tyr Ala Gln
            980                 985                 990

Leu Phe Ser Thr Gly Leu Asn Thr Ile Thr Asp Ala Ala Lys Val Val
        995                 1000                1005

Glu Leu Val Ser Thr Ala Leu Asp Glu Thr Ile Asp Leu Leu Pro Thr
    1010                1015                1020
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Leu Ser Glu Gly Leu Pro Ile Ile Ala Thr Ile Ile Asp Gly Val Ser
1025                1030                1035                1040

Leu Gly Ala Ala Ile Lys Glu Leu Ser Glu Thr Ser Asp Pro Leu Leu
                1045                1050                1055

Arg Gln Glu Ile Glu Ala Lys Ile Gly Ile Met Ala Val Asn Leu Thr
            1060                1065                1070

Thr Ala Thr Thr Ala Ile Ile Thr Ser Ser Leu Gly Ile Ala Ser Gly
        1075                1080                1085

Phe Ser Ile Leu Leu Val Pro Leu Ala Gly Ile Ser Ala Gly Ile Pro
    1090                1095                1100

Ser Leu Val Asn Asn Glu Leu Val Leu Arg Asp Lys Ala Thr Lys Val
1105                1110                1115                1120

Val Asp Tyr Phe Lys His Val Ser Leu Val Glu Thr Glu Gly Val Phe
                1125                1130                1135

Thr Leu Leu Asp Asp Lys Ile Met Met Pro Gln Asp Asp Leu Val Ile
            1140                1145                1150

Ser Glu Ile Asp Phe Asn Asn Asn Ser Ile Val Leu Gly Lys Cys Glu
        1155                1160                1165

Ile Trp Arg Met Glu Gly Gly Ser Gly His Thr Val Thr Asp Asp Ile
    1170                1175                1180

Asp His Phe Phe Ser Ala Pro Ser Ile Thr Tyr Arg Glu Pro His Leu
1185                1190                1195                1200

Ser Ile Tyr Asp Val Leu Glu Val Gln Lys Glu Glu Leu Asp Leu Ser
                1205                1210                1215

Lys Asp Leu Met Val Leu Pro Asn Ala Pro Asn Arg Val Phe Ala Trp
            1220                1225                1230

Glu Thr Gly Trp Thr Pro Gly Leu Arg Ser Leu Glu Asn Asp Gly Thr
        1235                1240                1245

Lys Leu Leu Asp Arg Ile Arg Asp Asn Tyr Glu Gly Glu Phe Tyr Trp
    1250                1255                1260

Arg Tyr Phe Ala Phe Ile Ala Asp Ala Leu Ile Thr Thr Leu Lys Pro
1265                1270                1275                1280

Arg Tyr Glu Asp Thr Asn Ile Arg Ile Asn Leu Asp Ser Asn Thr Arg
                1285                1290                1295

Ser Phe Ile Val Pro Ile Ile Thr Thr Glu Tyr Ile Arg Glu Lys Leu
            1300                1305                1310

Ser Tyr Ser Phe Tyr Gly Ser Gly Gly Thr Tyr Ala Leu Ser Leu Ser
        1315                1320                1325

Gln Tyr Asn Met Gly Ile Asn Ile Glu Leu Ser Glu Ser Asp Val Trp
    1330                1335                1340

Ile Ile Asp Val Asp Asn Val Val Arg Asp Val Thr Ile Glu Ser Asp
1345                1350                1355                1360

Lys Ile Lys Lys Gly Asp Leu Ile Glu Gly Ile Leu Ser Thr Leu Ser
                1365                1370                1375

Ile Glu Glu Asn Lys Ile Ile Leu Asn Ser His Glu Ile Asn Phe Ser
            1380                1385                1390

Gly Glu Val Asn Gly Ser Asn Gly Phe Val Ser Leu Thr Phe Ser Ile
        1395                1400                1405

Leu Glu Gly Ile Asn Ala Ile Ile Glu Val Asp Leu Leu Ser Lys Ser
    1410                1415                1420

Tyr Lys Leu Leu Ile Ser Gly Glu Leu Lys Ile Leu Met Leu Asn Ser
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1425                1430                1435                1440

Asn His Ile Gln Gln Lys Ile Asp Tyr Ile Gly Phe Asn Ser Glu Leu
                1445                1450                1455

Gln Lys Asn Ile Pro Tyr Ser Phe Val Asp Ser Glu Gly Lys Glu Asn
            1460                1465                1470

Gly Phe Ile Asn Gly Ser Thr Lys Glu Gly Leu Phe Val Ser Glu Leu
        1475                1480                1485

Pro Asp Val Val Leu Ile Ser Lys Val Tyr Met Asp Asp Ser Lys Pro
    1490                1495                1500

Ser Phe Gly Tyr Tyr Ser Asn Asn Leu Lys Asp Val Lys Val Ile Thr
1505                1510                1515                1520

Lys Asp Asn Val Asn Ile Leu Thr Gly Tyr Tyr Leu Lys Asp Asp Ile
                1525                1530                1535

Lys Ile Ser Leu Ser Leu Thr Leu Gln Asp Glu Lys Thr Ile Lys Leu
            1540                1545                1550

Asn Ser Val His Leu Asp Glu Ser Gly Val Ala Glu Ile Leu Lys Phe
        1555                1560                1565

Met Asn Arg Lys Gly Asn Thr Asn Thr Ser Asp Ser Leu Met Ser Phe
    1570                1575                1580

Leu Glu Ser Met Asn Ile Lys Ser Ile Phe Val Asn Phe Leu Gln Ser
1585                1590                1595                1600

Asn Ile Lys Phe Ile Leu Asp Ala Asn Phe Ile Ile Ser Gly Thr Thr
                1605                1610                1615

Ser Ile Gly Gln Phe Glu Phe Ile Cys Asp Glu Asn Asp Asn Ile Gln
            1620                1625                1630

Pro Tyr Phe Ile Lys Phe Asn Thr Leu Glu Thr Asn Tyr Thr Leu Tyr
        1635                1640                1645

Val Gly Asn Arg Gln Asn Met Ile Val Glu Pro Asn Tyr Asp Leu Asp
    1650                1655                1660

Asp Ser Gly Asp Ile Ser Ser Thr Val Ile Asn Phe Ser Gln Lys Tyr
1665                1670                1675                1680

Leu Tyr Gly Ile Asp Ser Cys Val Asn Lys Val Val Ile Ser Pro Asn
                1685                1690                1695

Ile Tyr Thr Asp Glu Ile Asn Ile Thr Pro Val Tyr Glu Thr Asn Asn
            1700                1705                1710

Thr Tyr Pro Glu Val Ile Val Leu Asp Ala Asn Tyr Ile Asn Glu Lys
        1715                1720                1725

Ile Asn Val Asn Ile Asn Asp Leu Ser Ile Arg Tyr Val Trp Ser Asn
    1730                1735                1740

Asp Gly Asn Asp Phe Ile Leu Met Ser Thr Ser Glu Glu Asn Lys Val
1745                1750                1755                1760

Ser Gln Val Lys Ile Arg Phe Val Asn Val Phe Lys Asp Lys Thr Leu
                1765                1770                1775

Ala Asn Lys Leu Ser Phe Asn Phe Ser Asp Lys Gln Asp Val Pro Val
            1780                1785                1790

Ser Glu Ile Ile Leu Ser Phe Thr Pro Ser Tyr Tyr Glu Asp Gly Leu
        1795                1800                1805

Ile Gly Tyr Asp Leu Gly Leu Val Ser Leu Tyr Asn Glu Lys Phe Tyr
    1810                1815                1820

Ile Asn Asn Phe Gly Met Met Val Ser Gly Leu Ile Tyr Ile Asn Asp
1825                1830                1835                1840
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Ser Leu Tyr Tyr Phe Lys Pro Pro Val Asn Asn Leu Ile Thr Gly Phe
                1845                1850                1855

Val Thr Val Gly Asp Asp Lys Tyr Tyr Phe Asn Pro Ile Asn Gly Gly
            1860                1865                1870

Ala Ala Ser Ile Gly Glu Thr Ile Ile Asp Asp Lys Asn Tyr Tyr Phe
        1875                1880                1885

Asn Gln Ser Gly Val Leu Gln Thr Gly Val Phe Ser Thr Glu Asp Gly
    1890                1895                1900

Phe Lys Tyr Phe Ala Pro Ala Asn Thr Leu Asp Glu Asn Leu Glu Gly
1905                1910                1915                1920

Glu Ala Ile Asp Phe Thr Gly Lys Leu Ile Ile Asp Glu Asn Ile Tyr
                1925                1930                1935

Tyr Phe Asp Asp Asn Tyr Arg Gly Ala Val Glu Trp Lys Glu Leu Asp
            1940                1945                1950

Gly Glu Met His Tyr Phe Ser Pro Glu Thr Gly Lys Ala Phe Lys Gly
        1955                1960                1965

Leu Asn Gln Ile Gly Asp Tyr Lys Tyr Tyr Phe Asn Ser Asp Gly Val
    1970                1975                1980

Met Gln Lys Gly Phe Val Ser Ile Asn Asp Asn Lys His Tyr Phe Asp
1985                1990                1995                2000

Asp Ser Gly Val Met Lys Val Gly Tyr Thr Glu Ile Asp Gly Lys His
                2005                2010                2015

Phe Tyr Phe Ala Glu Asn Gly Glu Met Gln Ile Gly Val Phe Asn Thr
            2020                2025                2030

Glu Asp Gly Phe Lys Tyr Phe Ala His His Asn Glu Asp Leu Gly Asn
        2035                2040                2045

Glu Glu Gly Glu Glu Ile Ser Tyr Ser Gly Ile Leu Asn Phe Asn Asn
    2050                2055                2060

Lys Ile Tyr Tyr Phe Asp Asp Ser Phe Thr Ala Val Val Gly Trp Lys
2065                2070                2075                2080

Asp Leu Glu Asp Gly Ser Lys Tyr Tyr Phe Asp Glu Asp Thr Ala Glu
                2085                2090                2095

Ala Tyr Ile Gly Leu Ser Leu Ile Asn Asp Gly Gln Tyr Tyr Phe Asn
            2100                2105                2110

Asp Asp Gly Ile Met Gln Val Gly Phe Val Thr Ile Asn Asp Lys Val
        2115                2120                2125

Phe Tyr Phe Ser Asp Ser Gly Ile Ile Glu Ser Gly Val Gln Asn Ile
    2130                2135                2140

Asp Asp Asn Tyr Phe Tyr Ile Asp Asp Asn Gly Ile Val Gln Ile Gly
2145                2150                2155                2160

Val Phe Asp Thr Ser Asp Gly Tyr Lys Tyr Phe Ala Pro Ala Asn Thr
                2165                2170                2175

Val Asn Asp Asn Ile Tyr Gly Gln Ala Val Glu Tyr Ser Gly Leu Val
            2180                2185                2190

Arg Val Gly Glu Asp Val Tyr Tyr Phe Gly Glu Thr Tyr Thr Ile Glu
        2195                2200                2205

Thr Gly Trp Ile Tyr Asp Met Glu Asn Glu Ser Asp Lys Tyr Tyr Phe
    2210                2215                2220

Asn Pro Glu Thr Lys Lys Ala Cys Lys Gly Ile Asn Leu Ile Asp Asp
2225                2230                2235                2240
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Ile Lys Tyr Tyr Phe Asp Glu Lys Gly Ile Met Arg Thr Gly Leu Ile
                2245                2250                2255

Ser Phe Glu Asn Asn Asn Tyr Tyr Phe Asn Glu Asn Gly Glu Met Gln
            2260                2265                2270

Phe Gly Tyr Ile Asn Ile Glu Asp Lys Met Phe Tyr Phe Gly Glu Asp
        2275                2280                2285

Gly Val Met Gln Ile Gly Val Phe Asn Thr Pro Asp Gly Phe Lys Tyr
    2290                2295                2300

Phe Ala His Gln Asn Thr Leu Asp Glu Asn Phe Glu Gly Glu Ser Ile
2305                2310                2315                2320

Asn Tyr Thr Gly Trp Leu Asp Leu Asp Glu Lys Arg Tyr Tyr Phe Thr
                2325                2330                2335

Asp Glu Tyr Ile Ala Ala Thr Gly Ser Val Ile Ile Asp Gly Glu Glu
            2340                2345                2350

Tyr Tyr Phe Asp Pro Asp Thr Ala Gln Leu Val Ile Ser Glu
        2355                2360                2365


<210> SEQ ID NO 3
<211> LENGTH: 183
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: fragment of toxin B

<400> SEQUENCE: 3

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

Phe Asn Ser Lys Gly Ile Ile Asn Gln Gly Leu Ile Ser Val Lys Asp
            20                  25                  30

Ser Tyr Cys Ser Asn Leu Ile Val Lys Gln Ile Glu Asn Arg Tyr Lys
        35                  40                  45

Ile Leu Asn Asn Ser Leu Asn Pro Ala Ile Ser Glu Asp Asn Asp Phe
    50                  55                  60

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

Ala Asp Asn Gly Arg Phe Met Met Glu Leu Gly Lys Tyr Leu Arg Val
                85                  90                  95

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

Ala Tyr Ala Ala Ala Tyr Gln Asp Leu Leu Met Phe Lys Glu Gly Ser
        115                 120                 125

Met Asn Ile His Leu Ile Glu Ala Asp Leu Arg Asn Phe Glu Ile Ser
    130                 135                 140

Lys Thr Asn Ile Ser Gln Ser Thr Glu Gln Glu Met Ala Ser Leu Trp
145                 150                 155                 160

Ser Phe Asp Asp Ala Arg Ala Lys Ala Gln Phe Glu Glu Tyr Lys Arg
                165                 170                 175

Asn Tyr Phe Glu Gly Ser Leu
            180


<210> SEQ ID NO 4
<211> LENGTH: 407
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<223> OTHER INFORMATION: fragment of toxin B

<400> SEQUENCE: 4

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

Phe Asn Ser Lys Gly Ile Ile Asn Gln Gly Leu Ile Ser Val Lys Asp
            20                  25                  30

Ser Tyr Cys Ser Asn Leu Ile Val Lys Gln Ile Glu Asn Arg Tyr Lys
        35                  40                  45

Ile Leu Asn Asn Ser Leu Asn Pro Ala Ile Ser Glu Asp Asn Asp Phe
    50                  55                  60

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

Ala Asp Asn Gly Arg Phe Met Met Glu Leu Gly Lys Tyr Leu Arg Val
                85                  90                  95

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

Ala Tyr Ala Ala Ala Tyr Gln Asp Leu Leu Met Phe Lys Glu Gly Ser
        115                 120                 125

Met Asn Ile His Leu Ile Glu Ala Asp Leu Arg Asn Phe Glu Ile Ser
    130                 135                 140

Lys Thr Asn Ile Ser Gln Ser Thr Glu Gln Glu Met Ala Ser Leu Trp
145                 150                 155                 160

Ser Phe Asp Asp Ala Arg Ala Lys Ala Gln Phe Glu Glu Tyr Lys Arg
                165                 170                 175

Asn Tyr Phe Glu Gly Ser Leu Gly Glu Asp Asp Asn Leu Asp Phe Ser
            180                 185                 190

Gln Asn Ile Val Val Asp Lys Glu Tyr Leu Leu Glu Lys Ile Ser Ser
        195                 200                 205

Leu Ala Arg Ser Ser Glu Arg Gly Tyr Ile His Tyr Ile Val Gln Leu
    210                 215                 220

Gln Gly Asp Lys Ile Ser Tyr Glu Ala Ala Cys Asn Leu Phe Ala Lys
225                 230                 235                 240

Thr Pro Tyr Asp Ser Val Leu Phe Gln Lys Asn Ile Glu Asp Ser Glu
                245                 250                 255

Ile Ala Tyr Tyr Tyr Asn Pro Gly Asp Gly Glu Ile Gln Glu Ile Asp
            260                 265                 270

Lys Tyr Lys Ile Pro Ser Ile Ile Ser Asp Arg Pro Lys Ile Lys Leu
        275                 280                 285

Thr Phe Ile Gly His Gly Lys Asp Glu Phe Asn Thr Asp Ile Phe Ala
    290                 295                 300

Gly Phe Asp Val Asp Ser Leu Ser Thr Glu Ile Glu Ala Ala Ile Asp
305                 310                 315                 320

Leu Ala Lys Glu Asp Ile Ser Pro Lys Ser Ile Glu Ile Asn Leu Leu
                325                 330                 335

Gly Cys Asn Met Phe Ser Tyr Ser Ile Asn Val Glu Glu Thr Tyr Pro
            340                 345                 350

Gly Lys Leu Leu Leu Lys Val Lys Asp Lys Ile Ser Glu Leu Met Pro
        355                 360                 365

Ser Ile Ser Gln Asp Ser Ile Ile Val Ser Ala Asn Gln Tyr Glu Val
    370                 375                 380
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Arg Ile Asn Ser Glu Gly Arg Arg Glu Leu Leu Asp His Ser Gly Glu
385                 390                 395                 400

Trp Ile Asn Lys Glu Glu Ser
                405


<210> SEQ ID NO 5
<211> LENGTH: 123
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 1..25
<223> OTHER INFORMATION: FR1
<220> FEATURE:
<223> OTHER INFORMATION: heavy chain
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 26..33
<223> OTHER INFORMATION: CDRH1
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 34..50
<223> OTHER INFORMATION: FR2
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 51..58
<223> OTHER INFORMATION: CDRH2
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 59..96
<223> OTHER INFORMATION: FR3
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 97..112
<223> OTHER INFORMATION: CDRH3
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 113..123
<223> OTHER INFORMATION: FR4

<400> SEQUENCE: 5

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

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

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

Gly Trp Ile Asn Pro Gly Asn Gly Asn Thr Lys Tyr Ser Gln Thr Phe
    50                  55                  60

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

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

Ala Arg Val Ile Arg Pro Ser Val Ile Val Thr Thr Pro Phe Asp Phe
            100                 105                 110

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


<210> SEQ ID NO 6
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 1..25
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<223> OTHER INFORMATION: FR1
<220> FEATURE:
<223> OTHER INFORMATION: light chain
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 26..34
<223> OTHER INFORMATION: CDRL1
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 35..51
<223> OTHER INFORMATION: FR2
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 52..54
<223> OTHER INFORMATION: CDRL2
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 55..90
<223> OTHER INFORMATION: FR3
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 91..101
<223> OTHER INFORMATION: CDRL3
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 102..111
<223> OTHER INFORMATION: FR4

<400> SEQUENCE: 6

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

Ser Ile Thr Ile Ser Cys Thr Gly Thr Asn Ser Asp Ile Gly Gly His
20 25 30

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

Ile Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

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

Gln Ala Glu Asp Glu Ala Asp Tyr Phe Cys Gly Ser Tyr Thr Ser Arg
85 90 95

Gly Ala Arg Tyr Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu
100 105 110

<210> SEQ ID NO 7
<211> LENGTH: 128
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 1..25
<223> OTHER INFORMATION: FR1
<220> FEATURE:
<223> OTHER INFORMATION: heavy chain
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 26..33
<223> OTHER INFORMATION: CDRH1
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 34..50
<223> OTHER INFORMATION: FR2
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 51..58
<223> OTHER INFORMATION: CDRH2
<220> FEATURE:
<221> NAME/KEY: CHAIN

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<222> LOCATION: 59..96
<223> OTHER INFORMATION: FR3
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 97..117
<223> OTHER INFORMATION: CDRH3
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 118..128
<223> OTHER INFORMATION: FR4

<400> SEQUENCE: 7

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

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

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

Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
50 55 60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Ala Arg Asp Leu Val Phe Gln Gly Arg Phe Leu Glu Trp Leu Ser Pro
100 105 110

Tyr Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> SEQ ID NO 8
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 1..24
<223> OTHER INFORMATION: FR1
<220> FEATURE:
<223> OTHER INFORMATION: light chain
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 25..33
<223> OTHER INFORMATION: CDRL1
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 34..50
<223> OTHER INFORMATION: FR2
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 51..53
<223> OTHER INFORMATION: CDRL2
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 54..89
<223> OTHER INFORMATION: FR3
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 90..100
<223> OTHER INFORMATION: CDRL3
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 101..110
<223> OTHER INFORMATION: FR4

<400> SEQUENCE: 8

Gln Ala Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln

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1               5                   10                  15

Arg Val Ala Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn
            20                  25                  30

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

Ile Tyr Ala Lys Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
    50                  55                  60

Ala Ser Lys Ser Gly Ser Ser Ala Ser Leu Ala Ile Thr Gly Leu Gln
65                  70                  75                  80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Thr Trp Asp Asp Ser Leu
                85                  90                  95

Ser Ala Trp Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu
            100                 105                 110


<210> SEQ ID NO 9
<211> LENGTH: 272
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 1..123
<223> OTHER INFORMATION: heavy chain
<220> FEATURE:
<223> OTHER INFORMATION: scFv
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 124..141
<223> OTHER INFORMATION: linker
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 142..252
<223> OTHER INFORMATION: light chain

<400> SEQUENCE: 9

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

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

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

Gly Trp Ile Asn Pro Gly Asn Gly Asn Thr Lys Tyr Ser Gln Thr Phe
    50                  55                  60

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

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

Ala Arg Val Ile Arg Pro Ser Val Ile Val Thr Thr Pro Phe Asp Phe
            100                 105                 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Ser Ala Ser Ala
        115                 120                 125

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

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

Ile Ser Cys Thr Gly Thr Asn Ser Asp Ile Gly Gly His Asn Tyr Val
                165                 170                 175

Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu Ile Ile Tyr
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            180                 185                 190

Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe Ser Gly Ser
        195                 200                 205

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

Asp Glu Ala Asp Tyr Phe Cys Gly Ser Tyr Thr Ser Arg Gly Ala Arg
225                 230                 235                 240

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

Ala Asn Pro Thr Val Thr Leu Phe Pro Pro Ser Ser Ala Ala Ala Ser
            260                 265                 270


<210> SEQ ID NO 10
<211> LENGTH: 276
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 1..128
<223> OTHER INFORMATION: heavy chain
<220> FEATURE:
<223> OTHER INFORMATION: scFv
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 129..146
<223> OTHER INFORMATION: linker
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 147..256
<223> OTHER INFORMATION: heavy chain

<400> SEQUENCE: 10

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

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

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

Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

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

Ala Arg Asp Leu Val Phe Gln Gly Arg Phe Leu Glu Trp Leu Ser Pro
            100                 105                 110

Tyr Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120                 125

Gly Ser Ala Ser Ala Pro Lys Leu Glu Glu Gly Glu Phe Ser Glu Ala
    130                 135                 140

Arg Val Gln Ala Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro
145                 150                 155                 160

Gly Gln Arg Val Ala Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly
                165                 170                 175

Ser Asn Thr Val Asn Trp Tyr Gln Gln Leu Pro Gly Glu Ala Pro Arg
            180                 185                 190

Leu Leu Ile Tyr Ala Lys Asn Gln Arg Pro Ser Gly Val Pro Asp Arg
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        195                 200                 205

Phe Ser Ala Ser Lys Ser Gly Ser Ser Ala Ser Leu Ala Ile Thr Gly
    210                 215                 220

Leu Gln Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Thr Trp Asp Asp
225                 230                 235                 240

Ser Leu Ser Ala Trp Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu
                245                 250                 255

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

Ala Ala Ala Ser
        275


<210> SEQ ID NO 11
<211> LENGTH: 2366
<212> TYPE: PRT
<213> ORGANISM: Clostridioides difficile
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 1..543
<223> OTHER INFORMATION: GTD domain
<220> FEATURE:
<223> OTHER INFORMATION: Toxin B R20291 (clade 2)
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 402..437
<223> OTHER INFORMATION: epitope
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 544..767
<223> OTHER INFORMATION: CPD domain
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 768..1852
<223> OTHER INFORMATION: TLD domain
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 1853..2366
<223> OTHER INFORMATION: CROPs
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 1875..2005
<223> OTHER INFORMATION: E1 domain
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 2006..2137
<223> OTHER INFORMATION: E2 domain
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 2138..2271
<223> OTHER INFORMATION: E3 domain
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 2272..2366
<223> OTHER INFORMATION: E4 domain

<400> SEQUENCE: 11

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

Phe Arg Val Gln Glu Asp Glu Tyr Val Ala Ile Leu Asp Ala Leu Glu
            20                  25                  30

Glu Tyr His Asn Met Ser Glu Asn Thr Val Val Glu Lys Tyr Leu Lys
        35                  40                  45

Leu Lys Asp Ile Asn Ser Leu Thr Asp Ile Tyr Ile Asp Thr Tyr Lys
    50                  55                  60

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

Thr Glu Val Leu Glu Leu Lys Asn Asn Asn Leu Thr Pro Val Glu Lys
                85                  90                  95

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

Asn Tyr Ile Asn Gln Trp Lys Asp Val Asn Ser Asp Tyr Asn Val Asn
        115                 120                 125

Val Phe Tyr Asp Ser Asn Ala Phe Leu Ile Asn Thr Leu Lys Lys Thr
    130                 135                 140

Ile Val Glu Ser Ala Thr Asn Asp Thr Leu Glu Ser Phe Arg Glu Asn
145                 150                 155                 160

Leu Asn Asp Pro Arg Phe Asp Tyr Asn Lys Phe Tyr Arg Lys Arg Met
                165                 170                 175

Glu Ile Ile Tyr Asp Lys Gln Lys Asn Phe Ile Asn Tyr Tyr Lys Thr
            180                 185                 190

Gln Arg Glu Glu Asn Pro Asp Leu Ile Ile Asp Asp Ile Val Lys Ile
        195                 200                 205

Tyr Leu Ser Asn Glu Tyr Ser Lys Asp Ile Asp Glu Leu Asn Ser Tyr
    210                 215                 220

Ile Glu Glu Ser Leu Asn Lys Val Thr Glu Asn Ser Gly Asn Asp Val
225                 230                 235                 240

Arg Asn Phe Glu Glu Phe Lys Gly Gly Glu Ser Phe Lys Leu Tyr Glu
                245                 250                 255

Gln Glu Leu Val Glu Arg Trp Asn Leu Ala Ala Ala Ser Asp Ile Leu
            260                 265                 270

Arg Ile Ser Ala Leu Lys Glu Val Gly Gly Val Tyr Leu Asp Val Asp
        275                 280                 285

Met Leu Pro Gly Ile Gln Pro Asp Leu Phe Glu Ser Ile Glu Lys Pro
    290                 295                 300

Ser Ser Val Thr Val Asp Phe Trp Glu Met Val Lys Leu Glu Ala Ile
305                 310                 315                 320

Met Lys Tyr Lys Glu Tyr Ile Pro Gly Tyr Thr Ser Glu His Phe Asp
                325                 330                 335

Met Leu Asp Glu Glu Val Gln Ser Ser Phe Glu Ser Val Leu Ala Ser
            340                 345                 350

Lys Ser Asp Lys Ser Glu Ile Phe Ser Ser Leu Gly Asp Met Glu Ala
        355                 360                 365

Ser Pro Leu Glu Val Lys Ile Ala Phe Asn Ser Lys Gly Ile Ile Asn
    370                 375                 380

Gln Gly Leu Ile Ser Val Lys Asp Ser Tyr Cys Ser Asn Leu Ile Val
385                 390                 395                 400

Lys Gln Ile Glu Asn Arg Tyr Lys Ile Leu Asn Asn Ser Leu Asn Pro
                405                 410                 415

Ala Ile Ser Glu Asp Asn Asp Phe Asn Thr Thr Thr Asn Ala Phe Ile
            420                 425                 430

Asp Ser Ile Met Ala Glu Ala Asn Ala Asp Asn Gly Arg Phe Met Met
        435                 440                 445

Glu Leu Gly Lys Tyr Leu Arg Val Gly Phe Phe Pro Asp Val Lys Thr
    450                 455                 460

Thr Ile Asn Leu Ser Gly Pro Glu Ala Tyr Ala Ala Ala Tyr Gln Asp
465                 470                 475                 480
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Leu Leu Met Phe Lys Glu Gly Ser Met Asn Ile His Leu Ile Glu Ala
                485                 490                 495

Asp Leu Arg Asn Phe Glu Ile Ser Lys Thr Asn Ile Ser Gln Ser Thr
            500                 505                 510

Glu Gln Glu Met Ala Ser Leu Trp Ser Phe Asp Asp Ala Arg Ala Lys
        515                 520                 525

Ala Gln Phe Glu Glu Tyr Lys Lys Asn Tyr Phe Glu Gly Ser Leu Gly
    530                 535                 540

Glu Asp Asp Asn Leu Asp Phe Ser Gln Asn Thr Val Val Asp Lys Glu
545                 550                 555                 560

Tyr Leu Leu Glu Lys Ile Ser Ser Leu Ala Arg Ser Ser Glu Arg Gly
                565                 570                 575

Tyr Ile His Tyr Ile Val Gln Leu Gln Gly Asp Lys Ile Ser Tyr Glu
            580                 585                 590

Ala Ala Cys Asn Leu Phe Ala Lys Thr Pro Tyr Asp Ser Val Leu Phe
        595                 600                 605

Gln Lys Asn Ile Glu Asp Ser Glu Ile Ala Tyr Tyr Tyr Asn Pro Gly
    610                 615                 620

Asp Gly Glu Ile Gln Glu Ile Asp Lys Tyr Lys Ile Pro Ser Ile Ile
625                 630                 635                 640

Ser Asp Arg Pro Lys Ile Lys Leu Thr Phe Ile Gly His Gly Lys Asp
                645                 650                 655

Glu Phe Asn Thr Asp Ile Phe Ala Gly Leu Asp Val Asp Ser Leu Ser
            660                 665                 670

Thr Glu Ile Glu Thr Ala Ile Asp Leu Ala Lys Glu Asp Ile Ser Pro
        675                 680                 685

Lys Ser Ile Glu Ile Asn Leu Leu Gly Cys Asn Met Phe Ser Tyr Ser
    690                 695                 700

Val Asn Val Glu Glu Thr Tyr Pro Gly Lys Leu Leu Leu Arg Val Lys
705                 710                 715                 720

Asp Lys Val Ser Glu Leu Met Pro Ser Ile Ser Gln Asp Ser Ile Ile
                725                 730                 735

Val Ser Ala Asn Gln Tyr Glu Val Arg Ile Asn Ser Glu Gly Arg Arg
            740                 745                 750

Glu Leu Leu Asp His Ser Gly Glu Trp Ile Asn Lys Glu Glu Ser Ile
        755                 760                 765

Ile Lys Asp Ile Ser Ser Lys Glu Tyr Ile Ser Phe Asn Pro Lys Glu
    770                 775                 780

Asn Lys Ile Ile Val Lys Ser Lys Asn Leu Pro Glu Leu Ser Thr Leu
785                 790                 795                 800

Leu Gln Glu Ile Arg Asn Asn Ser Asn Ser Ser Asp Ile Glu Leu Glu
                805                 810                 815

Glu Lys Val Met Leu Ala Glu Cys Glu Ile Asn Val Ile Ser Asn Ile
            820                 825                 830

Asp Thr Gln Val Val Glu Gly Arg Ile Glu Glu Ala Lys Ser Leu Thr
        835                 840                 845

Ser Asp Ser Ile Asn Tyr Ile Lys Asn Glu Phe Lys Leu Ile Glu Ser
    850                 855                 860

Ile Ser Asp Ala Leu Tyr Asp Leu Lys Gln Gln Asn Glu Leu Glu Glu
865                 870                 875                 880
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Ser His Phe Ile Ser Phe Glu Asp Ile Leu Glu Thr Asp Glu Gly Phe
                885                 890                 895

Ser Ile Arg Phe Ile Asp Lys Glu Thr Gly Glu Ser Ile Phe Val Glu
            900                 905                 910

Thr Glu Lys Ala Ile Phe Ser Glu Tyr Ala Asn His Ile Thr Glu Glu
        915                 920                 925

Ile Ser Lys Ile Lys Gly Thr Ile Phe Asp Thr Val Asn Gly Lys Leu
    930                 935                 940

Val Lys Lys Val Asn Leu Asp Ala Thr His Glu Val Asn Thr Leu Asn
945                 950                 955                 960

Ala Ala Phe Phe Ile Gln Ser Leu Ile Glu Tyr Asn Ser Ser Lys Glu
                965                 970                 975

Ser Leu Ser Asn Leu Ser Val Ala Met Lys Val Gln Val Tyr Ala Gln
            980                 985                 990

Leu Phe Ser Thr Gly Leu Asn Thr Ile Thr Asp Ala Ala Lys Val Val
        995                 1000                1005

Glu Leu Val Ser Thr Ala Leu Asp Glu Thr Ile Asp Leu Leu Pro Thr
    1010                1015                1020

Leu Ser Glu Gly Leu Pro Val Ile Ala Thr Ile Ile Asp Gly Val Ser
1025                1030                1035                1040

Leu Gly Ala Ala Ile Lys Glu Leu Ser Glu Thr Ser Asp Pro Leu Leu
                1045                1050                1055

Arg Gln Glu Ile Glu Ala Lys Ile Gly Ile Met Ala Val Asn Leu Thr
            1060                1065                1070

Ala Ala Thr Thr Ala Ile Ile Thr Ser Ser Leu Gly Ile Ala Ser Gly
        1075                1080                1085

Phe Ser Ile Leu Leu Val Pro Leu Ala Gly Ile Ser Ala Gly Ile Pro
    1090                1095                1100

Ser Leu Val Asn Asn Glu Leu Ile Leu Arg Asp Lys Ala Thr Lys Val
1105                1110                1115                1120

Val Asp Tyr Phe Ser His Ile Ser Leu Ala Glu Ser Glu Gly Ala Phe
                1125                1130                1135

Thr Ser Leu Asp Asp Lys Ile Met Met Pro Gln Asp Asp Leu Val Ile
            1140                1145                1150

Ser Glu Ile Asp Phe Asn Asn Asn Ser Ile Thr Leu Gly Lys Cys Glu
        1155                1160                1165

Ile Trp Arg Met Glu Gly Gly Ser Gly His Thr Val Thr Asp Asp Ile
    1170                1175                1180

Asp His Phe Phe Ser Ala Pro Ser Ile Thr Tyr Arg Glu Pro His Leu
1185                1190                1195                1200

Ser Ile Tyr Asp Val Leu Glu Val Gln Lys Glu Glu Leu Asp Leu Ser
                1205                1210                1215

Lys Asp Leu Met Val Leu Pro Asn Ala Pro Asn Arg Val Phe Ala Trp
            1220                1225                1230

Glu Thr Gly Trp Thr Pro Gly Leu Arg Ser Leu Glu Asn Asp Gly Thr
        1235                1240                1245

Lys Leu Leu Asp Arg Ile Arg Asp Asn Tyr Glu Gly Glu Phe Tyr Trp
    1250                1255                1260

Arg Tyr Phe Ala Phe Ile Ala Asp Ala Leu Ile Thr Thr Leu Lys Pro
1265                1270                1275                1280

Arg Tyr Glu Asp Thr Asn Ile Arg Ile Asn Leu Asp Ser Asn Thr Arg
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                1285                1290                1295

Ser Phe Ile Val Pro Val Ile Thr Thr Glu Tyr Ile Arg Glu Lys Leu
            1300                1305                1310

Ser Tyr Ser Phe Tyr Gly Ser Gly Gly Thr Tyr Ala Leu Ser Leu Ser
        1315                1320                1325

Gln Tyr Asn Met Asn Ile Asn Ile Glu Leu Asn Glu Asn Asp Thr Trp
    1330                1335                1340

Val Ile Asp Val Asp Asn Val Val Arg Asp Val Thr Ile Glu Ser Asp
1345                1350                1355                1360

Lys Ile Lys Lys Gly Asp Leu Ile Glu Asn Ile Leu Ser Lys Leu Ser
                1365                1370                1375

Ile Glu Asp Asn Lys Ile Ile Leu Asp Asn His Glu Ile Asn Phe Ser
            1380                1385                1390

Gly Thr Leu Asn Gly Gly Asn Gly Phe Val Ser Leu Thr Phe Ser Ile
        1395                1400                1405

Leu Glu Gly Ile Asn Ala Val Ile Glu Val Asp Leu Leu Ser Lys Ser
    1410                1415                1420

Tyr Lys Val Leu Ile Ser Gly Glu Leu Lys Thr Leu Met Ala Asn Ser
1425                1430                1435                1440

Asn Ser Val Gln Gln Lys Ile Asp Tyr Ile Gly Leu Asn Ser Glu Leu
                1445                1450                1455

Gln Lys Asn Ile Pro Tyr Ser Phe Met Asp Asp Lys Gly Lys Glu Asn
            1460                1465                1470

Gly Phe Ile Asn Cys Ser Thr Lys Glu Gly Leu Phe Val Ser Glu Leu
        1475                1480                1485

Ser Asp Val Val Leu Ile Ser Lys Val Tyr Met Asp Asn Ser Lys Pro
    1490                1495                1500

Leu Phe Gly Tyr Cys Ser Asn Asp Leu Lys Asp Val Lys Val Ile Thr
1505                1510                1515                1520

Lys Asp Asp Val Ile Ile Leu Thr Gly Tyr Tyr Leu Lys Asp Asp Ile
                1525                1530                1535

Lys Ile Ser Leu Ser Phe Thr Ile Gln Asp Glu Asn Thr Ile Lys Leu
            1540                1545                1550

Asn Gly Val Tyr Leu Asp Glu Asn Gly Val Ala Glu Ile Leu Lys Phe
        1555                1560                1565

Met Asn Lys Lys Gly Ser Thr Asn Thr Ser Asp Ser Leu Met Ser Phe
    1570                1575                1580

Leu Glu Ser Met Asn Ile Lys Ser Ile Phe Ile Asn Ser Leu Gln Ser
1585                1590                1595                1600

Asn Thr Lys Leu Ile Leu Asp Thr Asn Phe Ile Ile Ser Gly Thr Thr
                1605                1610                1615

Ser Ile Gly Gln Phe Glu Phe Ile Cys Asp Lys Asp Asn Asn Ile Gln
            1620                1625                1630

Pro Tyr Phe Ile Lys Phe Asn Thr Leu Glu Thr Lys Tyr Thr Leu Tyr
        1635                1640                1645

Val Gly Asn Arg Gln Asn Met Ile Val Glu Pro Asn Tyr Asp Leu Asp
    1650                1655                1660

Asp Ser Gly Asp Ile Ser Ser Thr Val Ile Asn Phe Ser Gln Lys Tyr
1665                1670                1675                1680

Leu Tyr Gly Ile Asp Ser Cys Val Asn Lys Val Ile Ile Ser Pro Asn
                1685                1690                1695
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Ile Tyr Thr Asp Glu Ile Asn Ile Thr Pro Ile Tyr Glu Ala Asn Asn
            1700                1705                1710

Thr Tyr Pro Glu Val Ile Val Leu Asp Thr Asn Tyr Ile Ser Glu Lys
        1715                1720                1725

Ile Asn Ile Asn Ile Asn Asp Leu Ser Ile Arg Tyr Val Trp Ser Asn
    1730                1735                1740

Asp Gly Ser Asp Phe Ile Leu Met Ser Thr Asp Glu Glu Asn Lys Val
1745                1750                1755                1760

Ser Gln Val Lys Ile Arg Phe Thr Asn Val Phe Lys Gly Asn Thr Ile
                1765                1770                1775

Ser Asp Lys Ile Ser Phe Asn Phe Ser Asp Lys Gln Asp Val Ser Ile
            1780                1785                1790

Asn Lys Val Ile Ser Thr Phe Thr Pro Ser Tyr Tyr Val Glu Gly Leu
        1795                1800                1805

Leu Asn Tyr Asp Leu Gly Leu Ile Ser Leu Tyr Asn Glu Lys Phe Tyr
    1810                1815                1820

Ile Asn Asn Phe Gly Met Met Val Ser Gly Leu Val Tyr Ile Asn Asp
1825                1830                1835                1840

Ser Leu Tyr Tyr Phe Lys Pro Pro Ile Lys Asn Leu Ile Thr Gly Phe
                1845                1850                1855

Thr Thr Ile Gly Asp Asp Lys Tyr Tyr Phe Asn Pro Asp Asn Gly Gly
            1860                1865                1870

Ala Ala Ser Val Gly Glu Thr Ile Ile Asp Gly Lys Asn Tyr Tyr Phe
        1875                1880                1885

Ser Gln Asn Gly Val Leu Gln Thr Gly Val Phe Ser Thr Glu Asp Gly
    1890                1895                1900

Phe Lys Tyr Phe Ala Pro Ala Asp Thr Leu Asp Glu Asn Leu Glu Gly
1905                1910                1915                1920

Glu Ala Ile Asp Phe Thr Gly Lys Leu Thr Ile Asp Glu Asn Val Tyr
                1925                1930                1935

Tyr Phe Gly Asp Asn Tyr Arg Ala Ala Ile Glu Trp Gln Thr Leu Asp
            1940                1945                1950

Asp Glu Val Tyr Tyr Phe Ser Thr Asp Thr Gly Arg Ala Phe Lys Gly
        1955                1960                1965

Leu Asn Gln Ile Gly Asp Asp Lys Phe Tyr Phe Asn Ser Asp Gly Ile
    1970                1975                1980

Met Gln Lys Gly Phe Val Asn Ile Asn Asp Lys Thr Phe Tyr Phe Asp
1985                1990                1995                2000

Asp Ser Gly Val Met Lys Ser Gly Tyr Thr Glu Ile Asp Gly Lys Tyr
                2005                2010                2015

Phe Tyr Phe Ala Glu Asn Gly Glu Met Gln Ile Gly Val Phe Asn Thr
            2020                2025                2030

Ala Asp Gly Phe Lys Tyr Phe Ala His His Asp Glu Asp Leu Gly Asn
        2035                2040                2045

Glu Glu Gly Glu Ala Leu Ser Tyr Ser Gly Ile Leu Asn Phe Asn Asn
    2050                2055                2060

Lys Ile Tyr Tyr Phe Asp Asp Ser Phe Thr Ala Val Val Gly Trp Lys
2065                2070                2075                2080

Asp Leu Glu Asp Gly Ser Lys Tyr Tyr Phe Asp Glu Asp Thr Ala Glu
                2085                2090                2095
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Ala Tyr Ile Gly Ile Ser Ile Ile Asn Asp Gly Lys Tyr Tyr Phe Asn
            2100                2105                2110

Asp Ser Gly Ile Met Gln Ile Gly Phe Val Thr Ile Asn Asn Glu Val
        2115                2120                2125

Phe Tyr Phe Ser Asp Ser Gly Ile Val Glu Ser Gly Met Gln Asn Ile
    2130                2135                2140

Asp Asp Asn Tyr Phe Tyr Ile Asp Glu Asn Gly Leu Val Gln Ile Gly
2145                2150                2155                2160

Val Phe Asp Thr Ser Asp Gly Tyr Lys Tyr Phe Ala Pro Ala Asn Thr
                2165                2170                2175

Val Asn Asp Asn Ile Tyr Gly Gln Ala Val Glu Tyr Ser Gly Leu Val
            2180                2185                2190

Arg Val Gly Glu Asp Val Tyr Tyr Phe Gly Glu Thr Tyr Thr Ile Glu
        2195                2200                2205

Thr Gly Trp Ile Tyr Asp Met Glu Asn Glu Ser Asp Lys Tyr Tyr Phe
    2210                2215                2220

Asp Pro Glu Thr Lys Lys Ala Tyr Lys Gly Ile Asn Val Ile Asp Asp
2225                2230                2235                2240

Ile Lys Tyr Tyr Phe Asp Glu Asn Gly Ile Met Arg Thr Gly Leu Ile
                2245                2250                2255

Thr Phe Glu Asp Asn His Tyr Tyr Phe Asn Glu Asp Gly Ile Met Gln
            2260                2265                2270

Tyr Gly Tyr Leu Asn Ile Glu Asp Lys Thr Phe Tyr Phe Ser Glu Asp
        2275                2280                2285

Gly Ile Met Gln Ile Gly Val Phe Asn Thr Pro Asp Gly Phe Lys Tyr
    2290                2295                2300

Phe Ala His Gln Asn Thr Leu Asp Glu Asn Phe Glu Gly Glu Ser Ile
2305                2310                2315                2320

Asn Tyr Thr Gly Trp Leu Asp Leu Asp Glu Lys Arg Tyr Tyr Phe Thr
                2325                2330                2335

Asp Glu Tyr Ile Ala Ala Thr Gly Ser Val Ile Ile Asp Gly Glu Glu
            2340                2345                2350

Tyr Tyr Phe Asp Pro Asp Thr Ala Gln Leu Val Ile Ser Glu
        2355                2360                2365


<210> SEQ ID NO 12
<211> LENGTH: 2367
<212> TYPE: PRT
<213> ORGANISM: Clostridioides difficile
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 1..543
<223> OTHER INFORMATION: GTD domain
<220> FEATURE:
<223> OTHER INFORMATION: Toxin B 1470 (clade 4)
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 403..438
<223> OTHER INFORMATION: epitope
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 544..767
<223> OTHER INFORMATION: CPD domain
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 768..1852
<223> OTHER INFORMATION: TLD domain
<220> FEATURE:
<221> NAME/KEY: CHAIN
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<222> LOCATION: 1853..2366
<223> OTHER INFORMATION: CROPs
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 1875..2005
<223> OTHER INFORMATION: E1 domain
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 2006..2137
<223> OTHER INFORMATION: E2 domain
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 2138..2271
<223> OTHER INFORMATION: E3 domain
<220> FEATURE:
<221> NAME/KEY: CHAIN
<222> LOCATION: 2272..2366
<223> OTHER INFORMATION: E4 domain

<400> SEQUENCE: 12

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

Phe Arg Val Gln Glu Asp Glu Tyr Val Ala Ile Leu Asp Ala Leu Glu
            20 25 30

Glu Tyr His Asn Met Ser Glu Asn Thr Val Val Glu Lys Tyr Leu Lys
        35 40 45

Leu Lys Asp Ile Asn Ser Leu Thr Asp Thr Tyr Ile Asp Thr Tyr Lys
    50 55 60

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

Ile Glu Ile Leu Glu Leu Lys Asn Ser Asn Leu Thr Pro Val Glu Lys
                85 90 95

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

Asn Tyr Ile Asn Gln Trp Lys Asp Val Asn Ser Asp Tyr Asn Val Asn
        115 120 125

Val Phe Tyr Asp Ser Asn Ala Phe Leu Ile Asn Thr Leu Lys Lys Thr
    130 135 140

Ile Ile Glu Ser Ala Ser Asn Asp Thr Leu Glu Ser Phe Arg Glu Asn
145 150 155 160

Leu Asn Asp Pro Glu Phe Asn His Thr Ala Phe Phe Arg Lys Arg Met
                165 170 175

Gln Ile Ile Tyr Asp Lys Gln Gln Asn Phe Ile Asn Tyr Tyr Lys Ala
            180 185 190

Gln Lys Glu Glu Asn Pro Asp Leu Ile Ile Asp Asp Ile Val Lys Thr
        195 200 205

Tyr Leu Ser Asn Glu Tyr Ser Lys Asp Ile Asp Glu Leu Asn Ala Tyr
    210 215 220

Ile Glu Glu Ser Leu Asn Lys Val Thr Glu Asn Ser Gly Asn Asp Val
225 230 235 240

Arg Asn Phe Glu Glu Phe Lys Thr Gly Glu Val Phe Asn Leu Tyr Glu
                245 250 255

Gln Glu Ser Val Glu Arg Trp Asn Leu Ala Gly Ala Ser Asp Ile Leu
            260 265 270

Arg Val Ala Ile Leu Lys Asn Ile Gly Gly Val Tyr Leu Asp Val Asp
        275 280 285

Met Leu Pro Gly Ile His Pro Asp Leu Phe Lys Asp Ile Asn Lys Pro

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    290                 295                 300

Asp Ser Val Lys Thr Ala Val Asp Trp Glu Glu Met Gln Leu Glu Ala
305                 310                 315                 320

Ile Met Lys His Lys Glu Tyr Ile Pro Glu Tyr Thr Ser Lys His Phe
                325                 330                 335

Asp Thr Leu Asp Glu Glu Val Gln Ser Ser Phe Glu Ser Val Leu Ala
            340                 345                 350

Ser Lys Ser Asp Lys Ser Glu Ile Phe Leu Pro Leu Gly Asp Ile Glu
        355                 360                 365

Val Ser Pro Leu Glu Val Lys Ile Ala Phe Ala Lys Gly Ser Ile Ile
    370                 375                 380

Asn Gln Ala Leu Ile Ser Ala Lys Asp Ser Tyr Cys Ser Asp Leu Leu
385                 390                 395                 400

Ile Lys Gln Ile Gln Asn Arg Tyr Lys Ile Leu Asn Asp Thr Leu Gly
                405                 410                 415

Pro Ile Ile Ser Gln Gly Asn Asp Phe Asn Thr Thr Met Asn Asn Phe
            420                 425                 430

Gly Glu Ser Leu Gly Ala Ile Ala Asn Glu Glu Asn Ile Ser Phe Ile
        435                 440                 445

Ala Lys Ile Gly Ser Tyr Leu Arg Val Gly Phe Tyr Pro Glu Ala Asn
    450                 455                 460

Thr Thr Ile Thr Leu Ser Gly Pro Thr Ile Tyr Ala Gly Ala Tyr Lys
465                 470                 475                 480

Asp Leu Leu Thr Phe Lys Glu Met Ser Ile Asp Thr Ser Ile Leu Ser
                485                 490                 495

Ser Glu Leu Arg Asn Phe Glu Phe Pro Lys Val Asn Ile Ser Gln Ala
            500                 505                 510

Thr Glu Gln Glu Lys Asn Ser Leu Trp Gln Phe Asn Glu Glu Arg Ala
        515                 520                 525

Lys Ile Gln Phe Glu Glu Tyr Lys Lys Asn Tyr Phe Glu Gly Ala Leu
    530                 535                 540

Gly Glu Asp Asp Asn Leu Asp Phe Ser Gln Asn Thr Val Thr Asp Lys
545                 550                 555                 560

Glu Tyr Leu Leu Glu Lys Ile Ser Ser Ser Thr Lys Ser Ser Glu Gly
                565                 570                 575

Gly Tyr Val His Tyr Ile Val Gln Leu Gln Gly Asp Lys Ile Ser Tyr
            580                 585                 590

Glu Ala Ala Cys Asn Leu Phe Ala Lys Asn Pro Tyr Asp Ser Ile Leu
        595                 600                 605

Phe Gln Arg Asn Ile Glu Asp Ser Glu Val Ala Tyr Tyr Tyr Asn Pro
    610                 615                 620

Thr Asp Ser Glu Ile Gln Glu Ile Asp Lys Tyr Arg Ile Pro Asp Arg
625                 630                 635                 640

Ile Ser Asp Arg Pro Lys Ile Lys Leu Thr Phe Ile Gly His Gly Lys
                645                 650                 655

Ala Glu Phe Asn Thr Asp Ile Phe Ala Gly Leu Asp Val Asp Ser Leu
            660                 665                 670

Ser Ser Glu Ile Glu Thr Ala Ile Gly Leu Ala Lys Glu Asp Ile Ser
        675                 680                 685

Pro Lys Ser Ile Glu Ile Asn Leu Leu Gly Cys Asn Met Phe Ser Tyr
    690                 695                 700
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Ser Val Asn Val Glu Glu Thr Tyr Pro Gly Lys Leu Leu Leu Arg Val
705                 710                 715                 720

Lys Asp Lys Val Ser Glu Leu Met Pro Ser Met Ser Gln Asp Ser Ile
                725                 730                 735

Ile Val Ser Ala Asn Gln Tyr Glu Val Arg Ile Asn Ser Glu Gly Arg
            740                 745                 750

Arg Glu Leu Leu Asp His Ser Gly Glu Trp Ile Asn Lys Glu Glu Ser
        755                 760                 765

Ile Ile Lys Asp Ile Ser Ser Lys Glu Tyr Ile Ser Phe Asn Pro Lys
    770                 775                 780

Glu Asn Lys Ile Ile Val Lys Ser Lys Asn Leu Pro Glu Leu Ser Thr
785                 790                 795                 800

Leu Leu Gln Glu Ile Arg Asn Asn Ser Asn Ser Ser Asp Ile Glu Leu
                805                 810                 815

Glu Glu Lys Val Met Leu Ala Glu Cys Glu Ile Asn Val Ile Ser Asn
            820                 825                 830

Ile Glu Thr Gln Val Val Glu Glu Arg Ile Glu Glu Ala Lys Ser Leu
        835                 840                 845

Thr Ser Asp Ser Ile Asn Tyr Ile Lys Asn Glu Phe Lys Leu Ile Glu
    850                 855                 860

Ser Ile Ser Glu Ala Leu Cys Asp Leu Lys Gln Gln Asn Glu Leu Glu
865                 870                 875                 880

Asp Ser His Phe Ile Ser Phe Glu Asp Ile Ser Glu Thr Asp Glu Gly
                885                 890                 895

Phe Ser Ile Arg Phe Ile Asn Lys Glu Thr Gly Glu Ser Ile Phe Val
            900                 905                 910

Glu Thr Glu Lys Thr Ile Phe Ser Glu Tyr Ala Asn His Ile Thr Glu
        915                 920                 925

Glu Ile Ser Lys Ile Lys Gly Thr Ile Phe Asp Thr Val Asn Gly Lys
    930                 935                 940

Leu Val Lys Lys Val Asn Leu Asp Thr Thr His Glu Val Asn Thr Leu
945                 950                 955                 960

Asn Ala Ala Phe Phe Ile Gln Ser Leu Ile Glu Tyr Asn Ser Ser Lys
                965                 970                 975

Glu Ser Leu Ser Asn Leu Ser Val Ala Met Lys Val Gln Val Tyr Ala
            980                 985                 990

Gln Leu Phe Ser Thr Gly Leu Asn Thr Ile Thr Asp Ala Ala Lys Val
        995                 1000                1005

Val Glu Leu Val Ser Thr Ala Leu Asp Glu Thr Ile Asp Leu Leu Pro
    1010                1015                1020

Thr Leu Ser Glu Gly Leu Pro Ile Ile Ala Thr Ile Ile Asp Gly Val
1025                1030                1035                1040

Ser Leu Gly Ala Ala Ile Lys Glu Leu Ser Glu Thr Ser Asp Pro Leu
                1045                1050                1055

Leu Arg Gln Glu Ile Glu Ala Lys Ile Gly Ile Met Ala Val Asn Leu
            1060                1065                1070

Thr Thr Ala Thr Thr Ala Ile Ile Thr Ser Ser Leu Gly Ile Ala Ser
        1075                1080                1085

Gly Phe Ser Ile Leu Leu Val Pro Leu Ala Gly Ile Ser Ala Gly Ile
    1090                1095                1100
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Pro Ser Leu Val Asn Asn Glu Leu Val Leu Arg Asp Lys Ala Thr Lys
1105                1110                1115                1120

Val Val Asp Tyr Phe Lys His Val Ser Leu Val Glu Thr Glu Gly Val
                1125                1130                1135

Phe Thr Leu Leu Asp Asp Lys Val Met Met Gln Gln Asp Asp Leu Val
            1140                1145                1150

Ile Ser Glu Ile Asp Phe Asn Asn Asn Ser Ile Val Leu Gly Lys Cys
        1155                1160                1165

Glu Ile Trp Arg Met Glu Gly Gly Ser Gly His Thr Val Thr Asp Asp
    1170                1175                1180

Ile Asp His Phe Phe Ser Ala Pro Ser Ile Thr Tyr Arg Glu Pro His
1185                1190                1195                1200

Leu Ser Ile Tyr Asp Val Leu Glu Val Gln Lys Glu Glu Leu Asp Leu
                1205                1210                1215

Ser Lys Asp Leu Met Val Leu Pro Asn Ala Pro Asn Arg Val Phe Ala
            1220                1225                1230

Trp Glu Thr Gly Trp Thr Pro Gly Leu Arg Ser Leu Glu Asn Asp Gly
        1235                1240                1245

Thr Lys Leu Leu Asp Arg Ile Arg Asp Asn Tyr Glu Gly Glu Phe Tyr
    1250                1255                1260

Trp Arg Tyr Phe Ala Phe Ile Ala Asp Ala Leu Ile Thr Thr Leu Lys
1265                1270                1275                1280

Pro Arg Tyr Glu Asp Thr Asn Ile Arg Ile Asn Leu Asp Ser Asn Thr
                1285                1290                1295

Arg Ser Phe Ile Val Pro Ile Ile Thr Thr Glu Tyr Ile Arg Glu Lys
            1300                1305                1310

Leu Ser Tyr Ser Phe Tyr Gly Ser Gly Gly Thr Tyr Ala Leu Pro Leu
        1315                1320                1325

Ser Gln Tyr Asn Met Gly Ile Asn Ile Glu Leu Ser Glu Ser Asp Val
    1330                1335                1340

Trp Ile Ile Asp Val Asp Asn Val Val Arg Asp Val Thr Ile Glu Ser
1345                1350                1355                1360

Asp Lys Ile Lys Lys Gly Asp Leu Ile Glu Gly Ile Leu Ser Thr Leu
                1365                1370                1375

Ser Ile Glu Glu Asn Lys Ile Ile Leu Asn Ser His Glu Ile Asn Phe
            1380                1385                1390

Ser Gly Glu Val Asn Gly Ser Asn Gly Phe Val Ser Leu Thr Phe Ser
        1395                1400                1405

Ile Leu Glu Gly Ile Asn Ala Ile Ile Glu Val Asp Leu Leu Ser Lys
    1410                1415                1420

Ser Tyr Lys Leu Leu Ile Ser Gly Glu Leu Lys Ile Leu Met Leu Asn
1425                1430                1435                1440

Ser Asn His Ile Gln Gln Lys Ile Asp Tyr Ile Gly Phe Asn Ser Glu
                1445                1450                1455

Leu Gln Lys Asn Ile Pro Tyr Ser Phe Val Asp Ser Glu Gly Lys Glu
            1460                1465                1470

Asn Gly Phe Ile Asn Gly Ser Thr Lys Glu Gly Leu Phe Val Ser Glu
        1475                1480                1485

Leu Pro Asp Val Val Leu Ile Ser Lys Val Tyr Met Asp Asp Ser Lys
    1490                1495                1500

Pro Ser Phe Gly Tyr Tyr Ser Asn Asn Leu Lys Asp Val Lys Val Ile
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Thr Lys Asp Asn Val Asn Ile Leu Thr Gly Tyr Tyr Leu Lys Asp Asp
                1525                1530                1535

Ile Lys Ile Ser Leu Ser Leu Thr Leu Gln Asp Glu Lys Thr Ile Lys
            1540                1545                1550

Leu Asn Ser Val His Leu Asp Glu Ser Gly Val Ala Glu Ile Leu Lys
        1555                1560                1565

Phe Met Asn Arg Lys Gly Ser Thr Asn Thr Ser Asp Ser Leu Met Ser
    1570                1575                1580

Phe Leu Glu Ser Met Asn Ile Lys Ser Ile Phe Val Asn Phe Leu Gln
1585                1590                1595                1600

Ser Asn Ile Lys Phe Ile Leu Asp Ala Asn Phe Ile Ile Ser Gly Thr
                1605                1610                1615

Thr Ser Ile Gly Gln Phe Glu Phe Ile Cys Asp Glu Asn Asn Asn Ile
            1620                1625                1630

Gln Pro Tyr Phe Ile Lys Phe Asn Thr Leu Glu Thr Asn Tyr Thr Leu
        1635                1640                1645

Tyr Val Gly Asn Arg Gln Asn Met Ile Val Glu Pro Asn Tyr Asp Leu
    1650                1655                1660

Asp Asp Ser Gly Asp Ile Ser Ser Thr Val Ile Asn Phe Ser Gln Lys
1665                1670                1675                1680

Tyr Leu Tyr Gly Ile Asp Ser Cys Val Asn Lys Val Val Ile Ser Pro
                1685                1690                1695

Asn Ile Tyr Thr Asp Glu Ile Asn Ile Thr Pro Val Tyr Glu Thr Asn
            1700                1705                1710

Asn Thr Tyr Pro Glu Val Ile Val Leu Asp Ala Asn Tyr Ile Asn Glu
        1715                1720                1725

Lys Ile Asn Val Asn Ile Asn Asp Leu Ser Ile Arg Tyr Val Trp Ser
    1730                1735                1740

Asn Asp Gly Asn Asp Phe Ile Leu Met Ser Thr Ser Glu Glu Asn Lys
1745                1750                1755                1760

Val Ser Gln Val Lys Ile Arg Phe Val Asn Val Phe Lys Asp Lys Thr
                1765                1770                1775

Leu Ala Asn Lys Leu Ser Phe Asn Phe Ser Asp Lys Gln Asp Val Pro
            1780                1785                1790

Val Ser Glu Ile Ile Leu Ser Phe Thr Pro Ser Tyr Tyr Glu Asp Gly
        1795                1800                1805

Leu Ile Gly Tyr Asp Leu Gly Leu Val Ser Leu Tyr Asn Glu Lys Phe
    1810                1815                1820

Tyr Ile Asn Asn Phe Gly Met Met Val Ser Gly Leu Ile Tyr Ile Asn
1825                1830                1835                1840

Asp Ser Leu Tyr Tyr Phe Lys Pro Pro Val Asn Asn Leu Ile Thr Gly
                1845                1850                1855

Phe Val Thr Val Gly Asp Asp Lys Tyr Tyr Phe Asn Pro Ile Asn Gly
            1860                1865                1870

Gly Ala Ala Ser Ile Gly Glu Thr Ile Ile Asp Asp Lys Asn Tyr Tyr
        1875                1880                1885

Phe Asn Gln Ser Gly Val Leu Gln Thr Gly Val Phe Ser Thr Glu Asp
    1890                1895                1900

Gly Phe Lys Tyr Phe Ala Pro Ala Asn Thr Leu Asp Glu Asn Leu Glu
1905                1910                1915                1920
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Gly Glu Ala Ile Asp Phe Thr Gly Lys Leu Ile Ile Asp Glu Asn Ile
                1925                1930                1935

Tyr Tyr Phe Glu Asp Asn Tyr Arg Gly Ala Val Glu Trp Lys Glu Leu
            1940                1945                1950

Asp Gly Glu Met His Tyr Phe Ser Pro Glu Thr Gly Lys Ala Phe Lys
        1955                1960                1965

Gly Leu Asn Gln Ile Gly Asp Asp Lys Tyr Tyr Phe Asn Ser Asp Gly
    1970                1975                1980

Val Met Gln Lys Gly Phe Val Ser Ile Asn Asp Asn Lys His Tyr Phe
1985                1990                1995                2000

Asp Asp Ser Gly Val Met Lys Val Gly Tyr Thr Glu Ile Asp Gly Lys
                2005                2010                2015

His Phe Tyr Phe Ala Glu Asn Gly Glu Met Gln Ile Gly Val Phe Asn
            2020                2025                2030

Thr Glu Asp Gly Phe Lys Tyr Phe Ala His His Asn Glu Asp Leu Gly
        2035                2040                2045

Asn Glu Glu Gly Glu Glu Ile Ser Tyr Ser Gly Ile Leu Asn Phe Asn
    2050                2055                2060

Asn Lys Ile Tyr Tyr Phe Asp Asp Ser Phe Thr Ala Val Val Gly Trp
2065                2070                2075                2080

Lys Asp Leu Glu Asp Gly Ser Lys Tyr Tyr Phe Asp Glu Asp Thr Ala
                2085                2090                2095

Glu Ala Tyr Ile Gly Leu Ser Leu Ile Asn Asp Gly Gln Tyr Tyr Phe
            2100                2105                2110

Asn Asp Asp Gly Ile Met Gln Val Gly Phe Val Thr Ile Asn Asp Lys
        2115                2120                2125

Val Phe Tyr Phe Ser Asp Ser Gly Ile Ile Glu Ser Gly Val Gln Asn
    2130                2135                2140

Ile Asp Asp Asn Tyr Phe Tyr Ile Asp Asp Asn Gly Ile Val Gln Ile
2145                2150                2155                2160

Gly Val Phe Asp Thr Ser Asp Gly Tyr Lys Tyr Phe Ala Pro Ala Asn
                2165                2170                2175

Thr Val Asn Asp Asn Ile Tyr Gly Gln Ala Val Glu Tyr Ser Gly Leu
            2180                2185                2190

Val Arg Val Gly Glu Asp Val Tyr Tyr Phe Gly Glu Thr Tyr Thr Ile
        2195                2200                2205

Glu Thr Gly Trp Ile Tyr Asp Met Glu Asn Glu Ser Asp Lys Tyr Tyr
    2210                2215                2220

Phe Val Pro Glu Thr Lys Lys Ala Cys Lys Gly Ile Asn Leu Ile Asp
2225                2230                2235                2240

Asp Ile Lys Tyr Tyr Phe Asp Glu Lys Gly Ile Met Arg Thr Gly Leu
                2245                2250                2255

Ile Ser Phe Glu Asn Asn Asn Tyr Tyr Phe Asn Glu Asn Gly Glu Ile
            2260                2265                2270

Gln Phe Gly Tyr Ile Asn Ile Glu Asp Lys Met Phe Tyr Phe Gly Glu
        2275                2280                2285

Asp Gly Val Met Gln Ile Gly Val Phe Asn Thr Pro Asp Gly Phe Lys
    2290                2295                2300

Tyr Phe Ala His Gln Asn Thr Leu Asp Glu Asn Phe Glu Gly Glu Ser
2305                2310                2315                2320
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Ile Asn Tyr Thr Gly Trp Leu Gly Leu Asp Glu Lys Arg Tyr Tyr Phe
                2325                2330                2335

Thr Asp Glu Tyr Ile Ala Ala Thr Gly Ser Val Ile Ile Asp Gly Glu
            2340                2345                2350

Glu Tyr Tyr Phe Asp Pro Asp Thr Ala Gln Leu Val Ile Ser Glu
        2355                2360                2365


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Gln Ile Xaa Asn Arg Tyr Lys Ile Leu Asn Xaa Xaa Leu Asn Pro Xaa
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Ile Ser Xaa Xaa Asn Asp Phe Asn Thr Thr Xaa Asn Xaa Phe Xaa Xaa
            20                  25                  30

Ser Xaa Xaa Ala
        35
```

1. Antigenic peptide for use in the treatment or prevention of an infection by *Clostridioides difficile*, the peptide comprising the epitope of SEQ ID NO: 13, which peptide is devoid of an amino acid sequence of amino acids No. 2138 to 2271 of SEQ ID NO: 2 and/or is devoid of amino acids No. 2272 to 2366 of SEQ ID NO: 2.

2. Antigenic peptide for use in the treatment or prevention of an infection by *Clostridioides difficile* according to claim **1**, wherein the peptide is devoid of the amino acid sequence of the CPD and of the amino acid sequence of the CROPs of a sequence having at least 90% homology to SEQ ID NO: 2.

3. Antigenic peptide for use in the treatment or prevention of an infection by *Clostridioides difficile* according to claim **1**, wherein the peptide does not contain one or more of the group consisting of a catalytically active GTD, a functional TLD, a catalytically active CPD, and the CROPs.

4. Antigenic peptide for use in the treatment or prevention of an infection by *Clostridioides difficile* according to claim **1**, wherein the antigenic peptide as a continuous segment of *Clostridioides difficile* toxin B comprises only the fraction of amino acids of SEQ ID NO: 3 or SEQ ID NO: 4, wherein the peptide optionally contains further epitopes of *Clostridioides difficile* toxin A and/or toxin B, which further epitopes are contained in segments which do not contain a catalytically active GTD, nor a catalytically active CPD, nor the CROPs.

5. Antigenic peptide for use in the treatment or prevention of an infection by *Clostridioides difficile* according to claim **1**, wherein the antigenic peptide does not contain additional epitopes of *Clostridioides difficile* toxin B.

6. Antigenic peptide for use in the treatment or prevention of an infection by *Clostridioides difficile* according to claim **1**, comprising at least two copies of the epitope of SEQ ID NO: 13.

7. Antigenic peptide for use in the treatment or prevention of an infection by *Clostridioides difficile* according to claim **1**, comprising at least one or at least two of the epitopes of amino acid Nos. 322 to 325 and/or of amino acid Nos. 340 to 351, and/or the domain of amino acid Nos. 290 to 360 of SEQ ID NO: 2 or of SEQ ID NO: 11.

8. Binding peptide for use in the treatment or prevention of an infection by *Clostridioides difficile*, the peptide comprising a paratope of framework regions (FR) and of complementarity determining regions (CDR) in an arrangement of FR1-CDR1-FR2-CDR2-FR3-CDR3, preferably additionally FR4, wherein the heavy chain complementarity determining regions (CDRH) are

CDRH1 consisting of amino acids 26 to 33 of SEQ ID NO: 5,

CDRH2 consisting of amino acids 51 to 58 of SEQ ID NO: 5,

CDRH3 consisting of amino acids 97 to 112 of SEQ ID NO: 5,

or

CDRH1 consisting of amino acids 26 to 33 of SEQ ID NO: 7,

CDRH2 consisting of amino acids 51 to 58 of SEQ ID NO: 7, and

CDRH3 consisting of amino acids 97 to 117 of SEQ ID NO: 7.

9. Binding peptide for use according to claim **8**, wherein the

FR1 consists of amino acids 1 to 25 of SEQ ID NO: 5,
FR2 consists of amino acids 34 to 50 of SEQ ID NO: 5,
FR3 consists of amino acids 59 to 96 of SEQ ID NO: 5,
and optional FR4 consists of amino acids 113 to 123 of SEQ ID NO: 5,

or

FR1 consists of amino acids 1 to 25 of SEQ ID NO: 7,
FR2 consists of amino acids 34 to 50 of SEQ ID NO: 7,
FR3 consists of amino acids 59 to 96 of SEQ ID NO: 7,
and optional FR4 consists of amino acids 118 to 128 of SEQ ID NO: 7

10. Binding peptide for use according to claim **8**, comprising a light chain of FR1-CDR1-FR2-CDR2-FR3-CDR3, preferably additionally FR4, with the light chain complementarity determining regions (CDRL)

CDRL1 consisting of amino acids 26 to 34 of SEQ ID NO: 6,

CDRL2 consisting of amino acids 52 to 54 of SEQ ID NO: 6,

CDRL3 consisting of amino acids 91 to 101 of SEQ ID NO: 6,

or

CDRL1 consisting of amino acids 25 to 33 of SEQ ID NO: 8,

CDRL2 consisting of amino acids 51 to 53 of SEQ ID NO: 8,

CDRL3 consisting of amino acids 90 to 100 of SEQ ID NO: 8.

11. Binding peptide for use according to claim **10**, wherein the framework regions (FR) of the light chain are

FR1 consisting of amino acids 1 to 25 of SEQ ID NO: 6,

FR2 consisting of amino acids 35 to 51 of SEQ ID NO: 6,

FR3 consisting of amino acids 55 to 90 of SEQ ID NO: 6,

and optional FR4 consisting of amino acids 102 to 111 of SEQ ID NO: 6

or

FR1 consisting of amino acids 1 to 24 of SEQ ID NO: 8,

FR2 consisting of amino acids 34 to 50 of SEQ ID NO: 8,

FR3 consisting of amino acids 54 to 89 of SEQ ID NO: 8,

and optional FR4 consisting of amino acids 101 to 110 of SEQ ID NO: 8.

12. Binding peptide for use according to claim **8**, wherein the paratope is contained in an IgG, IgM, IgA or IgE, scFv, scFv-Fc, minibody or diabody.

13. Process for producing and/or selecting binding peptides directed against *Clostridioides difficile* toxin B, characterized by the use of an antigenic peptide according to claim **1**.

* * * * *