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TI_WPI: Reducing and/or delaying pathological effects of HIV or reducing risk of developing AIDS in human infected with HIV, by measuring amount of antibodies against epitope of HIV envelope glycoproteins (gp)l20 or gp41 and treating humans

AB_WPI: NOVELTY: Method for reducing and/or delaying pathological effects of HIV or for reducing the risk of developing AIDS in a human infected with HIV, involves (a) measuring amount of antibodies against one or more epitope of HIV envelope glycoproteins (gp)l20 and/or gp41 in a suitable assay in a biological sample, such as serum or plasma, from a human infected with HIV, (b) selecting a subgroup of humans from (a), and (c) treating humans infected with HIV selected under (b) with one or more peptide(s).

DESCRIPTION: Method for reducing and/or delaying pathological effects of HIV or for reducing the risk of developing AIDS in a human infected with HIV, involves (a) measuring amount of antibodies against one or more epitope of HIV envelope glycoproteins (gp)l20 and/or gp41 in a suitable assay in a biological sample, such as serum or plasma, from a human infected with HIV, (b) selecting a subgroup of humans from (a), where the amount of measured antibodies corresponds to an amount of above background level of uninfected humans, such as above 1 μ g/ml of antibodies against Vacc-C5 in serum as measured by an enzyme-linked immunosorbent assay (ELISA) assay, and (c) treating humans infected with HIV selected under (b) with one or more peptide(s) to stimulate a cell-mediated immune response and/or a compound that stimulate a humoral response in human. An INDEPENDENT CLAIM is included for kit, which comprises test assay for measuring in a biological sample, such as serum or plasma, one or more peptide to stimulate a cell-mediated immune response and/or a compound that stimulate a humoral response in human, and optionally one or more immunomodulatory compound and/or a reservoir purging agent.

ACTIVITY: Anti-HIV. Test details are described but no results given.

MECHANISM OF ACTION: None given.

USE: The method is useful for reducing and/or delaying pathological effects of HIV or for reducing risk of developing AIDS in a human infected with AIDS (claimed).

BIOTECHNOLOGY: Preferred Biomolecule: The amino acid sequence of SEQ ID NO: 47 is 20 amino acid sequence (SEQ ID NO: 48 or 49) fully defined in the specification. The amino acid sequence of SEQ ID NO: 50 is one of 4 (23-24) amino acid sequence (SEQ ID NOs: 51-54) all fully defined in the specification. The amino acid sequence of SEQ ID NO: 55 is one of 5 (22-26) amino acid sequence (SEQ ID NOs: 57-60) all fully defined in the specification. The amino acid sequence of SEQ ID NO: 61 is one of 5 (24-28) amino acid sequence (SEQ ID NOs: 62-66) all fully defined in the specification. One or more peptide is in the form of an acetate salt. One, two, three or four peptides are used in the therapeutic HIV-1 immunization phase. All four peptide as acetate salts are used in the therapeutic HIV-1 immunization phase. The peptides have amide C-terminal ends of formula -C(O)NH_2, or its acetate salts. All four peptide are used in the ratio of 1:1:1:1 weight/weight. One, two, three or four peptide acetate salts are in a dissolved liquid state. The liquid is water. At least one compound that stimulate a humoral response stabilizing association of the C5 domain of HIV gpl20 with the transmembrane domain of gp41 and/or with the constant C2 domain of gpl20 is a molecule comprising at least one amino acid sequence selected independently from an amino acid sequence derived from the transmembrane domain of gp41 and an amino acid sequence derived from the C2 domain, where the at least one amino acid sequence binds the C5 domain, optionally comprising at least one D-amino acid. The molecule is a peptide. The peptide consists of at least one amino acid sequence. The amino acid sequence derived from the transmembrane domain of gp41 has an amino acid sequence of at most 10 amino acid residues. The agent is a peptide multimer comprising a first peptide comprising the amino acid sequence of the 13 amino acid residue amino acid sequence of the C5 domain of HIV gpl20 including between 0 and 4 amino acid substitutions, a subsequence, or an amino acid sequence comprising the inverso-, retro- or retro-inverso form of amino acid sequence or subsequence, and at least one second peptide comprising an amino acid stretch present in the transmembrane domain of gp41 or present in the constant C2 domain of gpl20 or comprising an amino acid stretch or comprising a inverso-, retro- or retro-inverso form of an amino acid stretch present in the transmembrane domain of gp41 or present in the constant C2 domain of gpl20, where peptide multimer is capable of inducing an antibody which can bind and stabilise the association of the C5 domain of HIV gpl20 with the transmembrane domain of gp41 and/or with the constant C2 domain of gpl20, and where peptide multimer lacks amino acids N-terminal of C5 in gpl20. The first peptide further comprises dipeptide Ala-Pro linked to the N-terminus of the amino acid sequence. The second peptide includes at least 5 consecutive amino acid residues. The first peptide and the at least one second peptide are associated through linker. The linker is chosen from bis-maleimide linker, a disulfide linker, a polyethylene glycol (PEG) linker, a glycine linker, a lysine linker, and an arginine linker. At least one of the first and at least one second peptides comprises an N- or C-terminal modification, such as an amidation, acylation, or acetylation. The peptide multimer is coupled to a carrier molecule, such as an immunogenic carrier. The carrier is a virus like particle. The peptide multimer comprises at most 70 amino acids. The peptide multimer comprises at least 6 amino acid residues. The peptide multimer comprises number of amino acid residues chosen from 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, and 70 amino acid residues. The peptide multimer comprises one of 15 (16-31) amino acid sequences (SEQ ID NO: 28-33, 39-43 and 68) all fully defined in the specification. The peptide multimer is (H-Gly-Ala-Lys-Arg-Arg-Val-Val-Gly-Gly-Cys(2-oxo-ethyl)-Gly-Gly-Ala-Lys-Arg-Arg-Val-Val-Gln-Arg-Glu-Lys-Arg-Ala-Gly-Glu-Arg-Glu-Lys-Arg-Ala-NH2) (H-Gly-Lys-Gly-Gly-Ile-Glu-Glu-Glu-Gly-Gly-Arg-Asp-Arg-Asp-Arg-Gly-Gly-Gln-Asp-Arg-Asp-Arg-NH2), acetate salt (amide bond between Cys(2-oxo-ethyl)10 (A-chain) and Lys2 (B-

chain)). Preferred Method: The human under step (c) is treated with one or more peptides that elicit a cell-mediated immune response in a subject. One or more peptide that stimulate cell-mediated immune response is at least one HIV-specific peptide chosen from amino acid sequences of SEQ ID NOs: 47, 50, 55 and 61. The method further involves administering immunomodulatory compound and/or a reservoir purging agent, such as a histone deacetylase (HDAC) inhibitor, and adjuvant, such as recombinant human granulocyte-macrophage colony-stimulating factor (rhuGM-CSF). The immunomodulatory compound is chosen from anti-programmed cell death protein 1 (PD1) antibodies, such as MDX-1106 (Merck), THALOMID (RTM: Thalidomide), cyclophosphamide, levamisole, lenalidomide, pomalidomide, and celgene. The immunomodulatory compound is chosen from 4-(amino)-2-(2,6-dioxo(3-piperidyl))-isoindoline-1,3-dione and a 3-(4-amino-1-oxo-1,3-dihydro-isoindol-2-yl)-piperidine-2,6-dione. Xaa1-Xaa2-Xaa3-Xaa4-Xaa5-Xaa6-Ala-Xaa7-Xaa8-Gln-Thr-Pro-Trp-Xaa9-Xaa10-Xaa11-Xaa12-Xaa13-Val-Xaa14 (SEQ ID NO: 47), Xaa15-Xaa16-Xaa17-Xaa18-Xaa19-Gly-Leu-Asn-Pro-Leu-Val-$[Gly]_n$-Xaa20-Xaa21-Tyr-Xaa22-Pro-Xaa23-Xaa24-Ile-Leu-Xaa25-Xaa26 (SEQ ID NO: 50), Xaa27-Xaa28-Xaa29-Pro-Ile-Pro-Xaa30-Xaa31-Xaa32-Xaa33-Xaa34-Xaa35-[Gly]n-Xaa36-Xaa37-Xaa38-Xaa39-Xaa40-Xaa41-Xaa42-Xaa43-Xaa44-Xaa45-Xaa46-Xaa47 (SEQ ID NO: 55), Xaa48-Xaa49-Ile-Ile-Xaa50-Xaa51-Xaa52-Xaa53-Xaa54-Leu-Xaa55$[Gly]_n$-$[Arg]_m$-Xaa56-Xaa57-Xaa58-Xaa59-Xaa60-Xaa61-Xaa62-Xaa63-Xaa64-Xaa65-Xaa66-Xaa67-Xaa68-Xaa69 (SEQ ID NO: 61).
Xaa1 := Lys or Arg;
Xaa2 := Ala, Gly, Ser or Arg;
Xaa3 := Leu or Met;
Xaa4 := Gly or Arg;
Xaa5 := Pro, Thr, Val, Ser, Gln or Ala;
Xaa6 := Gly, Ala, Lys, Arg, Gln or Glu;
Xaa7 := Thr or Ser;
Xaa8 := Leu or Ile;
Xaa9 := Thr, Ser or Val;
Xaa10 := Ala or Ser;
Xaa11 := Cys or Ser;
Xaa12 := Gln or Leu;
Xaa13 := Gly, Glu or Arg;
Xaa14 := Gly or Arg;
Xaa15 := Arg, Lys, Asp or none;
Xaa16 := Trp, Gly, Lys or Arg;
Xaa17 := Ile, Leu, Val or Met;
Xaa18 := Ile, Val or Leu;
Xaa19 := Leu, Met, Val or Pro;
Xaa20 := Arg or Lys;
Xaa21 := Met or Leu;
Xaa22 := Ser, Cys or Gln;
Xaa23 := Thr, Val, Ile, Ser or Ala;
Xaa24 := Ser, Gly or Thr;
Xaa25 := Asp, Glu, Cys or Gly;
Xaa26 := Gly or none;
Xaa27 := Asn, Ser, Gly, His, Ala, Pro, Arg or none;
Xaa28 := Asn, Ala or Lys;
Xaa29 := Pro, Gln, Gly, He or Leu;
Xaa30 := Val or Ala;
Xaa31 := Gly or Lys;
Xaa32 := Glu, Asp, Lys, Phe or Thr;
Xaa33 := Ile, Met, Val or Leu;
Xaa34 := Tyr, Leu or none;
Xaa35 := Ser or none;
Xaa36 := Arg or none;
Xaa37 := Asp, Arg, Trp, Ala or none;
Xaa38 := Ile or none;
Xaa39 := Tyr or none;
Xaa40 := Lys or Arg;
Xaa41 := Arg, Lys or Asp;
Xaa42 := Trp or Gly;
Xaa43 := Ile, Met, Val, Gln or Ala;
Xaa44 := Ile, Val or Ala;
Xaa45 := Leu, Met or Val;
Xaa46 := Gly or Cys;
Xaa47 := Leu or none;
Xaa48 := Pro, Lys, Arg or none;
Xaa49 := Glu, Arg, Phe or Lys;
Xaa50 := Pro or Thr;
Xaa51 := Met, Thr or leu;
Xaa52 := Phe or Leu;
Xaa53 := Ser, Thr, Ala or Met;
Xaa54 := Ala, Glu or Leu;
Xaa55 := Ser or none;
Xaa56 := Ala, Arg or none;
Xaa57 := Ile, Leu or none;
Xaa58 := Ser, Ala, Leu or none;
Xaa59 := Tyr, Glu or Asp;
Xaa60 := Gly or Asp;
Xaa61 := Ala or Leu;
Xaa62 := Thr, lie, Val, Leu or Asn;
Xaa63 := Pro, Thr or Ser;
Xaa64 := Tyr, Phe, Leu, His or Gln;
Xaa65 := Asp, Asn, Leu or Ala;
Xaa66 := Leu, Ile, Val or Asn;
Xaa67 := Asn, Tyr, Cys or Gly;
Xaa68 := Thr, Met, lie, Ala, Val or none;

Xaa69 := Gly or none;
n := 0, 1, 2 or 3, or 1, 2 or 3;and
m := 0, 1, 2 or 3.
Where the terminal ends of each HIV specific peptide is free carboxyl- or amino-groups, amides, acyls or acetyls or their salts, and each peptide is in the form of an acetate salt.
EXAMPLE: No suitable example given.

IW_WPI: REDUCE DELAY PATHOLOGICAL EFFECT HIV RISK DEVELOP AID HUMAN INFECT MEASURE AMOUNT ANTIBODY EPITOPE ENVELOPE GROUP TREAT
DC_WPI: A96, B05, D16
MC_WPI: A12V01, B04B04D4, B04C01, B04E99, B04G21, B05B01J, B06H, B07H, B08D03, B10A08, B10A12C, B10A18, B10B02A, B10C04E6, B10G02, B11C07A, B12K04A4A, B14A02B1, B14G01B, B14G03, B14S18, D05H09

[DE]VERFAHREN ZUR IMPFUNG GEGEN HIV

[EN]METHOD FOR THE VACCINATION AGAINST HIV

[FR]MÉTHODE DE VACCINATION CONTRE LE VIH