other cell types, macrophages, T lymphocytes, eosinophils, neutrophils, dendritic cells, and basophils. There also exist the chemokines lymphotactin-1, lymphotactin-2 (both C chemokines), and fractalkine (a CX3C chemokine) that do not fall into either of the major chemokine subfamilies.

As used herein, the term "antigenic determinant" is meant to refer to that portion of an antigen that is specifically recognized by either B-or T-lymphocytes. B-lymphocytes respond to foreign antigenic determinants via antibody production, whereas T-lymphocytes are the mediator of cellular immunity. Thus, antigenic determinants or epitopes are those parts of an antigen that are recognized by antibodies, or in the context of an MHC, by T-cell receptors. An antigenic determinant contains one or more epitopes.

As used herein, the term "antibody" refers to molecules which are capable of binding an epitope or antigenic determinant. The term is meant to include whole antibodies and antigen-binding fragments thereof, including single-chain antibodies. Such antibodies include human antigen binding antibody fragments and include, but are not limited to, Fab, Fab' and F(ab')2, Fd, single-chain Fvs (scFv), single-chain antibodies, disulfide-linked Fvs (sdFv) and fragments comprising either a VL or VH domain. The antibodies can be from any animal origin including

Examples of Chikungunya virus include, but are not limited to, strains of 37997 and LR2006 OPY-1.

Examples of Venezuelan equine encephalitis virus include, but are not limited to, TC-83.

Chikungunya or Venezuelan equine encephalitis virus structural polypeptide used in the present invention may naturally occurring virus structural polypeptide or modified polypeptide thereof. The modified polypeptide may be a fragment of the naturally occurring virus structural polypeptide. In one embodiment, the modified polypeptide has at least 70%, 75%, 80%, 85%, 90%, 95% or 98% amino acid sequence identity to a naturally occurring viral capsid and/or envelope protein. In one embodiment, the modified polypeptide is a mutant where at most 10% of the amino acids are deleted, substituted, and/or added based on a naturally occurring viral capsid and/or envelope protein. For example, K64A or K64N mutation may be introduced into a capsid of Venezuelan equine encephalitis virus structural polypeptide used in the present invention.

Chikungunya or Venezuelan equine encephalitis virus envelope protein may comprise at least one selected from the group consisting of E3, E2, 6K and E1.

Examples of Chikungunya virus structural polypeptide include, but are not limited to, E3-E2-6K-E1 of Chikungunya virus Strain 37997, Capsid-E3-E2-6K-E1 of Chikungunya virus

hegkvmgyaclvgdkvmkpahvkgtidnadlaklafkrsskydlecaqipvhmksdask
fthekpegyynwhhgavqysggrftiptgagkpgdsgrpifdnkgrvvaivlgganega
rtalsvvtwnkdivtkitpegaeewslalpvlcllanttfpcsqppctpccyekepest
lrmlednvmrpgyyqllkasltcsphrqrrstkdnfnvykatrpylahcpdcgeghsch
spialerirneatdgtlkiqvslqigiktddshdwtklrymdshtpadaeragllvrts
apctitgtmghfilarcpkgetltvgftdsrkishtcthpfhheppvigrerfhsrpqh
gkelpcstyvqstaataeeievhmppdtpdrtlmtqqsgnvkitvngqtvrykcncggs
neglttdkvinnckidqchaavtnhknwqynsplvprnaelgdrkgkihipfplanvt
crvpkarnptvtygknqvtmllypdhptllsyrnmgqepnyheewvthkkevtltvpte
glevtwgnnepykywpqmstngtahghpheiilyyyelyptmtvvivsvasfvllsmvg
tavgmcvcarrrcitpyeltpgatvpfllsllccvrttkaatyyeaaaylwneqqplfw
lqaliplaalivlcnclkllpcccktlaflavmsigahtvsayehvtvipntvgvpykt
lvnrpgyspmvlemelqsvtleptlsldyitceyktvipspyvkccgtaeckdkslpdy
sckvftgvypfmwggaycfcdaentqlseahveksescktefasayrahtasasaklrv
lyqgnnitvaayangdhavtvkdakfvvgpmssawtpfdnkivvykgdvynmdyppfga
grpgqfgdiqsrtpeskdvyantqlvlqrpaagtvhvpysqapsgfkywlkergaslqh
tapfgcqiatnpvravncavgnipisidipdaaftrvvdapsvtdmscevpacthssdf
ggvaiikytaskkgkcavhsmtnavtireadvevegnsqlqisfstalasaefrvqvcs
tqvhcaaachppkdhivnypashttlgvqdisttamswvqkitggvglivavaaliliv
vlcvsfsrh.

An exemplary Venezuelan equine encephalitis virus structural polypeptide is described below (SEQ ID No.:3):

mfpfqpmypmqpmpyrnpfaaprrpwfprtdpflamqvqeltrsmanltfkqrrdappe
gpsaakpkkeasqkqkgggqgkkkknqgkkkaktgppnpkaqngnkkktnkkpgkrqrm
vmklesdktfpimlegkingyacvvggklfrpmhvegkidndvlaalktkkaskydley
advpqnmradtfkythekpqgyyswhhgavqyengrftvpkgvgakgdsgrpildnqgr
vvaivlggvnegsrtalsvvmwnekgvtvkytpenceqwslvttmcllanvtfpcaqpp
icydrkpaetlamlsvnvdnpgydelleaavkcpgrkrrsteelfneykltrpymarci
rcavgschspiaieavksdghdgyvrlqtssqyglдssgnlkgrtmrydmhgtikeipl
hqvslytsrpchivdghgyfllarcpagdsitmefkkdsvrhscsvpyevkfnpvgrel
ythppehgveqacqvyahdaqnrgayvemhlpgsevdsslvslsgssvtvtppdgtsal
vececggtkisetinktkqfsqctkkeqcrayrlqndkwvynsdklpkaagatlkgklh
vpflladgkctvplapepmitfgfrsvslklhpknptylitrqladephythelisepa
vrnftvtekgwefvwgnhppkrfwaqetapgnphglphevithyyhrypmstilglsic
aaiatvsvaastwlfcrsrvacltpyrltpnaripfclavlccartaraettwesldhl
wnnnqqmfwiqlliplaalivvtrllrcvccvvpflvmagaagagayehattmpsqagi
syntivnragyaplpisitptkikliptvnleyvtchyktgmdspaikccgsqectpty
rpdeqckvftgvypfmwggaycfcdtentqvskayvmksddcladhaeaykahtasvqa
flnitvgehsivttvyvngetpvnfngvkitagplstawtpfdrkivqyageiynydfp
eygagqpgafgdiqsrtvsssdlyantnlvlqrpkagaihvpytqapsgfeqwkkdkap
slkftapfgceiytnpiraencavgsiplafdipdalftrvsetptlsaaectlnecvy
ssdfggiatvkysasksgkcavhvpsgtatlkeaavelteqggsatihfstanihpefrl
qictsyvtckgdchppkdhivthpqyhaqtftaavsktawtwltsllggsaviiiiglv
lativamyvltnqkhn.

In one embodiment, a first attachment site comprises an amino group, preferably an amino group of a lysine

present invention can be useful for the treatment of Alzheimer's disease.

For example, when at least one antigen used for the present invention is TNF alpha, the isolated nucleic acid, the vector, the composition and the method provided by the present invention can be useful for the treatment of inflammation; auto immune disease including rheumatoid arthritis; psoriasis, Crohn's disease; ulcerative colitis etc.

For example, when at least one antigen used for the present invention is CD20, the isolated nucleic acid, the vector, the composition and the method provided by the present invention can be useful for the treatment of auto immune disease including rheumatoid arthritis and SLE; cancer including Non-Hodgkin lymphoma etc.

For example, when at least one antigen used for the present invention is CTLA4, the isolated nucleic acid, the vector, the composition and the method provided by the present invention can be useful for the treatment of cancer including melanoma; and useful for activating T cells etc.

Given the symptom of patients infected with Chikungunya or Venezuelan equine encephalitis together with unusual big molecule of Chikungunya or Venezuelan equine

Chikungunya virus like particles comprising a virus structural polypeptide and a fragment of human or mouse CD20 were prepared using VLP_CHI 532 vector and a fragment of human or mouse TNF alpha antibody. The fragment of human and mouse TNF alpha antibody are described below: CD20 Human iyncepanpseknspstqycysiq (SEQ ID No.:21); CD20 Mouse ydcepsnsseknspstqycnsi (SEQ ID No.:41).

Linkers (e.g. SGG, SG, GS or GGS) were used to insert the fragment of CD20 as described below between G at 519-position and Q at 520-position of SEQ ID No.2:

CD20 Human: SGGiyncepanpseknspstqycysiqGS (SEQ ID No.:42)

CD20 Mouse version2: SGydcepsnsseknspstqycnsiGGS (SEQ ID No.:43)

CD20 Mouse version3: SGGydcepsnsseknspstqycnsiGS (SEQ ID No.:44).

Plasmids: VLP_CHI VLP 532 CD20H, VLP_CHI VLP 532 CD20-2 mouse and VLP_CHI VLP 532 CD20-3 mouse were used for the expression of Chikungunya virus like particles comprising a virus structural polypeptide and a fragment of human or mouse CD20 (SEQ ID No.: 45 (the amino acid sequence of the expressed polypeptide is represented by SEQ ID No.: 46), SEQ ID No.: 47 (the amino acid sequence of the expressed

CLAIMS

1. A particle comprising

a virus structural polypeptide and

at least one antigen which is different from the virus structural polypeptide,

wherein the spatial distance between the N-terminal residue and C-terminal residue of the antigen is 30 Å or less,

wherein the envelope protein of said virus structural polypeptide comprises at least one first attachment site and said at least one antigen comprises at least one second attachment site,

wherein said envelope protein of the virus structural polypeptide and said antigen are linked through said at least one first and said at least one second attachment site,

wherein said particle is virus like particle, and

wherein said virus structural polypeptide is derived from Chikungunya virus (CHIKV) or Venezuelan equine encephalitis virus (VEEV).

2. The particle according to claim 1, wherein the virus structural polypeptide is derived from Chikungunya virus (CHIKV).

3. The particle according to Claim 1 or 2, wherein said polypeptide is virus structural polypeptide comprising the capsid and/or the envelope proteins E3, E2, 6K and E1.

4. The particle according to Claim 3, wherein said at least one antigen is inserted in E2 of the envelope protein.

5. The particle according to any one of Claims 1-4, wherein said antigen is at least one selected from the group consisting of self-antigens and cancer antigens.

6. The particle according to any one of Claims 1-5, wherein said antigen is a polypeptide derived from TNF-α, CD20 or CTLA4.

7. The particle according to any one of Claims 1-6, wherein said polypeptide and said at least one antigen are:
i) a polypeptide derived from Chikungunya virus (CHIKV) and a polypeptide of TNF-α;
ii) a polypeptide derived from Chikungunya virus (CHIKV) and a polypeptide of CD20;
iii) a polypeptide derived from Venezuelan equine encephalitis virus (VEEV) and a polypeptide of TNF-α;
iv) a polypeptide derived from Venezuelan equine encephalitis virus (VEEV) and a polypeptide of CD20; or
v) a polypeptide derived from Venezuelan equine encephalitis virus (VEEV) and a polypeptide of CTLA4.

8. The particle according to any one of Claims 1-7, wherein said at least one antigen and said polypeptide are expressed as a fusion protein.

9. The particle according to Claim 8, wherein said polypeptide and said at least one antigen are directly fused.

10. The particle according to Claim 8, wherein said at least one antigen are fused with said polypeptide, wherein one or two linkers intervenes between N-terminal residue of

said antigen and said polypeptide and/or between C-terminal residue of said antigen and said polypeptide.

11. The particle according to Claims 9 or 10, wherein said at least one antigen is inserted between residues 519 and 520 of SEQ ID No.1 or 2, between residues 530 and 531 of SEQ ID No.1 or 2, between residues 531 and 532 of SEQ ID No.1 or 2 or between residues 532 and 533 of SEQ ID No.1 or 2.

12. The particle according to any one of Claims 8-11, wherein said fusion protein is a protein consisting of an amino acid sequence represented by SEQ ID No. 4, 5, 6, 7 or 8.

13. The particle according to any one of Claims 1-7, wherein said at least one antigen is linked to said polypeptide by way of chemical cross-linking.

14. An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the particle according to any one of Claims 1-13.

15. An isolated nucleic acid molecule according to claim 14, consisting of a nucleotide sequence represented by SEQ ID No. 13, 14, 15, 16 or 17.

16. A vector comprising the nucleic acid molecule according to Claim 14 or 15, wherein the vector comprises an expression control sequence operably linked to the nucleic acid molecule.

17. A composition comprising the particle according to any

one of Claims 1-13 and/or the nucleic acid molecule according to any one of Claims 14-16.

18. A pharmaceutical composition comprising:
(a) the particle according to any one of Claims 1-13 and/or the nucleic acid molecule according to any one of Claims 14-16; and
(b) a pharmaceutically acceptable carrier.

19. A vaccine composition comprising the particle according to any one of Claims 1-13.

20. A DNA vaccine composition comprising the nucleic acid molecule according to any one of Claims 14-16.

21. Use of the particle according to any one of Claims 1-13 and/or the nucleic acid molecule according to any one of Claims 14-16 in the manufacture of a medicament for producing an antibody in a mammal other than a human.

22. The use according to Claim 21, wherein said antibody is a monoclonal antibody.

23. The composition according to any one of claims 17-20 for use in immunomodulation.

24. The composition according to any one of claims 17-20 for use in treating an autoimmune disease.

25. The composition according to any one of claims 17-20 for use in inducing and/or enhancing immune response against an antigen in a mammal.

26. The composition according to any one of claims 17–20 for use in treating cancer.

27. The use according to claim 21 or 22, wherein the antibody is to be used for providing passive immunization against at least one antigen.

28. The use according to Claim 27, wherein the antibody is to be used for the treatment of cancer.

29. The use according to Claim 27 or 28, wherein said at least one antigen is a cancer antigen.

30. The use according to Claim 27 or 28, wherein said at least one antigen is one or more cancer antigens.

31. The particle according to any one of Claims 1–13 and/or the nucleic acid molecule according to any one of Claims 14–16 for use in presenting an antigen on a macrophage.

32. A method for producing the particle according to any one of Claims 8–12, comprising preparing a gene comprising a nucleotide sequence encoding said particle; culturing a cell which is transfected with said gene to express said particle; and recovering said particle.