NANOCAPSULES CARRYING CHIKUNGUNYA-ASSOCIATED PEPTIDES

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of priority of Singapore provisional application No. 10201500725U, filed 29 January 2015, the contents of it being hereby incorporated by reference in its entirety for all purposes.

FIELD OF THE INVENTION

[0002] The present invention relates generally to the field of nanotechnology. In particular, the present invention relates to nanocapsules for peptide delivery.

BACKGROUND OF THE INVENTION

[0003] Chikungunya virus (CHIKV) is a human pathogen and one of the leading causes of mosquito-borne arthralgia in parts of Africa, India and Southeast Asia. The disease of the same name, Chikungunya is a transmitted by Chikungunya virus (CHIKV)-carrying Aedes mosquitoes. Since Chikungunya symptoms are very similar to Dengue fever, it is often misdiagnosed. In the year 2006, total number of 1,390,322 suspected Chikungunya fever cases was reported in India. The disease was unknown in Singapore until 2008, when it experienced its first successive waves of Chikungunya fever. According to Singapore Ministry of Health and The Strait Times, the total number of infections in the last five years is about 1500. With no specific treatment or any licensed vaccine to prevent Chikungunya, the disease remains a public health threat.

[0004] Therefore, there is a need to develop an effective vaccine against the disease caused by the Chikungunya virus.

SUMMARY

[0005] In one aspect, the present invention refers to a composition comprising a viral protein or fragment thereof, wherein the viral protein, or fragment thereof is enclosed within a nanocapsule, wherein the viral protein or fragment thereof is an epitope of the Chikungunya virus, wherein the viral protein or fragment thereof differs by at least 1, at least 2 or at least 3 amino acids from the viral protein or fragment thereof selected from the group consisting of E2EP3 (SEQ ID NO: 7), E2EP4 (SEQ ID NO: 9), E2EP5 (SEQ ID NO: 10), and CV (SEQ ID NO: 12); or wherein the viral protein or fragment thereof is selected from the group consisting of E2EP3 (SEQ ID NO: 7), E2EP3 mutant (SEQ ID NO: 8) E2EP4 (SEQ ID NO: 9), E2EP5 (SEQ ID NO: 10), E2EP5 mutant (SEQ ID NO: 11), and CV (SEQ ID NO: 12) and wherein the nanocapsule is formed by a scaffold protein selected from the group consisting of ferritin, apoferritin and bacterioferritin. In one example, there is disclosed a composition comprising a viral protein or fragment thereof, wherein the viral protein, or fragment thereof is enclosed within a nanocapsule, and wherein the viral protein, or fragment thereof is selected from a virus of the Togaviridae family.

Claims

1. A composition comprising a viral protein or fragment thereof, wherein the viral protein, or fragment thereof is enclosed within a nanocapsule, wherein the viral protein or fragment thereof is an epitope of the Chikungunya virus, wherein the viral protein or fragment thereof differs by at least 1, at least 2 or at least 3 amino acids from the viral protein or fragment thereof selected from the group consisting of E2EP3 (SEQ ID NO: 7), E2EP4 (SEQ ID NO: 9), E2EP5 (SEQ ID NO: 10), and CV (SEQ ID NO: 12); or wherein the viral protein or fragment thereof is selected from the group consisting of E2EP3 (SEQ ID NO: 7), E2EP3 mutant (SEQ ID NO: 8) E2EP4 (SEQ ID NO: 9), E2EP5 (SEQ ID NO: 10), E2EP5 mutant (SEQ ID NO: 11), and CV (SEQ ID NO: 12) and wherein the nanocapsule is formed by a scaffold protein selected from the group consisting of ferritin, apoferritin and bacterioferritin.

2. The composition of claim 1, wherein the viral protein or fragment thereof has an identity of at least about 70%, about 80%, about 90%, about 92%, about 95%, about 97%, about 98% or about 99% of the viral protein or fragment thereof selected from the group consisting of E2EP3 (SEQ ID NO: 7), E2EP3 mutant (SEQ ID NO: 8), E2EP4 (SEQ ID NO: 9), E2EP5 (SEQ ID NO: 10), E2EP5 mutant (SEQ ID NO: 11), and CV (SEQ ID NO: 12).

3. The composition of claims 1 or 2, wherein the nanocapsule comprises viral proteins or fragments thereof of one type only, or wherein the nanocapsule comprises 2, or 3, or 4 or more viral proteins or fragments thereof.

4. The composition of any one of claims 1-3, wherein the nanocapsule is a nanocage.

5. The composition of any one of claims 1-4, wherein the scaffold protein is a recombinant scaffold protein.

6. The composition of claim 5, wherein the scaffold protein is a mutated ferritin protein, wherein at least 1, at least 2, at least 3 or more amino acids differ from the wild-type

ferritin of SEQ ID NO: 15 or SEQ ID NO: 16; or wherein the mutated ferritin has the sequence according to SEQ ID NO: 13 or SEQ ID NO: 14.

7. The composition of any one of claims 1-6, wherein the viral protein or fragment thereof, is attached to the scaffold protein according to any of claims 5 to 7.

8. The composition of claim 7, wherein the viral protein, or fragment thereof, is attached to the scaffold protein via a linker sequence.

9. The composition of claim 8, wherein the linker sequence comprises the amino acids of the format $(G_XS_Y)_Z$; or wherein the linker sequence comprises the amino acids SGG.

10. The composition according to any one of claims 1 to 9 for use in eliciting an immune response in a subject.

11. Use of a vaccine comprising the composition according to any one of claims 1 to 10 in the manufacture of a medicament for preventing an infection caused by an agent selected from the group consisting of Chikungunya virus, O'nyong'nyong virus, Semliki Forest virus, Sindbis virus, Aura virus, Babanki virus, Barmah Forest virus, Bebaru virus, Buggy Creek virus, Cabassou virus, Eastern equine encephalitis virus, Everglades virus, Fort Morgan virus, Getah virus, Highlands J virus, Kyzykagach virus, Mayaro virus, Middleburg virus, Mosso das Pedras virus, Mucambo virus, Ndumu virus, Ockelbo virus, Paramana virus, Pixuna virus, Rio Negro virus, Tonate virus, Trocara virus, Sagiyama virus, sleeping disease virus, Salmon pancreatic disease virus, Southern elephant seal virus, Una virus, Venezuelan equine encephalitis virus, Western equine encephalitis virus, Whataroa virus and Ross River virus.

12. Use of the composition according to any one of claims 1 to 10 in the manufacture of a medicament for preventing or ameliorating an infection caused by an agent selected from the group consisting of Chikungunya virus, O'nyong'nyong virus, Semliki Forest virus, Sindbis virus, Aura virus, Babanki virus, Barmah Forest virus, Bebaru virus, Buggy Creek virus, Cabassou virus, Eastern equine encephalitis virus, Everglades

virus, Fort Morgan virus, Getah virus, Highlands J virus, Kyzykagach virus, Mayaro virus, Middleburg virus, Mosso das Pedras virus, Mucambo virus, Ndumu virus, Ockelbo virus, Paramana virus, Pixuna virus, Rio Negro virus, Tonate virus, Trocara virus, Sagiyama virus, sleeping disease virus, Salmon pancreatic disease virus, Southern elephant seal virus, Una virus, Venezuelan equine encephalitis virus, Western equine encephalitis virus, Whataroa virus and Ross River virus.

13. A nucleic acid sequence comprising a gene encoding the viral protein or fragment thereof according to any one of claims 1 to 3, the linker sequence according to any one of claims 9 or 10 and the scaffold protein according to any one of claims 5 to 7.

14. A vector comprising the nucleic acid sequence according to claim 13.

15. An isolated host cell comprising the vector according to claim 14.

16. A method of producing the composition according to any one of claims 1 to 10, the method comprising

- isolating the protein expressed by the vector of claim 14, and
- adding a catalyst in an amount sufficient to catalyse the formation of the nanocapsule; optionally wherein the catalyst is selected from the group consisting of Mn^{2+}, Mg^{2+}, Co^{2+}, Pt, Fe^{3+} and Fe^{2+}.