CLAIMS

1. An attenuated influenza A virus inducing a cross-protective response against influenza A and B viruses, comprising a chimeric NS fragment including a truncated reading frame of an NS1 protein and a Nep gene heterologous sequence, wherein said truncated reading frame of the NS1 protein is derived from H1N1 influenza virus subtype, and the Nep gene heterologous sequence is derived from H2N2 influenza virus subtype and wherein said truncated reading frame encodes the NS1 protein consisting of 124 amino acid residues corresponding to SEQ ID NO: 4.

2. An attenuated influenza virus vector expressing a protein or a fragment thereof selected from the group consisting of proteins or fragments thereof from bacteria, viruses, and protozoa, wherein the vector is an attenuated influenza A virus according to claim 1, in which the truncated reading frame of the NS1 protein gene is elongated by an insertion of a sequence of at least one transgene encoding the protein or the fragment thereof from bacteria, viruses, and protozoa, wherein the bacteria, virus, or protozoa is pathogenic.

3. The attenuated influenza virus vector according to claim 2, wherein the protein or the fragment thereof is selected from the group consisting of proteins of an influenza A virus, influenza B virus, mycobacterium tuberculosis, herpes virus, respiratory syncytial virus, human immunodeficiency virus, hepatitis C virus, malaria parasite, Trichomonas, Trypanosoma, Leishmania, Chlamydia, brucellosis causative agent, or a combination thereof.

4. The attenuated influenza virus vector according to claim 2, wherein the protein or the fragment thereof consists of 10 to 400 amino acids.

5. The attenuated influenza virus vector according to claim 2, wherein the insertion encodes an HA protein region from influenza virus.

6. The attenuated influenza virus vector according to claim 5, wherein the HA protein region is an HA2 subunit region selected from the group consisting of 1–185 amino acids from influenza A virus, 1–186 amino acids from influenza B virus, 23–185 amino acids from influenza A virus, or 65–222 amino acids from influenza A virus.

7. The attenuated influenza virus vector according to claim 2, wherein the insertion encodes a sequence of an influenza A or B virus HA2 subunit region of from 1 to 21 amino acids and a sequence of an influenza A virus NP protein region of from 243 to 251 amino acids.

8. The attenuated influenza virus vector according to claim 2, wherein the insertion encodes protein ESAT-6, Ag85A, Ag85B, Mpt64, HspX, Mtb8.4, or 10.4 of mycobacterium tuberculosis, or a fragment thereof.

9. The attenuated influenza virus vector according to claim 8, wherein the viral genome sequence further comprises a sequence encoding a self-cleaving 2A peptide between the truncated reading frame of the NS1 protein gene and the insertion encoding protein ESAT6.

10. An attenuated influenza virus vector expressing an influenza virus protein or a fragment thereof, wherein said vector is an attenuated influenza virus according to claim 1, wherein the truncated reading frame of an NS1 protein gene is elongated by an insertion of a sequence encoding 1-21 aa of an influenza B HA2 protein and 243-251 aa of an influenza A NP protein.

11. An attenuated influenza virus vector having oncolytic activity, wherein said vector is an attenuated influenza A virus according to claim 1, wherein the truncated reading frame of an NS1 protein gene is elongated by an insertion of a sequence encoding a mycobacterium tuberculosis protein ESAT-6 or a fragment thereof.

12. The attenuated influenza virus vector according to claim 11, wherein the protein or a fragment thereof consists of 10 to 400 amino acids.

13. The attenuated influenza virus vector according to claim 11, wherein the truncated reading frame of an NS1 protein gene is further elongated by an insertion of a sequence encoding self-cleaving 2A peptide.

14. An attenuated influenza virus vector inducing a cross-protective response against influenza A and B viruses, comprising:

a nucleotide sequence of a PB2 protein gene of SEQ ID NO: 14 or a nucleotide sequence having at least 95% sequence identity to SEQ ID NO: 14;

a nucleotide sequence of a PB1 protein gene of SEQ ID NO: 15 or a nucleotide sequence having at least 95% sequence identity to SEQ ID NO: 15;

a nucleotide sequence of a PA protein gene of SEQ ID NO: 16 or a nucleotide sequence having at least 95% sequence identity to SEQ ID NO: 16;

a nucleotide sequence of an NP protein gene of SEQ ID NO: 17 or a nucleotide sequence having at least 95% sequence identity to SEQ ID NO: 17;

a nucleotide sequence of an M protein gene of SEQ ID NO: 18 or a nucleotide sequence having at least 95% sequence identity to SEQ ID NO: 18;

a nucleotide sequence of an HA protein gene of SEQ ID NO: 19 or a nucleotide sequence having at least 95% sequence identity to SEQ ID NO: 19;

a nucleotide sequence of an NA protein gene of SEQ ID NO: 20 or a nucleotide sequence having at least 95% sequence identity to SEQ ID NO: 20;

a nucleotide sequence of an NS protein chimeric gene of SEQ ID NO: 21 including:

an NS1 protein reading frame derived from influenza A/PR/8/34 (H1N1), wherein said reading frame is truncated and encodes an NS1 protein consisting of 124 amino acid residues,

and a Nep gene sequence derived from influenza A/Singapore/1/57-like (H2N2) virus, or

a nucleotide sequence having at least 95% sequence identity to SEQ ID NO: 21;

wherein said NS1 protein truncated reading frame is elongated by an insertion of a nucleotide sequence encoding a fusion peptide of an influenza B subunit HA2 region and a nucleotide sequence encoding a conservative B-cell epitope of influenza A virus nucleoprotein (NP).

15. The attenuated influenza virus vector according to claim 14, wherein the nucleotide sequence of the NS protein chimeric gene is set forth in SEQ ID NO:21.

16. An immunogenic composition for the induction of an immune response against an infectious pathogen in a subject, comprising an effective amount of an attenuated influenza virus vector according to claim 2, and a pharmaceutically acceptable carrier.

17. A pharmaceutical composition for the prophylaxis of influenza disease, comprising in an effective amount of an attenuated influenza virus vector according to claim 14 and a pharmaceutically acceptable carrier.

18. The immunogenic or pharmaceutical composition according to claim 16 or 17, respectively, comprising 6.5 to 10.5 log EID50/ml of the attenuated influenza A virus and a buffer solution comprising 0 to 1.5 wt.% of a monovalent salt, 0 to 5 wt.% of an imidazole-containing compound, 0 to 5 wt.% of a carbohydrate component, 0 to 2 wt.% of a protein component, 0 to 2 wt.% of an amino acid component, and 0 to 10 wt.% of hydroxyethylated starch.

19. The immunogenic composition according to claim 16, wherein the buffer solution comprises 0.5 to 1.5 wt.% of a monovalent salt, 0.01 to 5 wt.% of an imidazole-containing compound, 1 to 5 wt.% of a carbohydrate component, 0.1 to 2 wt.% of a protein component, 0.01 to 2 wt.% of an amino acid component, and 1 to 10 wt.% of hydroxyethylated starch.

20. The immunogenic composition according to claim 19, wherein the monovalent salt is sodium chloride, the carbohydrate component is sucrose, trehalose, or lactose, the protein component is a human recombinant albumin, casitone, lactalbumin hydrolysate, or gelatin, the amino acid component is arginine, glycine, or sodium glutamate, and the imidazole-containing compound is L-carnosine or N,N'-bis[2-(1H-imidazol-5yl)ethyl]propanediamide.

21. The immunogenic composition according to claim 16, wherein the infectious pathogen is selected from the group consisting of an influenza A virus, influenza B virus, mycobacterium tuberculosis, herpes simplex virus types I and II, respiratory syncytial virus, human immunodeficiency virus, hepatitis C virus, malaria parasite, Trichomonas, Chlamydia, Trypanosoma, Leishmania, or a brucellosis causative agent.

22. The immunogenic composition according to claim 16, wherein the subject is a mammal or a bird.

23. The immunogenic composition according to claim 22, wherein the subject is a human subject.

24. A vaccine against an influenza, comprising an effective amount of an attenuated influenza virus vector according to claim 1, and a pharmaceutically acceptable carrier.

25. A vaccine against influenza comprising an effective amount of an attenuated influenza virus vector according to claim 14 and a pharmaceutically acceptable carrier.

26. The vaccine according to claim 24 or 25, comprising 6.5 to 10.5 log EID50/ml of the attenuated influenza virus vector and a buffer solution comprising 0 to 1.5 wt.% of a monovalent salt, 0 to 5 wt.% of an imidazole-containing compound, 0 to 5 wt.% of a carbohydrate component, 0 to 2 wt.% of a protein component, 0 to 2 wt.% of an amino acid component, and 0 to 10 wt.% of hydroxyethylated starch.

27. The vaccine according to claim 24, wherein the buffer solution comprises 0.5 to 1.5 wt.% of a monovalent salt, 0.01 to 5 wt.% of an imidazole-containing compound, 1 to 5 wt.% of a carbohydrate component, 0.1 to 2 wt.% of a protein component, 0.01 to 2 wt.% of an amino acid component, and 1 to 10 wt.% of hydroxyethylated starch.

28. The vaccine according to claim 27, wherein the monovalent salt is sodium chloride, the carbohydrate component is sucrose, trehalose, or lactose, the protein component is a human recombinant albumin, casitone, lactalbumin hydrolysate, or gelatin, the amino acid component is arginine, glycine, or sodium glutamate, and the imidazole-containing compound is L-carnosine or N,N'-bis[2-(1H-imidazol-5yl)ethyl]propanediamide.

29. Use of the attenuated influenza virus vector according to claim 2 for preparing a medicament for treating and/or prophylaxis of influenza disease in a subject in need thereof.

30. The use according to claim 29, wherein the infectious disease is caused by a pathogen selected from

the group consisting of an influenza A virus and an influenza B virus.

31. The use according to claim 30, wherein the subject is a mammal or a bird.

32. The use according to claim 31, wherein the subject is a human subject.

33. A pharmaceutical composition for the treatment of an oncological disease in a subject, comprising an attenuated influenza vector according to claim 11 in an effective amount, and a pharmaceutically acceptable carrier.

34. The pharmaceutical composition according to claim 33, comprising 8.5 to 10.5 log EID50/ml of the attenuated influenza virus vector, and a buffer solution comprising 0 to 1.5 wt.% of a monovalent salt, 0 to 5 wt.% of an imidazole-containing compound, 0 to 5 wt.% of a carbohydrate component, 0 to 2 wt.% of a protein component, 0 to 2 wt.% of an amino acid component, and 0 to 10 wt.% of hydroxyethylated starch.

35. The pharmaceutical composition according to claim 34, wherein buffer solution comprises 0.5 to 1.5 wt.% of a monovalent salt, 0.01 to 5 wt.% of an imidazole-containing compound, 1 to 5 wt.% of a carbohydrate component, 0.1 to 2 wt.% of a protein component, 0.01 to 2 wt.% of an amino acid component, and 1 to 10 wt.% of hydroxyethylated starch.

36. The pharmaceutical composition according to claim 35, wherein the monovalent salt is sodium chloride, the carbohydrate component is starch, the protein component is a human albumin, the amino acid component is arginine, and the an imidazole-containing compound is L-carnosine or N,N'-bis[2-(1H-imidazol-5yl)ethyl]propanediamide.

37. Use of the attenuated influenza virus vector according to claim 11 for preparing a medicament for treating an oncological disease in a subject in need thereof.

38. The use according to claim 37, wherein the oncological disease is selected from the group consisting of colorectal cancer, cardioesophageal cancer, pancreatic cancer, cholangiocellular cancer, glioma, glioblastoma, and melanoma.