[Non-Patent Documents]

[0007]

[Non-Patent Document 1] Ngwuta J. O. et al., Science Translational Medicine 2015; 309: 309ra162.

[Non-Patent Document 2] Jason S. McLellan et al., Science 2013; 340: 1113.

[Non-Patent Document 3] Morgan S. A. Gilman et al., 2016, Science Immunology, 1 (6), pii: eaaj1879.

[Non-Patent Document 4] Eileen Goodwin et al., Immunity 2018; 48 (2): 339.

[Non-Patent Document 5] Jason S. McLellan et al., Science 2013; 342:592.

[Non-Patent Document 6] M. Gordon Joyce et al., Nature structural and molecular biology 2016; 23 (9): 811.

[Summary of the Invention]

[0007a]

In one aspect, provided herein is a mutant RSV F protein having a mutation, wherein the mutation is a substitution of a leucine corresponding to a leucine at position 141 of an amino acid sequence of SEQ ID NO: 1 or a leucine corresponding to a leucine at position 142 with a cysteine, and a substitution of a leucine corresponding to a leucine at position 373 with a cysteine, and a disulfide bond is formed between the cysteines.

[0007b]

In another aspect, provided herein is a mutant RSV F protein having a mutation, wherein the mutation is a substitution of a glutamic acid corresponding to a glutamic acid at position 60 of an amino acid sequence of SEQ ID NO: 1 with a non-acidic amino acid.

[0007c]

In another aspect, provided herein is a fusion protein comprising: the mutant RSV F protein as disclosed herein; and a multimerization domain fused to a C-terminal of the mutant RSV F protein.

[0007d]

In another aspect, provided herein is a multimer of the mutant RSV F protein as disclosed herein, wherein the fusion protein as disclosed herein is associated via the multimerization domain.

[0007e]

In another aspect, provided herein is a particulate product of the mutant RSV F protein as disclosed herein or the multimer as disclosed herein, wherein

the mutant RSV F protein or the fusion protein contains a particle-forming domain,

two or more of the mutant RSV F proteins or the multimers are aggregated via the particle-forming domain to form a particle, and

the particle-forming domain is located at a position closer to an epitope I than to an epitope Φ on a steric structure of the mutant RSV F protein or the multimer.

[0007f]

In another aspect, provided herein is a fusion protein for producing a particulate product comprising: the mutant RSV F protein as disclosed herein, or the fusion protein as disclosed herein, and a particle-forming domain fused to a C-terminal thereof.

[0007g]

In another aspect, provided herein is a polynucleotide encoding the mutant RSV F protein as disclosed herein, the fusion protein as disclosed herein, or the fusion protein for producing a particulate product as disclosed herein.

[0007h]

In another aspect, provided herein is an expression unit comprising the as disclosed herein.

[0007i]

In another aspect, provided herein is a host cell comprising the expression unit as disclosed herein.

[0007j]

In another aspect, provided herein is an immunogen comprising: the mutant RSV F protein as disclosed herein, the fusion protein as disclosed herein, the as disclosed herein, or the particulate product as disclosed herein.

[0007k]

In another aspect, provided herein is a pharmaceutical composition comprising the expression unit as disclosed herein or the immunogen as disclosed herein.

[0007l]

In another aspect, provided herein is an RSV vaccine comprising the expression unit as disclosed herein or the immunogen as disclosed herein.

[0007m]

In yet another aspect, provided herein is the pharmaceutical composition as disclosed herein or the RSV vaccine as disclosed herein which is used for humans.

[Problems to Be Solved by the Invention]

[0008]

The present invention is intended to provide a technique for efficiently inducing an antibody having a high RSV infection neutralization capacity.

[Means for Solving the Problems]

[0009]

The present inventors have found that a mutant RSV F protein including a specific amino acid mutation efficiently induces an antibody having a high RSV infection neutralization capacity, and thus have accomplished the present invention.

The present invention is as follows.

[0010]

[1] A mutant RSV F protein having a mutation, wherein the mutation is a substitution of a leucine corresponding to a leucine at position 141 of an amino acid sequence of SEQ ID NO: 1 or a leucine corresponding to a leucine at position 142 with a cysteine, and a substitution of a