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(54) Titre : ANTIGENE MUTANT DU VIRUS DES MOULES ET CODAGE DES GENES DE CE VIRUS
(54) Title: MEASLES VIRUS MUTANT ANTIGEN AND GENE CODING FOR THE SAME

(57) **Abrégé/Abstract:**

Disclosed is a measles virus mutant antigen, comprising at least one protein antigen selected from the group consisting of (I) a measles virus mutant H protein antigen and (II) a measles virus mutant F protein antigen, the measles virus mutant H protein antigen (I) being at least one member selected from the group consisting of the whole protein and fragmentary peptides identified with the positional amino acid numbers of either SEQ ID NO: 2 or SEQ ID NO: 10; and the measles virus mutant F protein antigen (II) being at least one member selected from the group consisting of the whole protein and fragmentary peptides identified with the positional amino acid numbers of either SEQ ID NO: 18 or SEQ ID NO: 20. Also disclosed is a measles virus mutant gene coding for the measles virus mutant antigen. By the use of the measles virus mutant antigen or the gene coding for the same of the present invention, it has become possible to provide efficiently and economically a live attenuated measles vaccine or gene vaccine which is adapted for an epidemic strain of measles virus, and a diagnostic reagent capable of accurately detecting infections with an epidemic strain of measles virus.



ABSTRACT

Disclosed is a measles virus mutant antigen,
comprising at least one protein antigen selected from
the group consisting of (I) a measles virus mutant H
protein antigen and (II) a measles virus mutant F
protein antigen,

the measles virus mutant H protein antigen (I)
being at least one member selected from the group con-
sisting of the whole protein and fragmentary peptides
identified with the positional amino acid numbers of
either SEQ ID NO: 2 or SEQ ID NO: 10; and

the measles virus mutant F protein antigen (II)
being at least one member selected from the group con-
sisting of the whole protein and fragmentary peptides
identified with the positional amino acid numbers of
either SEQ ID NO: 18 or SEQ ID NO: 20.

Also disclosed is a measles virus mutant gene coding
for the measles virus mutant antigen. By the use of
the measles virus mutant antigen or the gene coding for
the same of the present invention, it has become possi-
ble to provide efficiently and economically a live
attenuated measles vaccine or gene vaccine which is
adapted for an epidemic strain of measles virus, and a
diagnostic reagent capable of accurately detecting
infections with an epidemic strain of measles virus.

TITLE OF THE INVENTION

Measles virus mutant antigen and gene coding
for the same

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BACKGROUND OF THE INVENTIONField of the Invention

The present invention relates to a measles virus
mutant antigen and a gene coding for the same. More
particularly, the present invention is concerned with a
10 measles virus mutant antigen comprising at least one
protein antigen selected from the group consisting of a
measles virus mutant H protein antigen and a measles
virus mutant F protein antigen, and a measles virus
mutant gene coding for the measles virus mutant anti-
15 gen. By the use of the measles virus mutant antigen or
the gene coding for the same of the present invention,
it has become possible to provide efficiently and
economically a live attenuated measles vaccine or gene
vaccine which is adapted for an epidemic strain of
20 measles virus, and a diagnostic reagent capable of
accurately detecting infections with an epidemic strain
of measles virus.

Prior Art

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(1) Pathogenicity: Measles virus is the pathogen

of measles, and it is distributed widely throughout the world. This virus is highly infectious, and when a person suffers a droplet infection with a measles virus, damage occurs mainly in the respiratory system and reticuloendothelial tissue, thereby causing an acute disease. A person suffering from measles shows systemic symptoms, such as high fever, catarrh and rash. Further, in severe cases, measles is complicated with bacterial pneumonia, tympanitis and acute encephalitis. In 1996, the number of measles patients and number of deaths due to measles in the world were estimated to be about 42 million and about 1 million 10 thousand, respectively ["The World Health Report 1997", p. 15, WHO (World Health Organization) published in 1997]. As apparent from the above, measles is an infectious disease which should be taken into serious consideration, and eradication of measles by vaccines is desired throughout the world. In this situation, the Expanded Program on Immunization (EPI) of World Health Organization (WHO) has already adopted a measles eradication program with the goal of controlling measles by the year 2010.

(2) Viral morphology and genomic structure:
According to the Sixth Report of the International Committee on Taxonomy of Viruses, the measles virus is

classified under the order Mononegavirales, family Paramyxoviridae, genus *Morbillivirus*. The virion of the measles virus is generally spherical (diameter: about 150 nm) and has an envelope composed of a lipid bilayer. On the surface of the envelope are spike-like projections composed of an H (hemagglutinin) protein and composed of an F (fusion) protein, and the bases of the projections (proteins) are supported by a matrix membrane protein at the inner layer of the envelope. The nucleocapsid present in the inside of the envelope consists of measles virus genomic RNA which is a linear, non-segmented (-) sense (that is, mononega) RNA having a length of about 16 kb, and proteins. The genomic RNA codes for N (nucleocapsid-associated proteins), P/C/V (phosphoprotein / C protein / V protein: coded for by tricistronic gene), M (matrix protein), F (fusion protein), H (hemagglutinin protein) and L (large putative polymerase protein), and the coding regions are located in this order from the 3' end to the 5' end of the genome ("Virus Taxonomy: Sixth Report of the International Committee on Taxonomy of Viruses", Archives of Virology, Supplement 10, pp. 268-270 and pp. 271-272, 1995).

(3) Conventional virus strain for live attenuated measles vaccine: Examples of the virus strains known

for live attenuated measles vaccine are: CAM-70,
Schwarz FF8, AIK-C, AIK-HDC, TD97, Moraten, Connaught,
Schwarz, Edmonston B, Edmonston-Zagreb, Leningrad-16,
Shanghai-191, Changchum-47 and Beijing (S.A. Plotokin
5 and E.A. Mortimer, "Vaccines", 2nd edition, pp. 238-
239, published by W.B. Saunders Company, 1994). These
virus strains are either a host-range mutant or a
temperature mutant of measles virus which are attenuat-
ed to ensure safety and effectiveness so as to be used
10 as an active component for a live vaccine, and such
viruses are obtained by sequentially subjecting an
isolated strain (wild measles virus) to passages of
culture under different conditions prepared by combin-
ing various factors, such as host cell, culture temper-
15 ature, and pH and composition of a culture medium.

(4) Prevention: Vaccines for preventing measles
were put to practical use in the early 1960's. At the
beginning, the majority of the measles vaccines used
was killed (or inactivated) vaccines (abbreviated "K")
20 containing killed measles viruses as an active compon-
ent of the vaccine. However, the killed measles vac-
cine had an unsatisfactory immunological effect, and
further, it induced serious atypical measles. In this
situation, the use of a live vaccine (abbreviated "L")
25 containing live attenuated measles viruses as an active

component of the vaccine gradually became predominant in the late 1960's. A combination of K and L vaccines was adopted, but since the 1970's, a further attenuated live vaccine (abbreviated "FL") obtained by further
5 attenuating the above-mentioned live vaccine virus has become commercially available throughout the world for practical use. With respect to the live vaccine, each of the live attenuated measles vaccine strains mentioned in item (3) above is used as an active component
10 of the vaccine.

(5) Problems of measles vaccine and diagnosis:
With respect to the maintenance of immunity obtained by using a conventional live attenuated measles virus vaccine, some problems have arisen since the early
15 1970's. Illustratively stated, reports on secondary vaccine failure and modified measles have been made, in which it is reported that, people who have been vaccinated with measles vaccine were reinfected with measles and suffered from symptoms which are different from
20 that of the natural infection (in general, the symptoms are mild compared to those of the natural infection, but serious in rare cases). Such reports on reinfection in various parts of the world were made sporadically in the latter half of the 1980's, and the reports
25 are frequently made in the 1990's. Therefore, the

development of means for preventing the reinfection and for determining the infecting virus has been earnestly desired by not only the people in various countries of the world, but also by the WHO from the viewpoint of the above-mentioned eradication program on measles. However, a measles vaccine or diagnostic reagent effective for preventing the infection with the currently prevailing measles viruses has not yet been realized.

10 SUMMARY OF THE INVENTION

15 The inventors of the present invention have not only studied measles from the viewpoint of clinics, epidemiology and vaccine, but also studied various measles viruses, such as vaccine strains, epidemic strains and isolated fresh strains, from the viewpoint of virology and immunology, together with the genetic analyses of these virus strains. In particular, the primary inventor of the present invention has been continuing his studies for more than 30 years. The inventors of the present invention have further made extensive and intensive studies for elucidating the differences in antigenicity or immunogenicity between conventional virulent strains, and virulent mutants including epidemic strains, and also for identifying the causes of such differences. As a result, they have

surprisingly found that, with respect to the mutants, the specific regions in each of the genes coding for the H protein and F protein possess mutations which result in amino acid substitutions. Further, the
5 inventors of the present invention have found that the mutated regions in the H protein and F protein are effective as mutant antigens of the measles virus. The present invention has been completed, based on these novel findings.

10 Therefore, it is an object of the present invention to provide a measles virus mutant antigen, comprising at least one protein antigen selected from the group consisting of a measles virus mutant H protein antigen and a measles virus mutant F protein antigen,
15 which is advantageous for preparing a vaccine and a diagnostic reagent for a virus of epidemic measles.

It is a further object of the present invention to provide a measles virus mutant gene, comprising at least one gene selected from the group consisting of a
20 gene coding for a measles virus mutant H protein antigen and a gene coding for a measles virus mutant F protein antigen, which is advantageous for preparing a gene vaccine and a diagnostic reagent for a virus of epidemic measles.

25 The foregoing and other objects, features and

advantages of the present invention will be apparent to those skilled in the art from the following detailed description and the appended claims taken in connection with the accompanying sequence listing.

5 BRIEF DESCRIPTION OF THE SEQUENCE LISTING

In each of SEQ ID NOs: 1 to 20, the left end and the right end of the amino acid sequence are the N-terminus and the C-terminus, respectively.

10 SEQ ID NO: 1 is the nucleotide sequence of the cDNA corresponding to the genomic RNA coding for the H protein of the attenuated measles virus CAM-70 strain and the whole amino acid sequence encoded by the nucleotide sequence;

15 SEQ ID NO: 2 is the whole amino acid sequence of the H protein of the attenuated measles virus CAM-70 strain;

SEQ ID NO: 3 is the amino acid sequence of the fragmentary peptide consisting of the 93rd to 616th amino acids in SEQ ID NO: 2;

20 SEQ ID NO: 4 is the amino acid sequence of the fragmentary peptide consisting of the 176th to 316th amino acids in SEQ ID NO: 2;

25 SEQ ID NO: 5 is the amino acid sequence of the fragmentary peptide consisting of the 172nd to 178th amino acids in SEQ ID NO: 2;

SEQ ID NO: 6 is the amino acid sequence of the fragmentary peptide consisting of the 238th to 244th amino acids in SEQ ID NO: 2;

5 SEQ ID NO: 7 is the amino acid sequence of the fragmentary peptide consisting of the 277th to 282nd amino acids in SEQ ID NO: 2;

SEQ ID NO: 8 is the amino acid sequence of the fragmentary peptide consisting of the 301st to 307th amino acids in SEQ ID NO: 2;

10 SEQ ID NO: 9 is the nucleotide sequence of the cDNA corresponding to the genomic RNA coding for the H protein of the virulent measles virus NA strain and the whole amino acid sequence encoded by the nucleotide sequence;

15 SEQ ID NO: 10 is the whole amino acid sequence of the H protein of the virulent measles virus NA strain;

SEQ ID NO: 11 is the amino acid sequence of the fragmentary peptide consisting of the 93rd to 616th amino acids in SEQ ID NO: 10;

20 SEQ ID NO: 12 is the amino acid sequence of the fragmentary peptide consisting of the 176th to 316th amino acids in SEQ ID NO: 10;

25 SEQ ID NO: 13 is the amino acid sequence of the fragmentary peptide consisting of the 172nd to 178th amino acids in SEQ ID NO: 10;

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SEQ ID NO: 14 is the amino acid sequence of the fragmentary peptide consisting of the 238th to 244th amino acids in SEQ ID NO: 10;

5 SEQ ID NO: 15 is the amino acid sequence of the fragmentary peptide consisting of the 277th to 282nd amino acids in SEQ ID NO: 10;

SEQ ID NO: 16 is the amino acid sequence of the fragmentary peptide consisting of the 301st to 307th amino acids in SEQ ID NO: 10;

10 SEQ ID NO: 17 is the nucleotide sequence of the cDNA corresponding to the genomic RNA coding for the F protein of the attenuated measles virus CAM-70 strain and the whole amino acid sequence encoded by the nucleotide sequence;

15 SEQ ID NO: 18 is the whole amino acid sequence of the F protein of the attenuated measles virus CAM-70 strain;

20 SEQ ID NO: 19 is the nucleotide sequence of the cDNA corresponding to the genomic RNA coding for the F protein of the virulent measles virus NA strain and the whole amino acid sequence encoded by the nucleotide sequence; and

SEQ ID NO: 20 is the whole amino acid sequence of the F protein of the virulent measles virus NA strain.

25

DETAILED DESCRIPTION OF THE INVENTION

In one aspect of the present invention, there is provided a measles virus mutant antigen, comprising at least one protein antigen selected from the group consisting of (I) a measles virus mutant H protein antigen and (II) a measles virus mutant F protein antigen,

the measles virus mutant H protein antigen (I) being at least one member selected from the group consisting of the following amino acid sequences (a) to (f) identified with the positional amino acid numbers of either SEQ ID NO: 2 or SEQ ID NO: 10:

(a) the whole sequence of the 1st to 617th amino acids;

(b) a fragmentary sequence of the 93rd to 616th amino acids;

(c) a fragmentary sequence of the 176th to 316th amino acids;

(d) fragmentary sequences of the 172nd to 178th amino acids, the 238th to 244th amino acids, the 277th to 282nd amino acids, and the 301st to 307th amino acids;

(e) fragmentary, contiguous sequences of at least 6 amino acids in either SEQ ID NO: 2 or SEQ ID NO: 10, wherein the sequences each comprise an amino acid

selected from the group consisting of the 174th, 176th, 243rd, 279th and 302nd amino acids, and neighboring amino acids of the selected amino acid in either SEQ ID NO: 2 or SEQ ID NO: 10, wherein the fragmentary, contiguous sequences are exclusive of the fragmentary sequences (d); and

(f) fragmentary, contiguous sequences of at least 6 amino acids in either SEQ ID NO: 2 or SEQ ID NO: 10, wherein the sequences each comprise an amino acid selected from the group consisting of the 93rd, 157th, 169th, 175th, 211th, 252nd, 276th, 284th, 285th, 296th, 316th, 338th, 387th, 416th, 455th, 481st, 484th, 505th, 546th, 592nd, 600th, 603rd and 616th amino acids, and neighboring amino acids of the selected amino acid in either SEQ ID NO: 2 or SEQ ID NO: 10 wherein the fragmentary, contiguous sequences are exclusive of the fragmentary sequences (d) and (e); and

the measles virus mutant F protein antigen (II) being at least one member selected from the group consisting of the following amino acid sequences (g) and (h) identified with the positional amino acid numbers of either SEQ ID NO: 18 or SEQ ID NO: 20:

(g) the whole sequence of the 1st to 550th amino acids; and

(h) fragmentary, contiguous sequences of at least

6 amino acids in either SEQ ID NO: 18 or SEQ ID NO: 20,
wherein the sequences each comprise an amino acid
selected from the group consisting of the 11th, 52nd,
107th, 165th, 398th, 417th and 523rd amino acids, and
5 neighboring amino acids of the selected amino acid in
either SEQ ID NO: 18 or SEQ ID NO: 20.

For easy understanding of the present invention,
the essential features and various preferred embodi-
ments of the present invention are enumerated below.

10

1. A measles virus mutant antigen, comprising at
least one protein antigen selected from the group
consisting of (I) a measles virus mutant H protein
antigen and (II) a measles virus mutant F protein
15 antigen,

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the measles virus mutant H protein antigen (I)
being at least one member selected from the group
consisting of the following amino acid sequences (a) to
(f) identified with the positional amino acid numbers
of either SEQ ID NO: 2 or SEQ ID NO: 10:

20

(a) the whole sequence of the 1st to 617th amino
acids;

(b) a fragmentary sequence of the 93rd to 616th
amino acids;

25

(c) a fragmentary sequence of the 176th to 316th

amino acids;

(d) fragmentary sequences of the 172nd to 178th amino acids, the 238th to 244th amino acids, the 277th to 282nd amino acids, and the 301st to 307th amino acids;

(e) fragmentary, contiguous sequences of at least 6 amino acids in either SEQ ID NO: 2 or SEQ ID NO: 10, wherein the sequences each comprise an amino acid selected from the group consisting of the 174th, 176th, 243rd, 279th and 302nd amino acids, and neighboring amino acids of the selected amino acid in either SEQ ID NO: 2 or SEQ ID NO: 10, wherein the fragmentary, contiguous sequences are exclusive of the fragmentary sequences (d); and

(f) fragmentary, contiguous sequences of at least 6 amino acids in either SEQ ID NO: 2 or SEQ ID NO: 10, wherein the sequences each comprise an amino acid selected from the group consisting of the 93rd, 157th, 169th, 175th, 211th, 252nd, 276th, 284th, 285th, 296th, 316th, 338th, 387th, 416th, 455th, 481st, 484th, 505th, 546th, 592nd, 600th, 603rd and 616th amino acids, and neighboring amino acids of the selected amino acid in either SEQ ID NO: 2 or SEQ ID NO: 10, wherein the fragmentary, contiguous sequences are exclusive of the fragmentary sequences (d) and (e); and

the measles virus mutant F protein antigen (II) being at least one member selected from the group consisting of the following amino acid sequences (g) and (h) identified with the positional amino acid numbers of either SEQ ID NO: 18 or SEQ ID NO: 20:

(g) the whole sequence of the 1st to 550th amino acids; and

(h) fragmentary, contiguous sequences of at least 6 amino acids in either SEQ ID NO: 18 or SEQ ID NO: 20, wherein the sequences each comprise an amino acid selected from the group consisting of the 11th, 52nd, 107th, 165th, 398th, 417th and 523rd amino acids, and neighboring amino acids of the selected amino acid in either SEQ ID NO: 18 or SEQ ID NO: 20.

2. A measles virus mutant gene, comprising at least one gene selected from the group consisting of (I) a gene coding for a measles virus mutant H protein antigen and (II) a gene coding for a measles virus mutant F protein antigen,

the gene coding for a measles virus mutant H protein antigen (I) being at least one member selected from the group consisting of the following genes (a) to (f) identified with the positional amino acid numbers of either SEQ ID NO: 2 or SEQ ID NO: 10:

(a) a gene coding for the whole sequence of the 1st to 617th amino acids;

(b) a gene coding for a fragmentary sequence of the 93rd to 616th amino acids;

5 (c) a gene coding for a fragmentary sequence of the 176th to 316th amino acids;

(d) genes coding for fragmentary sequences of the 172nd to 178th amino acids, the 238th to 244th amino acids, the 277th to 282nd amino acids, and the 301st to
10 307th amino acids;

(e) genes coding for fragmentary, contiguous sequences of at least 6 amino acids in either SEQ ID NO: 2 or SEQ ID NO: 10, wherein the sequences each comprise an amino acid selected from the group consisting of the 174th, 176th, 243rd, 279th and 302nd amino acids, and neighboring amino acids of the selected amino acid in either SEQ ID NO: 2 or SEQ ID NO: 10, wherein the genes are exclusive of the genes (d); and
15

(f) genes coding for fragmentary, contiguous sequences of at least 6 amino acids in either SEQ ID NO: 2 or SEQ ID NO: 10, wherein the sequences each comprise an amino acid selected from the group consisting of the 93rd, 157th, 169th, 175th, 211th, 252nd, 276th, 284th, 285th, 296th, 316th, 338th, 387th, 416th, 455th, 481st, 484th, 505th, 546th, 592nd, 600th, 603rd
20
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and 616th amino acids, and neighboring amino acids of the selected amino acid in either SEQ ID NO: 2 or SEQ ID NO: 10, wherein the genes are exclusive of the genes (d) and (e); and

5 the gene coding for measles virus mutant F protein antigen (II) being at least one member selected from the group consisting of the following genes (g) and (h) identified with the positional amino acid numbers of either SEQ ID NO: 18 or SEQ ID NO: 20:

10 (g) a gene coding for the whole sequence of the 1st to 550th amino acids; and

 (h) genes coding for fragmentary, contiguous sequences of at least 6 amino acids in either SEQ ID NO: 18 or SEQ ID NO: 20, wherein the sequences each
15 comprise an amino acid selected from the group consisting of the 11th, 52nd, 107th, 165th, 398th, 417th and 523rd amino acids, and neighboring amino acids of the selected amino acid in either SEQ ID NO: 18 or SEQ ID NO: 20.

20 Hereinbelow, the present invention is described in detail.

 In the present invention, with respect to the nucleotide sequences, A represents adenine, C represents cytosine, G represents guanine and T represents
25 thymine.

In the present invention, with respect to the amino acid sequences, Ala represents an alanine residue, Arg represents an arginine residue, Asn represents an asparagine residue, Asp represents an aspartic acid residue, Cys represents a cysteine residue, Gln represents a glutamine residue, Glu represents a glutamic acid residue, Gly represents a glycine residue, His represents a histidine residue, Ile represents an isoleucine residue, Leu represents a leucine residue, Lys represents a lysine residue, Met represents a methionine residue, Phe represents a phenylalanine residue, Pro represents a proline residue, Ser represents a serine residue, Thr represents a threonine residue, Trp represents a tryptophan residue, Tyr represents a tyrosine residue and Val represents a valine residue.

For making more clear the essential features of the present invention, the technical features of the present invention will be described in detail below by explaining how the present invention has been developed.

All of the conventional live measles vaccines are produced from virus strains which were obtained by attenuating the viruses which prevailed in the 1950's and 1960's. Therefore, the antigenicity of convention-

al vaccine strains corresponds to the antigenicity of virus strains which were epidemic half a century ago.

On the other hand, it has been found that the most recent epidemic strains and the relatively recent epidemic strains have mutations in the H protein gene and the F protein gene which are genes responsible for a virion to adsorb on and penetrate into cells to thereby cause an infection with the virus. Specifically, the mutation in the H protein gene causes substitution of 17 to 19 amino acids in a specific region in the whole amino acid sequence (consisting of 617 amino acids) of the H protein and, such a substitution changes the three-dimensional structure of the protein, so that an antigenic mutation occurs. This antigenic mutation is as large as the antigenic shift of the H protein, and important.

Further, the present inventors have found that the antigenic mutation of the epidemic strain is an important factor causing the above-mentioned secondary vaccine failure and modified measles.

Based on these findings, the present inventors have succeeded in providing a viral genome of a measles virus mutant, particularly a mutant H protein gene and a mutant F protein gene, and the mutant antigens (not only the whole protein but also fragmentary peptides

thereof) encoded by the genes.

In addition, the present inventors have successfully developed the following utilities (i) to (iii) of the above-mentioned genes, mutant antigens and their epitopes, and the like.

(i) Modification of a viral genome of a live vaccine strain: A recombinant virus is prepared by replacing the H protein gene of a conventional live vaccine strain with the H protein gene of an epidemic strain. By using this method, a live attenuated vaccine strain which is adapted for the antigenicity of the epidemic strain is obtained speedily. In other words, the recombinant virus obtained in the above-mentioned manner can be used as an active component of an excellent vaccine which is capable of effectively preventing infections with the epidemic strains. This method is also advantageous from an economical viewpoint. That is, the time, labor and costs necessary for attenuating a virus can be decreased to a large extent. As mentioned above, with respect to the production of conventional vaccines, there is no specific limitation on the method for attenuating viruses, and conventionally, the attenuation was conducted mainly by passage, which requires at least several years to about 10 years for establishing an attenuated strain for a

live vaccine.

(ii) Preparation of an active component for a gene vaccine: A gene vaccine is prepared by inserting the H protein gene and the F protein gene of an epidemic strain into various vectors, such as a plasmid vector, a cosmid vector, a phage vector, a shuttle vector, a viral vector of a non-proliferating viral vector and the like.

For example, when a non-proliferating recombinant virus, which is prepared by inserting the cDNAs for the above-mentioned H protein gene and F protein gene into a non-proliferating viral vector, is used as an active component for a gene vaccine or DNA vaccine, such a vaccine is capable of inducing both humoral immunity and cellular immunity like a conventional live measles vaccine. A remarkable feature of this vaccine is that nasal injection is possible.

In addition, a cDNA fragment comprising the mutated region of the H protein gene of an epidemic strain can be inserted into, for example, a plasmid vector, to prepare a naked DNA. The thus prepared naked DNA can also be used as an active component for a DNA vaccine or gene vaccine for preventing measles.

(iii) Preparation of a suitable reagent for diagnosis of epidemic strains: PCR primers are synthe-

sized so that the synthesized primers reflect the mutations in the H protein gene or F protein gene of the epidemic strains. The synthesized primers can be used as a reagent for gene diagnosis not only for
5 identifying the epidemic strains, but also for differentiating a virulent strain from an attenuated strain, or vice versa.

Further, the mutant antigens (whole proteins or fragmentary peptides thereof) encoded by the above-mentioned genes are prepared, and their epitopes are
10 chemically synthesized. The antigens and epitopes are provided as suitable antigens for diagnosis of epidemic measles.

15 An explanation is made below with respect to the preparation of a measles virus mutant antigen and a measles virus mutant gene of the present invention, and the use of the prepared antigens and genes as a vaccine and a diagnostic reagent.

20 [I] Preparation of measles virus mutant antigen and measles virus mutant gene

(1) Antigen analysis of various measles virus antigens: The antigenicity of the measles virus mutant antigen can be evaluated by a neutralization test, an
25 HI (hemagglutination inhibition) test, a PA (passive

agglutination) test, an enzyme immunoassay and a fluorescent antibody technique each using a monoclonal antibody, and the like. However, for determining the effectiveness of the virus antigen as antigen for a vaccine, it is requisite to evaluate the antibody titer by the neutralization test, and it can be performed in accordance with the modified Ueda method (Biken Journal, 14, 155-160, 1971) which employs microplates.

With respect to the antibodies used in the antigen analysis, sera, such as a serum from a measles patient and mouse immune sera against measles viruses as mentioned below, can be employed.

With respect to the antigens (challenge viruses) used in the antigen analysis, it is important to select different measles strains from the strains isolated in the past to the present. Representative examples of epidemic strains of the 1950's and 1960's (virulent strains of the past) include Tanabe strain and Edmonston strain; and examples of live vaccine strains established by attenuating the above-mentioned virulent strains (conventional attenuated strains) include CAM-70 strain and Edmonston B strain. As the recent epidemic strains (virulent strains), use can be made of the measles strains isolated in various countries in the 1990's. For example, the virus strains isolated from

various resources by the present inventors, such as F-t strain (isolated in 1991 from throat swab of a reinfected patient), F-b strain (isolated in 1991 from blood of a reinfected patient), U-t strain (isolated in 1991 from throat swab of a non-vaccinated patient), U-b strain (isolated in 1991 from blood of a non-vaccinated patient), Momo strain (isolated in 1995 from a patient) and NA strain (isolated in 1996 from a patient) can be used as the recent epidemic strain.

Hereinafter, the following strains will be frequently referred to as indicated in the parentheses: Tanabe (Tana) strain, Edmonston (Edmo) strain, CAM-70 (CAM) strain and Momo (MO) strain.

(2) Determination of the mutated regions in the nucleotide sequence of a gene, and translation of the gene into an amino acid sequence: The analysis of the viral genome of each of the measles strains mentioned in item (1) above is carried out as follows. First, the viral RNA genome is extracted and the cDNA is prepared using primers. The nucleotide sequence of the prepared cDNA is determined by the direct sequencing method which employs PCR method (hereinafter, simply referred to as "PCR-direct sequencing method"). The search for DNA sequence homology between different measles virus strains is performed while determining

the nucleotide sequence of the genes, to thereby specify the mutated regions within the genes.

Next, each of the above-specified mutated regions are translated into amino acid sequence in accordance with the universal code, and the deductive analyses of the amino acid sequences are performed as follows. Analysis of the hydrophobicity pattern and determination of the secondary structure of a protein by Chou-Fasman analysis are performed by computer using the computer software "DNASIS-Mac (version 3.6)" (manufactured and sold by Hitachi Software Engineering Co., Ltd., Japan). Epitopes can be identified, for example, by computer using the computer software "Epitope Advisor" [manufactured and sold by Fujitsu Kyushu System Engineering (FQS) Ltd., Japan].

(3) Measles virus mutant antigens and genes coding for the same: Based on the antigen analyses mentioned in item (1) above and the studies on the nucleotide and amino acid sequences mentioned in item (2) above, the present inventors have conducted comparative analyses between the strains of recent epidemic measles, the virulent strains of the past and the conventional strains for a live attenuated measles vaccine, and they identified the respective regions in the H protein and the F protein which contain amino

acid substitutions. Further, the present inventors specified the antigens useful for the vaccine or the reagent for diagnosis of epidemic strain of measles virus. The measles virus mutant antigen of the present invention is the whole protein or a fragmentary peptide of the H protein and F protein of the attenuated measles virus CAM-70 strain or the epidemic measles virus NA strain. Each of the amino acid sequences is disclosed for the first time by the inventors of the present invention. Specifically, the measles virus mutant antigen of the present invention is an antigen comprising at least one protein antigen selected from the group consisting of (I) an H protein antigen of a measles mutant and (II) an F protein antigen of a measles mutant.

The measles virus mutant H protein antigen (I) is at least one member selected from the group consisting of the following amino acid sequences (a) to (f) identified with the positional amino acid numbers of either SEQ ID NO: 2 or SEQ ID NO: 10:

- (a) the whole sequence of the 1st to 617th amino acids;
- (b) a fragmentary sequence of the 93rd to 616th amino acids;
- (c) a fragmentary sequence of the 176th to 316th

amino acids;

(d) fragmentary sequences of the 172nd to 178th amino acids, the 238th to 244th amino acids, the 277th to 282nd amino acids, and the 301st to 307th amino acids;

(e) fragmentary, contiguous sequences of at least 6 amino acids in either SEQ ID NO: 2 or SEQ ID NO: 10, wherein the sequences each comprise an amino acid selected from the group consisting of the 174th, 176th, 243rd, 279th and 302nd amino acids, and neighboring amino acids of the selected amino acid in either SEQ ID NO: 2 or SEQ ID NO: 10, wherein the fragmentary, contiguous sequences are exclusive of the fragmentary sequences (d); and

(f) fragmentary, contiguous sequences of at least 6 amino acids in either SEQ ID NO: 2 or SEQ ID NO: 10, wherein the sequences each comprise an amino acid selected from the group consisting of the 93rd, 157th, 169th, 175th, 211th, 252nd, 276th, 284th, 285th, 296th, 316th, 338th, 387th, 416th, 455th, 481st, 484th, 505th, 546th, 592nd, 600th, 603rd and 616th amino acids, and neighboring amino acids of the selected amino acid in either SEQ ID NO: 2 or SEQ ID NO: 10, wherein the fragmentary, contiguous sequences are exclusive of the fragmentary sequences (d) and (e).

The measles virus mutant F protein antigen (II) is at least one member selected from the group consisting of the following amino acid sequences (g) and (h) identified with the positional amino acid numbers of either SEQ ID NO: 18 or SEQ ID NO: 20:

(g) the whole sequence of the 1st to 550th amino acids; and

(h) fragmentary, contiguous sequences of at least 6 amino acids in either SEQ ID NO: 18 or SEQ ID NO: 20, wherein the sequences each comprise an amino acid selected from the group consisting of the 11th, 52nd, 107th, 165th, 398th, 417th and 523rd amino acids, and neighboring amino acids of the selected amino acid in either SEQ ID NO: 18 or SEQ ID NO: 20.

Among the protein antigens included in the measles virus mutant antigens of the present invention, the protein antigens as defined in items (a) and (g) above are H protein and F protein, respectively, and the protein antigens as defined in items (b) to (f) and (h) above are peptides (fragmentary sequences). Further, the four fragmentary sequences as defined in item (d) above, namely, the fragmentary sequences of the 172nd to 178th amino acids, the 238th to 244th amino acids, the 277th to 282nd amino acids, and the 301st to 307th amino acids, identified with the positional amino acid

numbers of either SEQ ID NO: 2 or SEQ ID NO: 10, are epitopes of the H protein which are disclosed for the first time by the inventors of the present invention. With respect to the protein antigens as defined in items (a) to (d) and (g) above, the specific sequences are shown in the Sequence Listing. Each of the anti-
gens of the present invention can be chemically synthesized, based on the sequences shown in the Sequence Listing (see Example 5).

The measles virus mutant antigen of the present invention comprises at least one protein antigen selected from the group consisting of the above-mentioned whole proteins and fragmentary peptides, and the protein antigen can be chosen, based on the intended utility of the measles virus mutant antigen. Occasionally, several protein antigens can be used in combination.

In a further aspect of the present invention, a gene coding for the above-mentioned measles virus mutant antigen is provided. Specifically, the measles virus mutant gene comprising at least one gene selected from the group consisting of (I) a gene coding for an H protein antigen of a measles mutant and (II) a gene coding for an F protein antigen of a measles mutant is provided.

The gene (I) coding for a measles virus mutant H protein antigen is at least one member selected from the group consisting of the following genes (a) to (f) identified with the positional amino acid numbers of either SEQ ID NO: 2 or SEQ ID NO: 10:

(a) a gene coding for the whole sequence of the 1st to 617th amino acids;

(b) a gene coding for a fragmentary sequence of the 93rd to 616th amino acids;

(c) a gene coding for a fragmentary sequence of the 176th to 316th amino acids;

(d) genes coding for fragmentary sequences of the 172nd to 178th amino acids, the 238th to 244th amino acids, the 277th to 282nd amino acids, and the 301st to 307th amino acids;

(e) genes coding for fragmentary, contiguous sequences of at least 6 amino acids in either SEQ ID NO: 2 or SEQ ID NO: 10, wherein said sequences each comprise an amino acid selected from the group consisting of the 174th, 176th, 243rd, 279th and 302nd amino acids, and neighboring amino acids of the selected amino acid in either SEQ ID NO: 2 or SEQ ID NO: 10, wherein the genes are exclusive of the genes (d); and

(f) genes coding for fragmentary, contiguous sequences of at least 6 amino acids in either SEQ ID

NO: 2 or SEQ ID NO: 10, wherein said sequences each
comprise an amino acid selected from the group consist-
ing of the 93rd, 157th, 169th, 175th, 211th, 252nd,
276th, 284th, 285th, 296th, 316th, 338th, 387th, 416th,
5 455th, 481st, 484th, 505th, 546th, 592nd, 600th, 603rd
and 616th amino acids, and neighboring amino acids of
the selected amino acid in either SEQ ID NO: 2 or SEQ
ID NO: 10, wherein the genes are exclusive of the genes
(d) and (e).

10 The gene (II) coding for measles virus mutant F
protein antigen is at least one member selected from
the group consisting of the following genes (g) and (h)
identified with the positional amino acid numbers of
either SEQ ID NO: 18 or SEQ ID NO: 20:

15 (g) a gene coding for the whole sequence of the
1st to 550th amino acids; and

 (h) genes coding for fragmentary, contiguous
sequences of at least 6 amino acids in either SEQ ID
NO: 18 or SEQ ID NO: 20, wherein the sequences each
20 comprise an amino acid selected from the group consist-
ing of the 11th, 52nd, 107th, 165th, 398th, 417th and
523rd amino acids, and neighboring amino acids of the
selected amino acid in either SEQ ID NO: 18 or SEQ ID
NO: 20.

25 With respect to the gene coding for the measles

virus mutant antigen of the present invention, there is no particular limitation as long as the gene codes for the whole protein or a fragmentary peptide of the measles virus mutant antigen. Therefore, the gene is not limited to the nucleotide sequence of the genomic RNA of CAM-70 strain or NA strain. As the measles virus mutant gene, use can be made of the cDNAs shown in SEQ ID NOs: 1, 9, 17 and 19, or the gene can be prepared by synthesizing a nucleotide sequence on the basis of an amino acid sequence of a measles virus mutant antigen.

The measles virus mutant gene of the present invention comprises at least one gene selected from the group consisting of the above-mentioned genes, and the gene can be chosen, based on the intended utility of the measles virus mutant gene. Like the measles virus mutant antigen of the present invention, the measles virus mutant gene of the present invention comprises both the genes of the attenuated strain and the genes of the epidemic strain. Based on the disclosure of the present invention, for example, a live vaccine effective for preventing the infection with the epidemic strains can be produced {see the below-mentioned item [II](1), and Examples 2 and 3}. When several genes are used in combination, they can also be used in such a

form as ligated to each other {see the below-mentioned item [II](2) and Example 4}.

The antigens and genes coding for the same of the present invention, which respectively comprise the above-mentioned sequences, are effective as a marker for identifying a virulent strain or an attenuated strain, and are also important and advantageous for improving conventional vaccines and developing diagnostic reagents.

[II] Use of measles virus mutant antigen and measles virus mutant gene of the present invention as vaccine and diagnostic reagent

(1) Preparation of an effective live vaccine for epidemic measles strains: A recombinant virus is prepared by replacing a gene of a live vaccine strain with a corresponding gene of an epidemic strain. With respect to the live vaccine strain, various strains mentioned under "Prior Art" of the specification can be used, but preferably, use is made of a strain which has been employed as an active component of a live vaccine in various countries for at least 10 years. That is, a strain having approved safety and effectiveness as an active component for a vaccine, such as CAM-70 strain, is preferred.

With respect to the epidemic strain used for

preparing a live vaccine, the epidemic strain is selected so that when the selected strain is compared with a live vaccine strain, the epidemic strain has a marked, broad antigenic mutation due to the genetic mutation thereof. Specifically, a preferred epidemic strain is a recent epidemic strain which is being isolated at high frequency and is widely prevailing, and having an universal antigenic mutation (that is, an antigenic mutation which is not peculiar to a particular strain), for example, MO strain or NA strain isolated by the inventors of the present invention in 1995 to 1996.

With respect to the gene to be used for replacement, the gene can be selected from the genes coding for the antigens mentioned in item [I](3) above, and the genes can be used individually or in combination. However, for preventing any possible reversion of a recombinant virus from an attenuated state to a virulent state, and also from the viewpoint of ease in preparing a recombinant virus, it is preferred to use the gene described in item (c), that is, the gene coding for the fragmentary sequence of the 176th to 316th amino acids of the H protein (the peptide of SEQ ID NO: 4 and the peptide of SEQ ID NO: 12). The amino acid substitutions in this region are characteristic of

the epidemic strains and such substitutions are not found in the H protein of the attenuated strains. Therefore, by using the gene coding for this region, an epitope of the epidemic strain can be introduced into the attenuated strain without changing the sequences which are characteristic of the attenuated strains (that is, the sequences which may be causative of attenuation).

The recombinant virus can be produced by the method of Radecke et al. (EMBO Journal, Vol. 14, No. 23, pp. 5773-5784, 1995) which is a method for genetic recombination of a non-segmented negative-strand RNA viral (mononegaviral) genome, or by the modified method of Radecke et al., which has been developed by the inventors of the present invention.

The method of Radecke et al. (frequently referred to as "reverse genetics") will be explained below. First, the cells of 293 cell line (American Type Culture Collection, Accession No. ATCC CRL-1573) were transfected with a recombinant vector containing genes coding for T7 RNA polymerase and measles virus N protein and P protein, thereby obtaining transfectants (i.e., helper cells) capable of expressing T7 RNA polymerase, N protein and P protein. Next, an expression vector capable of expressing L protein (polymer-

ase) of the measles virus under the control of T7 promoter is constructed (hereinafter, the constructed expression vector is simply referred to as "V1"). Further, a cDNA for the (+) sense RNA of the whole genome of CAM-70 strain is prepared, and a DNA fragment coding for a region in the H protein which contains the above-mentioned amino acid substitutions is cleaved and removed from the cDNA for CAM-70 strain by means of restriction enzymes. Then, the DNA sequence of the corresponding region of the viral genome of epidemic MO strain or NA strain is prepared therefrom and inserted into the restriction site of the cDNA for CAM-70 strain, to thereby obtain a recombinant cDNA. The obtained recombinant cDNA is inserted into plasmid pBluescriptTM SK or KS (manufactured and sold by Stratagene Co., Ltd., England), thereby obtaining an expression vector (hereinafter, the obtained expression vector is simply referred to as "V0"), wherein the expression vector is prepared so that the recombinant cDNA is capable of transcription by T7 RNA polymerase. V0 and V1 are co-transfected to the helper cells prepared above, and the desired recombinant measles virus can be obtained by subsequently culturing the transfected cells. The proliferation of the recombinant virus in the transfected cells can be confirmed by detecting the occurrence

of CPE (cytopathic effect), wherein the transfected cells generate syncytia, or by conducting a microscopic observation using a fluorescent antibody technique with a monoclonal antibody against the epitope of the protein encoded by the replaced gene.

The recombinant attenuated measles virus of CAM-70 strain, in which the gene coding for the 176th to 316th amino acids of the H protein of CAM-70 strain (SEQ ID NO: 4) is replaced by the gene coding for the 176th to 316th amino acids of the H protein of MO strain or NA strain (SEQ ID NO: 12), is obtained by using the above-mentioned method.

Further, the modified method of Radecke et al. is explained below. This modified method is such that the helper cells are not required, and any desired permissive cells can be used as host cells for the recombinant virus. With respect to the host cells employed, cells which are ensured to be safe as a culture host for the live vaccine strains and are approved as the host cells therefor, such as, MRC-5 cells and WI-38 cells are preferably used to prevent an introduction of an unidentified factor, a carcinogen and the like into the virus. First, the expression vectors for each of the genes coding for N, P, and L proteins of CAM-70 strain are individually prepared using plasmids

pcDNA3.1(+)TM or pcDNA3.1(-)TM (manufactured and sold by Invitrogen Co., Ltd., Canada). For example, each of the genes encoding N, P and L proteins of CAM-70 strain is individually inserted into an appropriate restriction site of pcDNA3.1(-), thereby constructing the expression vectors. For the expression of T7 RNA polymerase, recombinant MVA (hereinafter, simply referred to as "recMVA"; FEBS Letter, vol. 371, no. 1, pp. 9-12, 1995) can be used. The above-prepared three expression vectors and the expression vector V0 mentioned in connection with the method of Radecke et al. are co-transfected to either the MRC-5 cells or WI-38 cells which have already been transfected with recMVA. The desired recombinant attenuated measles virus is obtained by culturing the transfected cells at about 35° to 38 °C. The proliferation of the virus can be confirmed by detecting the occurrence of CPE or by conducting the microscopic observation using the fluorescent monoclonal antibody technique mentioned above. Further, the antigenicity and immunogenicity of the obtained recombinant virus can be qualified in accordance with the antigen analysis mentioned in item [I](1) above.

(2) Preparation of an active component of a gene vaccine: The non-proliferating recombinant adenovirus

can be prepared by inserting a gene of an epidemic measles virus into a non-proliferating adenoviral genome. The prepared recombinant adenovirus is effective as an active component of a gene vaccine. For preparing the recombinant virus, COS-TPC method developed by Saito et al. [Cell Technology (Saibo Kogaku), vol. 13, no. 8, pp. 757-763, 1994] can be employed. In this method, DNA-TPC (viral DNA-Terminal Protein Complex) of the genome of human adenovirus 5, and a cassette cosmid carrying almost all of the whole genome of the non-proliferating adenovirus (cassette cosmid pAdex1; U.S. Patent No. 5,700,470) are used. The non-proliferating adenovirus is derived from human adenovirus 5 and it lacks E1A and E1B genes which are essential for viral proliferation, and therefore, this virus is incapable of proliferation in cells other than the 293 cells which constantly express E1A and E1B genes. Further, this virus lacks gene coding for E3 protein, a protein which antagonizes the recognition of viral antigens by CTL (cytotoxic T lymphocytes). Due to this contrived design of the adenovirus, cellular immunity induced by CTL is expected to develop even in the presence of this virus.

With respect to a measles virus gene used for preparing the recombinant virus, the gene can be se-

lected from the genes coding for the antigens mentioned in item [I](3) above, and the genes can be used individually or in combination. However, for improving the immunogenicity which is necessary for providing a protection against the viral infection (that is, adsorption and penetration of a measles virus to a cell), it is preferred to use in combination the gene coding for the whole H protein mentioned in item (a) (SEQ ID NO: 2 or SEQ ID NO: 10) and the gene coding for the whole F protein mentioned in item (g) (SEQ ID NO: 18 or SEQ ID NO: 20).

Specifically, the cDNAs for the above mentioned H protein gene and F protein gene (for example, the nucleotide sequences of SEQ ID NO: 9 and SEQ ID NO: 19) are prepared [when the cDNAs are ligated, they are ligated in the order of H protein - F protein (HF) or F protein - H protein (FH) in the direction of from the 5' end to the 3' end], and the prepared cDNAs are inserted into the E1A·E1B deletion site of the cassette cosmid pAdex1, to thereby obtain recombinant cosmid pAdex1/HF or pAdex1/FH. On the other hand, DNA-TPC is extracted from the parent adenovirus strain, and the DNA-TPC is digested with the restriction enzyme *Eco* T22I (manufactured and sold by Takara Shuzo Co., Ltd., Japan), to thereby obtain digestion product DNA-TPC/*Eco*

T22I. Subsequently, pAdex1/HF or pAdex1/FH, and DNA-TPC/Eco T22I are co-transfected to the 293 cells by calcium phosphate method. As a result of the co-transfection, homologous recombination between the transfected DNAs occurs in the cells, and a non-proliferating recombinant adenovirus containing measles virus H protein gene and F protein gene is obtained. The presence of measles virus H and F proteins in the non-proliferating recombinant adenovirus can be confirmed by testing Hela cells infected with the obtained adenovirus by fluorescent antibody technique using the monoclonal antibodies against the measles proteins.

(3) Production of a measles vaccine: The live attenuated measles vaccine can be produced by using the recombinant attenuated measles virus mentioned in item [II](1) above as a seed virus. For example, the recombinant virus is proliferated in permissive cells, such as chicken embryo cells, thereby obtaining a virus suspension. The cells are removed from the obtained virus suspension by low-speed centrifugation, thereby obtaining a supernatant. Then, the obtained supernatant is subjected to filtration to thereby prepare a bulk vaccine solution. The prepared bulk vaccine solution is diluted with a medium, such as BME medium (Eagle's Basal Medium), so as to obtain a vaccine

solution comprising the virus in a sufficient antigenic amount, for example, not less than 5,000 TCID₅₀ (Median Tissue Culture Infective Dose) per 0.5 ml of vaccine solution. A stabilizer for stabilizing the virus can
5 be added to the vaccine solution when the bulk vaccine solution is being diluted. Subsequently, the diluted vaccine solution is dispensed into suitable containers, such as 1 to 20 ml volume vials, and then, the containers are sealed hermetically, and the sealed vaccine is
10 provided as a vaccine preparation. The vaccine preparation can be provided as a liquid preparation or as a lyophilized preparation obtained by lyophilizing the vaccine after dispensation. Prior to the use of the vaccine preparation, it is requisite to subject the
15 vaccine preparation to various tests on effectiveness and safety to assure its quality as a vaccine. The tests are conducted in accordance with Pharmaceutical Affairs Law (the Law No. 145 established in 1960) and a provision entitled "Dried Attenuated Measles Virus Live
20 Vaccine" in the Notification No. 217 of the Japanese Ministry of Health and Welfare: Seibutsugakuteki Seizai Kijun (Minimum Requirements for Biological Products) established in 1993. With respect to the manner of administration, for example, the vaccine preparation is
25 administered by subcutaneous injection in an amount of

0.25 to 0.5 ml per dose.

The non-proliferating recombinant virus mentioned in item [II](2) above can be produced in large yield using the 293 cells. The recombinant virus can be prepared from the liquid culture of 293 cells in substantially the same manner as mentioned above for preparing the vaccine preparation, so that the final virus content of a liquid or lyophilized preparation is 10^6 to 10^8 PFU (plaque-forming unit) per 1 ml of preparation. Such virus preparation can be provided as an active component for a gene vaccine. With respect to the manner of administration, the gene vaccine can be administered by subcutaneous, intramuscular or nasal injection in an amount of 0.25 to 0.5 ml per dose, and from the viewpoint of ease in injection procedure, nasal injection is especially preferred.

(4) Preparation of a diagnostic reagent: The antigens mentioned in item [I](3) above (whole protein or fragmentary peptide thereof) can be used individually or in combination as an antigen for diagnosis. When using several antigens in combination, the antigens containing different epitopes are preferably used to broaden the spectrum of reactivity with antibody. The antigen of the present invention can be provided as an antigen to be used in various diagnoses, such as diag-

nosis using precipitation reaction, agglutination reaction, neutralization reaction, fluorescent antibody technique, enzyme immunoassay, and radioimmunoassay. Further, the antigens can be inoculated intraperitoneally, subcutaneously or intramuscularly to an animal, such as rabbit, guinea pig and mouse, to prepare an immune serum, antibody or the like. The thus prepared antibody can be also provided as an antibody for detecting antigens in various diagnoses.

The antigen or antibody of the present invention is diluted so as to prepare a diagnostic reagent containing the antigen or antibody in an amount sufficient to cause an antigen-antibody reaction.

Further, the genes coding for the antigen mentioned in item [I](3) above can be used individually or in combination, for example, as a probe reagent for gene diagnosis and a reagent for identifying the measles virus strains. PCR primers can be designed, based on the amino acid sequences of the H protein and F protein of the attenuated strain and epidemic strain (for example, SEQ ID NOs: 2, 10, 18 and 20) and based the nucleotide sequences of the genes coding for the same (for example, SEQ ID NOs: 1, 9, 17 and 19) which are disclosed in the present specification. Such PCR primers can be provided as a reagent for diagnosis

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using the PCR method.

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BEST MODE FOR CARRYING OUT THE INVENTION

Hereinbelow, the present invention will be described in more detail with reference to the following Examples, but they should not be construed as limiting the scope of the present invention.

Example 1

Antigen analyses and gene analyses are performed as follows, to thereby identify the differences in nucleotide sequences and amino acid sequences between the past epidemic strains (virulent strains), conventional live vaccine strains (attenuated strains) and recent epidemic strains (virulent strains). In addition, the amino acid sequences of mutant antigens and their epitopes are determined.

(1) Antigen Analyses

Measurement of neutralizing antibody titers (1):

Each of the neutralizing antibody titers for a vaccine strain and an epidemic strain in a test serum is measured separately by the modified Ueda method which employs microplates. As a challenge virus, CAM-70 strain is used as a vaccine strain, and Momo strain is used as an epidemic strain. B95a cells are used for proliferating the viruses. The test sera are selected

from sample sera individually obtained from infants who received vaccination with measles CAM-70 strain vaccine during the period of 1994 to 1996, in which the sera were sampled from each infant before the vaccination and 1 to 2 months after the vaccination. Two groups of test sera (i.e., groups A and B) are prepared, so that group A consists of eleven (11) sample sera each having HI (hemagglutination inhibition) antibody titer of 8-fold, and group B consists of fourteen (14) sample sera each having HI antibody titer of 64-fold, both measured using HI antigen of Toyoshima strain (isolated in 1959). Two rows of microplate wells were used for determining the neutralizing antibody titer in a test serum.

20 μ l of culture medium is dispensed into each well of a microplate, and serial 2-fold dilution of each test serum (20 μ l) with the dispensed culture medium is performed. 20 μ l of a challenge virus solution (viral infective dose is already adjusted to 10 TCID₅₀/20 μ l) is placed in each well and mixed with the diluted test serum, and then, a reaction is allowed to proceed at 37 °C for 1 hour. Subsequently, 100 μ l of cultured B95a cells is added to each reaction mixture in the well, and the cells are cultured for 1 week. The neutralizing antibody titer is measured by

detecting the occurrence of CPE (cytopathic effect).
The results are shown below.

Group A: The relative antibody titer (antibody
titer for epidemic strain/antibody titer for vaccine
5 strain) is less than $1/2$ in nine (9) test sera out of
the total of eleven (11) test sera (9/11; 81.8 %).
Particularly, among the above-mentioned nine (9) test
sera, the antibody titer for the epidemic strain is not
detected (that is, the value of antibody titer is less
10 than 0 as expressed in terms of $\log_2$) in six (6) test
sera (6/11; 54.5 %), even though the antibody titer for
the vaccine strain is from 2.6 to 3.6 (the values are
expressed in terms of $\log_2$) in these test sera. With
respect to the remaining two (2) test sera, the rela-
15 tive antibody titer is 1 (i.e., $1/1$).

Group B: With respect to ten (10) test sera out of
the total of fourteen (14) test sera (10/14; 71.4 %),
the relative antibody titer (antibody titer of epidemic
strain/antibody titer of vaccine strain) is so low as
20 to fall within the range of from $1/2$ to $1/8$. Each of
the remaining four (4) test sera has a relative anti-
body titer of approximately 1 (i.e., $1/1$). Since test
sera having a relative antibody titer (antibody titer
of epidemic strain/antibody titer of vaccine strain) of
25 less than $1/2$ are frequently found among the sera

containing antibodies against a conventional measles virus, it is concluded that the recent epidemic strain has certain mutation in its antigens (that is, both the H and F proteins) which are related to the neutralization of antibodies and viral infection.

Measurement of neutralizing antibody titers (2):

The neutralizing antibody titers in a mouse immune serum against the H protein of NA strain is determined in substantially the same manner as mentioned in measurement (1) above, except that CAM-70 strain, Tanabe strain and NA strain are separately used as a challenging virus, and the mouse immune sera prepared in the following manner are used as the test sera.

Ten BALB/C mice (4 weeks old) are individually injected intramuscularly with 100 μ l of a solution of expression vector pcDNA3.1(-)/H capable of expressing the H protein of NA strain (hereinafter, simply referred to as "naked DNA"). After 2 weeks from the first injection, as a booster injection, the intramuscular injection of the naked DNA is repeated in substantially the same manner as the first injection. As a control, physiological saline is injected instead of the naked DNA to each of the five mice in substantially the same manner as mentioned above. After 4 weeks from

the booster injection, blood is sampled individually from each of the ten immunized mice and five control mice to thereby obtain mouse immune sera.

5 The above-mentioned naked DNA is the expression vector for NA strain H protein prepared in connection with Example 3 below, and it is obtained by amplifying plasmid pCDNA3.1(-)/H in *E. coli*, and substantially purifying the plasmid from the *E. coli* culture.

10 As a result, it is found that the average neutralizing antibody titer (the value expressed in terms of $\log_2$) for NA strain, CAM-70 strain and Tanabe strain is 4.0, 3.8 and 4.0, respectively. From the above results and the results of measurement (1) mentioned above, it is concluded that the antigen of the recent epidemic
15 strain (i.e., NA strain) has a broader spectrum with respect to the reactivity with antibody than that of the vaccine strain or the epidemic strain of the past, and that the antigenicities of the vaccine strain and the past epidemic strain are embraced by that of the
20 recent epidemic strain.

(2) Gene Analyses

Determination of the nucleotide sequences of the H protein and F protein:

25 The nucleotide sequences of the H and F proteins

are determined in accordance with the method of Isegawa
et al. (Mol. Cell. Prob., 6, 467-475, 1992). Each of
the measles strains shown in Tables 2 and 3 is infected
individually to B95a cells, and RNA is extracted from
each of the infected cells by GTC/CsCl method of Chirg-
win et al. (Biochemistry, 18, 5294-5299, 1979). Subse-
quently, the cDNA for each measles strain is synthe-
sized using random primers (6 mer). Based on the cDNA
sequence of the gene of Edmonston strain (Virology,
vol. 173, no. 2, pp. 415-425, 1989), specific primers
(shown in Table 1) are synthesized, and the nucleotide
sequence of each of the measles strains is determined
by the PCR-direct sequencing method using the synthe-
sized primers. The amino acid sequence is deduced from
each nucleotide sequence in accordance with the univer-
sal code, and in addition, the amino acids which are
substituted as a result of genetic mutations are iden-
tified. The results are shown in Tables 2 and 3 and
SEQ ID NOS: 1, 2, 9, 10, and 17 to 20.

Table 1

Primers used for PCR-direct sequencing method

	Primer	Nucleic acid sequence
Gene coding for F protein	F28	AGAATCAAGACTCATCCAATGTC
	CF7	TTGAGAGTTCAGCATGGACTGGT
	CF3	ACAATGAAGTAGGACTCTGTGTC
	F3	GGAACCTAATAGCCAATTGTGCA
	CF2	CGAGGTCAATTCTGTGCAAGTAC
	F4	AAAGGGAGAACAAGTTGGTATGT
	CF1	GATATTGTTTCGGCCAGAGGGAAG
Gene coding for H protein	MP5	ATGTCACCACAACGAGACCGGAT
	MP4	GAGATTCACTGACCTAGTGAAAT
	MP2	TCGCTGTCCCTGTTAGACTTGTA
	H8	GAGCAACCAGTCAGTAATGATCT
	MP3	ATGCCTGATGTCTGGGTGACATC

Table 2

Amino acid substitutions in H protein

Amino acid number	Measles strain								
	Edmo	Tana	CAM-70	F-b	F-t	U-b	U-t	MO	NA
93	Thr		Ile						
157	Val		Ala						
169	Ser			Ala	Ala	Ala	Ala	Ala	Ala
174	Thr			Ala	Ala	Ala	Ala	Ala	Ala
175	Arg	Lys	Lys						
176	Thr			Ala	Ala	Ala	Ala	Ala	Ala
211	Gly			Ser	Ser	Ser	Ser	Ser	Ser
243	Arg			Gly	Gly	Gly	Gly	Gly	Gly
252	Tyr			His	His	His	His	His	His
276	Leu			Phe	Phe	Phe	Phe	Phe	Phe
279	Pro			Ser	Ser	Ser	Ser	Ser	Ser
284	Leu			Phe	Phe	Phe	Phe	Phe	Phe
285	Ser							Asn	Asn
296	Leu			Phe	Phe	Phe	Phe	Phe	Phe
302	Gly			Arg	Arg	Arg	Arg	Arg	Arg
316	Gly			Ser	Ser	Ser	Ser		
338	Pro		Ser						
387	Leu								Gln
416	Asp			Asn	Asn	Asn	Asn	Asn	Asn
455	Thr		Asn						
481	Tyr			Asn	Asn	Asn	Asn	Asn	Asn
484	Asn	Thr	Thr	Thr	Thr	Thr	Thr	Thr	Thr
505	Asp		Gly						
546	Ser	Gly							
592	Gly	Glu	Glu						
600	Glu	Val	Val	Val	Val	Val	Val	Val	Val
603	Gly		Glu						
616	Arg			Ser	Ser	Ser	Ser	Ser	Ser

[Note]

- (1) "Edmo" represents "Edmonston strain", "Tana" represents "Tanabe strain", and "MO" represents "Momo strain".
- (2) Amino acid sequence of H protein (deduced from cDNA) of Edmonston strain is used as a standard for determining the substituted amino acids in H protein of other measles strains. Amino acids which are the same as that of the Edmonston strain are not shown.

Table 3

Amino acid substitutions in F protein

Amino acid number	Measles strain								
	Edmo	Tana	CAM-70	F-b	F-t	U-b	U-t	MO	NA
11	Phe							Leu	Leu
52	Gln	His	His						
107	Ser	Gly	Gly						
165	Arg		Gly						
398	tyr		His						
417	Ala	Asp	Asp						
523	Lys			Arg	Arg	Arg	Arg	Arg	Arg

[Note]

- (1) "Edmo" represents "Edmonston strain", "Tana" represents "Tanabe strain", and "MO" represents "Momo strain".
- (2) Amino acid sequence of F protein (deduced from cDNA) of Edmonston strain is used as a standard for determining the substituted amino acids in F protein of other measles strains. Amino acids which are the same as that of the Edmonston strain are not shown.

Determination of the secondary structure of the H protein:

The secondary structure of the H protein is determined by analyzing the above-identified amino acid sequence by computer. Computer software "DNASIS-Mac (version 3.6)" (manufactured and sold by Hitachi Software Engineering Co., Ltd., Japan) is used to analyze the hydrophobicity pattern and to conduct Chou-Fasman analysis. As a result, with respect to the secondary structure of each of the regions respectively consisting of the 176th to 316th amino acids and the 317th to 616th amino acids of the whole amino acid sequence of the H protein shown in SEQ ID NO: 2, the positions of epitopes are flip-flopped between the vaccine strain and the epidemic strain [that is, when an analytical diagram for a vaccine strain (for example, CAM-70 strain) and an analytical diagram for an epidemic strain (for example, MO strain or NA strain) are arranged side by side, it is apparent that the diagram for the epidemic strain is transformed to look like a mirror image (axial symmetry) of the diagram for the vaccine strain]. On the other hand, with respect to the F protein, when the analytical diagrams are prepared for a vaccine strain and an epidemic strain, no such differences as would cause a mirror image (axial

symmetry) are observed.

Analysis of the mutated epitopes of the H protein:

5 With respect to the amino acid sequences of the
above-mentioned vaccine strain and epidemic strain, the
regions where the mutation (amino acid substitutions)
is concentrated are analyzed by computer using the
computer software "Epitope Advisor" [manufactured and
sold by Fujitsu Kyushu System Engineering (FQS) Co.,
10 Ltd., Japan] to determine the epitopes. As a result,
the following four regions, the 172nd to 178th amino
acids, the 238th to 244th amino acids, the 277th to
282nd amino acids, and the 301st to 307th amino acids,
identified with the positional amino acid numbers of
15 either SEQ ID NO: 2 or SEQ ID NO: 10, are determined as
the mutated epitope regions of the H protein.

Example 2

20 Modification of a genome of a live attenuated vaccine
strain:

A recombinant CAM-70 virus, which is vaccine virus
CAM-70 strain having a part of its H protein replaced
by the corresponding part of the H protein of epidemic
measles Momo strain, is prepared by the method of Radecke et
25 al. (reverse genetics) described in item [II](1) above.

The part of the H protein to be replaced is the restriction enzyme *HinfI* fragment of the cDNA derived from the viral genome comprising the region consisting of the 526th to 948th nucleotides (total of 423 nucleotides) of the nucleotide sequence of SEQ ID NO: 1 (encoding the 176th to 316th amino acids of H protein). The antigenicity of the prepared recombinant virus is confirmed by the fluorescent antibody technique and the enzyme immunoassay using the monoclonal antibodies against CAM-70 strain and Momo strain.

Example 3

Modification of a genome of a live attenuated vaccine strain:

A recombinant CAM-70 virus which is vaccine virus CAM-70 strain having a part of its H protein replaced by the corresponding part of the H protein of epidemic measles NA strain is prepared in substantially the same manner as mentioned in Example 2, except that the method is modified in the following manner {modified method described in item [II](1) above}.

First, the viral genomic RNA is extracted from the CAM-70 strain, and the cDNA is prepared from the genomic RNA by RT-PCR (reverse transcript-PCR) method. The genes coding for N, P and L proteins are cloned

individually from the prepared cDNA by a customary method using primers [hereinbelow, each of the clones are referred to as "pcDNA3.1(-)/N", "pcDNA3.1(-)/P" and "pcDNA3.1(-)/L"]. The clones are amplified in *E. coli* and stored for use in the subsequent procedure.

In addition to the above, the cDNA derived from the full length viral genomic RNA of CAM-70 strain, in which a part of its H protein gene is replaced by the corresponding part of the H protein gene of NA strain, is cloned by using plasmids pBluescript SK or KS in substantially the same manner as mentioned above, to thereby obtain clone pBluescript/MV. The obtained clone is amplified and stored for use in the subsequent procedure. With respect to the nucleotide sequence replaced in the cDNA for CAM-70 strain, the region consisting of the 526th to 948th nucleotides (total of 423 nucleotides encoding the 176th to 316th amino acids) of the CAM-70 strain H protein gene of SEQ ID NO: 1 is replaced with the corresponding region (the 526th to 948th nucleotides) in the NA strain H protein gene of SEQ ID NO: 9.

The above-mentioned pcDNA3.1(-)/N, pcDNA3.1(-)/P, pcDNA3.1(-)/L and pBluescript/MV are co-transfected to MRC-5 cells which have already been transfected with recMVA (FEBS Letter, vol. 371, no. 1, pp. 9-12, 1995),

and then, the transfected cells are cultured at 37 °C to thereby obtain a recombinant virus. The antigenicity of the recombinant virus is confirmed by the fluorescent antibody technique and the enzyme immunoassay using the monoclonal antibodies against CAM-70 strain and NA strain. The antigenicity of the recombinant virus is on the same level as that of the epidemic strains, and since the recombinant virus is attenuated, it can be used as an active component for a live attenuated measles vaccine.

Example 4

Preparation of an active component for a gene vaccine:

A non-proliferating recombinant adenovirus is prepared in accordance with the method of Saito et al. described in item [II](2) above. With respect to the gene which is inserted into the non-proliferating viral genome (i.e., cassette cosmid pAdex1), use is made of a ligation product of the cDNAs for the H protein gene and F protein gene of NA strain respectively shown in SEQ ID NO: 9 and SEQ ID NO: 19. The two cDNAs are ligated in the order of F protein - H protein in the direction from the 5' end to the 3' end, so that the F protein and the H protein are expressed in the form of an F-H fusion protein. The ligated cDNA is inserted

into the E1A·E1B deletion site of the cassette cosmid pAdex1 cleaved with a restriction enzyme *Swa*I, to thereby obtain pAdex1/FH.

5 With respect to the cDNAs for the H protein gene and the F protein gene, the cDNAs are prepared from the NA strain genomic RNA by RT-PCR method using primers which correspond to the respective genes. Further, pAdex1/FH is packaged into a λ phage so as to be amplified in *E. coli*, and stored for use in the subsequent
10 procedure.

Subsequently, the DNA-TPC (viral DNA-Terminal Protein Complex) of the parent adenovirus strain is extracted and purified from the infected cells by CsCl ultracentrifugation method, and the purified DNA-TPC is
15 digested with restriction enzyme *Eco* T22I to thereby obtain the digestion product DNA-TPC/*Eco* T22I. Then, using calcium phosphate method, the above-obtained pAdex1/FH and DNA-TPC/*Eco* T22I are co-transfected to the cultured cells of 293 cell line, thereby obtaining
20 transfectants, followed by culturing the transfectants at 37 °C for 18 hours to advance the homologous recombination between the DNAs. As a result of the homologous recombination, a non-proliferating recombinant adenovirus having both the H and F proteins of NA
25 strain is obtained from the cultured transfectants.

The fluorescent antibody technique using monoclonal antibodies against each of the H and F proteins is conducted to select the recombinant virus and confirm its proliferation in the transfected cells of 293 cell line (which are the permissive host cells for the adenovirus).

Example 5

Preparation of a diagnostic reagent:

10 The peptides having the following amino acid sequences are synthesized using a peptide synthesizer (Model ABI 432A manufactured and sold by Perkin-Elmer Cetus Co., Ltd., U.S.A.): "Leu Glu Ala Arg Ala Thr Asn", "Asn Leu Ser Ser Lys Gly Ser", "Glu Gln Ser Val
15 Ser Asn" and "His Arg Glu Asp Ser Ile Thr". Each of the synthesized peptides is used as an antigen for recognizing and identifying the infection with the epidemic strains.

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INDUSTRIAL APPLICABILITY

By the use of the measles virus mutant antigen or the gene coding for the same of the present invention, it has become possible to provide efficiently and economically a live attenuated measles vaccine or gene vaccine which is adapted for an epidemic strain of measles virus, and a diagnostic reagent capable of accurately detecting infections with an epidemic strain of measles virus.

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SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT:

- (A) NAME: The Research Foundation for Microbial Diseases of Osaka University
- (B) STREET: c/o Osaka University, 3-1 Yamadaoka
- (C) CITY: Suita-shi
- (D) STATE: Osaka
- (E) COUNTRY: Japan
- (F) ZIP: 565-0871

(ii) TITLE OF INVENTION: Measles virus mutant antigen and gene coding for the same

(iii) NUMBER OF SEQUENCES: 20

(v) COMPUTER READABLE FORM:

- (A) MEDIUM TYPE: Floppy disk
- (B) COMPUTER: IBM PC compatible
- (C) OPERATING SYSTEM: PC-DOS/MS-DOS
- (D) SOFTWARE: PatentIn Release #1.0, Version #1.30

(vi) CURRENT APPLICATION DATA:

- (A) APPLICATION NUMBER:
- (B) FILING DATE:
- (C) CLASSIFICATION:

(vii) PRIOR APPLICATION DATA:

- (A) APPLICATION NUMBER: WO PCT/JP98/02481
- (B) FILING DATE: 04-JUN-1998

(vii) PRIOR APPLICATION DATA:

- (A) APPLICATION NUMBER: JP 9-184285
- (B) FILING DATE: 04-JUN-1997

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1854 bases
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA to genomic RNA

(iii) HYPOTHETICAL: NO

64

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Measles virus

(B) STRAIN: Attenuated measles virus CAM-70 strain

(ix) FEATURE:

(A) NAME/KEY: CDS

(B) LOCATION: 1..1851

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

ATG TCA CCA CAA CGA GAC CGG ATA AAT GCC TTC TAC AAA GAT AAC CCC	48
Met Ser Pro Gln Arg Asp Arg Ile Asn Ala Phe Tyr Lys Asp Asn Pro	
1 5 10 15	
CAT CCC AAG GGA AGT AGG ATA GTC ATT AAC AGA GAA CAT CTT ATG ATT	96
His Pro Lys Gly Ser Arg Ile Val Ile Asn Arg Glu His Leu Met Ile	
20 25 30	
GAT AGA CCT TAT GTT TTG CTG GCT GTT CTG TTT GTC ATG TTT CTG AGC	144
Asp Arg Pro Tyr Val Leu Leu Ala Val Leu Phe Val Met Phe Leu Ser	
35 40 45	
TTG ATC GGG TTG CTA GCC ATT GCA GGC ATT AGA CTT CAT CGG GCA GCC	192
Leu Ile Gly Leu Leu Ala Ile Ala Gly Ile Arg Leu His Arg Ala Ala	
50 55 60	
ATC TAC ACC GCA GAG ATC CAT AAA AGC CTC AGC ACC AAT CTA GAT GTA	240
Ile Tyr Thr Ala Glu Ile His Lys Ser Leu Ser Thr Asn Leu Asp Val	
65 70 75 80	
ACT AAC TCA ATC GAG CAT CAG GTC AAG GAC GTG CTG ATA CCA CTC TTC	288
Thr Asn Ser Ile Glu His Gln Val Lys Asp Val Leu Ile Pro Leu Phe	
85 90 95	
AAA ATC ATC GGT GAT GAA GTG GGC CTG AGG ACA CCT CAG AGA TTC ACT	336
Lys Ile Ile Gly Asp Glu Val Gly Leu Arg Thr Pro Gln Arg Phe Thr	
100 105 110	
GAC CTA GTG AAA TTC ATC TCT GAC AAG ATT AAA TTC CTT AAT CCG GAT	384
Asp Leu Val Lys Phe Ile Ser Asp Lys Ile Lys Phe Leu Asn Pro Asp	
115 120 125	
AGG GAG TAC GAC TTC AGA GAT CTC ACT TGG TGT ATC AAC CCG CCA GAG	432
Arg Glu Tyr Asp Phe Arg Asp Leu Thr Trp Cys Ile Asn Pro Pro Glu	
130 135 140	

65

AGA Arg 145	ATC Ile	AAA Lys	TTG Leu	GAT Asp	TAT Tyr 150	GAT Asp	CAA Gln	TAC Tyr	TGT Cys	GCA Ala 155	GAT Asp	GCG Ala	GCT Ala	GCT Ala	GAA Glu 160	480
GAG Glu	CTC Leu	ATG Met	AAT Asn	GCA Ala 165	TTG Leu	GTG Val	AAC Asn	TCA Ser	ACT Thr 170	CTA Leu	CTG Leu	GAG Glu	ACC Thr	AAA Lys 175	ACA Thr	528
ACC Thr	AAT Asn	CAG Gln	TTC Phe 180	CTA Leu	GCT Ala	GTC Val	TCA Ser	AAG Lys 185	GGA Gly	AAC Asn	TGC Cys	TCA Ser	GGG Gly 190	CCC Pro	ACT Thr	576
ACA Thr	ATC Ile	AGA Arg 195	GGT Gly	CAA Gln	TTC Phe	TCA Ser	AAC Asn 200	ATG Met	TCG Ser	CTG Leu	TCC Ser	CTG Leu 205	TTA Leu	GAC Asp	TTG Leu	624
TAT Tyr 210	TTA Leu	GGT Gly	CGA Arg	GGT Gly	TAC Tyr	AAT Asn 215	GTG Val	TCA Ser	TCT Ser	ATA Ile	GTC Val 220	ACT Thr	ATG Met	ACA Thr	TCC Ser	672
CAG Gln 225	GGA Gly	ATG Met	TAT Tyr	GGG Gly	GGA Gly 230	ACT Thr	TAC Tyr	CTA Leu	GTG Val	GAA Glu 235	AAG Lys	CCT Pro	AAT Asn	CTG Leu	AGC Ser 240	720
AGC Ser	AAA Lys	AGG Arg	TCA Ser	GAG Glu 245	TTG Leu	TCA Ser	CAA Gln	CTG Leu	AGC Ser 250	ATG Met	TAC Tyr	CGA Arg	GTG Val 255	TTT Phe	GAA Glu	768
GTA Val	GGT Gly	GTT Val	ATC Ile 260	AGA Arg	AAT Asn	CCG Pro	GGT Gly	TTG Leu 265	GGG Gly	GCT Ala	CCG Pro	GTG Val 270	TTC Phe	CAT His	ATG Met	816
ACA Thr	AAC Asn	TAT Tyr 275	CTT Leu	GAG Glu	CAA Gln	CCA Pro	GTC Val 280	AGT Ser	AAT Asn	GAT Asp	CTC Leu	AGC Ser 285	AAC Asn	TGT Cys	ATG Met	864
GTG Val 290	GCT Ala	TTG Leu	GGG Gly	GAG Glu	CTC Leu	AAA Lys 295	CTC Leu	GCA Ala	GCC Ala	CTT Leu	TGT Cys 300	CAC His	GGG Gly	GAA Glu	GAT Asp	912
TCT Ser 305	ATC Ile	ACA Thr	ATT Ile	CCC Pro	TAT Tyr 310	CAG Gln	GGA Gly	TCA Ser	GGG Gly	AAA Lys 315	GGT Gly	GTC Val	AGC Ser	TTC Phe	CAG Gln 320	960
CTC Leu	GTC Val	AAG Lys	CTA Leu	GGT Gly 325	GTC Val	TGG Trp	AAA Lys	TCC Ser	CCA Pro 330	ACC Thr	GAC Asp	ATG Met	CAA Gln	TCC Ser 335	TGG Trp	1008
GTC Val	TCC Ser	TTA Leu	TCA Ser	ACG Thr	GAT Asp	GAT Asp	CCA Pro	GTG Val	ATA Ile	GAC Asp	AGG Arg	CTT Leu	TAC Tyr	CTC Leu	TCA Ser	1056

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340			345			350														
TCT	CAC	AGA	GGT	GTT	ATC	GCT	GAC	AAT	CAA	GCA	AAA	TGG	GCT	GTC	CCG					
Ser	His	Arg	Gly	Val	Ile	Ala	Asp	Asn	Gln	Ala	Lys	Trp	Ala	Val	Pro					1104
		355					360					365								
ACA	ACA	CGA	ACA	GAT	GAC	AAG	TTG	CGA	ATG	GAG	ACA	TGC	TTC	CAA	CAG					
Thr	Thr	Arg	Thr	Asp	Asp	Lys	Leu	Arg	Met	Glu	Thr	Cys	Phe	Gln	Gln					1152
		370				375					380									
GCG	TGT	AAG	GGT	AAA	ATC	CAA	GCA	CTC	TGC	GAG	AAT	CCC	GAG	TGG	GCA					
Ala	Cys	Lys	Gly	Lys	Ile	Gln	Ala	Leu	Cys	Glu	Asn	Pro	Glu	Trp	Ala					1200
385					390					395					400					
CCA	TTG	AAG	GAT	AAC	AGG	ATT	CCT	TCA	TAC	GGG	GTC	TTG	TCT	GTT	GAT					
Pro	Leu	Lys	Asp	Asn	Arg	Ile	Pro	Ser	Tyr	Gly	Val	Leu	Ser	Val	Asp					1248
				405					410					415						
CTG	AGT	CTG	ACA	GTT	GAG	CTT	AAA	ATC	AAA	ATT	GCT	TCG	GGA	TTC	GGG					
Leu	Ser	Leu	Thr	Val	Glu	Leu	Lys	Ile	Lys	Ile	Ala	Ser	Gly	Phe	Gly					1296
			420					425				430								
CCA	TTG	ATC	ACA	CAC	GGT	TCA	GGG	ATG	GAC	CTA	TAC	AAA	TCC	AAC	CAC					
Pro	Leu	Ile	Thr	His	Gly	Ser	Gly	Met	Asp	Leu	Tyr	Lys	Ser	Asn	His					1344
		435					440					445								
AAC	AAT	GTG	TAT	TGG	CTG	AAT	ATC	CCG	CCA	ATG	AAG	AAC	CTA	GCC	TTA					
Asn	Asn	Val	Tyr	Trp	Leu	Asn	Ile	Pro	Pro	Met	Lys	Asn	Leu	Ala	Leu					1392
		450				455					460									
GGT	GTA	ATC	AAC	ACA	TTG	GAG	TGG	ATA	CCG	AGA	TTC	AAG	GTT	AGC	CCC					
Gly	Val	Ile	Asn	Thr	Leu	Glu	Trp	Ile	Pro	Arg	Phe	Lys	Val	Ser	Pro					1440
465					470					475					480					
TAC	CTC	TTC	ACT	GTC	CCA	ATT	AAG	GAA	GCA	GGC	GAA	GAC	TGC	CAT	GCC					
Tyr	Leu	Phe	Thr	Val	Pro	Ile	Lys	Glu	Ala	Gly	Glu	Asp	Cys	His	Ala					1488
				485					490				495							
CCA	ACA	TAC	CTA	CCT	GCG	GAG	GTG	GGT	GGT	GAT	GTC	AAA	CTC	AGT	TCC					
Pro	Thr	Tyr	Leu	Pro	Ala	Glu	Val	Gly	Gly	Asp	Val	Lys	Leu	Ser	Ser					1536
			500					505					510							
AAT	CTG	GTG	ATT	CTA	CCT	GGT	CAA	GAT	CTC	CAA	TAT	GTT	TTG	GCA	ACC					
Asn	Leu	Val	Ile	Leu	Pro	Gly	Gln	Asp	Leu	Gln	Tyr	Val	Leu	Ala	Thr					1584
		515					520					525								
TAC	GAT	ACT	TCC	AGG	GTT	GAA	CAT	GCT	GTG	GTT	TAT	TAC	GTT	TAC	AGC					
Tyr	Asp	Thr	Ser	Arg	Val	Glu	His	Ala	Val	Val	Tyr	Tyr	Val	Tyr	Ser					1632
	530					535						540								

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CCA	AGC	CGC	TCA	TTT	TCT	TAC	TTT	TAT	CCT	TTT	AGG	TTG	CCT	ATA	AAG	1680
Pro	Ser	Arg	Ser	Phe	Ser	Tyr	Phe	Tyr	Pro	Phe	Arg	Leu	Pro	Ile	Lys	
545					550					555					560	
GGG	GTC	CCC	ATC	GAA	TTA	CAA	GTG	GAA	TGC	TTC	ACA	TGG	GAC	CAA	AAA	1728
Gly	Val	Pro	Ile	Glu	Leu	Gln	Val	Glu	Cys	Phe	Thr	Trp	Asp	Gln	Lys	
				565					570					575		
CTC	TGG	TGC	CGT	CAC	TTC	TGT	GTG	CTT	GCG	GAC	TCA	GAA	TCT	GGT	GAA	1776
Leu	Trp	Cys	Arg	His	Phe	Cys	Val	Leu	Ala	Asp	Ser	Glu	Ser	Gly	Glu	
			580					585						590		
CAT	ATC	ACT	CAC	TCT	GGG	ATG	GTG	GGC	ATG	GAA	GTC	AGC	TGC	ACA	GTC	1824
His	Ile	Thr	His	Ser	Gly	Met	Val	Gly	Met	Glu	Val	Ser	Cys	Thr	Val	
		595					600					605				
ACC	CGG	GAA	GAT	GGA	ACC	AAT	CGC	AGA	TAG							1854
Thr	Arg	Glu	Asp	Gly	Thr	Asn	Arg	Arg								
	610					615										

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 617 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Met	Ser	Pro	Gln	Arg	Asp	Arg	Ile	Asn	Ala	Phe	Tyr	Lys	Asp	Asn	Pro
1				5					10					15	
His	Pro	Lys	Gly	Ser	Arg	Ile	Val	Ile	Asn	Arg	Glu	His	Leu	Met	Ile
			20					25					30		
Asp	Arg	Pro	Tyr	Val	Leu	Leu	Ala	Val	Leu	Phe	Val	Met	Phe	Leu	Ser
		35					40					45			
Leu	Ile	Gly	Leu	Leu	Ala	Ile	Ala	Gly	Ile	Arg	Leu	His	Arg	Ala	Ala
	50					55					60				
Ile	Tyr	Thr	Ala	Glu	Ile	His	Lys	Ser	Leu	Ser	Thr	Asn	Leu	Asp	Val
65					70					75				80	
Thr	Asn	Ser	Ile	Glu	His	Gln	Val	Lys	Asp	Val	Leu	Ile	Pro	Leu	Phe
				85					90					95	

Lys	Ile	Ile	Gly	Asp	Glu	Val	Gly	Leu	Arg	Thr	Pro	Gln	Arg	Phe	Thr
			100					105					110		
Asp	Leu	Val	Lys	Phe	Ile	Ser	Asp	Lys	Ile	Lys	Phe	Leu	Asn	Pro	Asp
		115					120					125			
Arg	Glu	Tyr	Asp	Phe	Arg	Asp	Leu	Thr	Trp	Cys	Ile	Asn	Pro	Pro	Glu
	130					135					140				
Arg	Ile	Lys	Leu	Asp	Tyr	Asp	Gln	Tyr	Cys	Ala	Asp	Ala	Ala	Ala	Glu
145					150					155					160
Glu	Leu	Met	Asn	Ala	Leu	Val	Asn	Ser	Thr	Leu	Leu	Glu	Thr	Lys	Thr
				165					170					175	
Thr	Asn	Gln	Phe	Leu	Ala	Val	Ser	Lys	Gly	Asn	Cys	Ser	Gly	Pro	Thr
			180					185					190		
Thr	Ile	Arg	Gly	Gln	Phe	Ser	Asn	Met	Ser	Leu	Ser	Leu	Leu	Asp	Leu
		195					200					205			
Tyr	Leu	Gly	Arg	Gly	Tyr	Asn	Val	Ser	Ser	Ile	Val	Thr	Met	Thr	Ser
	210					215					220				
Gln	Gly	Met	Tyr	Gly	Gly	Thr	Tyr	Leu	Val	Glu	Lys	Pro	Asn	Leu	Ser
225					230					235					240
Ser	Lys	Arg	Ser	Glu	Leu	Ser	Gln	Leu	Ser	Met	Tyr	Arg	Val	Phe	Glu
				245				250						255	
Val	Gly	Val	Ile	Arg	Asn	Pro	Gly	Leu	Gly	Ala	Pro	Val	Phe	His	Met
			260					265					270		
Thr	Asn	Tyr	Leu	Glu	Gln	Pro	Val	Ser	Asn	Asp	Leu	Ser	Asn	Cys	Met
		275					280					285			
Val	Ala	Leu	Gly	Glu	Leu	Lys	Leu	Ala	Ala	Leu	Cys	His	Gly	Glu	Asp
	290					295					300				
Ser	Ile	Thr	Ile	Pro	Tyr	Gln	Gly	Ser	Gly	Lys	Gly	Val	Ser	Phe	Gln
305					310					315					320
Leu	Val	Lys	Leu	Gly	Val	Trp	Lys	Ser	Pro	Thr	Asp	Met	Gln	Ser	Trp
				325					330					335	
Val	Ser	Leu	Ser	Thr	Asp	Asp	Pro	Val	Ile	Asp	Arg	Leu	Tyr	Leu	Ser
			340					345					350		
Ser	His	Arg	Gly	Val	Ile	Ala	Asp	Asn	Gln	Ala	Lys	Trp	Ala	Val	Pro
		355					360					365			

Thr	Thr	Arg	Thr	Asp	Asp	Lys	Leu	Arg	Met	Glu	Thr	Cys	Phe	Gln	Gln	
	370					375					380					
Ala	Cys	Lys	Gly	Lys	Ile	Gln	Ala	Leu	Cys	Glu	Asn	Pro	Glu	Trp	Ala	
385					390					395					400	
Pro	Leu	Lys	Asp	Asn	Arg	Ile	Pro	Ser	Tyr	Gly	Val	Leu	Ser	Val	Asp	
				405					410					415		
Leu	Ser	Leu	Thr	Val	Glu	Leu	Lys	Ile	Lys	Ile	Ala	Ser	Gly	Phe	Gly	
			420					425					430			
Pro	Leu	Ile	Thr	His	Gly	Ser	Gly	Met	Asp	Leu	Tyr	Lys	Ser	Asn	His	
		435					440					445				
Asn	Asn	Val	Tyr	Trp	Leu	Asn	Ile	Pro	Pro	Met	Lys	Asn	Leu	Ala	Leu	
	450					455					460					
Gly	Val	Ile	Asn	Thr	Leu	Glu	Trp	Ile	Pro	Arg	Phe	Lys	Val	Ser	Pro	
465					470					475					480	
Tyr	Leu	Phe	Thr	Val	Pro	Ile	Lys	Glu	Ala	Gly	Glu	Asp	Cys	His	Ala	
				485					490					495		
Pro	Thr	Tyr	Leu	Pro	Ala	Glu	Val	Gly	Gly	Asp	Val	Lys	Leu	Ser	Ser	
			500					505					510			
Asn	Leu	Val	Ile	Leu	Pro	Gly	Gln	Asp	Leu	Gln	Tyr	Val	Leu	Ala	Thr	
		515					520					525				
Tyr	Asp	Thr	Ser	Arg	Val	Glu	His	Ala	Val	Val	Tyr	Tyr	Val	Tyr	Ser	
	530					535					540					
Pro	Ser	Arg	Ser	Phe	Ser	Tyr	Phe	Tyr	Pro	Phe	Arg	Leu	Pro	Ile	Lys	
545					550					555					560	
Gly	Val	Pro	Ile	Glu	Leu	Gln	Val	Glu	Cys	Phe	Thr	Trp	Asp	Gln	Lys	
				565					570					575		
Leu	Trp	Cys	Arg	His	Phe	Cys	Val	Leu	Ala	Asp	Ser	Glu	Ser	Gly	Glu	
			580					585					590			
His	Ile	Thr	His	Ser	Gly	Met	Val	Gly	Met	Glu	Val	Ser	Cys	Thr	Val	
		595					600					605				
Thr	Arg	Glu	Asp	Gly	Thr	Asn	Arg	Arg								
	610					615										

(2) INFORMATION FOR SEQ ID NO:3:

70

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 524 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Measles virus
- (B) STRAIN: Attenuated measles virus CAM-70 strain

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

Ile	Pro	Leu	Phe	Lys	Ile	Ile	Gly	Asp	Glu	Val	Gly	Leu	Arg	Thr	Pro	1	5	10	15
Gln	Arg	Phe	Thr	Asp	Leu	Val	Lys	Phe	Ile	Ser	Asp	Lys	Ile	Lys	Phe	20	25	30	
Leu	Asn	Pro	Asp	Arg	Glu	Tyr	Asp	Phe	Arg	Asp	Leu	Thr	Trp	Cys	Ile	35	40	45	
Asn	Pro	Pro	Glu	Arg	Ile	Lys	Leu	Asp	Tyr	Asp	Gln	Tyr	Cys	Ala	Asp	50	55	60	
Ala	Ala	Ala	Glu	Glu	Leu	Met	Asn	Ala	Leu	Val	Asn	Ser	Thr	Leu	Leu	65	70	75	80
Glu	Thr	Lys	Thr	Thr	Asn	Gln	Phe	Leu	Ala	Val	Ser	Lys	Gly	Asn	Cys	85	90	95	
Ser	Gly	Pro	Thr	Thr	Ile	Arg	Gly	Gln	Phe	Ser	Asn	Met	Ser	Leu	Ser	100	105	110	
Leu	Leu	Asp	Leu	Tyr	Leu	Gly	Arg	Gly	Tyr	Asn	Val	Ser	Ser	Ile	Val	115	120	125	
Thr	Met	Thr	Ser	Gln	Gly	Met	Tyr	Gly	Gly	Thr	Tyr	Leu	Val	Glu	Lys	130	135	140	
Pro	Asn	Leu	Ser	Ser	Lys	Arg	Ser	Glu	Leu	Ser	Gln	Leu	Ser	Met	Tyr	145	150	155	160
Arg	Val	Phe	Glu	Val	Gly	Val	Ile	Arg	Asn	Pro	Gly	Leu	Gly	Ala	Pro	165	170	175	

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Val	Phe	His	Met	Thr	Asn	Tyr	Leu	Glu	Gln	Pro	Val	Ser	Asn	Asp	Leu
			180					185					190		
Ser	Asn	Cys	Met	Val	Ala	Leu	Gly	Glu	Leu	Lys	Leu	Ala	Ala	Leu	Cys
		195					200					205			
His	Gly	Glu	Asp	Ser	Ile	Thr	Ile	Pro	Tyr	Gln	Gly	Ser	Gly	Lys	Gly
	210					215					220				
Val	Ser	Phe	Gln	Leu	Val	Lys	Leu	Gly	Val	Trp	Lys	Ser	Pro	Thr	Asp
225					230					235					240
Met	Gln	Ser	Trp	Val	Ser	Leu	Ser	Thr	Asp	Asp	Pro	Val	Ile	Asp	Arg
				245					250					255	
Leu	Tyr	Leu	Ser	Ser	His	Arg	Gly	Val	Ile	Ala	Asp	Asn	Gln	Ala	Lys
				260					265					270	
Trp	Ala	Val	Pro	Thr	Thr	Arg	Thr	Asp	Asp	Lys	Leu	Arg	Met	Glu	Thr
		275					280					285			
Cys	Phe	Gln	Gln	Ala	Cys	Lys	Gly	Lys	Ile	Gln	Ala	Leu	Cys	Glu	Asn
	290					295					300				
Pro	Glu	Trp	Ala	Pro	Leu	Lys	Asp	Asn	Arg	Ile	Pro	Ser	Tyr	Gly	Val
305					310					315					320
Leu	Ser	Val	Asp	Leu	Ser	Leu	Thr	Val	Glu	Leu	Lys	Ile	Lys	Ile	Ala
				325					330					335	
Ser	Gly	Phe	Gly	Pro	Leu	Ile	Thr	His	Gly	Ser	Gly	Met	Asp	Leu	Tyr
			340					345					350		
Lys	Ser	Asn	His	Asn	Asn	Val	Tyr	Trp	Leu	Asn	Ile	Pro	Pro	Met	Lys
		355					360					365			
Asn	Leu	Ala	Leu	Gly	Val	Ile	Asn	Thr	Leu	Glu	Trp	Ile	Pro	Arg	Phe
	370					375					380				
Lys	Val	Ser	Pro	Tyr	Leu	Phe	Thr	Val	Pro	Ile	Lys	Glu	Ala	Gly	Glu
385					390					395					400
Asp	Cys	His	Ala	Pro	Thr	Tyr	Leu	Pro	Ala	Glu	Val	Gly	Gly	Asp	Val
				405					410					415	
Lys	Leu	Ser	Ser	Asn	Leu	Val	Ile	Leu	Pro	Gly	Gln	Asp	Leu	Gln	Tyr
			420					425					430		
Val	Leu	Ala	Thr	Tyr	Asp	Thr	Ser	Arg	Val	Glu	His	Ala	Val	Val	Tyr
		435					440					445			

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Tyr Val Tyr Ser Pro Ser Arg Ser Phe Ser Tyr Phe Tyr Pro Phe Arg
 450 455 460
 Leu Pro Ile Lys Gly Val Pro Ile Glu Leu Gln Val Glu Cys Phe Thr
 465 470 475 480
 Trp Asp Gln Lys Leu Trp Cys Arg His Phe Cys Val Leu Ala Asp Ser
 485 490 495
 Glu Ser Gly Glu His Ile Thr His Ser Gly Met Val Gly Met Glu Val
 500 505 510
 Ser Cys Thr Val Thr Arg Glu Asp Gly Thr Asn Arg
 515 520

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 141 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Measles virus
- (B) STRAIN: Attenuated measles virus CAM-70 strain

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

Thr Thr Asn Gln Phe Leu Ala Val Ser Lys Gly Asn Cys Ser Gly Pro
 1 5 10 15
 Thr Thr Ile Arg Gly Gln Phe Ser Asn Met Ser Leu Ser Leu Leu Asp
 20 25 30
 Leu Tyr Leu Gly Arg Gly Tyr Asn Val Ser Ser Ile Val Thr Met Thr
 35 40 45
 Ser Gln Gly Met Tyr Gly Gly Thr Tyr Leu Val Glu Lys Pro Asn Leu
 50 55 60
 Ser Ser Lys Arg Ser Glu Leu Ser Gln Leu Ser Met Tyr Arg Val Phe
 65 70 75 80
 Glu Val Gly Val Ile Arg Asn Pro Gly Leu Gly Ala Pro Val Phe His

73

				85						90					95
Met	Thr	Asn	Tyr	Leu	Glu	Gln	Pro	Val	Ser	Asn	Asp	Leu	Ser	Asn	Cys
				100				105					110		
Met	Val	Ala	Leu	Gly	Glu	Leu	Lys	Leu	Ala	Ala	Leu	Cys	His	Gly	Glu
			115				120					125			
Asp	Ser	Ile	Thr	Ile	Pro	Tyr	Gln	Gly	Ser	Gly	Lys	Gly			
			130				135					140			

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 7 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Measles virus
- (B) STRAIN: Attenuated measles virus CAM-70 strain

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

Leu	Glu	Thr	Lys	Thr	Thr	Asn
1				5		

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 7 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Measles virus
- (B) STRAIN: Attenuated measles virus CAM-70 strain

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

74

Asn Leu Ser Ser Lys Arg Ser
1 5

(2) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 6 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Measles virus
- (B) STRAIN: Attenuated measles virus CAM-70 strain

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

Glu Gln Pro Val Ser Asn
1 5

(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 7 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Measles virus
- (B) STRAIN: Attenuated Measles virus CAM-70 strain

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

His Gly Glu Asp Ser Ile Thr
1 5

(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1854 bases
- (B) TYPE: nucleic acid

75

(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA to genomic RNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Measles virus

(B) STRAIN: Attenuated measles virus NA strain

(ix) FEATURE:

(A) NAME/KEY: CDS

(B) LOCATION: 1..1851

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

ATG TCA CCA CAA CGA GAC CGA ATA AAT GCC TTC TAC AAA GAC AAC CCC	48
Met Ser Pro Gln Arg Asp Arg Ile Asn Ala Phe Tyr Lys Asp Asn Pro	
1 5 10 15	
CAT CCT AAG GGA AGT AGG ATA GTT ATT AAC AGA GAA CAT CTT ATG ATT	96
His Pro Lys Gly Ser Arg Ile Val Ile Asn Arg Glu His Leu Met Ile	
20 25 30	
GAT AGA CCT TAT GTT TTG CTG GCT GTT CTA TTC GTC ATG TTT CTG AGC	144
Asp Arg Pro Tyr Val Leu Leu Ala Val Leu Phe Val Met Phe Leu Ser	
35 40 45	
TTG ATC GGG TTG CTA GCC ATT GCA GGC ATT AGA CTT CAT CGG GCA GCC	192
Leu Ile Gly Leu Leu Ala Ile Ala Gly Ile Arg Leu His Arg Ala Ala	
50 55 60	
ATC TAC ACT GCA GAG ATC CAT AAA AGC CTC AGC ACC AAT CTA GAT GTA	240
Ile Tyr Thr Ala Glu Ile His Lys Ser Leu Ser Thr Asn Leu Asp Val	
65 70 75 80	
ACT AAC TCA ATC GAG CAT CAG GTC AAG GAC GTG CTG ACA CCA CTC TTC	288
Thr Asn Ser Ile Glu His Gln Val Lys Asp Val Leu Thr Pro Leu Phe	
85 90 95	
AAG ATC ATC GGT GAT GAA GTG GGC CTG AGG ACA CCT CAG AGA TTC ACT	336
Lys Ile Ile Gly Asp Glu Val Gly Leu Arg Thr Pro Gln Arg Phe Thr	
100 105 110	
GAC CTA GTG AAA TTC ATC TCT GAC AAG ATT AAA TTC CTT AAT CCG GAT	384
Asp Leu Val Lys Phe Ile Ser Asp Lys Ile Lys Phe Leu Asn Pro Asp	

76

115					120					125						
AGG	GAG	TAC	GAC	TTC	AGG	GAT	CTC	ACT	TGG	TGT	ATC	AAC	CCG	CCA	GAG	432
Arg	Glu	Tyr	Asp	Phe	Arg	Asp	Leu	Thr	Trp	Cys	Ile	Asn	Pro	Pro	Glu	
	130					135					140					
AGA	ATC	AAA	TTG	GAT	TAT	GAT	CAA	TAC	TGT	GCA	GAT	GTG	GCT	GCT	GAA	480
Arg	Ile	Lys	Leu	Asp	Tyr	Asp	Gln	Tyr	Cys	Ala	Asp	Val	Ala	Ala	Glu	
145					150					155					160	
GAA	CTC	ATG	AAT	GCA	TTG	GTG	AAC	GCA	ACT	CTA	CTG	GAG	GCC	AGG	GCA	528
Glu	Leu	Met	Asn	Ala	Leu	Val	Asn	Ala	Thr	Leu	Leu	Glu	Ala	Arg	Ala	
				165					170					175		
ACC	AAT	CAG	TTC	CTA	GCT	GTC	TCA	AAG	GGA	AAC	TGC	TCA	GGG	CCC	ACT	576
Thr	Asn	Gln	Phe	Leu	Ala	Val	Ser	Lys	Gly	Asn	Cys	Ser	Gly	Pro	Thr	
			180					185					190			
ACA	ATC	AGA	GGT	CAA	TTC	TCA	AAC	ATG	TCG	CTG	TCC	CTG	TTG	GAC	TTG	624
Thr	Ile	Arg	Gly	Gln	Phe	Ser	Asn	Met	Ser	Leu	Ser	Leu	Leu	Asp	Leu	
		195					200					205				
TAC	TTA	AGT	CGA	GGT	TAC	AAT	GTG	TCA	TCT	ATA	GTC	ACT	ATG	ACA	TCC	672
Tyr	Leu	Ser	Arg	Gly	Tyr	Asn	Val	Ser	Ser	Ile	Val	Thr	Met	Thr	Ser	
	210					215					220					
CAG	GGA	ATG	TAC	GGG	GGA	ACT	TAC	CTA	GTG	GAA	AAG	CCT	AAT	CTG	AGC	720
Gln	Gly	Met	Tyr	Gly	Gly	Thr	Tyr	Leu	Val	Glu	Lys	Pro	Asn	Leu	Ser	
225					230					235					240	
AGT	AAA	GGG	TCA	GAG	TTG	TCA	CAA	CTG	AGC	ATG	CAC	CGA	GTG	TTT	GAA	768
Ser	Lys	Gly	Ser	Glu	Leu	Ser	Gln	Leu	Ser	Met	His	Arg	Val	Phe	Glu	
				245					250					255		
GTA	GGT	GTG	ATC	AGA	AAT	CCG	GGT	TTG	GGG	GCT	CCG	GTG	TTC	CAT	ATG	816
Val	Gly	Val	Ile	Arg	Asn	Pro	Gly	Leu	Gly	Ala	Pro	Val	Phe	His	Met	
			260					265					270			
ACG	AAC	TAT	TTT	GAG	CAA	TCA	GTC	AGT	AAT	GAT	TTC	AAC	AAC	TGC	ATG	864
Thr	Asn	Tyr	Phe	Glu	Gln	Ser	Val	Ser	Asn	Asp	Phe	Asn	Asn	Cys	Met	
		275					280					285				
GTG	GCT	TTG	GGG	GAG	CTC	AAA	TTC	GCA	GCC	CTC	TGT	CAC	AGG	GAA	GAT	912
Val	Ala	Leu	Gly	Glu	Leu	Lys	Phe	Ala	Ala	Leu	Cys	His	Arg	Glu	Asp	
	290					295					300					
TCT	ATC	ACA	ATT	CCC	TAT	CAG	GGG	TCA	GGG	AAA	GGT	GTC	AGC	TTC	CAG	960
Ser	Ile	Thr	Ile	Pro	Tyr	Gln	Gly	Ser	Gly	Lys	Gly	Val	Ser	Phe	Gln	
305					310					315					320	

CTC	GTC	AAG	CTA	GGT	GTC	TGG	AAA	TCC	CCA	ACC	GAC	ATG	CAA	TCC	TGG	1008
Leu	Val	Lys	Leu	Gly	Val	Trp	Lys	Ser	Pro	Thr	Asp	Met	Gln	Ser	Trp	
				325					330					335		
GTC	CCC	CTA	TCA	ACG	GAT	GAT	CCA	GTG	ATA	GAT	AGG	CTT	TAC	CTC	TCA	1056
Val	Pro	Leu	Ser	Thr	Asp	Asp	Pro	Val	Ile	Asp	Arg	Leu	Tyr	Leu	Ser	
			340					345					350			
TCT	CAC	AGA	GGT	GTT	ATC	GCT	GAC	AAT	CAA	GCA	AAA	TGG	GCT	GTC	CCG	1104
Ser	His	Arg	Gly	Val	Ile	Ala	Asp	Asn	Gln	Ala	Lys	Trp	Ala	Val	Pro	
		355					360					365				
ACA	ACA	CGA	ACA	GAT	GAC	AAG	TTG	CGA	ATG	GAG	ACA	TGC	TTC	CAG	CAG	1152
Thr	Thr	Arg	Thr	Asp	Asp	Lys	Leu	Arg	Met	Glu	Thr	Cys	Phe	Gln	Gln	
	370					375					380					
GCG	TGT	CAG	GGC	AAA	ATC	CAA	GCA	CTC	TGC	GAG	AAT	CCC	GAG	TGG	GCA	1200
Ala	Cys	Gln	Gly	Lys	Ile	Gln	Ala	Leu	Cys	Glu	Asn	Pro	Glu	Trp	Ala	
385					390					395					400	
CCA	CTG	AAG	GAC	AAC	AGG	ATT	CCT	TCA	TAC	GGG	GTC	TTG	TCT	GTT	AAT	1248
Pro	Leu	Lys	Asp	Asn	Arg	Ile	Pro	Ser	Tyr	Gly	Val	Leu	Ser	Val	Asn	
			405					410					415			
CTG	AGT	CTG	ACA	GTT	GAG	CTC	AAA	ATC	AAA	ATT	GCT	TCA	GGA	TTC	GGG	1296
Leu	Ser	Leu	Thr	Val	Glu	Leu	Lys	Ile	Lys	Ile	Ala	Ser	Gly	Phe	Gly	
			420					425					430			
CCA	TTG	ATC	ACA	CAC	GGT	TCA	GGG	ATG	GAC	CTA	TAC	AAA	TCC	AAC	CAC	1344
Pro	Leu	Ile	Thr	His	Gly	Ser	Gly	Met	Asp	Leu	Tyr	Lys	Ser	Asn	His	
		435					440					445				
AAC	AAT	GTG	TAT	TGG	CTG	ACC	ATC	CCG	CCA	ATG	AAG	AAC	CTA	GCC	TTA	1392
Asn	Asn	Val	Tyr	Trp	Leu	Thr	Ile	Pro	Pro	Met	Lys	Asn	Leu	Ala	Leu	
	450					455					460					
GGT	GTA	ATC	AAC	ACA	TTA	GAG	TGG	ATA	CCG	AGA	TTC	AAG	GTT	AGT	CCC	1440
Gly	Val	Ile	Asn	Thr	Leu	Glu	Trp	Ile	Pro	Arg	Phe	Lys	Val	Ser	Pro	
465					470					475					480	
AAC	CTC	TTC	ACT	GTT	CCA	ATC	AAG	GAA	GCA	GGC	GAG	GAC	TGC	CAT	GCC	1488
Asn	Leu	Phe	Thr	Val	Pro	Ile	Lys	Glu	Ala	Gly	Glu	Asp	Cys	His	Ala	
			485					490					495			
CCA	ACA	TAC	CTG	CCT	GCG	GAG	GTG	GAT	GGT	GAT	GTC	AAA	CTC	AGT	TCC	1536
Pro	Thr	Tyr	Leu	Pro	Ala	Glu	Val	Asp	Gly	Asp	Val	Lys	Leu	Ser	Ser	
			500					505					510			
AAT	CTG	GTG	ATT	CTA	CCT	GGT	CAA	GAT	CTC	CAA	TAT	GTT	TTG	GCA	ACC	1584
Asn	Leu	Val	Ile	Leu	Pro	Gly	Gln	Asp	Leu	Gln	Tyr	Val	Leu	Ala	Thr	

78

515					520					525						
TAC	GAT	ACT	TCC	AGG	GTT	GAA	CAT	GCT	GTG	GTT	TAT	TAT	GTT	TAC	AGC	1632
Tyr	Asp	Thr	Ser	Arg	Val	Glu	His	Ala	Val	Val	Tyr	Tyr	Val	Tyr	Ser	
	530					535					540					
CCG	AGC	CGC	TCA	TTT	TCT	TAC	TTT	TAT	CCC	TTT	AGG	TTG	CCT	ATA	AAG	1680
Pro	Ser	Arg	Ser	Phe	Ser	Tyr	Phe	Tyr	Pro	Phe	Arg	Leu	Pro	Ile	Lys	
	545				550				555						560	
GGG	GTC	CCC	ATC	GAA	TTA	CAA	GTG	GAA	TGC	TTC	ACA	TGG	GAC	CAA	AAA	1728
Gly	Val	Pro	Ile	Glu	Leu	Gln	Val	Glu	Cys	Phe	Thr	Trp	Asp	Gln	Lys	
				565				570						575		
CTC	TGG	TGC	CGT	CAC	TTC	TGT	GTG	CTT	GCG	GAC	TCA	GAA	TCT	GGT	GGA	1776
Leu	Trp	Cys	Arg	His	Phe	Cys	Val	Leu	Ala	Asp	Ser	Glu	Ser	Gly	Gly	
			580				585						590			
CAT	ATC	ACT	CAC	TCT	GGA	ATG	GTG	GGC	ATG	GGA	GTC	AGC	TGC	ACA	GTC	1824
His	Ile	Thr	His	Ser	Gly	Met	Val	Gly	Met	Gly	Val	Ser	Cys	Thr	Val	
		595				600						605				
ACT	CGG	GAA	GAT	GGA	ACC	AAT	AGC	AGA	TAG							1854
Thr	Arg	Glu	Asp	Gly	Thr	Asn	Ser	Arg								
	610					615										

(2) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 617 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

Met	Ser	Pro	Gln	Arg	Asp	Arg	Ile	Asn	Ala	Phe	Tyr	Lys	Asp	Asn	Pro
1				5					10					15	
His	Pro	Lys	Gly	Ser	Arg	Ile	Val	Ile	Asn	Arg	Glu	His	Leu	Met	Ile
			20					25					30		
Asp	Arg	Pro	Tyr	Val	Leu	Leu	Ala	Val	Leu	Phe	Val	Met	Phe	Leu	Ser
		35					40					45			
Leu	Ile	Gly	Leu	Leu	Ala	Ile	Ala	Gly	Ile	Arg	Leu	His	Arg	Ala	Ala
	50					55					60				

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Ile 65	Tyr	Thr	Ala	Glu	Ile 70	His	Lys	Ser	Leu	Ser 75	Thr	Asn	Leu	Asp	Val 80
Thr	Asn	Ser	Ile	Glu 85	His	Gln	Val	Lys	Asp 90	Val	Leu	Thr	Pro	Leu	Phe 95
Lys	Ile	Ile	Gly 100	Asp	Glu	Val	Gly	Leu 105	Arg	Thr	Pro	Gln	Arg	Phe	Thr 110
Asp	Leu	Val 115	Lys	Phe	Ile	Ser	Asp 120	Lys	Ile	Lys	Phe	Leu	Asn	Pro	Asp 125
Arg	Glu 130	Tyr	Asp	Phe	Arg	Asp 135	Leu	Thr	Trp	Cys	Ile 140	Asn	Pro	Pro	Glu
Arg 145	Ile	Lys	Leu	Asp	Tyr 150	Asp	Gln	Tyr	Cys	Ala 155	Asp	Val	Ala	Ala	Glu 160
Glu	Leu	Met	Asn	Ala 165	Leu	Val	Asn	Ala	Thr 170	Leu	Leu	Glu	Ala	Arg	Ala 175
Thr	Asn	Gln	Phe 180	Leu	Ala	Val	Ser	Lys 185	Gly	Asn	Cys	Ser	Gly	Pro	Thr 190
Thr	Ile 195	Arg	Gly	Gln	Phe	Ser	Asn 200	Met	Ser	Leu	Ser	Leu	Leu	Asp	Leu 205
Tyr 210	Leu	Ser	Arg	Gly	Tyr	Asn 215	Val	Ser	Ser	Ile	Val 220	Thr	Met	Thr	Ser
Gln 225	Gly	Met	Tyr	Gly	Gly 230	Thr	Tyr	Leu	Val	Glu 235	Lys	Pro	Asn	Leu	Ser 240
Ser	Lys	Gly	Ser	Glu 245	Leu	Ser	Gln	Leu	Ser 250	Met	His	Arg	Val	Phe	Glu 255
Val	Gly	Val	Ile 260	Arg	Asn	Pro	Gly	Leu 265	Gly	Ala	Pro	Val	Phe	His	Met 270
Thr	Asn	Tyr 275	Phe	Glu	Gln	Ser	Val 280	Ser	Asn	Asp	Phe	Asn 285	Asn	Cys	Met
Val 290	Ala	Leu	Gly	Glu	Leu	Lys 295	Phe	Ala	Ala	Leu	Cys 300	His	Arg	Glu	Asp
Ser 305	Ile	Thr	Ile	Pro	Tyr 310	Gln	Gly	Ser	Gly	Lys 315	Gly	Val	Ser	Phe	Gln 320
Leu	Val	Lys	Leu	Gly 325	Val	Trp	Lys	Ser	Pro 330	Thr	Asp	Met	Gln	Ser	Trp 335

Val	Pro	Leu	Ser	Thr	Asp	Asp	Pro	Val	Ile	Asp	Arg	Leu	Tyr	Leu	Ser	
			340					345					350			
Ser	His	Arg	Gly	Val	Ile	Ala	Asp	Asn	Gln	Ala	Lys	Trp	Ala	Val	Pro	
		355					360					365				
Thr	Thr	Arg	Thr	Asp	Asp	Lys	Leu	Arg	Met	Glu	Thr	Cys	Phe	Gln	Gln	
	370					375					380					
Ala	Cys	Gln	Gly	Lys	Ile	Gln	Ala	Leu	Cys	Glu	Asn	Pro	Glu	Trp	Ala	
385					390					395					400	
Pro	Leu	Lys	Asp	Asn	Arg	Ile	Pro	Ser	Tyr	Gly	Val	Leu	Ser	Val	Asn	
				405					410					415		
Leu	Ser	Leu	Thr	Val	Glu	Leu	Lys	Ile	Lys	Ile	Ala	Ser	Gly	Phe	Gly	
			420					425					430			
Pro	Leu	Ile	Thr	His	Gly	Ser	Gly	Met	Asp	Leu	Tyr	Lys	Ser	Asn	His	
		435					440					445				
Asn	Asn	Val	Tyr	Trp	Leu	Thr	Ile	Pro	Pro	Met	Lys	Asn	Leu	Ala	Leu	
	450					455					460					
Gly	Val	Ile	Asn	Thr	Leu	Glu	Trp	Ile	Pro	Arg	Phe	Lys	Val	Ser	Pro	
465					470					475					480	
Asn	Leu	Phe	Thr	Val	Pro	Ile	Lys	Glu	Ala	Gly	Glu	Asp	Cys	His	Ala	
				485					490					495		
Pro	Thr	Tyr	Leu	Pro	Ala	Glu	Val	Asp	Gly	Asp	Val	Lys	Leu	Ser	Ser	
			500					505					510			
Asn	Leu	Val	Ile	Leu	Pro	Gly	Gln	Asp	Leu	Gln	Tyr	Val	Leu	Ala	Thr	
		515					520					525				
Tyr	Asp	Thr	Ser	Arg	Val	Glu	His	Ala	Val	Val	Tyr	Tyr	Val	Tyr	Ser	
	530					535					540					
Pro	Ser	Arg	Ser	Phe	Ser	Tyr	Phe	Tyr	Pro	Phe	Arg	Leu	Pro	Ile	Lys	
545					550					555					560	
Gly	Val	Pro	Ile	Glu	Leu	Gln	Val	Glu	Cys	Phe	Thr	Trp	Asp	Gln	Lys	
				565					570					575		
Leu	Trp	Cys	Arg	His	Phe	Cys	Val	Leu	Ala	Asp	Ser	Glu	Ser	Gly	Gly	
			580					585					590			
His	Ile	Thr	His	Ser	Gly	Met	Val	Gly	Met	Gly	Val	Ser	Cys	Thr	Val	

81

595

600

605

Thr Arg Glu Asp Gly Thr Asn Ser Arg
610 615

(2) INFORMATION FOR SEQ ID NO:11:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 524 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Measles virus
- (B) STRAIN: Attenuated measles virus NA strain

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

Thr	Pro	Leu	Phe	Lys	Ile	Ile	Gly	Asp	Glu	Val	Gly	Leu	Arg	Thr	Pro	1	5	10	15
Gln	Arg	Phe	Thr	Asp	Leu	Val	Lys	Phe	Ile	Ser	Asp	Lys	Ile	Lys	Phe	20	25	30	
Leu	Asn	Pro	Asp	Arg	Glu	Tyr	Asp	Phe	Arg	Asp	Leu	Thr	Trp	Cys	Ile	35	40	45	
Asn	Pro	Pro	Glu	Arg	Ile	Lys	Leu	Asp	Tyr	Asp	Gln	Tyr	Cys	Ala	Asp	50	55	60	
Val	Ala	Ala	Glu	Glu	Leu	Met	Asn	Ala	Leu	Val	Asn	Ala	Thr	Leu	Leu	65	70	75	80
Glu	Ala	Arg	Ala	Thr	Asn	Gln	Phe	Leu	Ala	Val	Ser	Lys	Gly	Asn	Cys	85	90	95	
Ser	Gly	Pro	Thr	Thr	Ile	Arg	Gly	Gln	Phe	Ser	Asn	Met	Ser	Leu	Ser	100	105	110	
Leu	Leu	Asp	Leu	Tyr	Leu	Ser	Arg	Gly	Tyr	Asn	Val	Ser	Ser	Ile	Val	115	120	125	
Thr	Met	Thr	Ser	Gln	Gly	Met	Tyr	Gly	Gly	Thr	Tyr	Leu	Val	Glu	Lys	130	135	140	

Pro	Asn	Leu	Ser	Ser	Lys	Gly	Ser	Glu	Leu	Ser	Gln	Leu	Ser	Met	His	145	150	155	160
Arg	Val	Phe	Glu	Val	Gly	Val	Ile	Arg	Asn	Pro	Gly	Leu	Gly	Ala	Pro		165	170	175
Val	Phe	His	Met	Thr	Asn	Tyr	Phe	Glu	Gln	Ser	Val	Ser	Asn	Asp	Phe		180	185	190
Asn	Asn	Cys	Met	Val	Ala	Leu	Gly	Glu	Leu	Lys	Phe	Ala	Ala	Leu	Cys		195	200	205
His	Arg	Glu	Asp	Ser	Ile	Thr	Ile	Pro	Tyr	Gln	Gly	Ser	Gly	Lys	Gly		210	215	220
Val	Ser	Phe	Gln	Leu	Val	Lys	Leu	Gly	Val	Trp	Lys	Ser	Pro	Thr	Asp	225	230	235	240
Met	Gln	Ser	Trp	Val	Pro	Leu	Ser	Thr	Asp	Asp	Pro	Val	Ile	Asp	Arg		245	250	255
Leu	Tyr	Leu	Ser	Ser	His	Arg	Gly	Val	Ile	Ala	Asp	Asn	Gln	Ala	Lys		260	265	270
Trp	Ala	Val	Pro	Thr	Thr	Arg	Thr	Asp	Asp	Lys	Leu	Arg	Met	Glu	Thr		275	280	285
Cys	Phe	Gln	Gln	Ala	Cys	Gln	Gly	Lys	Ile	Gln	Ala	Leu	Cys	Glu	Asn	290	295	300	
Pro	Glu	Trp	Ala	Pro	Leu	Lys	Asp	Asn	Arg	Ile	Pro	Ser	Tyr	Gly	Val	305	310	315	320
Leu	Ser	Val	Asn	Leu	Ser	Leu	Thr	Val	Glu	Leu	Lys	Ile	Lys	Ile	Ala		325	330	335
Ser	Gly	Phe	Gly	Pro	Leu	Ile	Thr	His	Gly	Ser	Gly	Met	Asp	Leu	Tyr		340	345	350
Lys	Ser	Asn	His	Asn	Asn	Val	Tyr	Trp	Leu	Thr	Ile	Pro	Pro	Met	Lys		355	360	365
Asn	Leu	Ala	Leu	Gly	Val	Ile	Asn	Thr	Leu	Glu	Trp	Ile	Pro	Arg	Phe		370	375	380
Lys	Val	Ser	Pro	Asn	Leu	Phe	Thr	Val	Pro	Ile	Lys	Glu	Ala	Gly	Glu	385	390	395	400
Asp	Cys	His	Ala	Pro	Thr	Tyr	Leu	Pro	Ala	Glu	Val	Asp	Gly	Asp	Val		405	410	415

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Lys Leu Ser Ser Asn Leu Val Ile Leu Pro Gly Gln Asp Leu Gln Tyr
 420 425 430
 Val Leu Ala Thr Tyr Asp Thr Ser Arg Val Glu His Ala Val Val Tyr
 435 440 445
 Tyr Val Tyr Ser Pro Ser Arg Ser Phe Ser Tyr Phe Tyr Pro Phe Arg
 450 455 460
 Leu Pro Ile Lys Gly Val Pro Ile Glu Leu Gln Val Glu Cys Phe Thr
 465 470 475 480
 Trp Asp Gln Lys Leu Trp Cys Arg His Phe Cys Val Leu Ala Asp Ser
 485 490 495
 Glu Ser Gly Gly His Ile Thr His Ser Gly Met Val Gly Met Gly Val
 500 505 510
 Ser Cys Thr Val Thr Arg Glu Asp Gly Thr Asn Ser
 515 520

(2) INFORMATION FOR SEQ ID NO:12:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 141 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Measles virus
- (B) STRAIN: Attenuated measles virus NA strain

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

Ala Thr Asn Gln Phe Leu Ala Val Ser Lys Gly Asn Cys Ser Gly Pro
 1 5 10 15
 Thr Thr Ile Arg Gly Gln Phe Ser Asn Met Ser Leu Ser Leu Leu Asp
 20 25 30
 Leu Tyr Leu Ser Arg Gly Tyr Asn Val Ser Ser Ile Val Thr Met Thr
 35 40 45
 Ser Gln Gly Met Tyr Gly Gly Thr Tyr Leu Val Glu Lys Pro Asn Leu

84

50		55		60											
Ser	Ser	Lys	Gly	Ser	Glu	Leu	Ser	Gln	Leu	Ser	Met	His	Arg	Val	Phe
65					70					75					80
Glu	Val	Gly	Val	Ile	Arg	Asn	Pro	Gly	Leu	Gly	Ala	Pro	Val	Phe	His
				85					90					95	
Met	Thr	Asn	Tyr	Phe	Glu	Gln	Ser	Val	Ser	Asn	Asp	Phe	Asn	Asn	Cys
				100				105					110		
Met	Val	Ala	Leu	Gly	Glu	Leu	Lys	Phe	Ala	Ala	Leu	Cys	His	Arg	Glu
		115					120					125			
Asp	Ser	Ile	Thr	Ile	Pro	Tyr	Gln	Gly	Ser	Gly	Lys	Gly			
130						135					140				

(2) INFORMATION FOR SEQ ID NO:13:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 7 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Measles virus
- (B) STRAIN: Attenuated measles virus NA strain

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

Leu	Glu	Ala	Arg	Ala	Thr	Asn
1				5		

(2) INFORMATION FOR SEQ ID NO:14:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 7 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Measles virus

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(B) STRAIN: Attenuated measles virus NA strain

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

Asn Leu Ser Ser Lys Gly Ser
1 5

(2) INFORMATION FOR SEQ ID NO:15:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 6 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Measles virus
- (B) STRAIN: Attenuated measles virus NA strain

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

Glu Gln Ser Val Ser Asn
1 5

(2) INFORMATION FOR SEQ ID NO:16:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 7 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Measles virus
- (B) STRAIN: Attenuated measles virus NA strain

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

His Arg Glu Asp Ser Ile Thr
1 5

(2) INFORMATION FOR SEQ ID NO:17:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1653 bases
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA to genomic RNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Measles virus
- (B) STRAIN: Attenuated measles virus CAM-70 strain

(ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 1..1650

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

ATG GGT CTC AAG GTG AAC GTC TCT GCC ATA TTC ATG GCA GTA CTG TTA	48
Met Gly Leu Lys Val Asn Val Ser Ala Ile Phe Met Ala Val Leu Leu	
1 5 10 15	
ACT CTC CAA ACA CCC ACC GGT CAA ATC CAT TGG GGC AAT CTC TCT AAG	96
Thr Leu Gln Thr Pro Thr Gly Gln Ile His Trp Gly Asn Leu Ser Lys	
20 25 30	
ATA GGG GTG GTA GGA ATA GGA AGT GCA AGC TAC AAA GTT ATG ACT CGT	144
Ile Gly Val Val Gly Ile Gly Ser Ala Ser Tyr Lys Val Met Thr Arg	
35 40 45	
TCC AGC CAT CAC TCA TTA GTC ATA AAA TTA ATG CCC AAT ATA ACT CTC	192
Ser Ser His His Ser Leu Val Ile Lys Leu Met Pro Asn Ile Thr Leu	
50 55 60	
CTC AAT AAC TGC ACG AGG GTA GAG ATT GCA GAA TAC AGG AGA CTA CTG	240
Leu Asn Asn Cys Thr Arg Val Glu Ile Ala Glu Tyr Arg Arg Leu Leu	
65 70 75 80	
AGA ACA GTT TTG GAA CCA ATT AGA GAT GCA CTT AAT GCA ATG ACC CAG	288
Arg Thr Val Leu Glu Pro Ile Arg Asp Ala Leu Asn Ala Met Thr Gln	
85 90 95	

AAT	ATA	AGA	CCG	GTT	CAG	AGT	GTA	GCT	TCA	GGT	AGG	AGA	CAC	AAG	AGA	336
Asn	Ile	Arg	Pro	Val	Gln	Ser	Val	Ala	Ser	Gly	Arg	Arg	His	Lys	Arg	
			100					105					110			
TTT	GCG	GGA	GTA	GTC	CTG	GCA	GGT	GCG	GCC	CTA	GGC	GTT	GCC	ACA	GCT	384
Phe	Ala	Gly	Val	Val	Leu	Ala	Gly	Ala	Ala	Leu	Gly	Val	Ala	Thr	Ala	
		115					120					125				
GCT	CAG	ATA	ACA	GCC	GGC	ATT	GCA	CTT	CAC	CAG	TCC	ATG	CTG	AAC	TCT	432
Ala	Gln	Ile	Thr	Ala	Gly	Ile	Ala	Leu	His	Gln	Ser	Met	Leu	Asn	Ser	
	130					135					140					
CAA	GCC	ATC	GAC	AAT	CTG	AGA	GCG	AGC	CTG	GAA	ACT	ACT	AAT	CAG	GCA	480
Gln	Ala	Ile	Asp	Asn	Leu	Arg	Ala	Ser	Leu	Glu	Thr	Thr	Asn	Gln	Ala	
145					150					155					160	
ATT	GAG	GCA	ATC	GGA	CAA	GCA	GGG	CAG	GAG	ATG	ATA	TTG	GCT	GTT	CAG	528
Ile	Glu	Ala	Ile	Gly	Gln	Ala	Gly	Gln	Glu	Met	Ile	Leu	Ala	Val	Gln	
				165				170						175		
GGT	GTC	CAA	GAC	TAC	ATC	AAT	AAT	GAG	CTG	ATA	CCG	TCT	ATG	AAC	CAA	576
Gly	Val	Gln	Asp	Tyr	Ile	Asn	Asn	Glu	Leu	Ile	Pro	Ser	Met	Asn	Gln	
			180					185					190			
CTA	TCT	TGT	GAT	TTA	ATC	GGC	CAG	AAG	CTC	GGG	CTC	AAA	TTG	CTC	AGA	624
Leu	Ser	Cys	Asp	Leu	Ile	Gly	Gln	Lys	Leu	Gly	Leu	Lys	Leu	Leu	Arg	
		195					200					205				
TAC	TAT	ACA	GAA	ATC	CTG	TCG	TTA	TTT	GGC	CCC	AGC	TTA	CGG	GAC	CCC	672
Tyr	Tyr	Thr	Glu	Ile	Leu	Ser	Leu	Phe	Gly	Pro	Ser	Leu	Arg	Asp	Pro	
	210					215					220					
ATA	TCT	GCG	GAG	ATA	TCT	ATC	CAG	GCT	TTG	AGC	TAT	GCG	CTT	GGA	GGA	720
Ile	Ser	Ala	Glu	Ile	Ser	Ile	Gln	Ala	Leu	Ser	Tyr	Ala	Leu	Gly	Gly	
225					230					235					240	
GAC	ATC	AAT	AAG	GTG	TTA	GAA	AAG	CTC	GGA	TAC	AGT	GGA	GGT	GAT	TTA	768
Asp	Ile	Asn	Lys	Val	Leu	Glu	Lys	Leu	Gly	Tyr	Ser	Gly	Gly	Asp	Leu	
				245					250					255		
CTG	GGC	ATC	TTA	GAG	AGC	AGA	GGA	ATA	AAG	GCC	CGG	ATA	ACT	CAC	GTC	816
Leu	Gly	Ile	Leu	Glu	Ser	Arg	Gly	Ile	Lys	Ala	Arg	Ile	Thr	His	Val	
			260					265					270			
GAC	ACA	GAG	TCC	TAC	TTC	ATT	GTC	CTC	AGT	ATA	GCC	TAT	CCG	ACG	CTG	864
Asp	Thr	Glu	Ser	Tyr	Phe	Ile	Val	Leu	Ser	Ile	Ala	Tyr	Pro	Thr	Leu	
		275					280					285				
TCC	GAG	ATT	AAG	GGG	GTG	ATT	GTC	CAC	CGG	CTA	GAG	GGG	GTC	TCG	TAC	912
Ser	Glu	Ile	Lys	Gly	Val	Ile	Val	His	Arg	Leu	Glu	Gly	Val	Ser	Tyr	

290	295	300	
AAC ATA GGC TCT CAA GAG TGG TAT ACC ACT GTG CCC AAG TAT GTT GCA Asn Ile Gly Ser Gln Glu Trp Tyr Thr Thr Val Pro Lys Tyr Val Ala 305 310 315 320			960
ACC CAA GGG TAC CTT ATC TCG AAT TTT GAT GAG TCA TCG TGT ACT TTC Thr Gln Gly Tyr Leu Ile Ser Asn Phe Asp Glu Ser Ser Cys Thr Phe 325 330 335			1008
ATG CCA GAG GGG ACT GTG TGC AGC CAA AAT GCC TTG TAC CCG ATG AGT Met Pro Glu Gly Thr Val Cys Ser Gln Asn Ala Leu Tyr Pro Met Ser 340 345 350			1056
CCT CTG CTC CAA GAA TGC CTC CGG GGG TTC ACC AAG TCC TGT GCT CGT Pro Leu Leu Gln Glu Cys Leu Arg Gly Phe Thr Lys Ser Cys Ala Arg 355 360 365			1104
ACA CTC GTA TCC GGG TCT TTT GGG AAC CGG TTC ATT TTA TCA CAA GGG Thr Leu Val Ser Gly Ser Phe Gly Asn Arg Phe Ile Leu Ser Gln Gly 370 375 380			1152
AAC CTA ATA GCC AAT TGT GCA TCA ATC CTT TGC AAG TGT CAC ACA ACA Asn Leu Ile Ala Asn Cys Ala Ser Ile Leu Cys Lys Cys His Thr Thr 385 390 395 400			1200
GGA ACG ATC ATT AAT CAA GAC CCT GAC AAG ATC CTA ACA TAC ATT GCT Gly Thr Ile Ile Asn Gln Asp Pro Asp Lys Ile Leu Thr Tyr Ile Ala 405 410 415			1248
GAC GAT CAC TGC CCG GTA GTC GAG GTG AAC GGC GTG ACC ATC CAA GTC Asp Asp His Cys Pro Val Val Glu Val Asn Gly Val Thr Ile Gln Val 420 425 430			1296
GGG AGC AGG AGG TAT CCA GAC GCT GTG TAC TTG CAC AGA ATT GAC CTC Gly Ser Arg Arg Tyr Pro Asp Ala Val Tyr Leu His Arg Ile Asp Leu 435 440 445			1344
GGT CCT CCC ATA TCA TTG GAG AGG TTG GAC GTA GGG ACA AAT CTG GGG Gly Pro Pro Ile Ser Leu Glu Arg Leu Asp Val Gly Thr Asn Leu Gly 450 455 460			1392
AAT GCA ATT GCT AAG TTG GAG GAT GCC AAG GAA TTG TTG GAG TCA TCG Asn Ala Ile Ala Lys Leu Glu Asp Ala Lys Glu Leu Leu Glu Ser Ser 465 470 475 480			1440
GAC CAG ATA TTG AGG AGT ATG AAA GGT TTA TCG AGC ACT AGC ATA GTC Asp Gln Ile Leu Arg Ser Met Lys Gly Leu Ser Ser Thr Ser Ile Val 485 490 495			1488

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TAC	ATC	CTG	ATT	GCA	GTG	TGT	CTT	GGA	GGG	TTG	ATA	GGG	ATC	CCC	GCT	1536
Tyr	Ile	Leu	Ile	Ala	Val	Cys	Leu	Gly	Gly	Leu	Ile	Gly	Ile	Pro	Ala	
			500					505					510			
TTA	ATA	TGT	TGC	TGC	AGG	GGG	CGT	TGT	AAC	AAA	AAG	GGA	GAA	CAA	GTT	1584
Leu	Ile	Cys	Cys	Cys	Arg	Gly	Arg	Cys	Asn	Lys	Lys	Gly	Glu	Gln	Val	
		515					520					525				
GGT	ATG	TCA	AGA	CCA	GGC	CTA	AAG	CCT	GAT	CTT	ACG	GGA	ACA	TCA	AAA	1632
Gly	Met	Ser	Arg	Pro	Gly	Leu	Lys	Pro	Asp	Leu	Thr	Gly	Thr	Ser	Lys	
	530					535					540					
TCC	TAT	GTA	AGG	TCG	CTC	TGA										1653
Ser	Tyr	Val	Arg	Ser	Leu											
545					550											

(2) INFORMATION FOR SEQ ID NO:18:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 550 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

Met	Gly	Leu	Lys	Val	Asn	Val	Ser	Ala	Ile	Phe	Met	Ala	Val	Leu	Leu	
1				5					10					15		
Thr	Leu	Gln	Thr	Pro	Thr	Gly	Gln	Ile	His	Trp	Gly	Asn	Leu	Ser	Lys	
			20					25					30			
Ile	Gly	Val	Val	Gly	Ile	Gly	Ser	Ala	Ser	Tyr	Lys	Val	Met	Thr	Arg	
		35					40					45				
Ser	Ser	His	His	Ser	Leu	Val	Ile	Lys	Leu	Met	Pro	Asn	Ile	Thr	Leu	
	50					55					60					
Leu	Asn	Asn	Cys	Thr	Arg	Val	Glu	Ile	Ala	Glu	Tyr	Arg	Arg	Leu	Leu	
65					70					75					80	
Arg	Thr	Val	Leu	Glu	Pro	Ile	Arg	Asp	Ala	Leu	Asn	Ala	Met	Thr	Gln	
				85					90					95		
Asn	Ile	Arg	Pro	Val	Gln	Ser	Val	Ala	Ser	Gly	Arg	Arg	His	Lys	Arg	
			100					105					110			
Phe	Ala	Gly	Val	Val	Leu	Ala	Gly	Ala	Ala	Leu	Gly	Val	Ala	Thr	Ala	

90

115					120					125					
Ala	Gln	Ile	Thr	Ala	Gly	Ile	Ala	Leu	His	Gln	Ser	Met	Leu	Asn	Ser
130					135					140					
Gln	Ala	Ile	Asp	Asn	Leu	Arg	Ala	Ser	Leu	Glu	Thr	Thr	Asn	Gln	Ala
145					150					155					
Ile	Glu	Ala	Ile	Gly	Gln	Ala	Gly	Gln	Glu	Met	Ile	Leu	Ala	Val	Gln
165					170					175					
Gly	Val	Gln	Asp	Tyr	Ile	Asn	Asn	Glu	Leu	Ile	Pro	Ser	Met	Asn	Gln
180					185					190					
Leu	Ser	Cys	Asp	Leu	Ile	Gly	Gln	Lys	Leu	Gly	Leu	Lys	Leu	Leu	Arg
195					200					205					
Tyr	Tyr	Thr	Glu	Ile	Leu	Ser	Leu	Phe	Gly	Pro	Ser	Leu	Arg	Asp	Pro
210					215					220					
Ile	Ser	Ala	Glu	Ile	Ser	Ile	Gln	Ala	Leu	Ser	Tyr	Ala	Leu	Gly	Gly
225					230					235					
Asp	Ile	Asn	Lys	Val	Leu	Glu	Lys	Leu	Gly	Tyr	Ser	Gly	Gly	Asp	Leu
245					250					255					
Leu	Gly	Ile	Leu	Glu	Ser	Arg	Gly	Ile	Lys	Ala	Arg	Ile	Thr	His	Val
260					265					270					
Asp	Thr	Glu	Ser	Tyr	Phe	Ile	Val	Leu	Ser	Ile	Ala	Tyr	Pro	Thr	Leu
275					280					285					
Ser	Glu	Ile	Lys	Gly	Val	Ile	Val	His	Arg	Leu	Glu	Gly	Val	Ser	Tyr
290					295					300					
Asn	Ile	Gly	Ser	Gln	Glu	Trp	Tyr	Thr	Thr	Val	Pro	Lys	Tyr	Val	Ala
305					310					315					
Thr	Gln	Gly	Tyr	Leu	Ile	Ser	Asn	Phe	Asp	Glu	Ser	Ser	Cys	Thr	Phe
325					330					335					
Met	Pro	Glu	Gly	Thr	Val	Cys	Ser	Gln	Asn	Ala	Leu	Tyr	Pro	Met	Ser
340					345					350					
Pro	Leu	Leu	Gln	Glu	Cys	Leu	Arg	Gly	Phe	Thr	Lys	Ser	Cys	Ala	Arg
355					360					365					
Thr	Leu	Val	Ser	Gly	Ser	Phe	Gly	Asn	Arg	Phe	Ile	Leu	Ser	Gln	Gly
370					375					380					

Asn	Leu	Ile	Ala	Asn	Cys	Ala	Ser	Ile	Leu	Cys	Lys	Cys	His	Thr	Thr
385					390					395					400
Gly	Thr	Ile	Ile	Asn	Gln	Asp	Pro	Asp	Lys	Ile	Leu	Thr	Tyr	Ile	Ala
				405					410					415	
Asp	Asp	His	Cys	Pro	Val	Val	Glu	Val	Asn	Gly	Val	Thr	Ile	Gln	Val
			420					425					430		
Gly	Ser	Arg	Arg	Tyr	Pro	Asp	Ala	Val	Tyr	Leu	His	Arg	Ile	Asp	Leu
		435					440					445			
Gly	Pro	Pro	Ile	Ser	Leu	Glu	Arg	Leu	Asp	Val	Gly	Thr	Asn	Leu	Gly
	450					455					460				
Asn	Ala	Ile	Ala	Lys	Leu	Glu	Asp	Ala	Lys	Glu	Leu	Leu	Glu	Ser	Ser
465					470					475					480
Asp	Gln	Ile	Leu	Arg	Ser	Met	Lys	Gly	Leu	Ser	Ser	Thr	Ser	Ile	Val
				485					490					495	
Tyr	Ile	Leu	Ile	Ala	Val	Cys	Leu	Gly	Gly	Leu	Ile	Gly	Ile	Pro	Ala
			500					505					510		
Leu	Ile	Cys	Cys	Cys	Arg	Gly	Arg	Cys	Asn	Lys	Lys	Gly	Glu	Gln	Val
		515					520					525			
Gly	Met	Ser	Arg	Pro	Gly	Leu	Lys	Pro	Asp	Leu	Thr	Gly	Thr	Ser	Lys
	530					535					540				
Ser	Tyr	Val	Arg	Ser	Leu										
545					550										

(2) INFORMATION FOR SEQ ID NO:19:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1653 bases
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA to genomic RNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Measles virus
- (B) STRAIN: Attenuated measles virus NA strain

(ix) FEATURE:

(A) NAME/KEY: CDS

(B) LOCATION: 1..1650

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

ATG	GGT	CTC	AAG	GTG	AAC	GTC	TCT	GCC	ATA	CTC	ATG	GCA	GTA	CTG	TTA	48
Met	Gly	Leu	Lys	Val	Asn	Val	Ser	Ala	Ile	Leu	Met	Ala	Val	Leu	Leu	
1				5					10					15		
ACT	CTC	CAA	ACA	CCC	ACC	GGT	CAA	ATC	CAT	TGG	GGC	AAT	CTC	TCT	AAG	96
Thr	Leu	Gln	Thr	Pro	Thr	Gly	Gln	Ile	His	Trp	Gly	Asn	Leu	Ser	Lys	
			20					25					30			
ATA	GGG	GTG	GTA	GGG	ATA	GGA	AGT	GCA	AGC	TAC	AAA	GTT	ATG	ACT	CGT	144
Ile	Gly	Val	Val	Gly	Ile	Gly	Ser	Ala	Ser	Tyr	Lys	Val	Met	Thr	Arg	
		35					40					45				
TCC	AGC	CAT	CAA	TCA	TTG	GTC	ATA	AAA	TTA	ATG	CCC	AAT	ATA	ACT	CTC	192
Ser	Ser	His	His	Ser	Leu	Val	Ile	Lys	Leu	Met	Pro	Asn	Ile	Thr	Leu	
	50					55					60					
CTC	AAT	AAC	TGC	ACG	AGG	GTA	GAG	ATT	GCA	GAA	TAC	AGG	AGA	CTA	CTG	240
Leu	Asn	Asn	Cys	Thr	Arg	Val	Glu	Ile	Ala	Glu	Tyr	Arg	Arg	Leu	Leu	
65					70					75					80	
AGA	ACA	GTT	TTG	GAA	CCA	ATT	AGA	GAT	GCA	CTT	AAT	GCA	ATG	ACC	CAG	288
Arg	Thr	Val	Leu	Glu	Pro	Ile	Arg	Asp	Ala	Leu	Asn	Ala	Met	Thr	Gln	
				85					90					95		
AAT	ATA	AGA	CCG	GTT	CAG	AGT	GTA	GCC	TCA	AGT	AGG	AGA	CAC	AAG	AGA	336
Asn	Ile	Arg	Pro	Val	Gln	Ser	Val	Ala	Ser	Gly	Arg	Arg	His	Lys	Arg	
			100					105					110			
TTT	GCG	GGA	GTT	GTC	CTG	GCA	GGT	GCG	GCC	CTA	GGC	GTT	GCC	ACA	GCT	384
Phe	Ala	Gly	Val	Val	Leu	Ala	Gly	Ala	Ala	Leu	Gly	Val	Ala	Thr	Ala	
		115					120					125				
GCT	CAG	ATA	ACA	GCC	GGC	ATT	GCA	CTT	CAC	CAG	TCC	ATG	CTG	AAC	TCT	432
Ala	Gln	Ile	Thr	Ala	Gly	Ile	Ala	Leu	His	Gln	Ser	Met	Leu	Asn	Ser	
	130					135					140					
CAA	GCC	ATC	GAC	AAT	CTG	AGA	GCA	AGC	CTG	GAA	ACT	ACT	AAT	CAG	GCG	480
Gln	Ala	Ile	Asp	Asn	Leu	Arg	Ala	Ser	Leu	Glu	Thr	Thr	Asn	Gln	Ala	
145					150					155					160	
ATT	GAG	GCA	ATC	AGA	CAA	GCA	GGG	CAG	GAG	ATG	ATA	TTG	GCT	GTT	CAG	528
Ile	Glu	Ala	Ile	Gly	Gln	Ala	Gly	Gln	Glu	Met	Ile	Leu	Ala	Val	Gln	

165								170				175					
GGT Gly	GTC Val	CAA Gln	GAC Asp	TAC Tyr	ATC Ile	AAT Asn	AAT Asn	GAG Glu	CTG Leu	ATA Ile	CCG Pro	TCT Ser	ATG Met	AAC Asn	CAA Gln	576	
180								185				190					
CTA Leu	TCT Ser	TGT Cys	GAT Asp	TTA Leu	ATC Ile	GGC Gly	CAG Gln	AAG Lys	CTA Leu	GGG Gly	CTC Leu	AAA Lys	TTG Leu	CTC Leu	AGA Arg	624	
195								200				205					
TAC Tyr	TAT Tyr	ACA Thr	GAA Glu	ATC Ile	CTG Leu	TCA Ser	TTA Leu	TTT Phe	GGC Gly	CCC Pro	AGC Ser	CTA Leu	CGG Arg	GAC Asp	CCC Pro	672	
210								215				220					
ATA Ile	TCT Ser	GCG Ala	GAG Glu	ATA Ile	TCC Ser	ATC Ile	CAG Gln	GCT Ala	TTG Leu	AGC Ser	TAT Tyr	GCG Ala	CTT Leu	GGA Gly	GGA Gly	720	
225								230				235				240	
GAT Asp	ATC Ile	AAT Asn	AAG Lys	GTG Val	TTA Leu	GAA Glu	AAG Lys	CTC Leu	GGA Gly	TAC Tyr	AGT Ser	GGA Gly	GGT Gly	GAT Asp	TTA Leu	768	
245								250				255					
CTG Leu	GGC Gly	ATC Ile	TTA Leu	GAG Glu	AGC Ser	AGA Arg	GGA Gly	ATA Ile	AAG Lys	GCC Ala	CGG Arg	ATA Ile	ACT Thr	CAC His	GTC Val	816	
260								265				270					
GAC Asp	ACA Thr	GAG Glu	TCC Ser	TAC Tyr	TTC Phe	ATT Ile	GTA Val	CTC Leu	AGT Ser	ATA Ile	GCC Ala	TAT Tyr	CCG Pro	ACG Thr	CTG Leu	864	
275								280				285					
TCC Ser	GAG Glu	ATT Ile	AAG Lys	GGG Gly	GTG Val	ATT Ile	GTC Val	CAC His	CGG Arg	CTA Leu	GAG Glu	GGG Gly	GTC Val	TCG Ser	TAC Tyr	912	
290								295				300					
AAT Asn	ATA Ile	GGC Gly	TCT Ser	CAA Gln	GAG Glu	TGG Trp	TAT Tyr	ACC Thr	ACT Thr	GTG Val	CCC Pro	AAG Lys	TAT Tyr	GTT Val	GCA Ala	960	
305								310				315				320	
ACC Thr	CAG Gln	GGG Gly	TAC Tyr	CTT Leu	ATC Ile	TCG Ser	AAT Asn	TTT Phe	GAT Asp	GAG Glu	TCA Ser	TCG Ser	TGT Cys	ACT Thr	TTC Phe	1008	
325								330				335					
ATG Met	CCA Pro	GAG Glu	GGG Gly	ACT Thr	GTG Val	TGC Cys	AGC Ser	CAA Gln	AAT Asn	GCC Ala	TTG Leu	TAC Tyr	CCG Pro	ATG Met	AGT Ser	1056	
340								345				350					
CCT Pro	CTG Leu	CTC Leu	CAA Gln	GAA Glu	TGC Cys	CTC Leu	CGG Arg	GGG Gly	TCC Phe	ACC Thr	AAG Lys	TCC Ser	TGT Cys	GCT Ala	CGT Arg	1104	
355								360				365					

ACA Thr	CTC Leu	GTA Val	TCC Ser	GGG Gly	TCT Ser	TTT Phe	GGG Gly	AAC Asn	CGG Arg	TTC Phe	ATT Ile	TTA Leu	TCA Ser	CAA Gln	GGG Gly	1152
370																
AAC Asn	CTA Leu	ATA Ile	GCC Ala	AAT Asn	TGT Cys	GCA Ala	TCA Ser	ATC Ile	CTC Leu	TGC Cys	AAG Lys	TGT Cys	TAC His	ACA Thr	ACA Thr	1200
385																
GGA Gly	ACG Thr	ATC Ile	ATT Ile	AAT Asn	CAA Gln	GAC Asp	CCT Pro	GAC Asp	AAG Lys	ATC Ile	CTA Leu	ACA Thr	TAC Tyr	ATT Ile	GCT Ala	1248
405																
GCC Asp	GAT Asp	CAC His	TGC Cys	CCG Pro	GTG Val	GTC Val	GAG Glu	GTG Val	AAC Asn	GGT Gly	GTG Val	ACC Thr	ATC Ile	CAG Gln	GTC Val	1296
420																
GGG Gly	AGC Ser	AGG Arg	AGG Arg	TAT Tyr	CCG Pro	GAC Asp	GCA Ala	GTG Val	TAC Tyr	TTG Leu	CAC His	AGA Arg	ATT Ile	GAC Asp	CTC Leu	1344
440																
GGT Gly	CCT Pro	CCC Pro	ATA Ile	TCA Ser	TTG Leu	GAG Glu	AGG Arg	TTG Leu	GAC Asp	GTG Val	GGG Gly	ACG Thr	AAT Asn	CTG Leu	GGG Gly	1392
450																
AAT Asn	GCA Ala	ATT Ile	GCT Ala	AAG Lys	TTG Leu	GAG Glu	GAT Asp	GCC Ala	AAA Lys	GAA Glu	TTG Leu	TTG Leu	GAG Glu	TCA Ser	TCG Ser	1440
465																
GAC Asp	CAG Gln	ATA Ile	TTG Leu	AGG Arg	AGT Ser	ATG Met	AAA Lys	GGT Gly	TTA Leu	TCG Ser	AGC Ser	ACT Thr	AGC Ser	ATA Ile	GTT Val	1488
485																
TAC Tyr	ATC Ile	CTG Leu	ATT Ile	GCA Ala	GTG Val	TGT Cys	CTT Leu	GGG Gly	GGG Gly	TTG Leu	ATA Ile	GGG Gly	ATC Ile	CCC Pro	GCT Ala	1536
500																
TTA Leu	ATA Ile	TGT Cys	TGC Cys	TGC Cys	AGG Arg	GGG Gly	CGT Arg	TGT Cys	AAC Asn	AGA Arg	AAG Lys	GGA Gly	GAG Glu	CAA Gln	GTT Val	1584
515																
GGT Gly	ATG Met	TCA Ser	AGA Arg	CCA Pro	GGC Gly	CTA Leu	AAG Lys	CCT Pro	GAT Asp	CTT Leu	ACA Thr	GGG Gly	ACA Thr	TCA Ser	AAA Lys	1632
530																
TCC Ser	TAT Tyr	GTA Val	AGG Arg	TCG Ser	CTC Leu	TGA ***										1653
545																
550																

95

(2) INFORMATION FOR SEQ ID NO:20:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 550 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

Met	Gly	Leu	Lys	Val	Asn	Val	Ser	Ala	Ile	Leu	Met	Ala	Val	Leu	Leu	1	5	10	15
Thr	Leu	Gln	Thr	Pro	Thr	Gly	Gln	Ile	His	Trp	Gly	Asn	Leu	Ser	Lys	20	25	30	
Ile	Gly	Val	Val	Gly	Ile	Gly	Ser	Ala	Ser	Tyr	Lys	Val	Met	Thr	Arg	35	40	45	
Ser	Ser	His	Gln	Ser	Leu	Val	Ile	Lys	Leu	Met	Pro	Asn	Ile	Thr	Leu	50	55	60	
Leu	Asn	Asn	Cys	Thr	Arg	Val	Glu	Ile	Ala	Glu	Tyr	Arg	Arg	Leu	Leu	65	70	75	80
Arg	Thr	Val	Leu	Glu	Pro	Ile	Arg	Asp	Ala	Leu	Asn	Ala	Met	Thr	Gln	85	90	95	
Asn	Ile	Arg	Pro	Val	Gln	Ser	Val	Ala	Ser	Ser	Arg	Arg	His	Lys	Arg	100	105	110	
Phe	Ala	Gly	Val	Val	Leu	Ala	Gly	Ala	Ala	Leu	Gly	Val	Ala	Thr	Ala	115	120	125	
Ala	Gln	Ile	Thr	Ala	Gly	Ile	Ala	Leu	His	Gln	Ser	Met	Leu	Asn	Ser	130	135	140	
Gln	Ala	Ile	Asp	Asn	Leu	Arg	Ala	Ser	Leu	Glu	Thr	Thr	Asn	Gln	Ala	145	150	155	160
Ile	Glu	Ala	Ile	Arg	Gln	Ala	Gly	Gln	Glu	Met	Ile	Leu	Ala	Val	Gln	165	170	175	
Gly	Val	Gln	Asp	Tyr	Ile	Asn	Asn	Glu	Leu	Ile	Pro	Ser	Met	Asn	Gln	180	185	190	
Leu	Ser	Cys	Asp	Leu	Ile	Gly	Gln	Lys	Leu	Gly	Leu	Lys	Leu	Leu	Arg	195	200	205	

Tyr Tyr Thr Glu Ile Leu Ser Leu Phe Gly Pro Ser Leu Arg Asp Pro
 210 215 220
 Ile Ser Ala Glu Ile Ser Ile Gln Ala Leu Ser Tyr Ala Leu Gly Gly
 225 230 235 240
 Asp Ile Asn Lys Val Leu Glu Lys Leu Gly Tyr Ser Gly Gly Asp Leu
 245 250 255
 Leu Gly Ile Leu Glu Ser Arg Gly Ile Lys Ala Arg Ile Thr His Val
 260 265 270
 Asp Thr Glu Ser Tyr Phe Ile Val Leu Ser Ile Ala Tyr Pro Thr Leu
 275 280 285
 Ser Glu Ile Lys Gly Val Ile Val His Arg Leu Glu Gly Val Ser Tyr
 290 295 300
 Asn Ile Gly Ser Gln Glu Trp Tyr Thr Thr Val Pro Lys Tyr Val Ala
 305 310 315 320
 Thr Gln Gly Tyr Leu Ile Ser Asn Phe Asp Glu Ser Ser Cys Thr Phe
 325 330 335
 Met Pro Glu Gly Thr Val Cys Ser Gln Asn Ala Leu Tyr Pro Met Ser
 340 345 350
 Pro Leu Leu Gln Glu Cys Leu Arg Gly Phe Thr Lys Ser Cys Ala Arg
 355 360 365
 Thr Leu Val Ser Gly Ser Phe Gly Asn Arg Phe Ile Leu Ser Gln Gly
 370 375 380
 Asn Leu Ile Ala Asn Cys Ala Ser Ile Leu Cys Lys Cys Tyr Thr Thr
 385 390 395 400
 Gly Thr Ile Ile Asn Gln Asp Pro Asp Lys Ile Leu Thr Tyr Ile Ala
 405 410 415
 Ala Asp His Cys Pro Val Val Glu Val Asn Gly Val Thr Ile Gln Val
 420 425 430
 Gly Ser Arg Arg Tyr Pro Asp Ala Val Tyr Leu His Arg Ile Asp Leu
 435 440 445
 Gly Pro Pro Ile Ser Leu Glu Arg Leu Asp Val Gly Thr Asn Leu Gly
 450 455 460
 Asn Ala Ile Ala Lys Leu Glu Asp Ala Lys Glu Leu Leu Glu Ser Ser
 465 470 475 480

[illegible]

WE CLAIM:

1. A measles virus mutant antigen, comprising at least one protein antigen selected from the group consisting of (I) a measles virus mutant H protein antigen and (II) a measles virus mutant F protein antigen,

said measles virus mutant H protein antigen (I) being at least one member selected from the group consisting of the following amino acid sequences (a) to (d):

(a) the amino acid sequence of SEQ ID NO:10;

(b) the amino acid sequence of SEQ ID NO:3 or SEQ ID NO:11;

(c) the amino acid sequence of SEQ ID NO:4 or SEQ ID NO:12; and

(d) the amino acid sequences of SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7 and SEQ ID NO:8, or the amino acid sequences of SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15 and SEQ ID NO:16; and

said measles virus mutant F protein antigen (II) being the amino acid sequence of SEQ ID NO:20.

2. A measles virus mutant gene, comprising at least one gene selected from the group consisting of (I) a gene coding for a measles virus mutant H protein antigen and (II) a gene coding for a measles virus mutant F protein antigen,

said gene coding for a measles virus mutant H protein antigen (I) being at least one member selected from the group consisting of the following genes (a) to (d):

(a) a gene coding for the amino acid sequence of SEQ ID NO:10;

(b) a gene coding for the amino acid sequence of SEQ ID NO:3 or SEQ ID NO:11;

(c) a gene coding for the amino acid sequence of SEQ ID NO:4 or SEQ ID NO:12; and

(d) genes coding for the amino acid sequences of SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7 and SEQ ID NO:8, or genes coding for the amino acid sequences of SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15 and SEQ ID NO:16; and

said gene coding for measles virus mutant F protein antigen (II) being a gene coding for the amino acid sequence of SEQ ID NO:20.

3. A recombinant measles virus mutant antigen obtained by replacing a part of the H protein of CAM-70 strain shown in SEQ ID NO:2 by a corresponding part of the H protein of NA strain shown in SEQ ID NO:10.

4. The recombinant measles virus antigen according to claim 3, wherein the 176th to 316th amino acids of SEQ ID NO:2 are replaced by the amino acid sequence of SEQ ID NO:12.

5. A recombinant measles virus mutant gene obtained by replacing a part of the gene coding for the H protein of CAM-70 strain shown in SEQ ID NO:2 by a corresponding part of the gene coding for the H protein of NA strain shown in SEQ ID NO:10.

6. The recombinant measles virus gene according to claim 5, wherein the gene coding for the 176th to 316th amino acids of SEQ ID NO:2 is replaced by the gene coding for the amino acid sequence of SEQ ID NO:12.