New live attenuated influenza vaccines

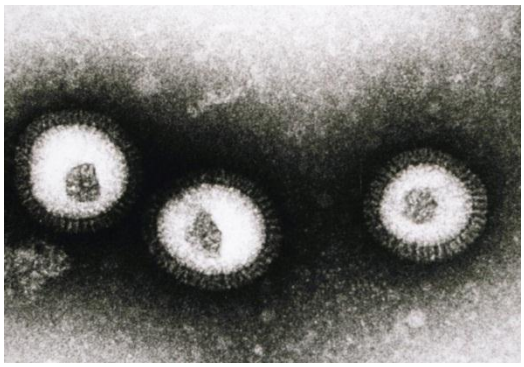
INRA's researchers within unit "Molecular Virology and Immunology" have identified new point mutations in Influenza A virus polymerase PA subunit, and generated new temperature-sensitive viruses. These mutant viruses could advantageously be used to develop new Influenza attenuated live vaccines.

Industrial application

Production of Influenza live attenuated vaccines for human and animal applications.

Advantages

- ✓ Temperature sensitivity limits the viral replication in the lower respiratory tract and lungs.
- ✓ To prevent appearance of a revertant on the substituted amino acid, it can be selected among the identified residues those requiring two nucleotide mutations to recover the initial amino acid.
- ✓ The invention allows to overcome vaccine manufacturing in embryonated eggs, and to shorten the production time of the vaccine.
- ✓ Implementation with standard techniques of production of recombinant Influenza virus (reverse genetic tools).



Technology transfer

- Patent application FR1353543 filed by INRA on April 18, 2013
- Licence or licence option with R&D program

Description of the innovation

Influenza viruses are among the major respiratory pathogens of Human and animals, and flu prevention primarily relies on vaccination. The most commonly marketed vaccines are inactivated vaccines based on viruses grown in embryonated chicken eggs, which is a complex, time-consuming and expensive process. More recently, live attenuated virus vaccines were built from donor strains with mutations alleviating their pathogenicity, but they are more rare.

In the frame of the Carnot Institute for Animal health "ICSA", within unit "Molecular Virology and Immunology", INRA's researchers steered by Dr Bernard Delmas have developed a method for preparing a temperature-sensitive "ts" Influenza virus characterized by the introduction of one or several mutation(s) located in the region corresponding to the linker region (aa 197 to 225) of Influenza A virus polymerase PA subunit.
These new point mutations lead to amino acids substitution resulting in the production of "ts" viruses. Researchers have demonstrated that between 33°C and 37°C these "ts" viruses were propagating with replication kinetics similar that of the parental virus, while at 39.5°C, this viral replication is blocked. Thermosensitivity limits the viral replication in the lower respiratory tract and lungs.
Preliminary experiments performed in the mouse model with these attenuated vaccines showed a reduced pathogenicity and elicitation of an antibody response.

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