

Information on the VLP influenza vaccine

On April 30, 2009, Cytos Biotechnology presented preclinical data for a novel influenza vaccine at the scientific conference „The Third International Conference on Influenza Vaccines for the World“, in Cannes, France. This novel influenza vaccine is produced entirely in *E.coli* bacteria, which allows manufacture of millions of doses within several weeks after a new influenza strain has been identified.

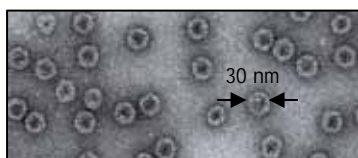
The novel vaccine comprises an antigen from the influenza hemagglutinin protein, which is displayed in a highly ordered fashion on virus like particles (VLPs). The resulting vaccine was shown to be highly immunogenic and able to protect mice from a lethal influenza challenge. Cytos Biotechnology's VLP technology has already been tested in several other indications in more than 1,100 people so far and has shown to be safe, well tolerated and highly immunogenic.

The VLP influenza vaccine candidate has several advantages over the approved influenza vaccines which are produced in embryonated chicken eggs or cell culture.

- Significantly higher production efficiency
- Faster availability of an antigenically matched vaccine compared to conventional production technology
- Seroconversion within days (as observed in animal models)
- Possibility of cross protection due to higher antibody levels induced by means of the VLP technology

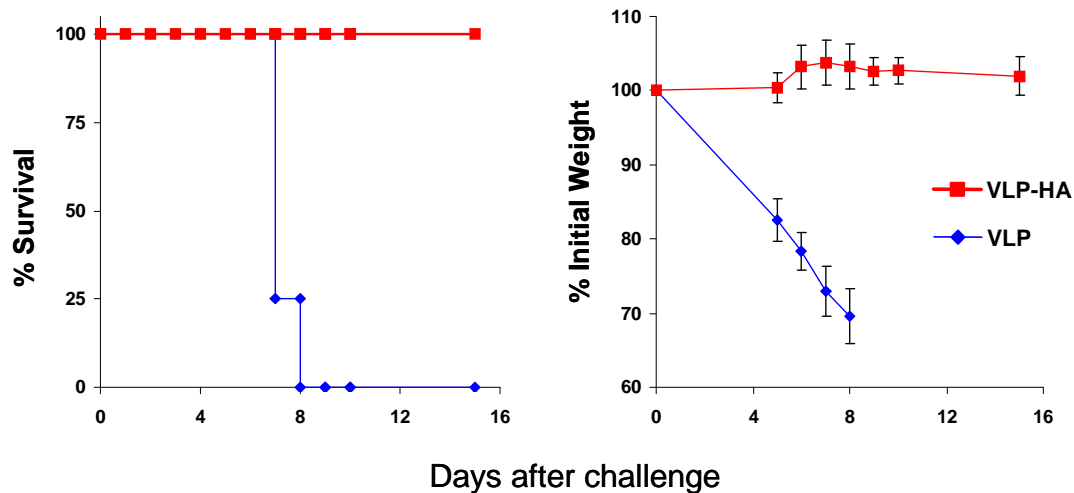
Since the VLP influenza vaccine is produced on a different production platform than conventional seasonal vaccines which are produced in embryonated chicken eggs or cell culture it can be manufactured without interrupting production of seasonal vaccines. This is especially important since seasonal influenza is a disease that every year causes up to 500,000 deaths in the world and a lack of seasonal vaccine would lead to a further increase in this number.

The development of a pandemic vaccine like the VLP influenza vaccine, which is based on an independent production platform is therefore crucial. Cytos Biotechnology intends to pursue this development in partnership with private as well as governmental bodies.



(Electron micrograph by T. Bächli, University of Zurich)

Picture 1: Electron micrograph of virus like particles



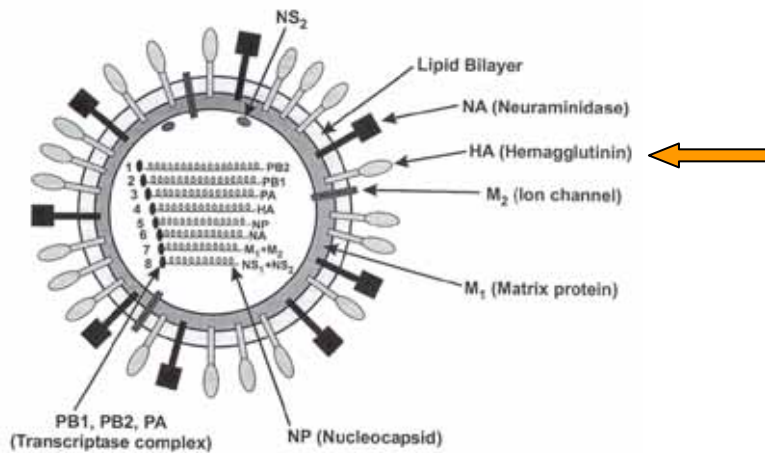
Picture 2: Protection of VLP-HA vaccinated mice against lethal challenge with influenza. Mice were immunized once with 15 μ g VLP influenza vaccine (VLP-HA) or VLP alone. 3 weeks later (day 0 on the graph) mice were challenged with a lethal dose of PR8/34, a H1N1 influenza strain. Survival and body weight was monitored following viral challenge.

Influenza – some facts

Influenza is one of the main viral diseases in man. Typically, 10-20 % of the world population are infected during seasonal epidemics resulting in 3 to 5 million cases of severe illness and up to 500,000 lethal cases per year (WHO, April 2009).

Development of protective vaccines against influenza virus has proven difficult due to the high mutation rate of the surface proteins hemagglutinin (HA) and neuraminidase (NA). Moreover, occasionally novel influenza strains containing new HA and/or NA genes acquired from animal influenza viruses appear in the human population and have high potential to cause pandemics. In the last century three major pandemics occurred (1918, 1957, 1968) that caused millions of deaths worldwide.

Immunization proves to be the most effective measure in preventing infection. Antigenically matched vaccines derived from the actual circulating strains have demonstrated up to 90% efficacy in protecting healthy adults from influenza illness. Conventional specific influenza vaccines, however, have inherent deficiencies, one of which is their time-consuming production in embryonated chicken eggs typically taking several months. Due to the complexity of the process, not enough doses to vaccinate a large population will be ready in time, should a new pandemic emerge. Indeed, in case of a new pandemic, vaccine would have to be available within weeks of the outbreak.



Classification of influenza strains:

Hemagglutinin (HA) 1-16

Neuraminidase (NA) 1-9

For example H3N2 and H1N1 which are strains currently circulating in the population.

Picture 3: Schematic view of an influenza virus

Further information on influenza virus and the current swine influenza (H1N1) are available under:

www.who.int

<http://www.bag.admin.ch/>