Göteborg, 2018

Broadly protective nanoparticle-based mucosal vaccine against Influenza virus infection

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i hörsal Arvid Carlsson, Medicinaregatan 3, Göteborg, fredagen den 30 november, klockan 13:00

av Valentina Bernasconi

Fakultetsopponent:

Professor **Bjarne Bogen,**
Institutt for klinisk medisin,
Universitetet i Oslo, Oslo, Norge

Avhandlingen baseras på följande delarbeten

I. "Porous nanoparticles with self-adjuvanted M2e-fusion protein and recombinant hemagglutinin provide strong and broadly protective immunity against influenza virus infections" Valentina Bernasconi, Beatrice Bernocchi, Liang Ye, Minh Quan Lê, Ajibola Omokanye, Rodolphe Carpentier, Karin Schön, Xavier Saelens, Peter Staeheli, Didier Betbeder, Nils Lycke
Frontiers in Immunology, 12 September 2018
https://doi.org/10.3389/fimmu.2018.02060

II. "A novel combined vaccine consisting of an enzymatically active fusion protein adjuvant and lipid nanoparticles provides broadly protective immunity against influenza infection" Valentina Bernasconi, Karin Norling, Sabina Burazerovic, Karin Schön, Anneli Strömberg, Marta Bally, Fredrik Höök, Nils Lycke
Manuscript

III. "Targeting follicular dendritic cells with CTA1-DD adjuvant effectively promotes immune responses in neonatal mice and recovery from influenza infection" Sophie Schussek, Valentina Bernasconi, Anneli Strömberg, Karin Schön, Nils Lycke
Manuscript

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Broadly protective nanoparticle-based mucosal vaccine against Influenza virus infection

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Abstract
Influenza is one of the major viral diseases affecting humans and it is responsible for three to five million cases of severe illness and about 250.000 to 500.000 deaths each year worldwide. A vaccine against pandemic influenza infection is much warranted and the most effective measure to reduce the risk of a global spread of novel emerging influenza strains. While injectable vaccines require trained medical staff and carry a substantial risk of spreading contaminating infections, mucosal vaccines are easier to administer and considered safer, but, unfortunately, also less effective. However, mucosal vaccines can be made more effective by using better formulations and adjuvants. We have designed two intranasal vaccine candidates against pandemic flu, which were based on the strain-conserved M2e peptide incorporated into the CTA1-DD mucosal adjuvant. Previously, the CTA1-3M2e-DD fusion protein was found to stimulate protective immunity. Here, we attempted to further improve its vaccine qualities by incorporating it into polysaccharide or liposome nanoparticles, which were administered intranasally. Our findings clearly indicate that mucosal vaccines based on combinations of the potent CTA1-DD immunomodulator and nanoparticles provide a strong basis for future mucosal vaccine development. Finally, my thesis work conveys optimism about the possibility to develop a broadly protective mucosal influenza vaccine not only for adults, but also for young children.

Keywords: Mucosal vaccination; Influenza A virus; CTA1-DD; Nanoparticle; Targeted adjuvant; Nasal immunization; Oral immunization; Neonatal vaccine; Universal vaccine.

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