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Vaccination with self-adjuvanted protein nanoparticles provides protection against lethal influenza challenge

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Subunit vaccines are generally less immunogenic than whole organism vaccines. One approach to reduce this deficiency is the development of repetitive antigen displays. One of the most promising repetitive antigen displays is our Self-Assembling Protein Nanoparticle (SAPN). Based off of coiled-coil oligomerization domains our SAPNs can self-assemble into spherical particles that mimic the size and shape of small viruses and are decorated on their surface with antigens. We have applied the SAPN technology to the development of a universal influenza virus vaccine. By incorporating two conserved antigens (M2e and Helix C), we aimed to generate a vaccine candidate that is broadly protective not only through different seasons but also against different subtypes. One of the most important considerations in vaccine development is adjuvant formulation. We have designed and implemented a new technology that incorporates the TLR5 agonist flagellin into the SAPN. Flagellin is an established adjuvant that is known to induce increased antigen processing as well as increased humoral and cellular immune responses. By adding flagellin to our SAPNs we have generated Self-Adjuvanted SAPNs. We have applied this technology to the development of universal influenza vaccine. In this study we demonstrate that addition of flagellin does not affect the ability of SAPNs to self-assemble, nor does it change the size or shape of the SAPNs. Self-Adjuvanted SAPNs are able to stimulate TLR5 *in vitro* in a dose dependent manner. Specific Pathogen-Free Chickens vaccinated with the Self-Adjuvanted SAPN induce significantly higher levels of antibodies than unadjuvanted SAPNs. Antibodies from chickens vaccinated with the Self-Adjuvanted SAPNs are cross-neutralizing towards group 1 influenza strains in *in vitro* experiments. Upon immunization with Self-Adjuvanted SAPN mice were completely protected against a lethal challenge with A/human/Puerto Rico/8/1934 (H1N1). Our data indicate that we have generated a Self-Adjuvanted SAPN has a great potential as a universal influenza vaccine.

Biography

Peter Burkhard has obtained his PhD from the University of Basel, Switzerland. He is currently a Professor of Nanobiotechnology at the University of Connecticut, Storrs, USA. He is also a Co-Founder and CEO of Alpha-O Peptides AG, Riehen, Switzerland. As a Structural Biologist he invented the self-assembling protein nanoparticles (SAPN) as a platform for vaccine design.

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