OMICS Group Conferences
Accelerating Scientific Discovery

2nd International Conference on
Vaccines and Vaccination

August 20-22, 2012 Hilton Chicago/Northbrook, USA

Modulation of peptide conformation in liposomal vaccines for targeting protein misfolding diseases

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Alzheimer´s disease (AD) is a neurological disorder characterized by the presence of Amyloid beta (Aβ) peptide fibrils and oligomers in the brain. It has been suggested that soluble Aβ oligomers, rather than Aβ fibrils, contribute to neurodegeneration and dementia due to their higher level of toxicity. Therefore, potential AD therapies should specifically target the pathological form of Aβ (oligomers) over the other aggregated states of the same protein. Here we present how pathological epitope conformation can be controlled on the surface of liposomes for generating conformationally specific immune responses [1]. A panel of synthetic lipopeptides was used in order to assess the impact of key parameters on the conformation adopted upon integration into liposomal bilayer. Results revealed that both the peptide lipidation pattern, lipid anchor chain length as well as the liposome surface charge, significantly affects peptide conformation independently of its primary aminoacid sequence [1]. Immunization of both mice and monkey with model liposomal vaccine containing β-sheet aggregated lipopeptide (Palm1-15) induced polyclonal IgG antibodies which specifically recognized β-sheet oligomers over monomers (non-pathological protein) [1]. The rational design of liposome-bound peptide immunogens with defined conformation opens up the possibility to generate vaccines against a wide-range of protein misfolding diseases (e.g. Alzheimer, Parkinson, Huntington and Diabetes type II). Finally, AC Immune's SupraAntigenTM Vaccine Technology has been demonstrated to be flexible (as varied antigens and adjuvants can be loaded on liposomes), efficacious in animal models and feasible under GMP-environment. [1] Hickman D.T. et al Sequence-Independent control of peptide Conformation in Liposomal Vaccines for targetting protein misfolding disease, JBC 2011; doi: 10.1074/jbc.M110.186338

Biography

Pedro Reis did a PhD on Biophysics in 2008 at Chalmers University of Technology, Sweden. Afterwards, he was appointed as Primer Researcher at Baylor College of Medicine, Houston and at UNIL's Biochemistry Department, Switzerland. Since August 2009, Pedro Reis has been working as a Project Leader of Vaccine Manufacturing at AC Immune SA, which is a Swiss-based biopharmaceutical company and a leader in Alzheimer's Disease drug development. AC Immune SA has been developing innovative therapeutics with "best in class" potential against Alzheimer's Disease and other conformational diseases along three axes: vaccines, antibodies and small molecules.

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