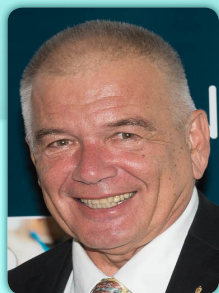


9th Global Summit and Expo on Vaccines & Vaccination

November 30-December 02, 2015 San Francisco, USA



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Dendritic vaccine delivery systems

Subunit vaccines that contain the minimal microbial components necessary to stimulate appropriate immune responses have the potential to overcome allergic response or autoimmunity that can result from using classical vaccines. We developed new delivery systems by combining the adjuvant and antigenic peptide epitopes into one chemically bonded dendritic entity. The presentation of epitopes on the nanoparticles surface was optimized to elicit a strong immune response in mouse models. Infection with Group A *Streptococci* (GAS), one of the most common and widespread human pathogens, can result in a broad range of diseases, with the potential to develop acute and post-infectious rheumatic fever and rheumatic heart disease. Immunity to GAS relies on the production of opsonic antibodies specific to the hyper-variable N-terminal and conserved C-terminal regions of the coiled-coil α -helical M protein, a GAS major virulence factor. To improve vaccine delivery, we developed a self-adjuncting lipid core peptide (LCP) dendrimer system that included the antigen, a T helper epitope, a carrier and the adjuvant within the same molecular entity. The system allowed the attachment of multiple copies of antigens. We investigated the structural requirements to elicit production of different antibodies (IgA, IgG) and assessed the influence of complex size on the level of antibody production. Recent developments in nanomedicine/vaccinology have identified that size and morphological characteristics of nanoparticle vaccines affect their efficacy. Preliminary investigations have demonstrated that polymer-based nanoparticles that displayed peptide epitopes on their surface induced very strong immune responses against those epitopes. We have also shown that this response was dependent on the size of the total construct. We explored the efficacy of nanoparticle vaccines using a *Human Papillomavirus* (HPV) model. HPV infection, most commonly HPV-16, is responsible for the vast majority of cases of cervical cancer, which is the second most common cancer in women worldwide. The development of therapeutic vaccines that eliminate HPV infected cells and eradicate established HPV-associated tumors would therefore be beneficial and desirable. We established a synthetic pathway to conjugate *Human papillomavirus* peptide antigens to the polymeric core to create macromolecular vaccine candidates to treat HPV-related cancers. These conjugates reduced tumor growth and eradicated established E7-expressing TC-1 tumors in mice after a single immunization, without the addition of an external adjuvant. We extended our vaccine delivery platform investigations by using Luteinizing Hormone-Releasing Hormone (LHRH) as antigen. An anti-LHRH vaccine aims to control the level of sex hormones FSH and LH by generating antibodies against LHRH in murine and ovine models. We have observed significant IgG antibody response after primary immunization without the use of additional adjuvant. The antibody response was enhanced and long-lasting when we co-administered commercial adjuvant AdjuVacTM with our LCP-LHRH vaccine formulation.

Biography

Istvan Toth, PhD, DSc ARC Australia Professorial Fellow is a chemical engineer and an internationally recognized expert in drug delivery. His major research interests are immuno-adjuncts, carbohydrates, lipids, peptides, nucleosides and nucleotides. At the School of Pharmacy, University of London and at the University of Queensland, he built up a strong, very productive research group where the research orientation well suited the direction of modern multidisciplinary pharmaceutical sciences. He has refereeing duties for many international scientific journals and for scientific granting bodies. He has also demonstrated track record in research commercialization he is a one of the key founders of Alchemia (ASX listed), Implicit Bioscience Pty Ltd., Neurotide Pty Ltd. and TetraQ. He is also a Scientific Advisory Board Member of Implicit Bioscience Pty Ltd. Brisbane, Australia and Proxima Concept Ltd., London, UK. He has obtained a Business/Higher Education Round Table (BHERT) Award: Outstanding Achievement in International Collaborative R&D. He has more than 300 peer-reviewed publications and 43 patents. He is the Editor in Chief of *Current Drug Delivery; Drug Delivery Letters*, Associate Editor of *Medicinal Chemistry*; Board Member of *Mini Reviews in Medicinal Chemistry*, *Open Drug Delivery*, *Open Medicinal Chemistry* and *Current Patents in Drug Delivery*. He has been appointed as a Member of the ARC College of Experts (2008-2010) and has been the funding President of the Australian Chapter of Controlled Release Society. He is a Fellow of the Royal Australian Chemical Institute (FRACI) and the Queensland Academy of Science and Art (FQA).

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