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How to elicit immediate and long-term immunity against influenza

When delivered intranasally a single dose of the TLR-2 agonist S-[2,3-bis(palmitoyl oxy)propyl] cysteine (Pam2Cys) affords up to 99% reduction in viral loads in the lungs of mice challenged with influenza virus strains of moderate virulence and significantly reduces weight loss and mortality following challenge with highly virulent virus strains. The effect is immediate, occurring in the first day of exposure, and is achieved with a single dose of Pam2Cys. Mice treated with Pam2Cys and subsequently challenged with influenza virus also demonstrate lower rates of contact transmission when compared to naive mice. The anti-viral activity is *antigen independent* and associated with activation of the innate immune system through Pam2Cys-dependent recruitment of neutrophils, macrophages and soluble factors including IL-6, IL-10, IFN- γ , MCP-1 and TNF- α into the pulmonary tract. The findings indicate that Pam2Cys is a *novel anti-viral agent* that can reduce both the severity of influenza infection, as well as the potential to transmit disease. An influenza vaccine formulated with Pam2Cys provides a similar immediate anti-viral effect but in addition provides anti-influenza antibodies cross reactive with the homologous, immunising strain, but also long-term *heterotypic* subtype immunity through the induction of cross-reactive CD8+ cytotoxic T cells. Vaccines formulated with Pam2Cys therefore would be suitable for use during influenza pandemics providing both an immediate anti-viral effect and long-term immunity. Finally, treatment with Pam2Cys also affords protection against secondary bacterial infection providing an option for the prevention of the secondary bacterial infections that often complicate the outcome of influenza.

Biography

David Jackson has been an active researcher in immunology and immunochemistry over the last 40 years. His research efforts are now focused on the design, assembly and evaluation of innovative vaccines which have led to pre-clinical and clinical evaluation of vaccine candidates for influenza, hepatitis C virus, Group A streptococcus, Mycobacterium tuberculosis and human papilloma virus. He has also developed candidate vaccines against methamphetamine and cocaine and against the reproductive hormone luteinizing hormone releasing hormone. He has trained more than 50 graduate, postgraduate, doctoral and postdoctoral scholars and published more than 200 original research papers, invited reviews and book chapters in immunology, chemistry, biochemistry and vaccinology. He was one of the founders of the Cooperative Research Centre for Vaccine Technology and is senior inventor of a number of patents with licenses issued to the pharmaceutical industry. One of his inventions resulted in a first-in-man clinical trial of a synthetic epitope-based vaccine against hepatitis C virus. He is co-founder of 2 start-up biotechnology companies both of which are based on his own inventions. In the last five years his work has attracted more than twenty million dollars in research grants from nationally and internationally competitive sources, industry and investors. He is a Senior Principal Research Fellow with the National Health & Medical Research Council of Australia, a Professor in The University of Melbourne and a Chief Investigator of an NH&MRC Program Grant. In 2014 he was appointed Distinguished Professor in Hokkaido University, Japan.

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