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Heat shock protein complex vaccines against mucosal pathogenic bacteria

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Heat shock proteins (Hsp) are highly conserved molecules with a range of functions, including acting as chaperones for cellular proteins and the ability to activate innate immune receptors. Hsp complex (HspC) vaccines, containing Hsp derived from pathogenic bacteria, are immunostimulatory without an exogenous adjuvant and induce immunity against their chaperoned bacterial proteins. HspC adjuvanticity is believed due to the ability of Hsp to activate toll-like receptors, though this has not been thoroughly examined. Further, the application of this vaccine technology against mucosal pathogens has not previously been explored.

Results: Helicobacter pylori infect the stomach and are the major aetiological factor in gastric cancer. Vaccination of mice with H. pylori HspC without exogenous adjuvant produced equivalent protection, and notably increased local cytokine levels but less inflammation, as similar adjuvanted vaccines. This is the first demonstration that HspC vaccines can induce protective immunity against a mucosal pathogen without a mucosal adjuvant. Neisseria meningitides colonise the nasopharynx and in some individuals, invade the host causing meningococcal disease, including meningitis. Vaccination of mice with N. meningitides B HspC induced a strong immune response. Using MyD88-/- mice, we examined the importance of TLR signalling in the HspC mechanism of action. While the immune cytokine response was dependent on MyD88, antibody induction occurred completely independently of MyD88.

Conclusion: HspC provide an effective vaccine strategy against mucosal pathogenic bacteria without the requirement for a mucosal adjuvant. While induction of a cellular response involves TLR signalling, the generation of humoral immunity occurs via a different, TLR-independent, mechanism.

Biography

Phil Sutton completed his PhD in Immunology at Manchester University in 1991 and has worked on vaccine research for almost 20 years, mostly in Australia. This includes academic Post-doctoral positions in universities and research institutes, and as an industry group leader working on vaccine R&D. Of his 64 peer reviewed publications, 32 are vaccine-related. He is also internationally recognised in the field of *Helicobacter pylori* pathogenesis. He is currently Head of the Mucosal Immunology Research group at the Murdoch Childrens Research Institute in Melbourne.

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