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DNA vaccines which encode natural adjuvants are more effective than canonical DNA vaccines

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Although DNA vaccines are attractive, suboptimal delivery, poor antigen expression and the lack of localised inflammation, essential for antigen presentation and the development of an effective immune response to the encoded antigens, has inhibited their potential. Consequently, we included the genes for membrane bound and secreted versions of HSP 70, which act as natural adjuvants, in DNA vaccines encoding the HIV protein, gag. Furthermore, as the non-cytolytic nature of DNA vaccination is likely to be a factor contributing to its inefficiency, a second vaccine encoding HIV gag and a cytolytic protein (perforin-PRF) that induces necrosis in vaccine-targeted cells after intradermal delivery was synthesized. This results in the expression and extracellular localization of damage associated molecular patterns, effective adjuvants that bind to pathogen recognition receptors in antigen presenting cells. Both vaccines generated greater cell mediated immunity resulting in significant increased protection against challenge with EcoHIV, a chimeric HIV that infects mice, compared with the canonical DNA vaccine. We also encoded PRF in a DNA vaccine encoding the HCV NS3 protein and vaccinated mice and pigs with this vaccine. The PRF-encoding vaccine generated statistically significant higher cell mediated immunity in mice and in pigs, as determined by ELIspot, after intradermal vaccination. To ensure effective, reproducible delivery the vaccine was delivered to the pig dermis by a microneedle device. As DNA vaccines fail to induce immunity to the vector, an effective DNA vaccine may be used in a homologous multi-dose regimen or as a DNA prime in a heterologous regimen.

Biography

Eric James Gowans is a Senior Research Fellow in the University of Adelaide. He has an interest in developing novel vaccine strategies for HIV and HCV and has published around 130 papers in reputed journals.

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