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Method to enhance immunogenicity of live typhoid vaccines and carriers

Live recombinant attenuated Salmonella-vectored vaccines hold great promise as a means to improve human health by generating long-lasting mucosal, humoral and cellular immunity against Salmonella and a variety of non-Salmonella pathogens at a low cost. Salmonella Typhimurium elicits a robust host immune response by targeting M cells present on the luminal surface of Peyer's patches. Because of this, much research has been done to develop attenuated S. Typhimurium strains for live Salmonella vaccines. S. Typhimurium, however, does not disseminate past the intestinal barrier in humans, thus focus has switched to Salmonella enterica serovar Typhi strains, as they are able to invade and colonize the spleen, liver and other immune tissues. Unfortunately, the immunogenicity of S. Typhi-vectored vaccines (STyVV) is low, hence no live STyVVs have been developed for humans.

Researchers at the Biodesign Institute of Arizona State University have created novel STyVV strains with enhanced immunogenicity. These mutated strains have a greater ability to target Peyer's patches, and attach to and invade M cells, enabling them to initiate a more robust mucosal, humoral and cellular response. These strains are attenuated such that they are nonpathogenic from a clinical standpoint and are excellent candidates for live Salmonella vaccines. The immunogenicity of these strains was validated in BALB/c mice by measuring markers of immune response in serum collected 7 weeks after primary immunization. As observed, mice inoculated with the mutated strains mounted a greater immune response when compared to strains without the mutations.

The attenuation and increased immunogenicity of these strains makes them great candidates for live Salmonella vaccines to improve human health and protect against Salmonella and non-Salmonella pathogens.

Potential Applications

- Live attenuated Salmonella vaccines
- Expression of genes from pathogens for further vaccine applications

Benefits and Advantages

- Attenuated strains with increased immunogenicity
- Reduced adherence to host intestinal enterocytes
- More effective at targeting Peyer's patches and attaching to and invading M cells
- More robust mucosal, humoral and cellular response
- Increased acid resistance
- Increased levels of IL-8 secreted by M cells

For more information about the inventor(s) and their research, please see Dr. Roland's departmental webpage