Immunization with Attenuated Salmonella-based Vaccine Vector for Influenza Hemagglutinin Domain 1 Elicits Antigen-specific Cell-mediated Immune Response in Broiler Chickens.

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Background/Objective

The influenza virus causes infection in humans and animals, with resultant disease ranging from asymptomatic or mild respiratory infections to loss of life. The current production method of influenza vaccines in eggs or cell culture is time and labour consuming. Alternative vaccines are required. Bacteria such as Salmonella can be used to express proteins from a heterologous pathogen.

Salmonella have many advantages as a vaccine delivery vector, as they are easy to produce, easy to administer (orally), are able to elicit both humoral immunity including serum and secretory IgA antibody, and they also elicit strong cell mediated immune responses that include cytotoxic and memory T lymphocytes. Furthermore, vaccinated recombinant Salmonella not only elicit immune responses against the heterologous antigen, but also to Salmonella itself, providing protective immunity against both Salmonella and the heterologous pathogen.

Method

In the study, attenuated Salmonella enterica serovar Typhimurium (STM-1), a ΔaroA- Δserc- mutant which is licensed for the prevention of Salmonelosis in poultry in Australia, , was used as a delivery vector for an influenza surface antigenic protein, Hemagglutinin domain 1 (HA1). HA1 was engineered and incorporated into a plasmid encoding the necessary components of the E. coli α-haemolysin secretion system, which enables the recombinant HA1 to be expressed and secreted as a secretory antigenic protein. An animal trial was carried out to evaluate the vaccine immunogenicity.

Result

In orally administered broiler chickens, the vaccine construct was capable of eliciting antigen-specific CD4+ Th1-biased cell-mediated immune response, but elicitation of humoral response was absent. In addition, the vaccine construct was able to persist in vivo for up to seven days after immunisation. Further studies were therefore designed to enhance the immunogenicity and genetic stability of the vaccine construct.

Conclusion

Here, attenuated Salmonella STM-1 was demonstrated as a possible alternative to deliver influenza protective antigen. However, such alternative requires in-depth understandings to the mechanism of antigen presentation hence to balance the vector-induced immune responses, as well as appropriate adjustments to enhance the genetic stability for optimal immunogenicity.

In the next step of our investigation, the pro-inflammatory cytokines including IFN-γ or IL-4 will be engineered to be co-expressed together with recombinant HA1 from the vaccine vector. IFN-γ and IL-4 are known as the crucial cytokines in the initiation of Th1 and Th2 immune responses, respectively. Therefore, co-delivery of either of these cytokines in conjunction with antigenic protein should, not only enhance the vaccine immunogenicity, but also enabled us to target a specific immunogenesis pathway for optimal disease protection. Also, to enhance the genetic stability of the vaccine construct, the expression cassette of influenza HA1 and the E. coli α-haemolysin secretion system will be incorporated into chromosomal DNA of the vector. Successful development of such strategy could serves as a technological platform for the future development of live-attenuated vaccine vector for the prevention of a wide array of diseases.

Reference

1. Coloe PJ, Alderton MR, Gerraty NL, Christopher W, Smith SC: Aromatic vitamin-dependent Salmonellae as vaccines in food animals: efficacy and persistence. Dev Biol Stand 1995, 84:263-267.
2. Gentschev I, Dietrich G, Spreng S, Neuhaus B, Maier E, Benz R, Goebel W, Fensterle J, Rapp UR: Use of the alpha-hemolysin secretion system of Escherichia coli for antigen delivery in the Salmonella typhi Ty21a vaccine strain. Int J Med Microbiol 2004, 294:363-371.
3. Van TTH, Lin YC, Van TNN, Nguyen TQ, Le TTH, Do TH, Truong NH, Coloe PJ, Smooker PM: Salmonella as a vaccine vector for influenza virus. Procedia in Vaccinology 2013, 7, 23-27.
4. Van TTH, Lin YC, Coloe PJ, Smooker PM: From animals to humans: can vaccines make the transition? In Vaccinations: Procedures, Types and Controversy. edition. Edited by Bezio AI, Campbell BE. U.S.A: Nova Science Publishers; 2012:1-63.