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Editorial OMICS International

Hot Points in Live Oral Salmonella Vaccine Development

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Editorial

As I have the privilege to be a member of the Editorial Board of the Journal of Mucosal Immunology and Research I would like to encourage taking a discussion on the research about mucosally applied vaccines against typhoid. Let me take up my considerations from the *Salmonella enterica* serovar typhi because of its high invasive nature [1]. The exceptional virulence properties of this pathogen rely on the capability to stimulate strong mucosal, humoral and cellular responses. S. Typhi can invade beyond the gut mucosa in healthy humans. This feature makes this microorganism a promising carrier of heterologous antigens [2]. In this paper, my intention is to focus on the development of new vaccine products against typhoid, based on the others' work and recent clinical trials. I would like to bypass the discussion about the advantages or disadvantages of vaccination. I am sure everybody who read now these words has his/her own reflections about the sense of immunization, but undoubtedly we may together conclude that this method of diseases prevention helped in the past to save hundreds of millions of lives from the deadly effects of infections.

Currently, Global Vaccine Action Plan proposed by World Health Organization involves 25 diseases for which vaccine development is a priority – among them is typhoid. This disease is transmitted by the faecal-oral route and is most common in areas with poor water and sanitation systems. What is more, multi-drug resistant strains have spread too many areas, reducing the effectiveness of common antibiotics. It is estimated that the typhoid disease results in 52,000 deaths per year. Remaining non-typhoidal *Salmonella spp.* are assessed to cause 93.8 million cases of acute gastroenteritis and 155 000 deaths globally each year [3]. It is worth emphasizing that non-typhoid *Salmonella enterica* serovars are reported to cause mild, self-limiting infections, but one, described as the most dangerous for humans S. Typhi can be fatal, especially in the areas of developing countries predominantly in children of school-age or younger. For example, in the excellent study of Obaro et al. [4] provided data showing that S. Typhi is the leading cause of childhood bacteremia in central Nigeria. A global priority area for research and development is to deliver new or improved vaccines. Live, attenuated *Salmonella* strains have been shown to be excellent carriers for prokaryotic or eukaryotic antigens, being able to stimulate strong systemic and local immune responses against the expressed antigens. For the oral and respiratory routes of administration, the goal is to mimic the natural course of infection. Regardless of few limitations in applying oral immunization, oral delivery seems still attractive. Why? Mainly because, oral vaccines are cheaper to administer since they can be delivered outside of a formal clinical setting without the need for trained personnel [5]. Moreover, mucosal immunization with live attenuated organisms induces local immune response including pathogen-specific CD4+ and CD8+ T cells that provides excellent protection against mucosal pathogens. Additionally, mucosal administration of antigen is more likely to induce a secretory IgA response for protection of mucosal surfaces than is a parenteral injection [6]. Finally, oral vaccines have a high potential to elicit cross-reactive multifunctional CD8+ T cell responses in humans against other than *S.* Typhi serovar [7]. There is currently lots of interest in improving protection of mucosal sites by direct immunization of mucosal tissues; however, most studies on bacterial vectors as vaccines are either in the discovery or preclinical development phase [8]. Some examples of recent clinical trials confirm this trend. In one case, recombinant, and avirulent *S.* Typhi strains each expressing the *Streptococcus pneumoniae* surface protein PspA was used to evaluate safe and tolerable oral dose levels in adult subjects. Other studies were aimed to examine the safety and immunogenicity of Ty800 oral vaccine and typhoid fever vaccine candidate M01ZH09 in healthy adult subjects. It was also investigated the immune response after giving a typhoid vaccine by mouth (an experimental vaccine, CVD 909) before providing a vaccine shot (Typhim Vi).

In summary, Salmonella-vectored vaccines in the future perspective seem to be the most attractive to protect also against other infectious diseases. In the case of typhoid, the priority is to develop a vaccine to be suitable for administration to children.

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