# Editorial
# Perspective of Bacterial Vaccines

In the battle against infectious disease, a serious threat confronting humanity is the escalating resistance of bacterial pathogens to conventional antibiotics, with *Yersinia*, *Salmonella*, *Escherichia*, *Klebsiella*, *Shigella*, and *Pseudomonas* all having acquired multiple drug resistances (MDR) (*Zhang S. et al., CPB, 2013*). In addition to the naturally acquired MDR, the deliberate introduction of MDR to the select agents also poses a desperate menace to humans. A vaccine capable of defending against these bacterial pathogens would constitute an important control measure. Although a majority of the bacterial pathogens do not have licensed vaccines available for human application, much progress in the vaccine research and development has been made to date. In this hot issue, I recruited 11 review articles based on a contemporary theme or topic of great importance to the field of vaccine development against the important human bacterial pathogens. Topics cover the bacterial diseases at the Biosafety Level II and III, live bacteria and the toxin produced by the bacteria, mucosal bacteria and systemic bacteria, intracellular bacteria and extracellular bacteria.

Needles are the most commonly used method for administering vaccines and therapeutics. Despite of their general use, needle-based immunizations have several limitations. The possible alternatives rose in past few decades are (i) nasal (ii) dermal and (iii) oral administration. In the past decade, Dr. Mansour Mohamadzadeh's laboratory has focused on the development of oral vaccine. The recombinant lactobacilli expressing immunogen used in his studies was able to break the existing tolerance and act as an adjuvant in such vaccine. In addition to targeting antigen-presenting cells, his group searched 12 amino acid long peptide sequence that can deliver antigens efficiently to dendritic cells of diverse species (*Erskine C.L. et al. J.I. 2011*). This strategy was used to deliver antigen derived from *Bacillus anthracis* (*Mohamadzadeh M. et al. 2009*), influenza virus, and set cancer antigens. Despite a protective immune response against pathogens, it was not clear, which is the site of immune reaction. Some primary data incorporated in the current manuscript, suggest the mesenteric lymph node to be the primary site of germinal center formation.

Currently, *Yersinia pestis* have been comprehensively recognized from evolutionary angels through complete analysis of Genomics and Bioinformatics. Through the comparison of the *Y. pestis* CO92 and *Y. pseudotuberculosis* IP32953 genomes, lots of genes in *Y. pestis* are absent or inactive. Loss or inactivation of some genetic elements such as *lpxL* and *flhD* offers the pathogens avoiding recognition by host innate immunity which render bacteria easily establish their colonies in host and destroy host immune system. Dr. Wei Sun's research is based on these important genetic losses to design, construct, and evaluate recombinant genetically modified *Y. pestis* as vaccines to control plague. Also, he tries to balance attenuation and effective colonization in lymphoid tissues of the vaccine strains *in vivo* through introduction of a regulated delayed attenuation system.

*Brucella* species survive and replicate in host macrophages, causing chronic infections which can produce abortion and infertility in animals and a debilitating condition in humans. To date, there are no ideal therapeutic drugs and vaccines used for animal and human. In order to develop novel and ideal products for prevention and control of brucellosis, the first goal of the research is to develop the highly safe and efficacious vaccines. The second goal is to create an effective detecting technique to differentiate infected from vaccinated animals (DIVA). Dr. Qingmin Wu's laboratory identified and characterized the important genes in the pathogenesis of *Brucella* and their roles in the host cell survivals, immunity escape, transplacental transmission, and their interactions with the host. These findings greatly facilitate reaching their goals for generating the DIVA vaccine against brucellosis.

The infections caused by the gram-negative bacteria *Acinetobacter baumannii* have become a significant clinical problem due to their increased incidence over the last three decades and a global emergence of multidrug resistant strains. In this context, the development of novel approaches for treating and preventing infections caused by this pathogen are warranted. Active and passive immunization strategies represent a novel approach that could contribute to prevention measures for *A. baumannii*. Dr. Michael J. McConnell reviewed the progress achieved in both active and passive immunization strategies in experimental animal models. He also evaluated the antigens used in these studies, including inactivated whole cells, mixtures of outer membrane components, outer membrane vesicles, purified outer membrane proteins, and membrane-associated polysaccharides. He suggests that both active and passive immunization against *A. baumannii* are possible, however there is still a great deal of work that must be carried out before it can be determined if these approaches represent a viable strategy for combating *A. baumannii*.

*Shigella* has been considered as a major causative agent of bacterial dysentery over a contrary, and it is still threatening human life today. Dr. Hyun-Jeong Ko's laboratory has been focused on the vaccine development against this disease. Dr. Ko believes that the major aspects that need to be considered in *Shigella* vaccine development is the animal model. Moreover, identification of the friction between host and microbes in pathology and immune surveillance may be helpful in establishing the defense strategy against *Shigella* infection. Currently, various approaches have been made to develop novel *Shigella* vaccines from preclinical to Phase III. The best candidate vaccine may sooner become licensed if they show promise in the Phase III assay.

The alpha-, beta-, epsilon- and iota-toxins are the major lethal toxins produced by *Clostridium perfringens* and play critical roles in disease development, particularly during the early stages of interaction between the bacteria and the host. Dr. Masahiro Nagahama's laboratory has been focusing on investigating the pathogenic mechanism of virulence factors (toxins) produced from *C. perfringens* at the molecular level. Toxins are multifunctional proteins and exhibit the ability to affect cellular processes by membrane disruption, pore-dependent cytotoxicity and modification of intracellular target proteins. Through studying such toxins, his group expects to better understand the molecular events that contribute to disease and to develop therapeutic inhibitors and vaccines treat or prevent these diseases.

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