

Attenuated bacteria as a DNA-delivery system for Chagas disease vaccine

Chagas disease caused by the parasite *Trypanosoma cruzi*, is considered by the World Health Organization (WHO) one of the most neglected tropical diseases worldwide. Prevalent in developing countries, it has a major social and economic impact in many regions of Latin America. Human infection mostly occurs through vector transmission by infected feces of bugs, and also by maternal transmission and blood and organ transplants. The acute phase of the disease is rarely detected, but a chemotherapeutic treatment is effective, although current drugs are toxic. In the absence of treatment the infection becomes chronic, and 20-30 % of infected individuals suffer severe cardiopathy or megaesophagus/megacolon leading to death. There is not available treatment or therapeutic vaccine for chronic infection.

Vector control efforts have had partial success because of the enormous extension of land and accessibility for people living in endemics areas. In addition, migration spread disease by organ and blood donation in non-endemic areas and countries where there is no systematic blood screening for Chagas disease. These facts strongly contribute to the expansion of Chagas disease geographic region, from rural to urban areas and to non-endemic countries in Europe and North America, a phenomenon referred to as the globalization of Chagas disease.

As a consequence, there is an urgent need for an effective vaccine that not only protects humans at risk of infection, but also may alleviate or prevent the pathogenic responses characteristic of chronic disease by reducing or perhaps eliminating tissue parasites from infected patients.

One important step in the searching for a *T. cruzi* vaccine was the identification of antigens able to elicited a strong and protective immune response against the parasite; just to mention some of them: Cruzipain, GP90, GP56, y GP82 TC52, ASP-2, Tc24, and the paraflagellar rod protein PFR-1 y PFR-2. Later on, DNA vaccine was introduced as a promising tool against *T. cruzi* through the induction of cytotoxic T cells and antibody response. However, studies employing needles to inject DNA vaccine into the muscle proved to be disappointed in animals and humans, producing only sporadic and low levels of immune response. An efficient antigen delivery system is a key issue for the development of an effective vaccine. In this regard, live vaccination strategies including various live bacterial and viral vectors have attracted great attention. The use of live attenuated bacteria as vector for *in vivo* delivery of relevant molecules, offers several advantages as compared to the administration of naked DNA. Thus, the vaccine can be administered by oral route mimicking the natural entry of many infectious agents, and facilitating its administration in pathogen eradication campaigns. In addition, components of the bacteria wall and methylated DNA sequences (CpG), act as natural adjuvants increasing the innate immunity and creating a favorable environment for antigen presentation.

Several bacterial strains such as *Salmonella* have been attenuated at several independent sites to

exclude potential reversion to pathogen *in vivo*. The development of *Salmonella* as live vector for heterologous antigens is based on the fact that upon bacterial infection, all bacterial antigens, and also the carried exogenous antigen, are delivered into antigen presenting cells (APC), such as macrophages and/or dendritic cells (DCs), which are *Salmonella* natural cell targets, and presented to the immune system.

Bacterial-based vaccines are an area of intensive research, providing number of advantages over other antigen-delivery strategies. Attenuated *Salmonella* strains have shown great potential as live vectors with broad applications in humans and animals. An impressively large, and still growing, number of reports published over the last decades have demonstrated the effectiveness in animal models of *Salmonella*-based therapies for the prevention and treatment of infectious and non-infectious diseases.

Bivona AE, Cerny N, Sánchez Alberti A, Cazorla SI, Malchiodi EL

*Universidad de Buenos Aires, Facultad de Farmacia y Bioquímica,
Instituto de Estudios de la Inmunidad Humoral (IDEHU, UBA-CONICET) and
Facultad de Medicina, Instituto de Microbiología y Parasitología Médica (IMPAM, UBA-CONICET),
Buenos Aires, Argentina*

Publication

[Attenuated *Salmonella* sp. as a DNA Delivery System for *Trypanosoma cruzi* Antigens.](#)

Bivona AE, Cerny N, Alberti AS, Cazorla SI, Malchiodi EL

Methods Mol Biol. 2016