SPI-I and SPI-2 defective mutants of salmonella enterica serovar enteritidis: promising future salmonella vaccine for poultry

Keywords: salmonella vaccine, poultry, SPI-1 and SPI-2 mutants

Abbreviations: SPI, salmonella pathogenicity island; T3SS, type iii secretion system; fliC, gene encoding for flagella; lon, gene coding for lon protease

Editorial

Non-typhoid Salmonella enterica serovars are among the most common causative agents of food-borne diseases in human worldwide. Since poultry is the most frequent reservoir of salmonellosis for humans, vaccination of chickens is considered as an effective measure to decrease S. enterica prevalence in poultry as well as to decrease S. enterica incidence in humans. Within the last 25 years, many live S. enterica vaccines have been described and those with inactivated aro or phoP genes were amongst the first ones tested. Recently, construction of attenuated vaccine strains of S. enterica is not an issue and many different mutants have been tested in mice, chickens and even humans. However, the main dilemma is which mode of attenuation to choose out of the many possibilities. The major pathogenicity islands of S. enterica include SPI-1, SPI-2, SPI-3, SPI-4 and SPI-5. The SPI-1 and SPI-2 genes code for proteins forming the type III secretion system (T3SS) which enable the transport of S. enterica proteins from the bacterial cell directly into the cytosol of eukaryotic cells. The SPI-1 encoded T3SS is required for the transport of S. enterica proteins across the cytoplasmic membrane of a host cell into its cytosol where they induce cytoskeletal rearrangements resulting in the uptake of S. enterica even by non-phagocytic cells. In addition, it has been reported that SPI-1 genes, independent of cell invasion, induce macrophage cytotoxicity. SPI-2 encoded T3SS is required for the transport of S. enterica proteins across the phagosomal membrane and increases S. enterica survival inside phagocytic cells. The function of genes localized on the remaining SPIs is less well characterized and according to recent reports these remaining SPIs individually have no effect on S. Enteritidis virulence although collectively they have a low effect on bacterial colonization.

Recently, with an increasing understanding of S. enterica pathogenesis, mutants without a functional type III secretion system (T3SS) encoded by either SPI-1 or SPI-2 have been tested for determining their virulence and vaccine potentials. Results of such studies show that whilst SPI2 mutants of S. enterica are attenuated in all warm-blooded hosts, SPI1 mutants seem to be attenuated only in hosts for which an endemic type of disease is characteristic and these genes are dispensable when the output of the infection is a typhoid disease. In agreement with the previous statement, the removal of SPI1 genes from S. Enteritidis or S. Typhimurium, i.e. the serovars which cause a mild enteric disease in chickens, results in a decrease in virulence with preserved immunogenicity in these hosts. Moreover, SPI1 mutants are defective in early interactions with macrophages which may enable the macrophage’s proper antigen processing and presentation though the role of SPI1 in the interactions with other antigen presenting cells in the chicken is less clear. When SPI1 and SPI2 mutants of S. enterica serovar Enteritidis have been tested for their vaccine potentials in chickens, both the mutants provide protection to chicken against S. Enteritidis challenge as documented by findings such as the bacterial counts in tissues, spleen weight, antibody production and cytokine response (namely IL-17 and IL-22). When the 2 mutants are compared, vaccination with the SPI1 mutant proved to be more effective in the protection of chicken against S. Enteritidis challenge than the vaccination with the SPI2 mutant. On the other hand, vaccination with the SPI2 mutant stimulates a slightly higher antibody production and such a mutant might therefore be a better choice if Salmonella is used as a vector for the delivery of heterologous antigens with a desired stimulation of the humoral part of the immune system. Recently, a triple SPI1-lon-fliC mutant of S. Enteritidis has been constructed and tested for its efficacy as a live attenuated marker vaccine for the oral vaccination of poultry. Deletion of fliC gene encoding for flagella in this mutant strain enables serological differentiation of vaccinated and infected chickens which is an increasing demand for the days and is something that the current commercial vaccines cannot provide. Lon protease is a negative regulator of SPI1 genes and is required for the resistance to multiple environmental stresses and removal of lon reduces the virulence of S. Enteritidis even for highly sensitive Balb/C mice. Therefore, the inactivation of gene encoding Lon protease results in further independent attenuation of S. Enteritidis in vitro. The SPI1-lon-fliC mutant might therefore be a suitable marker vaccine strain for oral vaccination of poultry in future.

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Conflict of interest

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References