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Immuno-Protective Role of Mucosal Delivery of Lactococcus lactis Expressing Functionally Active JlpA Protein on Campylobacter jejuni Colonization in Chickens

Authors : Ankita Singh, Chandan Gorain, Amirul I. Mallick

Abstract : Successful adherence of the mucosal epithelial cells is the key early step for Campylobacter jejuni pathogenesis (C. jejuni). A set of Surface Exposed Colonization Proteins (SECPs) are among the major factors involved in host cell adherence and invasion of C. jejuni. Among them, constitutively expressed surface-exposed lipoprotein adhesin of C. jejuni, JlpA, interacts with intestinal heat shock protein 90 (hsp90α) and contributes in disease progression by triggering pro-inflammatory response via activation of NF-κB and p38 MAP kinase pathway. Together with its ability to express in the bacterial surface, higher sequence conservation and predicted predominance of several B cells epitopes, JlpA protein reserves its potential to become an effective vaccine candidate against wide range of Campylobacter sps including C. jejuni. Given that chickens are the primary sources for C. jejuni and persistent gut colonization remain as major cause for foodborne pathogenesis to humans, present study explicitly used chickens as model to test the immune-protective efficacy of JlpA protein. Taking into account that gastrointestinal tract is the focal site for C. jejuni colonization, to extrapolate the benefit of mucosal (intragastric) delivery of JlpA protein, a food grade Nisin inducible Lactic acid producing bacteria, Lactococcus lactis (L. lactis) was engineered to express recombinant JlpA protein (rJlpA) in the surface of the bacteria. Following evaluation of optimal surface expression and functionality of recombinant JlpA protein expressed by recombinant L. lactis (rL. lactis), the immune-protective role of intragastric administration of live rL. lactis was assessed in commercial broiler chickens. In addition to the significant elevation of antigen specific mucosal immune responses in the intestine of chickens that received three doses of rL. lactis, marked upregulation of Toll-like receptor 2 (TLR2) gene expression in association with mixed pro-inflammatory responses (both Th1 and Th17 type) was observed. Furthermore, intragastric delivery of rJlpA expressed by rL. lactis, but not the injectable form, resulted in a significant reduction in C. jejuni colonization in chickens suggesting that mucosal delivery of live rL. lactis expressing JlpA serves as a promising vaccine platform to induce strong immune-protective responses against C. jejuni in chickens.

Keywords : chickens, lipoprotein adhesion of Campylobacter jejuni, immuno-protection, Lactococcus lactis, mucosal delivery
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