Autodisplay : efficacious surface exposure of antigenic UreA fragments from Helicobacter pylori in Salmonella vaccine strains

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Live attenuated Salmonella strains expressing antigens of pathogens are promising oral vaccine candidates. There is growing evidence that the topology of expression of the foreign antigens can have a dramatic impact on the immunogenicity. We examined the potential of the AIDA-I (Escherichia coli adhesin involved in diffuse adherence) autotransporter domain to display antigenic fragments of the urease A subunit of Helicobacter pylori for the induction of a protective immune response. In the murine H. pylori model, protection is mainly mediated by CD4(+) T cells, and we therefore used the AIDA-I expression system to successfully express both nearly full-length UreA and defined T-helper-cell epitopes on the surface of an attenuated Salmonella enterica serovar Typhimurium vaccine strain. Surface exposure of the large UreA fragment or of one UreA T-cell epitope mediated a significant reduction in the level of H. pylori in immunized mice after challenge infection, whereas conventional cytoplasmic expression of UreA in Salmonella had no effect. These results support the concept that surface display increases the immunogenicity of recombinant antigens expressed on oral live vaccine carriers and further demonstrate the feasibility of immunizing against H. pylori with Salmonella vaccine strains expressing CD4(+) T-cell epitopes.
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