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Systemic Vaccination with Aluminum Hydroxide Induces Protective Immunity against *Helicobacter Pylori* Infection in Mice

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H. pylori infection causes gastritis, ulcers, MALT lymphoma and gastric cancer. Since the prevalence of infection is high (50 to 80% worldwide) and pharmacological eradication therapy has several disadvantages, much effort has been undertaken to develop a preventative vaccine. Because the mucosal immune system is thought to be a rather autonomous entity, research has been focussed on mucosal immunization. However, mucosal adjuvants (e.g. cholera toxin) are too toxic for use in humans.
I investigated whether protection against *Helicobacter* infection can be achieved by systemic immunizations with the adjuvants Aluminum Hydroxide (ALOH), which is licensed for human use and the experimental adjuvant CFA. Using the *H. felis* and *H. pylori* mouse models I first characterized the immune response to our vaccines by ELISPOT and ELISA assay: Immunization with *Helicobacter* antigen and AlOH induced IL-5 secreting, antigen-specific T cells and low levels of IgG2a, thus eliciting a type-2 immune response. The adjuvant CFA led to induction of IFN-γ secreting, antigen-specific T cells and high levels of IgG2a, which is characteristic for type-1 immune responses. Both immune responses conferred protection after challenge with live *Helicobacter* organisms, as confirmed by the complete absence of any bacteria in histological sections of the stomach and culture of gastric biopsy samples. Next I studied the mechanism of protection: Antibodies are not required for protective immunity since μMT (immunoglobulin-gene knockout) mice are protected against *Helicobacter* infection after immunization with antigen and AlOH. Protective immunity can be transferred to otherwise immunodeficient $rag1^{-/-}$ mice by $CD4^+$ T cells from mice previously immunized with antigen and AlOH. However, adoptive transfer of $CD4^+$ spleen T cells from mice immunized with antigen and CFA into $rag1^{-/-}$ mice did not elicit protection against infection.
In summary, I have demonstrated that systemic immunization with Alum as adjuvant induces protective immunity against *H. pylori* in mice which is mediated by $CD4^+$ type-2 T cells. Perhaps the most important aspect of this work is that systemic immunization can result in mucosal immunity. This has a direct impact on the development of a vaccine against *Helicobater* and other mucosal pathogens. The fact that protective immunity in our model is antibody (i.e. IgA)-independent and can be transferred by $CD4^+$ T cells suggests the existence of a novel $CD4^+$ T cell-mediated effector mechanism at the gastric mucosa. We found that type-1 and type-2 immunity are equally protective when wild type mice are immunized. In adoptive transfer studies, however, only type-2 immunity seemed to be protective, possibly due to the absence of certain regulatory networks in $rag1^{-/-}$ mice. Further advantages of the type-2 adjuvant Alum are its low cost and its safety for use in humans.

The notion put forth in this work, that systemic immunization with *Helicobacter* antigens in Alum is suited to induce immune protection that has been accomplished previously only by the use of toxic mucosal adjuvants, should expedite the development of a *H. pylori* vaccine.