

## Protective efficacy of recombinant *Helicobacter suis* proteins against *Helicobacter suis* challenge in a mouse model

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*Helicobacter (H.) suis* has been associated with chronic gastritis, gastric ulcer disease and decreased weight gain in pigs. This agent can also cause gastric disorders in humans. In this study, the immunogenicity and protective efficacy of three recombinant *H. suis* proteins ( $\gamma$ -glutamyl transpeptidase, neutrophil-activating protein A and urease subunit B (rGGT, rNapA and rUreB)) were compared with those of *H. suis* whole-cell lysate (lysate) in a standardized mouse model. Mice were twice immunized intranasally with three weeks interval with either rGGT, rUreB, rNapA or lysate and subsequently intragastrically challenged with  $10^8$  *H. suis* bacteria. Control groups consisted of non-immunized and non-challenged mice (negative control group), or of sham-immunized and challenged mice (positive control group). Mice were sacrificed four weeks after challenge. Bacterial colonization and stomach cytokine-expressions were examined with (RT)-qPCR. Serum immunoglobulin G (IgG) levels were determined by ELISA. Intranasal immunization of mice with lysate gave a clearance of infection in 50% of the animals and induced a specific anti-lysate IgG response. *H. suis* colonization in mice vaccinated with rGGT or rUreB was significantly ( $p < 0.0001$ ) lower compared to the positive control group and induced production of specific IgG. Immunization with rUreB resulted in a higher reduction of bacterial load compared to rGGT (100-fold and 10-fold reduction, respectively, compared with positive controls). rNapA had no significant ( $p = 0.14$ ) protective effect, although it induced anti-rNapA IgG. Expression of  $\gamma$ -interferon was significantly higher ( $p < 0.05$ ) in the stomach of animals vaccinated with rGGT, rUreB or lysate compared to non-vaccinated infected animals. Only vaccination with rGGT caused a significant ( $p < 0.01$ ) upregulation of TNF- $\alpha$ . All immunizations showed upregulation ( $p < 0.05$ ) of IL-17 mRNA, being most pronounced in the rGGT immunized group. In conclusion, immunization with recombinant *H. suis* proteins rGGT and rUreB could be promising for future vaccination of pigs against *H. suis* infections.