ORAL VACCINATION IN PIGLETS THROUGH TARGETING OF ANTIBODY-ANTIGEN FUSION CONSTRUCTS TOWARDS AMINOPEPTIDASE N

Hans Van der Weken, Raquel Sanz Garcia, Eric Cox and Bert Devriendt

Laboratory of Immunology, Faculty of Veterinary Medicine, UGent

Many disease causing pathogens enter the host via the gut. A robust intestinal immune response is necessary to protect against these enteropathogens. Oral vaccination is required to induce adequate protection, but remains challenging due to problems inherent to the administration route, such as poor uptake by the gut epithelium. An interesting target to improve this epithelial uptake is aminopeptidase N (APN), present on small intestinal epithelial cells. Aim: We aimed to develop a novel oral vaccination strategy based on the targeting of antibody-antigen fusion constructs towards APN to promote antigen-specific intestinal immune responses. Methods: An APN-specific monoclonal antibody with strong binding and uptake characteristics was porcinized using the porcine IgA Fc-domain in an effort to improve gut stability and reduce mouse IgG-specific immune responses. This porcinized monoclonal antibody was genetically linked to the F18 fimbrial adhesion subunit FedF of enterotoxigenic E. coli. The immunogenicity of this recombinant antibody-antigen fusion construct was subsequently assessed in an oral immunization experiment in piglets. Results: The APN-specific monoclonal antibody was efficiently transcytosed by the intestinal epithelium, reached the mesenteric lymph nodes in gut-ligated loops and triggered antibody-specific immune responses after oral administration. Oral immunization with the porcinized antibody-antigen fusion construct elicited FedF-specific serum IgG responses and intestinal FedF-specific IgA+ antibody secreting cells. Conclusions: These findings show that the targeting of antigens towards APN induces antigen-specific immune responses upon oral immunization and might accelerate the development of oral subunit vaccines to protect against enteropathogens.