Passive immunity leads to enhanced priming of the immune system upon oral immunization with F4 fimbriae

Ut V Nguyen*, Bert Devriendt*, Bruno M Goddeeris and Eric Cox*†**

* Laboratory of Immunology, Faculty of Veterinary medicine, Ghent University, Salisburylaan 133, 9820 Merelbeke, Belgium; ** Department of Biosystems, Faculty of Bioscience Engineering, KU Leuven, Kasteelpark Arenberg 30, B-3001 Leuven, Belgium.
† presenting author: eric.cox@ugent.be

Introduction

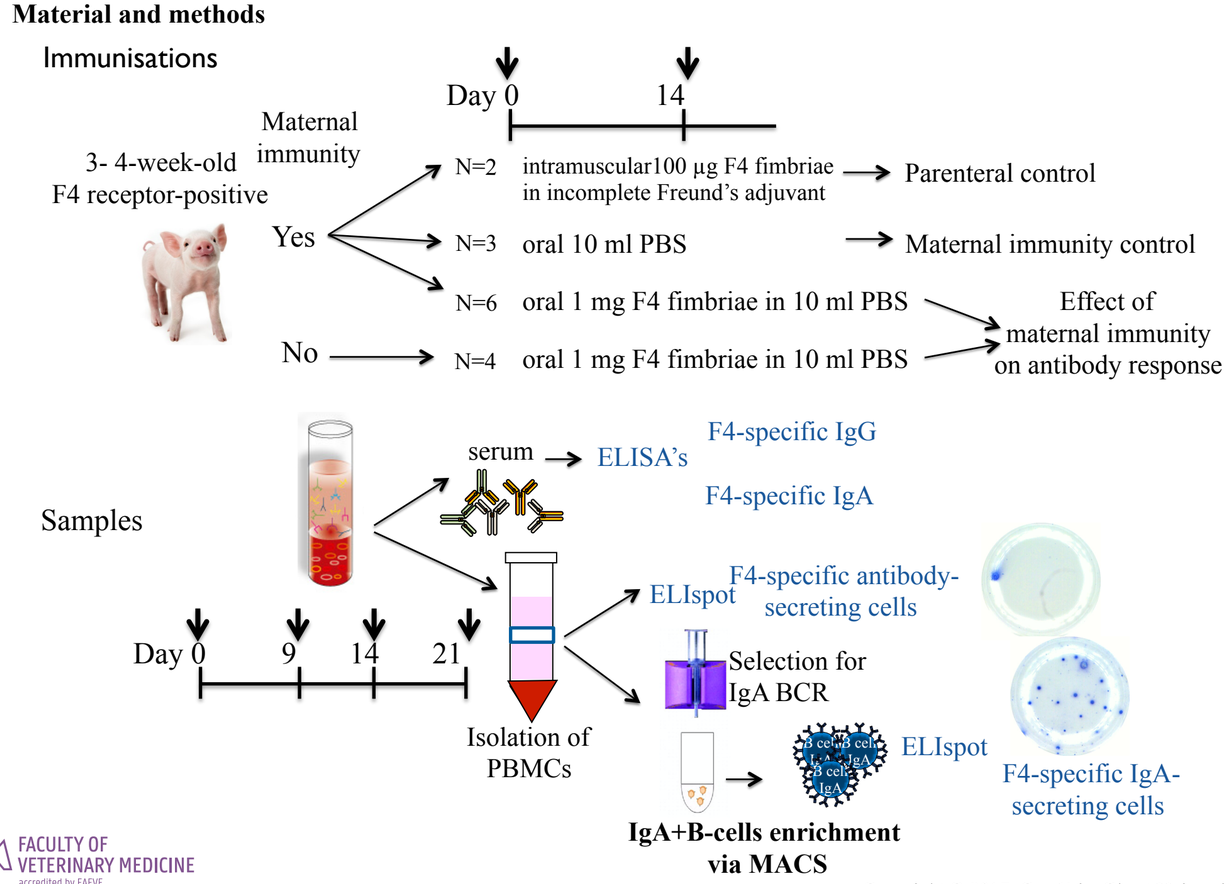
Whereas maternal immunity protects newborns against infectious pathogens, these antibodies can interfere with the active immune response against vaccines. In humans maternal antibodies are actively transported over the placenta. This is not the case in most large animals where these antibodies are derived from colostrum the first 12 hours after birth. As a result passive immunity can be steered allowing to study the impact on different immunization strategies. Structural and functional annotation of the immunome of pigs, mice and humans indicates a greater pig-human similarity (78%) than for mice-human (73%) or pig-mice. A large scale analysis of immune response genes revealed that pigs have 11-, 6- and 2- fold less unique genes than do the mouse, cow or human (Dawson et al., 2011; Dawson et al., 2013).

This together with the high similarity tissue structure and physiology makes the pig an interesting experimental animal for humans.

Maternal serum antibodies can interfere with successful parenteral vaccination of infants by cross-linking the B cell receptor of naive B cells with FcγRIIB. This inhibits B cell proliferation and secretion of antibodies. We previously demonstrated that oral immunization of 3-to 4-week-old F4-seronegative but F4 receptor-positive piglets with purified F4 fimbriae of enterotoxigenic *E. coli* (ETEC) can induce a protective intestinal mucosal immune response as evidenced by F4-specific IgA secreting cells in small intestinal tissues (Van den Broeck et al., 1999).

Here, we examined the effect of passive immunity on oral immunisation of piglets with a still immature immune system.

Material and methods

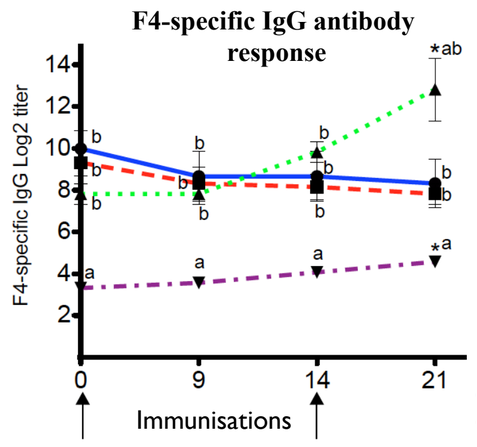


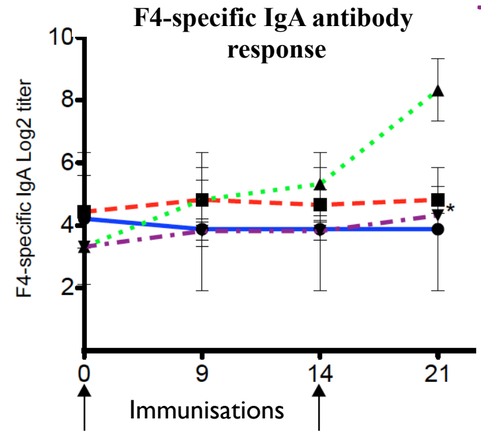
Results

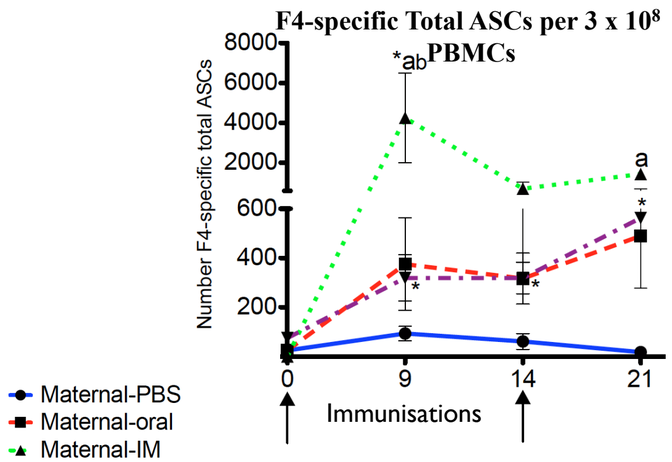
The **intramuscular immunisation** of pigs (green line) **with maternal antibodies** induced clear responses characterized by significant increases in F4-specific serum IgA and IgG titres and circulating F4 specific IgA antibody secreting cell numbers (ASC).

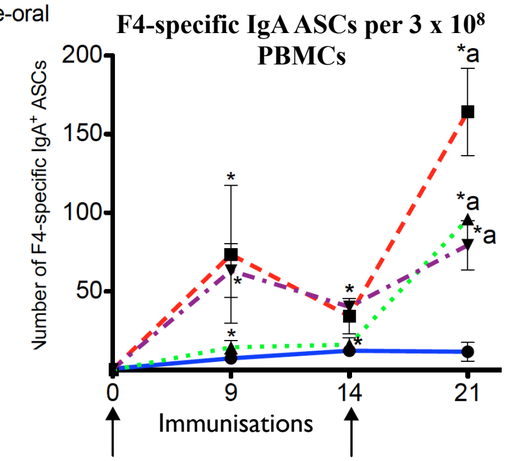
Oral immunisation of F4-seronegative animals (purple line) also induced increases in F4-specific serum IgA and IgG titres, but titres were only significantly higher one week after the booster immunisation (day 21), whereas no serum antibody responses where seen when **orally immunising pigs with maternal antibodies** (red line).

This suggests that maternal antibodies suppress or mask the immune response following oral immunisation.









This should be reflected in the circulating F4-specific ASCs after immunisation

When looking at the **total F4-specifc ASCs** only significant increases where seen in the intramuscularly immunized animals and the orally immunized seronegative animals. However a not significant increase occurred after the oral immunisation of pigs with maternal antibodies. When ELIspot assays were performed on **the enriched IgA B-cell populations**, the orally immunised pigs with maternal antibodies displayed the same primary response, but a more pronounced secondary response than pigs without maternal antibodies.

In conclusion, the presence of maternal antibodies seems to enhance the secondary response upon oral immunisation rather than to suppress it.