ETEC colonisation factors disrupt the antigen presenting capacity of porcine intestinal dendritic cells

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INTRODUCTION

Enterotoxigenic E. coli (ETEC) are not only a major cause of diarrhoea in travellers to developing countries, but also cause neonatal and postweaning diarrhoea in piglets, leading to a reduced feed conversion and a higher mortality rate. As a consequence ETEC infections result in severe economic losses in the swine production industry. This intestinal pathogen displays colonisation factors or fimbriae on its surface enabling the microorganism to adhere to the intestinal epithelium (Fig. 1). In pig, F4 and F18 fimbriae are the most frequently associated with ETEC-induced diarrhoea. Colonization factors or fimbriae are long, polymeric finger-like appendages on the bacterial surface. Fimbriae are composed of the structural subunit FedA and the tip adhesin FedF. In contrast, in F4 fimbriae the major structural subunit FedA is also a neutralizing carbohydrate.

RESULTS AND DISCUSSION

Fimbriae were purified from F4- and F18- ETEC strains and intestinal MCLs from small intestinal lamina propria (jejunum) were isolated as previously described. As opposed to F4 fimbriae, oral immunisation with F18 fimbriae doesn't protect piglets from a subsequent challenge infection. F18 fimbriae bind glycoprophages in the apical membrane of enterocytes, but no transcytosis occurs, resulting in lower surface-associated antigen concentrations as compared to F4 fimbriae, which bind the transcytotic receptor aminephorase N. However, M-cell mediated transport of F18 fimbriae still occur. Hence, besides a lower antigen concentration, these fimbriae could affect the function of intestinal antigen presenting cells. Here, we investigated the influence of purified F18 fimbriae on the antigen presentation capacity of small intestinal lamina propria dendritic cells (LPDCs).

Although the fimbriae were washed out from the LPDCs cultures prior to coculture, we assessed the effect of F18 fimbriae on ConA-induced T-cell proliferation to exclude the possibility of a direct inhibitory effect of residual F18 fimbriae on T-cell proliferation. As shown in figure 3C, F18 fimbriae were unable to reduce T-cell proliferation as compared to controls.

To assess the effect of F18 fimbriae on the function of LPDCs, F3B and F4 fimbriae-treated LPDCs were cocultured with T-cells. In contrast to F4 fimbriae, F18 fimbriae significantly diminished the T-cell proliferation inducing capacity of CD16+ and CD16- LPDCs as compared to mock-treated LPDCs (Fig. 3A). This inhibitory effect was not due to LPS present in the fimbrial preparations. Indeed, both in the presence of polymyxin B and upon removal of endotoxin (>90%) F18 fimbriae still drastically reduced the T-cell proliferation induction capacity of CD16+ and CD16- LPDCs as compared to mock- or F4 fimbriae-stimulated LPDCs (Fig. 3B).

CONCLUSION

F18 fimbriae diminished the antigen presentation capacity of porcine LPDCs. Although the exact mechanism is still unclear, we hypothesize that these F18 fimbriae disrupt lipid raft formation, resulting in a deformation of the intracellular synapse necessary to induce T-cell activation. Indeed, F18 fimbriae adhere to glycoprophages and these are important for the formation of lipid rafts. Alternatively, F18 fimbriae could drive the maturation of LPDCs towards a tolerogenic phenotype, which in turn could lead to the differentiation of regulatory T-cells, capable of suppressing CD4+ effector T-cell proliferation. Current efforts are going on unravel the molecular mechanism of this fimbriae-mediated reduction of LPDCs-induced T-cell proliferation. These results could lead to the development of an improved vaccine against F18 ETEC and deepen our understanding of potential novel immune evasive mechanisms employed by bacterial pathogens.

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