Preview Abstract IPVS Vancouver

Introduction: F18-fimbriated Escherichia coli are associated with porcine postweaning diarrhoea (PWD) and oedema disease. Adhesion of F18-fimbriated bacteria to the small intestine of susceptible pigs is a primary event in the infection process. However, the target cell receptor for F18+ E. coli (F18R) has remained unidentified. The objective of our study was to unravel the carbohydrate-binding specificity of F18-fimbriated E. coli and to examine whether these F18R molecules can inhibit the interaction between F18+ E. coli and the pig small intestine.
Materials and methods: To identify the F18R molecules, mixtures of glycosphingolipids (GSLs) isolated from pig intestines were separated on thin-layer plates, followed by a chromatogram binding assay with radiolabeled F18+ E. coli. In addition, the inhibitory capacity of the F18R molecules was assessed using an in vitro villous adhesion assay.
Results: We report that F18-fimbriated E. coli selectively interact with GSLs having blood group ABH determinants on type 1 core chains, and blood group A type 4 heptaglycosylceramide. F18-binding GSLs were isolated from the small intestinal epithelium of blood group O and A pigs, and characterized by mass spectrometry and proton NMR. The only GSL with F18 binding activity of the blood group O pig was an H type 1 pentaglycosylceramide (Fucα2Galβ3GlcNAcβ3Galβ4Glcβ1Cer). In contrast, the blood group A pig had a number of F18-binding GSLs, with the A type 1 hexa-glycosylceramide (GalNAcα3(Fucα2)Galβ3GlcNAcβ3Galβ4Glcβ1Cer) being the predominant one. The minimal binding epitope was identified as the blood group H type 1 determinant (Fucα2Galβ3GlcNAc), while an optimal binding epitope was created by addition of the terminal α3-linked galactose or N-acetylgalactosamine of the blood group B type 1 determinant (Galα3(Fucα2)Galβ3GlcNAc) and the blood group A type 1 determinant (GalNAcα3(Fucα2)Galβ3GlcNAc), respectively.
Using the in vitro villous adhesion assay, the inhibitory capacity of several blood group sugars on F18+ E. coli adhesion was examined. Strong inhibition of F18+ E. coli adherence was observed after pre-incubation of F18+ E. coli with 1 mg of the blood group H (52.4%, S.D. = 19.9), blood group A (72.9%, S.D. = 15.5) and blood group B sugar (86.8%, S.D. = 11.4), whereas the negative control sugar lacto-N-tetraose did not inhibit (-2.8%, S.D. = 12.4) the interaction with the intestinal villi.
Discussion: A highly specific interaction of the F18-fimbriated bacteria with GSLs having blood group ABH determinants on type 1 core chains was demonstrated. In addition, we showed that F18R molecules could be used to inhibit the interaction of F18+ E. coli with the porcine intestinal epithelium using an in vitro assay. In our future work, in vivo experiments will be performed to investigate whether these F18R molecules, when supplemented in pig feed, could provide a safe and efficient anti-adhesive therapy against F18+ E. coli infections. The use of F18R molecules in pig feed as prophylactic treatment of F18+ E. coli infections could be an alternative strategy for the use of antibiotics against edema disease and PWD in the future.

References:
Coddens A, Diswall M, Angström J, Breimer ME, Goddeeris B, Cox E, Teneberg S, 2009. Recognition of blood group ABH type 1 determinants by the FedF adhesin of F18-fimbriated Escherichia coli. J Biol Chem. 284(15):9713-26.