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Characterization of the small intestinal gene expression response in a preterm pig model of necrotizing enterocolitis

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In preterm infants, the serious gastrointestinal disease, necrotizing enterocolitis (NEC), is caused by the combined effect of abnormal bacterial colonization, enteral feeding, and prematurity, including immaturity of the immune system. In a well-established preterm pig model of NEC, the effect of diet on disease development has been studied thoroughly; however, the inflammatory response during NEC needs to be characterized to improve and promote the use of this model as a model for human disease. We investigated how expression of genes related to immune function and gut maturation in distal small intestinal tissue was affected by NEC development in a number of experimental diet groups. Preterm pigs delivered by Cesarean section received total parenteral nutrition for 2 d followed by enteral nutrition for an additional 2 d: bovine colostrum (n = 6), infant formula (FORM, n = 13), FORM for 6 h followed by bovine colostrum (n = 14), spray dried bovine colostrum (n = 8) or pasteurized, spray dried bovine colostrum (n = 9). At euthanasia, the gastrointestinal tract (stomach to colon) was evaluated for NEC lesions using a severity score ranging from 1–6 (6 being severe NEC). Pigs with a severity score of minimum three in any gastrointestinal region was regarded as a case of NEC. High throughput qPCR was used to investigate the gene expression of 48 genes in intestinal tissue. Across all enteral diet groups, a relatively higher expression of IL-6, IL-8, IL1-RA and CCL3 was seen in pigs suffering from NEC compared with healthy pigs. In conclusion, the expression of four genes coding for proteins involved in inflammation was increased in pigs suffering from NEC compared to healthy pigs irrespectively of enteral diet group, which points to inflammation as being an important component of NEC. Further studies will address the relationship of inflammation related gene expression and the development of NEC in order to elucidate cause-effect relationships leading to NEC.