Protective effects of transforming growth factor β2 in intestinal epithelial cells by regulation of proteins associated with stress and endotoxin responses

Transforming growth factor (TGF)-β2 is an important anti-inflammatory protein in milk and colostrum. TGF-β2 supplementation appears to reduce gut inflammatory diseases in early life, such as necrotizing enterocolitis (NEC) in young mice. However, the molecular mechanisms by which TGF-β2 protects immature intestinal epithelial cells (IECs) remain to be more clearly elucidated before interventions in infants can be considered. Porcine IECs PsIc1 were treated with TGF-β2 and/or lipopolysaccharide (LPS), and changes in the cellular proteome were subsequently analyzed using two-dimensional gel electrophoresis-MS and LC-MS-based proteomics. TGF-β2 alone induced the differential expression of 13 proteins and the majority of the identified proteins were associated with stress responses, TGF-β and Toll-like receptor 4 signaling cascades. In particular, a series of heat shock proteins had similar differential trends as previously shown in the intestine of NEC-resistant preterm pigs and young mice. Furthermore, LC-MS-based proteomics and Western blot analyses revealed 20 differentially expressed proteins following treatment with TGF-β2 in LPS-challenged IECs. Thirteen of these proteins were associated with stress response pathways, among which five proteins were altered by LPS and restored by TGF-β2, whereas six were differentially expressed only by TGF-β2 in LPS-challenged IECs. Based on previously reported biological functions, these patterns indicate the anti-stress and anti-inflammatory effects of TGF-β2 in IECs. We conclude that TGF-β2 of dietary or endogenous origin may regulate the IEC responses against LPS stimuli, thereby supporting cellular homeostasis and innate immunity in response to bacterial colonization, and the first enteral feeding in early life.