Characterizing the role of timing on the impact of interleukin-22 treatment during experimental necrotizing enterocolitis

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Necrotizing enterocolitis (NEC) is a severe intestinal disease of prematurity characterized by unrestrained inflammation and epithelial cell death. NEC impacts ~7% of premature infants, and mortality rates can approach 50%. Intensive research is focused on identifying targeted therapies. Dr. Misty Good's lab determined that administration of the cytokine interleukin-22 (IL-22) is protective in the mouse model of NEC when given at the initiation of the model. We subsequently characterized how the timing of recombinant IL-22 (rIL-22) administration impacted the outcomes of experimental NEC. Groups of neonatal mice were dam fed (DF), subjected to experimental NEC, or subjected to NEC and injected intraperitoneally with 100 μg/kg of rIL-22 at 6, 12, or 24 h after initiation of the model. Administration of rIL-22 at 6 h resulted in a significant downregulation of the pro-inflammatory cytokine *il1b* in the ileum, improved survival, reduced intestinal epithelial apoptosis, and increased intestinal epithelial proliferation compared to NEC alone. rIL-22 at 12 h did not downregulate *il1b*, but treatment improved survival, apoptosis, and proliferation. In contrast, administration at 24 h upregulated *il1b* and did not improve survival. Our results support the importance of optimizing the timing of rIL-22 administration for maximum benefits in treating NEC.