Delayed development of systemic immunity in preterm pigs as a model for preterm infants

Preterm neonates are highly sensitive to systemic infections in early life but little is known about systemic immune development following preterm birth. We hypothesized that preterm neonates have immature systemic immunity with distinct developmental trajectory for the first several weeks of life, relative to those born at near-term or term. Using pigs as a model, we characterized blood leukocyte subsets, antimicrobial activities and TLR-mediated cytokine production during the first weeks after preterm birth. Relative to near-term and term pigs, newborn preterm pigs had low blood leukocyte counts, poor neutrophil phagocytic rate, and limited cytokine responses to TLR1/2/5/7/9 and NOD1/2 agonists. The preterm systemic responses remained immature during the first postnatal week, but thereafter showed increased blood leukocyte numbers, NK cell proportion, neutrophil phagocytic rate and TLR2-mediated IL-6 and TNF-α production. These immune parameters remained different between preterm and near-term pigs at 2-3 weeks, even when adjusted for post-conceptional age. Our data suggest that systemic immunity follows a distinct developmental trajectory following preterm birth that may be influenced by postnatal age, complications of prematurity and environmental factors. Consequently, the immediate postnatal period may represent a window of opportunity to improve innate immunity in preterm neonates by medical, antimicrobial or dietary interventions.

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