Title: SPONTANEOUS NEUTROPHIL MIGRATION IS DECREASED IN PRETERM INFANTS LEAVING THEM VULNERABLE TO SEPSIS

Purpose: Preterm neonates, especially those born at less than 28 weeks gestational age, have reduced innate immune responses. In part, this is due to functional differences in neutrophil function. Here we evaluate PMN function in these infants using novel microfluidic technologies to quantify neutrophil migration. We sequentially analyzed neutrophil function in these infants until they reached full-term corrected gestational age. They were also compared to healthy, full-term infants.

Methods: Following IRB approval, serial low-volume blood samples (<300 µL) were collected from human preterm and full-term neonates. For preterm neonates, blood was drawn on day seven to nine of life, then weekly for the first three weeks of life, then biweekly thereafter until hospital discharge. Full-term infants underwent a single lab draw within 24 hours of birth. Microfluidic devices [1] were loaded with Hoechst-stained whole blood and spontaneous neutrophil migration was recorded for ten hours with a time-lapse fluorescent microscope. Trackmate® software and Matlab code were used to analyze the neutrophil motility parameters [2].

Results: 326 preterm whole blood samples were analyzed from 42 preterm neonates enrolled at an average gestational age of 29.1 weeks and were compared to 22 full-term infants (average gestational age of 39.4 weeks). PMN velocity was significantly lower at birth in preterm vs full-term infants ($p<0.05$). Linear regression revealed a significant, positive correlation between day of life and neutrophil velocity (R^2 0.99, $p<0.0001$).

Conclusions: Reduced spontaneous neutrophil migration may, in part, explain the decreased innate immune response seen in preterm infants. Neutrophil velocity increases as the patient matures and correlates strongly age, approaching that seen in healthy full-term infants. However, this prolonged period of depressed immune function leaves preterm infants vulnerable to infections early in life.

[1] S.L. Raymond, M.C. Lopez, H.V. Baker, S.D. Larson, P.A. Efron, T.E. Sweeney, P. Khatri, L.L. Moldawer, and J.L. Wynn, Unique transcriptomic response to sepsis is observed among patients of different age groups. PLoS One 12 (2017) e0184159.

[2] S. Muldur, A.L. Marand, F. Ellett, and D. Irimia, Measuring spontaneous neutrophil motility signatures from a drop of blood using microfluidics. Methods in cell biology 147 (2018) 93-107.