

Selective Modulation of Monocyte and Neutrophil Responses with Activated Protein C in Preterm Infants

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Abstract

Background: Inflammation is associated with many disorders of preterm infants including periventricular leukomalacia, chronic lung disease and necrotising enterocolitis. Activated Protein c (APC) has shown positive immunomodulatory effects. Objectives: We aimed to study neutrophil and monocyte function in response to lipopolysaccharide (LPS) and APC stimulation ex vivo in preterm infants <32 weeks gestation over the first week of life compared to neonatal and adult controls. Methods: Peripheral blood was taken on day 1, 3 and 7 and stimulated with LPS in the absence or presence of APC. Expression of Toll-like receptor 4 (TLR4) and CD11b and reactive oxygen intermediate release from neutrophils and monocytes was examined by flow cytometry. Results: LPS induced neutrophil ROI in adults and preterm infants and was significantly reduced by APC. Baseline and LPS-induced monocyte ROI production in preterm neonates was increased compared to adult and term controls. Neutrophil TLR4 baseline expression was higher in term controls compared to preterm infants. Conclusion: Increased systemic ROI release in preterm infants may mediate tissue damage, ROI was reduced by APC. However, due to the high risk of haemorrhage further examination of APC mutant forms with anti-inflammatory but decreased anticoagulant properties is merited.

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Figure 1

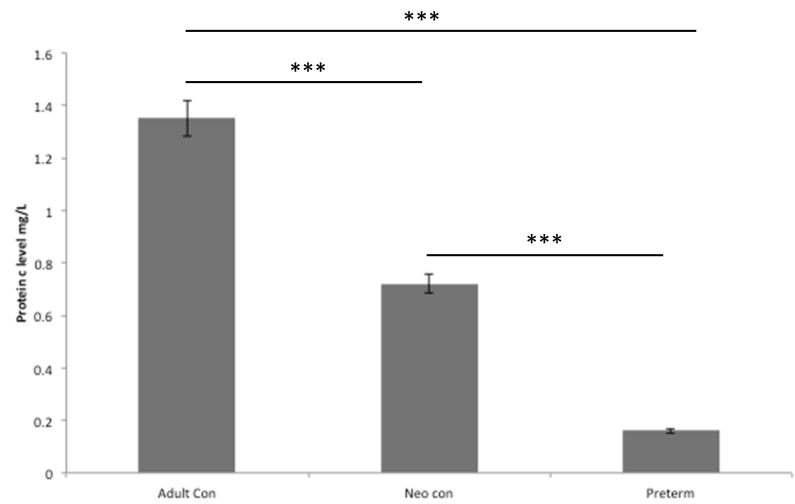
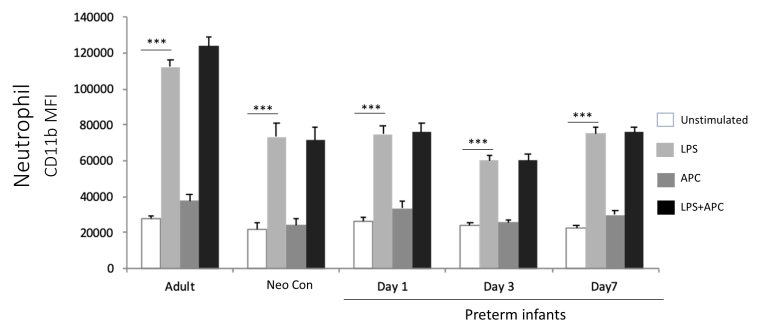


Figure 2

A



B

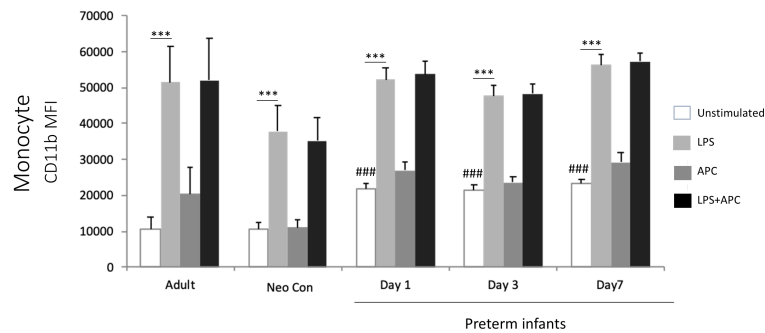
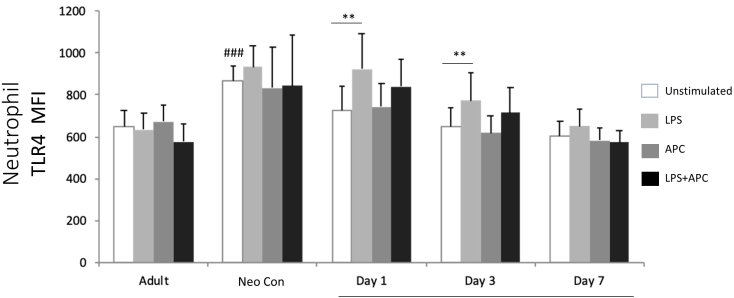


Figure 3

A



B

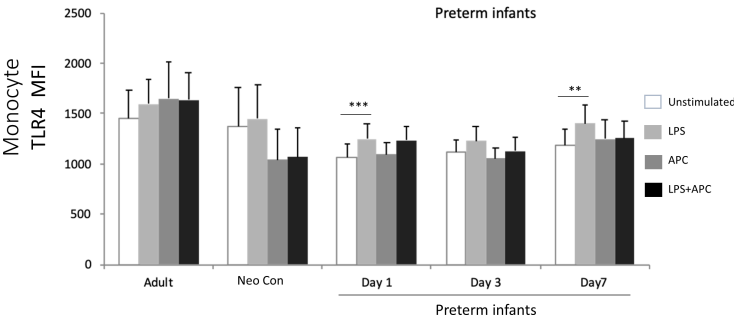
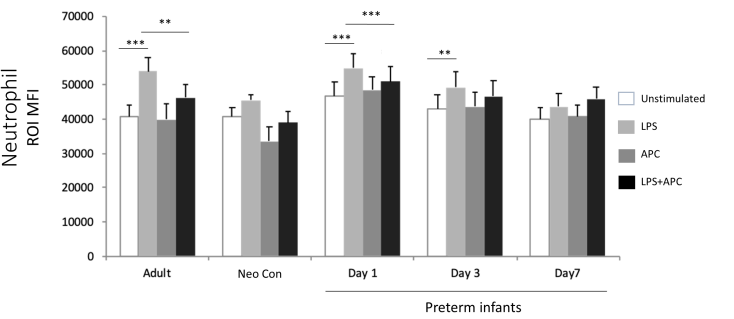


Figure 4

A



B

