Immature Inflammatory Response of Newborn (Nb) Compared to Adult (Ad) Human Microvascular Endothelial Cells (HMVEC) is Characterized by Reduced Tissue Factor (TF) Expression

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Our previous studies have demonstrated that cytokine and cytoadhesion molecule expression is altered in Nb vascular EC. To determine if aberrant coagulation factor regulation could also contribute to neonatal inflammatory coagulopathies, we have compared expression of five such factors between Nb and Ad HMVEC in response to the key inflammatory cytokine, IL-1α. Of these, only TF mRNA was differentially expressed, accumulating to just 25±4% of the Ad level in Nb HMVEC (p=0.0004) by RNA blot hybridization after activation for 2 hrs. Likewise, TF protein and activity were expressed at just 51±13% (p=0.03) and 52%, respectively, of the Ad level in Nb HMVEC extracts after activation for 4 hrs, as detected by ELISA (A.D.I.) and Factor X activation (A.D.I.). Macroarrays of 96 marker genes associated with 18 signal transduction pathways (SuperArray) were also used to compare expression of the marker transcripts by IL-1α-activated Nb vs. Ad HMVEC. While none of the marker genes was more highly expressed in Nb HMVEC, 26 were expressed more abundantly in Ad HMVEC. Eleven of these are associated with activation of the phospholipase C signaling pathway, known to participate in inflammatory responses and, notably, regulate both TF expression and mRNA turnover in general. The stability of TF mRNA, as well as the activity of the phospholipase C pathway itself, will be compared in Nb vs. Ad HMVEC to characterize the mechanism(s) regulating the weaker response of Nb HMVEC to IL-1α-activation.