Gene expression profile of the NF-κB signaling pathway in late-onset neonatal sepsis

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Aim: The availability of a genetic biomarker panel that could differentiate sepsis from Systemic Inflammatory Response Syndrome (SIRS) earlier and also identify different response patterns caused by different etiological agents may cause significant impact in the study of neonatal sepsis. The purpose is to investigate the gene expression related to the NF-κB signaling pathway in term newborns (NBs) with clinical late-onset sepsis and/or culture-positive caused by Gram-positive or Gram-negative bacteria at the day of diagnosis (day 0), in the intermediate stage (3rd day) and in the convalescence phase (7th and 10th post-diagnosis days). **Methods:** To date, blood samples from 5 Gram-positive, 5 Gram-negative and 6 NBs with SIRS were analyzed compared to 13 controls. Total RNA was isolated using the PAXgene Blood RNA System and the expression of 118 genes was performed using RNA-Seq method. Analyses were focused on gene expression relative to control samples. **Results:** On day 0, Gram-negative group showed the higher number of differentially expressed genes, 24 genes, in comparison with Gram-positive (8 genes) and SIRS (16 genes) groups. Of the 24 altered genes, 8 belonged to cytokine/chemokine category, which was not observed in Gram-positive and SIRS groups, that showed altered gene expression mainly in immunoreceptor and intracellular signaling categories. The number of altered genes decreased over the days of collection, probably in response to antibiotic therapy in the Gram-negative group, which was not observed in the other groups. The longitudinal analysis revealed overexpression of *CD80, IL10, HMOX1* and *IL1RN* genes corresponding to cytokine/chemokine, enzyme and adaptive immunity categories, in the Gram-negative group on day 0. In Gram-positive and SIRS groups, the *PLAU* gene, which encodes an acute phase protein, was up-regulated on days 3 and 7, which persisted on day 10 only in SIRS group. The longitudinal analysis focused on down-regulated genes demonstrated high number of gene repression corresponding to cytokine/chemokine, enzyme, immunoreceptor, intracellular signaling, transcription factor/modulator and apoptosis across all patient groups. **Conclusion**: Our preliminary results suggest that gene expression profile

could discriminate Gram-negative from Gram-positive and SIRS groups, mainly on the day of diagnosis. Further studies are needed to confirm these findings.