**Profiling tryptophan catabolites of human gut microbiota in neonatal dried blood spots and stool**

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**Abstract.** National screening programs use dried blood specimens to detect metabolic disorders or aberrant protein functions that are not clinically evident in the neonatal period. Similarly, gut microbiota metabolites may reveal latent immune aberrations. Microbial metabolites interact with xenobiotic receptors (i.e., aryl hydrocarbon and pregnane-X) to maintain gastrointestinal tissue health, functioning as sensors of microbial immunomodulation and homeostasis. The delivery (vaginal or cesarean section) shapes the microbial colonization, which substantially modulates both the immune system's response and mucosal homeostasis. This study profiled microbial metabolites of the kynurenine and tryptophan pathway in 134 neonatal dried blood specimens and stool samples of newborns. We newly established neonatal blood levels of microbial xenobiotic receptors ligands (i.e., indole-3-aldehyde, indole-3-butyric acid, and indole-3-acetamide) on the second day of life. Furthermore, we observed diverse microbial metabolic profiles in neonates born vaginally and via cesarean section in dried blood spots, potentially due to microbial immunomodulatory influence. In stool samples, significant differences were found in meconium and stool samples. In summary, these findings suggest the supportive role of human gut microbiota in developing and maintaining immune system homeostasis.

**Keywords.** Tryptophan and kynurenine metabolism, human gut microbiota, mass spectrometry