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Biomarker discovery in galactosemia: Metabolomics with UPLC/HRMS in dried blood spots

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Abstract: Introduction:Galactosemia (GAL) is a genetic disorder that results in disturbances in galactose metabolism and can lead to life-threatening complications. However, the underlying pathophysiology of long-term complications in GAL remains poorly understood. Methods: In this study, a metabolomics approach using ultra-performance liquid chromatography coupled with high-resolution mass spectrometry was used to investigate metabolomic changes in dried blood spots of 15 patients with GAL and 39 healthy individuals. Results: The study found that 2,819 metabolites underwent significant changes in patients with GAL compared to the control group. 480 human endogenous metabolites were identified, of which 209 and 271 were upregulated and downregulated, respectively. PA (8:0/LTE4) and ganglioside GT1c (d18:0/20:0) metabolites showed the most significant difference between GAL and the healthy group, with an area under the curve of 1 and 0.995, respectively. Additionally, the study identified potential biomarkers for GAL, such as 17-alpha-estradiol-3-glucuronide and 16-alpha-hydroxy DHEA 3-sulfatediphosphate. Conclusion: This metabolomics study deepened the understanding of the pathophysiology of GAL and presented potential biomarkers that might serve as prognostic biomarkers to monitor the progression or support the clinical diagnosis of GAL.