Proteome profiling identifies circulating biomarkers associated with hepatic steatosis in subjects with Prader-Willi syndrome.

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Introduction: Prader-Willi syndrome (PWS) is a rare genetic disorder characterized by loss of expression of paternal chromosome 15q11.2-q13 genes. Individuals with PWS exhibit unique physical, endocrine, and metabolic traits associated with severe obesity. Identifying liver steatosis in PWS is challenging, despite its lower prevalence compared to non-syndromic obesity. Reliable biomarkers are crucial for the early detection and management of this condition associated with the complex metabolic profile and cardiovascular risks in PWS.

Methods: Circulating proteome profiling was conducted in 29 individuals with PWS (15 with steatosis, 14 without) using the Olink Target 96 metabolism and cardiometabolic panels. Correlation analysis was performed to identify the association between protein biomarkes and clinical variables, while the geneenrichment analysis was conducted to identify pathways linked to deregulated proteins. Receiver operating characteristic (ROC) curves assessed the discriminatory power of circulating protein while a logistic regression model evaluated the potential of a combination of protein biomarkers.

Results: CDH2, CTSO, QDPR, CANT1, ALDH1A1, TYMP, ADGRE, KYAT1, MCFD, SEMA3F, THOP1, TXND5, SSC4D, FBP1, and CES1 exhibited a significant differential expression in liver steatosis, with a progressive increase from grade 1 to grade 3. FBP1, CES1, and QDPR showed predominant liver expression. The logistic regression model, -34.19 + 0.85 * QDPR*QDPR + 0.75 * CANT1*TYMP - 0.46 * THOP1*ALDH1A, achieved an AUC of 0.93 (95% CI: 0.63-0.99), with a sensitivity of 93% and specificity of 80% for detecting steatosis in individuals with PWS. These biomarkers showed strong correlations among themselves and were involved in an interconnected network of 62 nodes, related to seven metabolic pathways. They were also significantly associated with cholesterol, LDL, triglycerides, transaminases, HbA1c, FLI, APRI, and HOMA, and showed a negative correlation with HDL levels.

Conclusion: The biomarkers identified in this study offer the potential for improved patient stratification and personalized therapeutic protocols.