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Proteomic Analysis of Urinary Exosomes in Patients with Gitelman Syndrome

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Objectives: Gitelman syndrome (GS) are hereditary salt-losing tubulopathies resulting from defects of sodium-chloride cotransporter (NCC). Urinary exosome analysis of NCC by western blotting has been evaluated. However, the urine exosomal protein alterations in patients with GS remains unclear. Our purpose to examine urine exosomal protein alterations in patients with GS.

Methods: Urinary exosomes were further isolated by ultracentrifugation method. We applied isotopic demethylation labeling coupled with liquid chromatography-tandem mass spectrometry (LC–MS/MS) with CID to discover urinary exosomal target proteins in patients with GS (n=10) compared to health controls (n=10).

Results: We identified a total of 253 nonredundant proteins that were based on at least two distinct tryptic peptides. Of these, 241 proteins were quantified. Specifically, 90 proteins showed an altered pattern ($Log_2|GS/Control| \geq 1$) in patients with GS including 50 upregulated proteins and 40 down-regulated protein. Reninangiotensin system was the shared KEGG pathway/biological process in the upregulated differentially genes that compatible with the clinical presentation in GS patients with salt-losing tubulopathy and volume depletion. NCC has been identified in urinary exosome from health control but not from patients with GS that was consistent with the finding of NCC mutation in GS. Of interest, there is no significant change in specific exosome markers in CD9, CD81, phosphoglycerate kinase 1 (PGK1), L-lactate dehydrogenase A chain (LDHA), and Alpha-enolase (ENOA) that could be used as an internal control.

Conclusions: The identified proteins constitute potential targets for understanding the signal pathway or pathogenesis in in patients with GS. Further target protein needs to be validated in the future.