Application of multi-omic and functional network analysis for paediatric patients diagnosed with idiopathic nephrotic syndrome

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Idiopathic nephrotic syndrome (INS) is the most prevalent glomerular disease in children. In spite of some progress, its pathogenesis is still unknown and the therapy options are confined to gross immune modulation. A variety of methods for diagnostic and treatment purposes are available for the patients; however, the lack of understanding regarding the pathogenic mechanisms underlying INS can lead to poor therapeutic response and adverse side-effects. Here, we describe quantitative proteomic and metabolomic approaches to reveal new molecular factors involved in pathogenesis of INS with potential diagnostic and therapeutic significance. Urine samples were collected from 10 children diagnosed with INS receiving no therapy and 10 healthy children. Label-free protein expression data were acquired with a oa-TOF using an ion mobility data independent approach. Data were searched against a human database, which was amended to account for N-terminal processed peptides. Normalized label-free quantification results were generated using TransOmics software. In a similar fashion, diluted urine samples were analysed using a small molecule profiling approach. Interpretation of the data has shown a significant number of proteins to be over-expressed in the urine from INS patients, which includes a high percentage (approximately 80%) of glycosylated proteins. Metabolites of interest showing statistically significant changes include homocysteine, glutamate and uridine. Pathway analysis tools were used to review the complimentary datasets and hence provide an understanding of the underlying biology of differentially expressed proteins and metabolites. Review and validation of the suggested pathways, strongly suggests correlation with the neuronal system disorders network, specifically acute fatigue.