Mass spectrometry and SomaScan technologies to detect a plasma copper proteome in two human populations

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Micronutrient deficiencies represent a large, but often poorly assessed, public health burden in low-middle income countries. Protein biomarkers that associate with nutrient concentrations in plasma show potential for predicting prevalence rates of nutrient deficiencies on a single, future proteomics platform that are typically assessed by a variety of biochemical assays. However, degrees to which different proteomic methods yield comparable associations with any given nutrient remain unknown. Here, we compare two proteomics assays, iTRAQ tandem mass spectrometry (MS) and the SomaScan assay (SS), in their abilities to detect and quantify associations (by Pearson correlation) of plasma protein abundance and copper concentrations (measured by atomic absorption spectroscopy or inductively-coupled plasma mass spectrometry) in two populations: Nepalese school-aged children (n=500, by MS) and Bangladeshi 1st-trimester pregnant women (n=435, by SS). MS detected 982 proteins in >10% of sampled children while SS detected 6,431 proteins in all sampled pregnant women. Plasma cupromes, i.e., clusters of proteins whose relative abundance correlated with plasma copper at an FDR (q)<0.05, numbered 190 proteins by MS in children and 2416 by SS in gravida. Among the 982 MS-detected proteins, 568 (58%) were also measured by SS, of which 92 (16.2%) were positive in their association with copper (q<0.05) by both methods, and 246 (43.3%) were not associated with copper by either method (q>0.05), yielding a total agreement of 59.5%. Methods produced discordant correlations (q<0.05) for 230 proteins (40.5%). Among 92 concordant copper-protein correlates, 42 coefficients were stronger based on MS (r > 5 points further from null in either direction) versus SS, and another 29 coefficients were stronger based on SS. Thirty-one coefficients were comparable (r within 5 points). Despite two different populations and life stages that varied in health and nutrition, and sizes of detected proteomes, there was substantial overlap between MS and SS in identifying clusters of proteins associated with copper status, providing an initial proof-of-concept that different proteomics methods can co-detect a similar plasma nutrient proteome across populations.

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