an unbiased proteomics approach to identify candidate urine biomarkers (CUBMs) predictive of LN chronicity and further pursued their validation in a larger cohort.

**Methods** In this cross-sectional pilot study, we selected urine collected at kidney biopsy from 20 children with varying levels of LN damage (discovery cohort) and performed proteomic analysis using iTRAQ. We identified differentially expressed proteins based on degree of LN chronicity and sought to distinguish markers exhibiting different relative expression patterns using hierarchically-clustered log10-normalized relative abundance data with linked and distinct functions by biological network analyses. For each CUBM, we performed specific enzyme-linked immunosorbent assays (ELISAs) on urine from a validation cohort (n=41) and analysis of variance (ANOVA) to detect differences between LN chronicity, with LN activity adjustment. We evaluated for CUBM expression in LN biopsies with immunohistochemistry.

**Results** iTRAQ detected 112 proteins from urine samples in the discovery cohort, 51 of which were quantifiable in all replicates. Simple ANOVA revealed four differentially expressed, chronicity-correlated proteins (p-values<0.05). Further correlation and network analyses led us to select a total of seven CUBMs for LN chronicity: afamin (AFM), immunoglobulin heavy constant alpha 1 (IGHA1), alpha-1-antichymotrypsin (SERPINA3), transthyretin (TTR), retinol binding protein 4 (RBP4), alpha-1-acid glycoprotein, type 2 (ORM2) and transferrin (TF). In the validation cohort, urine SERPINA3 elevation was strikingly robust with respect to validation in high chronicity LN samples (3.3-fold change, p-value 0.012). Immunohistochemistry further demonstrated SERPINA3 staining in both endothelial and proximal tubular epithelial cells.

**Conclusions** Using advanced proteomic techniques followed by confirmation using specific ELISAs, we identified SERPINA3, a known inhibitor of neutrophil cathepsin G and angiotensin II production, as a potential urine biomarker to help quantify LN damage. SERPINA3 expression may be a protective mechanism from further kidney damage. Further validation of SERPINA3 as an LN damage biomarker in an independent cohort is needed to determine its ability to guide treatment and predict prognosis.

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**Conclusion** This project is a first step towards identifying subgroups of SLE patients through clinical and genetic databases. These findings will contribute to our understanding of SLE and illustrate how combining big data in both genetics and EHR has the potential to further define this heterogeneous disease.