**Supplemental Digital Content 1**

Detailed protocol for sample processing and proteomic analysis: Snap frozen samples were thawed, centrifuged (5000 rpm, 4°C, 30 min), and the isolated supernatant precipitated with 3 volumes of acetone overnight at -80°C. The acetone pellet was collected by centrifugation (5000 rpm, 4°C, 30 min). Soluble proteins were prepared as supernatants (14,000 rpm, 4°C, 15 min) from sequential extraction with 0.5 mL of phosphate buffer saline (PBS) with 1% Triton-X 100 (protein extraction). The protein extraction was diluted 5-10 fold with 50 mM Tris pH 9, filtered through a 0.45 m plate (Pall, Port Washington, NY) and then 300 L (50-200 g) were bound to a pre-equilibrated 96-well anion exchange Acro-Q filter plate (Pall, Port Washington, NY). Three separate fractions at pH 9, pH 6, and pH 4 were collected and the protein concentrations were measured in each using a bicinchoninic acid (BCA) assay (Pierce, Rockford, IL). The pH 9 fraction gave the best results with the most peaks in trial experiments, and so was used for the rest of the study. 20 g of protein of each pH 9 fraction was bound to 500 g of weak cation exchange (WCX) magnetic beads (MoBiTec, Goettingen, Germany) in binding buffer (100 L 0.2 M ammonium acetate pH 4, 0.01% Triton-X100). Beads were washed, desalted with 5 mM ammonium acetate (pH 4), pelleted, and bound proteins extracted with 25 L 1% trifluoroacetic acid (TFA), mixed with equal volume 5 mg/mL -cyano-hydroxycinnamic acid (CHCA) in 90% acetonitrile, and spotted 2 L twice on a 96-well MALDI chip (Perkin-Elmer Sciex, Waltham, MA). Liquid handling, magnetic bead binding, and MALDI target spotting were performed in triplicate with a STARlet 8-channel robot (Hamilton, Reno, NV).

The target plate was read in a high-resolution full-time reflectron prOTOF 2000 MALDI- MS (Perkin-Elmer Sciex, Waltham, MA) where the intact masses of the proteins between 1.5 to 20 kDa were determined to better than 50 ppm mass accuracy with external calibration. MALDI-MS spectra were converted to text files, and preprocessed using an established protocol (Li, X et. al., UCLA, manuscript in preparation). Briefly, each file was subjected to initial data cleanup using a Python-based algorithm, and then loaded to SpecAlign software for resolution reduction, background subtraction, outlier elimination, total ion current normalization, and peak selection. The preprocessed proteomic data were then exported from SpecAlign and further analyzed in R.

To identify specific protein candidates, IP-MALDI was carried out. Antibodies against specific proteins were used to precipitate the specific proteins from the pH 9 fractions using magnetic beads conjugated with either Protein A/G (Pierce, Rockford, IL) respectively. The beads were washed to remove non-specific proteins, desalted with 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES) buffer (20 mM, pH 7.5), and extracted with formic acid to release the bound peptides/proteins. The released peptides/proteins were mixed with matrix for spotting on a MALDI target. We then measured the accurate mass of the specific targets bound by antibody, as well as the immunodepleted protein extractions to confirm if the peaks corresponding to the targeted peptides/proteins were reduced or depleted.