Supplemental Methods

Tryptic digestion. Proteins aliquots, approximately 10 µg for each sample, were simultaneously denatured and their disulfide bond were reduced through the addition of a 10 mM ammonium bicarbonate solution (pH = 7.4) containing 6 M guanidine hydrochloride and 10 mM dithiothreitol and incubating the samples for 1 hr at 60^{o} C. After allowing the samples to cool to the room temperature, alkylation was accomplished through the addition of iodoacetamide resulting in a final concentration of 25 mM. This reaction was performed for 1 hr in the dark. Prior to the addition of trypsin, the proteins were desalted using Amicon Ultra centrifugal filters (0.5 ml capacity, 10 kDa MWCO). Digestion was accomplished by the addition of a 0.25-µg amount of proteomics-grade trypsin and incubating the samples for 24 hr at 37^{o} C.

LC-MS. Approximately 200 ng of each sample were injected (in mobile phase A), separated by nano-flow LC and detected and characterized using an LTQ FT-MS, using the dynamic exclusion function to avoid repeatedly analyzing previously-detected peptides within a 2-min time window. The samples were separated using a 75 µm ID x 15 cm capillary packed with 5 µm mean diameter Michrome Bioresources MagicQ C_{18} silica (mean pore size: 100 angstroms). The peptides were separated using a 45-min linear gradient, ranging from 5%-55%, mobile phase B. In this work, mobile phase A consisted of 95%/5%/0.1 water/acetonitrile/formic acid and mobile phase B was composed of 95%/5%/0.1% acetonitrile/water/formic acid.

Database Searching. The resulting data were searched against the human Swiss Prot database using Mascot 2.0 as the search engine. Fixed modifications were set as carbamidylmethylation and methionine was selected as a variable modification. Two missed tryptic cleavages were allowed. In this study, the MS mass tolerance was set at 0.02 Da for the FT-MS analysis, while

the tandem MS fragments were given a tolerance of 0.8 Da, since they were analyzed only by the ion trap, but not the FT-MS. Following the database searching, the identified peptides were parsed using a minimum ion score of 30 and selecting only the bold red peptides.