Supplemental Figure Legends

Supplemental Figure S1: Western blots for lysine acetylation (A) and arginine mono-methylation (B) of cancer patients' sera. Equal volumes of cancer patients' sera (2μL) were resolved by SDS-PAGE and transferred to nitrocellulose membranes. Pan-anti-AcK (#13420) and Rme motif antibodies (#8015/#8711) were used to probe corresponding modifications in each blot. Blots were developed using the LICOR Odyssey near-infrared imaging system.

Supplemental Figure S2: Venn diagram of protein level overlapping between proteins identified in the current study and a recent larger scale plasma proteomic analysis. Proteins for which acetyl lysine or mono-methyl arginine peptides were compared to protein identifications from Keshishian et al. (4). There were also a large number of proteins identified in the current study that were not identified in the large scale plasma proteomic analysis (4).

Supplemental Figure S3: Overlap of MS2 identifications in technical triplicates. Triplicate parallel experiments using pooled serum of NSCLC patients were processed independently. The overlap of unique lysine acetylated and arginine mono-methylated peptide is shown in the Venn Diagrams. About 46% (361 out of 778) of unique AcK peptides and 40% (226 out of 564) of unique Rme peptides were identified in all three samples, respectively.

Supplemental Figure S4: %CV distribution for intensity measurements across technical triplicates. Unique peptides were quantified using a label-free approach to measure the relative integrated peak area for a particular peptide across all LC-MS/MS runs. In total, 380 and 356 unique sites of lysine acetylation and arginine mono-methylation were quantified, respectively. A tight distribution of %CV of the relative peptide abundances across technical triplicates was observed. There were 297 (78%) lysine acetylation sites and 334 arginine methylation sites (94%) with %CV lower than 40%. The median %CVs were 23% and 17% for lysine acetylation and arginine mono-methylation, respectively.

Supplemental Figure S5: Quality control of retention time and intensity signal of standard peptide spiked in each sample for label free quantification. MassPrep digestion standards (Waters, Catalog # 186002865) were spiked into each sample at 33 fmol per injection. The sequence of each protein was added to the human database for SEQUEST searching. The consistency of retention time (top panel) and integrated peak area (bottom panel) was monitored by representative standard peptides spanning the entire gradient. Three isotopic peaks (blue, purple and red) are shown as an additional quality control metric.

Supplemental Figure S6: Distribution of %CV between analytical replicates of AcK (A) and Rme (B) enrichment data. %CV was calculated by measuring the variation between analytical replicates of each quantified modified peptide. A tight

distribution was observed for both AcK and Rme enrichment data. The median %CV was 14% and 15% for AcK and Rme enrichment, respectively.