**Protein Extraction and Digestion**

For protein extraction, the 4% 1-dodecyl-3-methylimidazolium chloride ([C12 -mim]Cl) (m/v, containing 1% (v/v) protease inhibitor cocktail) was added into the cell pellet and sonicated at 10% amplitude for 5 s on and 10 s off with the total working time of 3 min. The extracted proteins were denatured and reduced at 95 °C for 5 min. The insoluble debris was removed by centrifugation at 16,000 g for 10 min. The supernatant was collected and the protein concentration was determined using BCA quantification Kit. Proteins were reduced in 20 mM dithiothreitol at 95 °C for 5 min, and then alkylated in 40 mM iodoacetamide at room temperature in the dark for 30 min. Next, the proteins were transferred to 10 kDa filter devices and 8 Murea by centrifugation (14 0 0 0 g) three times. The concentrates were washed with 25 mM ABC three times. After that, the concentrates were diluted with 100 μL of 100mM mM TEAB containing 1 μg of trypsin, and incubated at 37 °C for 12 h.

**TMT 11-plex Labeling**

The isobaric labeling experiment was conducted according to the TMT kit instructions. For each set of TMT 10-plex labeling experiment, each channel was labeled with 100 mg peptides. Ten samples were labeled with the ten channels (127N, 128N, 129N, 130N, 131N, 127C, 128C, 129C, 130C and 131C). TMT reagents (0.4 mg) were dissolved in anhydrous acetonitrile (41 µL) and added to 100 mg peptides (dissolved in 60 µL 100 mM TEAB) to achieve a final acetonitrile concentration of approximately 30% (v/v). After 60 min of reaction at RT, 16 µL hydroxylamine 5% (w:V) was added in each tube, and mixed for 20 min. The aliquots were then combined for fractionation.

**High-pH RPLC Fractionation**

To increase the depth of protein identification, high-pH reverse phase liquid chromatography was used for peptide fractionation. combined peptides were separated and collected by an Agilent 2100 HPLC system (Agilent, CA) with a high pH-stable RP column (4.6 mm × 150 mm, 5 μm, 100 ˚ A, Durashel) at a flow rate of 0.3 mL per min using a gradient from 5 to 45% solvent B over 55 min (solvent A: 30 mM ammonium acetate, pH 10; solvent B: acetonitrile, 30 mM ammonium acetate, pH 10). A total of 50 fractions (0.5 mL) were collected from 6 min to 55 min and the fractions with equal collection time intervals (6 min) were pooled. Finally, 6 pooled fractions were lyophilized in a Speed Vac Concentrator (Thermo, MA).

**Proteomic Analysis**

Nanoflow reversed phase LC was performed on an EASY-nLC 1000 system coupled online to a Orbitrap Fusion Lumos mass spectrometer equipped with a nano-electrospray ion source (Thermo Fisher Scientific, Germany). Mobile phase buffer A was 2% ACN and 98% H2O (0.1% FA) and buffer B was 98% ACN and 2% H2O (0.1% FA). The tryptic peptides were dissolved in buffer A and loaded onto a 15 cm analytical column (ID. 150 μm) packed with ReproSil-Pur C18-AQ 1.9-µm beads. Peptides were separated at a flow rate of 600 nl/min with linear gradient of 8–36% mobile phase B within 78 min, followed by a linear increase from 36–50% mobile phase B within 8 min and 50-95% mobile B within 1min, then a 8 min washing. The spray voltage was set at 2,900 V in positive ion mode and the ion transfer tube temperature was set at 320 ° C. Data-dependent acquisition was performed using Xcalibur software in profile spectrum data type.

**Database Searching of MS Data**

All RAW data were analyzed using MaxQuant 1.5.1.0.against mouse reference proteomes (Uniprot, version 2019/06, 17331 sequences). Carbamidomethyl cysteine was searched as a fixed modification. Oxidized methionine and protein N-term acetylation were set as variable modifications. Enzyme specificity was set as trypsin. The maximum missing cleavage site was set as 2. The tolerances of first search and main search for peptides were set at 20 ppm and 4.5 ppm, respectively. The minimal peptide length was set at 7. The false discovery rates (FDR) of peptide, protein and site were all < 0.01.