## Supplementary Methods

*Preparation of cell lysates and protein digestion*. Frozen U373 glioblastoma cell pellets ($2x10^6$) were lysed with RIPA buffer (25 mM Tris•HCl pH 7.6, 150 mM NaCl, 1% NP-40, 1% sodium deoxycholate, 0.1% SDS), containing protease and phosphatase inhibitors and deoxyribonuclease (all products Thermo Fisher Scientific, Rockford, IL). The cell lysates were pipetted up and down 20 times and incubated on ice for 30 min. Cell lysates were centrifuged at 14,000× g for 15 min (4 °C) to remove cellular debris. The protein concentration was determined by the Bradford method. Volumes containing 100 µg total protein were aliquoted, and brominated albumin was spiked into the protein mixture (0.1%, 1% and 10% by weight). Five µL of 200 mM tris (2- carboxyethyl)-phosphine (TCEP) buffered with TEAB was added to each sample and incubated at 55 °C for 1 h. Five µL of 375 mM iodoacetamide (buffered with TEAB) was added and incubated in the dark for 30 min. Proteins were precipitated in four volumes (440 µL) of ice cold acetone for 2 h at -20 °C. Samples were centrifuged at 10,000× g for 30 min (4 °C) after which the supernatants were removed and discarded. Pellets were air dried and resuspended in 12.5 µL of 8 M urea. Trypsin (10 µg in 87.5 µL of TEAB buffer) was added, and the samples were incubated for 24 h at 37 °C. Peptides were stored at -80 °C.

*Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry*. HSA bromination was verified by screening of the HOBr-reacted protein by MALDI-TOF mass spectrometry (UltrafleXtreme, Bruker Daltonics) equipped with a 2 kHz solid state laser (Bruker Smartbeam-II). Saturated sinapinic acid matrix (Sigma-Aldrich) was prepared in 0.1% TFA: ACN (7:3 v/v). 1 µL of sample was mixed with 1 µL matrix solution; 0.5 µL was applied on a stainless steel target by the dried-droplet method18. Samples were analyzed by MALDI-TOF MS in linear positive mode. The accelerating voltage was 25 kV. Five thousand shots were accumulated in random walk mode. Spectra were processed in Compass™ with centroid peak picking (80%). For external quadratic calibration, masses of a protein mixture (trypsinogen, protein A, BSA, Bruker “Protein Calibration Standard II”) were used. In-solution trypsin digestion was performed on brominated and control HSA and desalted with ZipTip C18 (Millipore) materials. Control and brominated HSA were digested with trypsin and desalted. Further, digests were analyzed to determine the presence of brominated peptides in digests by MALDI-TOF MS in reflector mode (data not shown).

*MS/MS methods*. For low resolution data driven analyses, the survey scans (m/z 350-1600) (MS1) were acquired in the Orbitrap at 120,000 resolution (at m/z 400) in profile mode, and the MS/MS (MS2) spectra were acquired in the linear ion trap in centroid mode. The maximum injection time for the MS1 scans in the Orbitrap was 100 ms, and the automatic gain control target was $1 \times 10^6$. The MS1 scans were followed by ten MS2 events in the linear ion trap with collision activation in the ion trap (parent threshold of 15000, isolation width of 1.9 Da, normalized collision energy of 35%, activation Q of 0.250, and activation time of 10 msec). Maximum injection times for the MS2 scans were 100 msec, and the automatic gain control target for the LTQ was $1 \times 10^4$. Charge state screening was enabled, with charge state 1 and unassigned charge states

rejected. Monoisotopic precursor selection was enabled, and dynamic exclusion was used to remove selected precursor ions (+/- 10 ppm) for 15 sec after MS2 acquisitions. A repeat count of 1, a repeat duration of 30 s, and a maximal exclusion list size of 500 were used. The following ion source parameters were used: capillary temperature of 275 °C, source voltage of 2.2 kV, source current of 100 µA, capillary voltage of 33 V, and the S-lens RF level at 69%. The data were acquired using XCalibur, version 2.0.7 (Thermo Fisher Scientific).

For high-resolution data-driven analyses, the survey scans (m/z 350-1600) (MS1) were acquired at in the Orbitrap at 60,000 resolution (at m/z = 400) in profile mode and the HCD fragmentation MS2 spectra were acquired at 15,000 resolution in the Orbitrap in centroid mode. The maximum injection time for the MS1 scans in the Orbitrap was 10 msec, and the maximum injection time for the MSn scans was 100 msec. The automatic gain control targets for the Orbitrap were $1 \times 10^6$ for the MS1 scans and $1 \times 10^5$ for the MSn scans. The MS1 scans were followed by five HCD MS2 (parent threshold = 15,000; isolation width = 4.0 Da; normalized collision energy = 30%; activation Q = 0.250; activation time = 0.1 ms, FT first mass mode fixed at m/z, FT first mass value 100 Da). Other data acquisition parameters were identical to those described above.