S3.1 *Assessment of the protein components of the Fe3O4 NP-BC*. Briefly, following the last PBS wash, Fe3O4 NPs were pelleted and the supernatant was discarded. The Fe3O4 NP pellet was then resuspended in 8 M urea with 10 mM dithiothreitol and proteins were solubilized for 45 min at 60˚ C. The Fe3O4 NPs were then pelleted via centrifugation at 15,000 rcf for 10 min and the supernatant containing the solubilized proteins was collected. Protein samples were then treated with 20 mM iodoacetamide in the dark at room temperature for 30 min followed by the addition of 10 mM dithiothreitol in 50 mM ammonium bicarbonate for 30 min at room temperature. After incubation, 525 μl of ammonium bicarbonate was added to dilute the remaining urea. Samples were then proteolyzed using porcine trypsin (0.2 ng/μl) overnight at 37˚ C. Trypsin was then deactivated by heating samples to 90˚ C and the samples were concentrated to dryness prior to being resuspended in 0.1% trifluoroacetic acid in water. Following resuspension, UltraMicroSpin columns (The Nest Group, Southborough, MA) were used to purify samples as described by manufacturer's instructions. The purified samples were then concentrated to dryness and resuspended in 0.1% formic acid in HPLC-grade water for mass spectrometry analysis.

Purified peptides were loaded to the trap column (300 mm ID ´ 5 mm) packed with 5 mm 100 Å C18 PepMap™ medium and then separated on an Acclaim™ PepMap™ 100 C18 analytical column (75 mm ID x 15 cm) packed with 2 mm 100 Å PepMap C18 medium (Thermo Scientific). Instrument optimization and calibration was carried out at the start of the runs using calibration mix solution (Thermo Scientific), and the performance of the instrument was evaluated using E. coli digest (Waters, Milford, MA).

For each LC-MS/MS analysis, 1 µg of peptide solution was injected and separated using a 120 min method. Mobile phase solvent A was 0.1% formic acid (FA) in water and solvent B was 0.1% FA in 80% acetonitrile (ACN). Peptides were loaded to the trap column in 100% buffer A for 5 min, and eluted with a linear 80 min gradient of 5 to 30% buffer B in 80 and reaching 45% B in 91 min, 100% of B in 93 min at which point the gradient was held for 7 min before reverting back to 5% B in at 100 min. The columns were equilibrated at 5% B for 20 min. The samples were loaded at a flow rate of 5 ml/min for 5 min, and eluted from the analytical column at a flow rate of 300 nl/min. After each 120 min sample run, columns were washed 2x with a linear gradient of 5% to 45% of B to keep them clean and reduce sample carry over before running the next sample. Column temperature was maintained at 35˚C. The mass spectrometer was operated using standard data-dependent mode acquiring MS/MS for the top 20 precursors. The full scan MS spectra was collected in the 400-1,600 m/z range with a maximum injection time of 100 ms at a resolution of 120,000 (at 200 m/z). Fragmentation of precursor ions was performed by high-energy C-trap dissociation (HCD) with the normalized collision energy of 27 eV. MS/MS scans were acquired at a resolution of 15,000 (at m/z 200). The dynamic exclusion was set at 15 s to avoid repeated scanning of identical peptides.

The following settings were used for MaxQuant: default Orbitrap parameters, minimum peptides length of seven amino-acid, data was analyzed with ‘Label-free quantification’ (LFQ) checked and the ‘Match between runs’ interval set to 1 min, protein FDR was set to 1%, enzyme trypsin allowing for two missed cleavage and three modifications per peptide, fixed modifications were Carbamidomethyl (C), variable modifications were set to Acetyl (Protein N-term) and Oxidation (M). An in-house script was used to perform the following steps on the MaxQuant results: removed all the common contaminant proteins, log transformed [log2(x)] the LFQ intensity values, input the missing values using the average values of the other two samples when just one sample was missing and use half of the lowest intensity when all three samples were missing in one group and presented in all three samples in the other group.

S3.2 *Viability, Uptake, and Inflammation*

Total RNA was isolated from cells using TRIZOL (Ambion Inc, Carlsbad, CA) via manufacturer's instructions and quantified via nanodrop. Total RNA was reverse-transcribed to cDNA using an iScript cDNA Synthesis Kit.