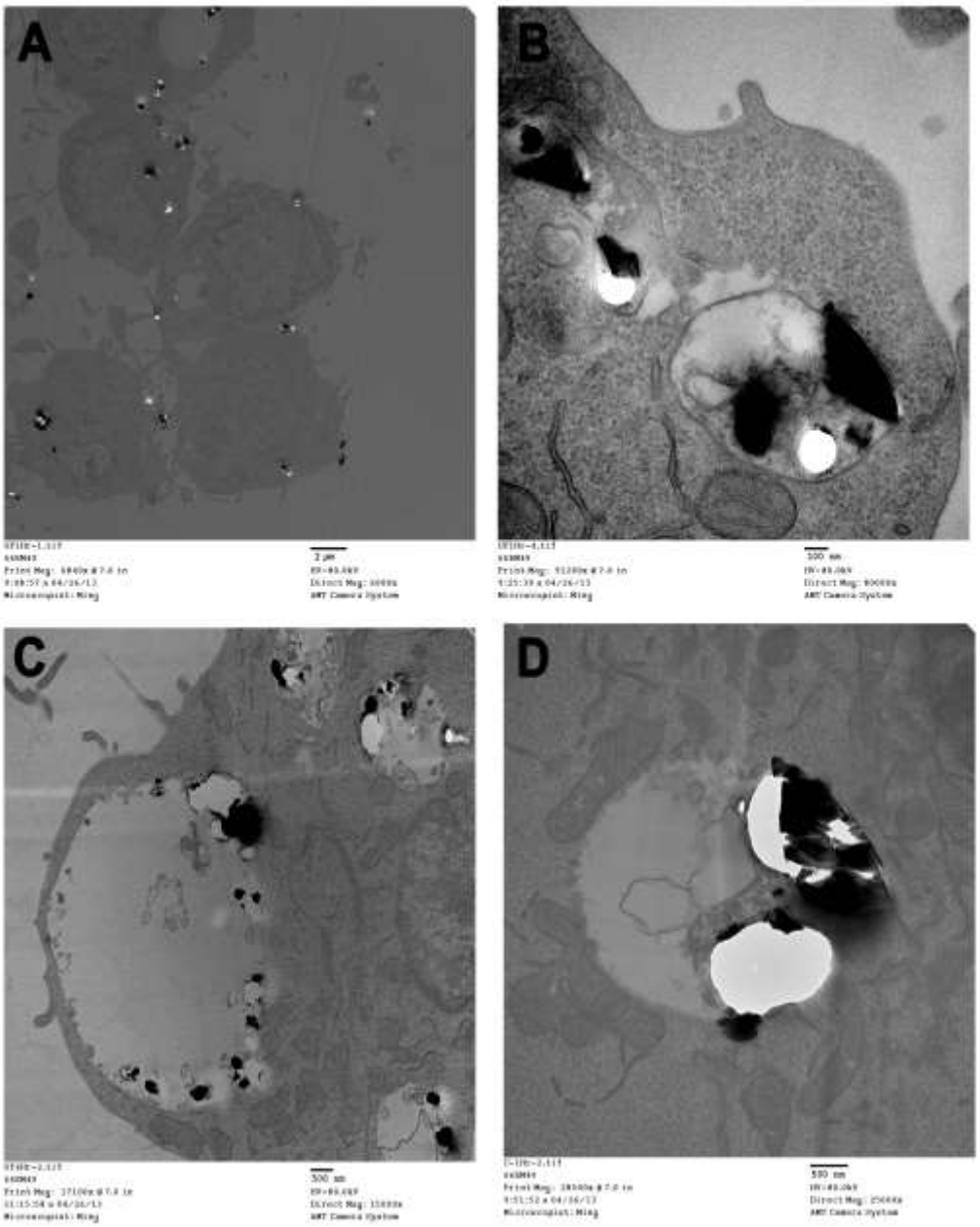
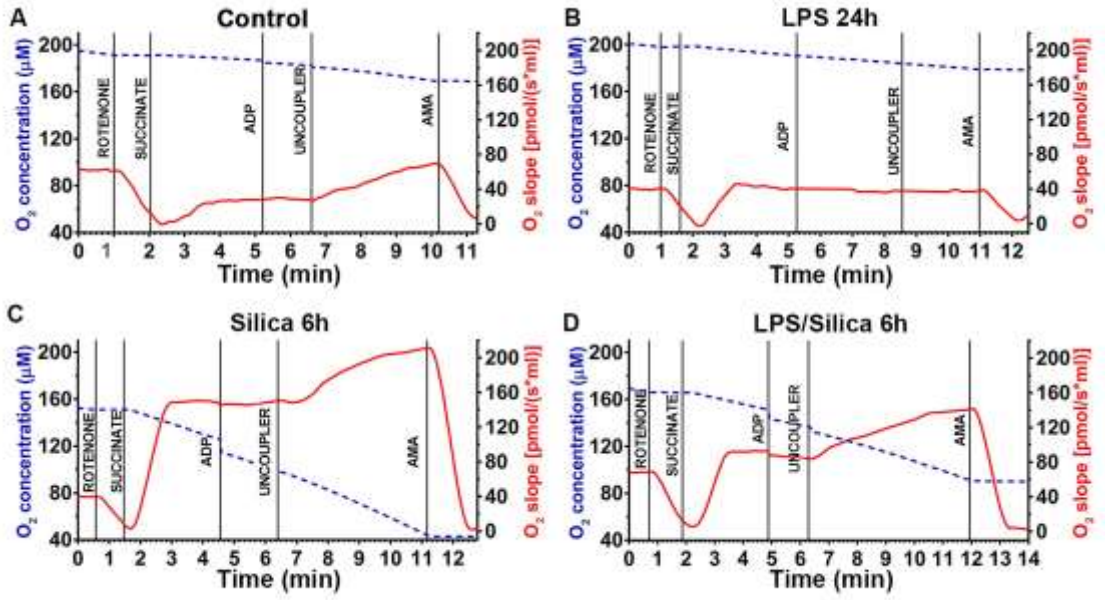
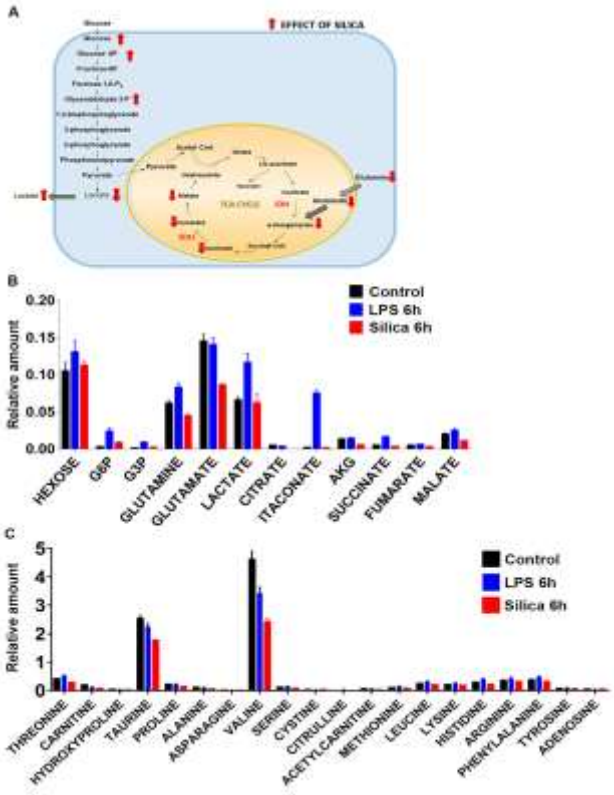


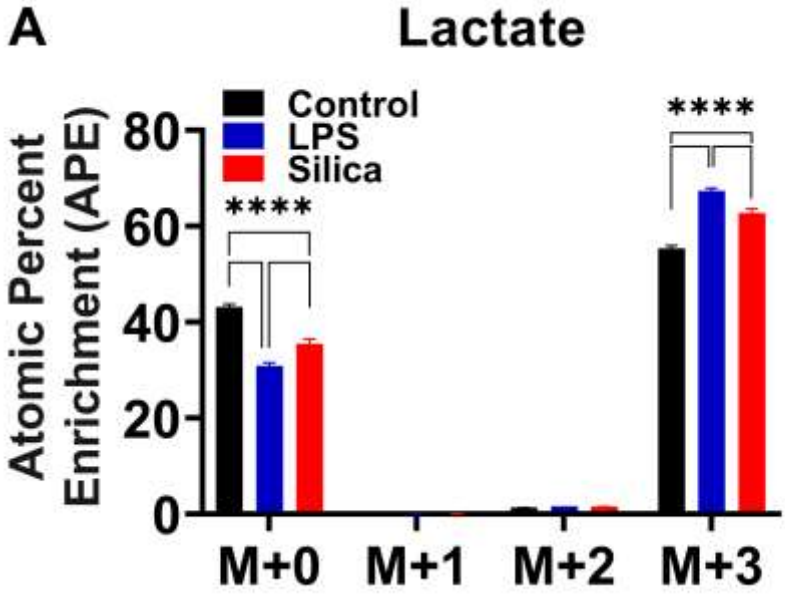
Supplemental Figure 1. Macrophages recruit mitochondria to silica-containing phagosomes. Transmission electron microscopy (TEM) images obtained from a RAW 264.7 macrophages, as a function of time, following silica (20 μg/cm^2) exposure. Images illustrate the incorporation of silica particles into phagosomes, 1h after exposure (A), and the subsequent recruitment of mitochondria to the silica-containing phagosomes 2h (B), 4h (C), and 6h (D) after silica exposures.



Supplemental Figure 2. Silica modulates ETC complexes activity. RAW 264.7 macrophages were exposed to (B) LPS (1 ng/ml) or (C) silica (50 µg/cm^2) for 6 hours or (D) primed with LPS (1ng/ml for 24h) and then exposed to silica (50 µg/cm^2) for 6h, or (A) left untreated. RAW 264.7 macrophages (5x10^6/chamber) were allowed to equilibrate in the chamber for about 10 minutes prior to measuring oxygen flux. Default respirometric settings of block temperature 37°C; stir bar speed 400 rpm, and data recording every 2s were used. Oxygen turnover (oxygen concentration, left *y*-axis, oxygen flux, right *y*-axis) by treated RAW 264.7 macrophages was followed after addition of Rotenone (f.c. 0.5 µM) Succinate (f.c. 10mM), ADP (f.c. 2.5mM), CCCP (f.c. 0.05 µM) and Antimycin A (f.c. 2.5 µM). After the addition of each compound, cells were allowed to come to equilibrium. Data are representative of 4 different experiments, with each experiment monitoring 5x10^6 cells.



Supplemental Figure 3. Silica increases the rate of glycolysis and suppresses the TCA cycle activity. (A) Schematic of metabolic changes showing increased glycolysis and suppression of the TCA cycle in RAW 264.7 macrophages exposed to silica. The arrows indicate increases or decreases of metabolite normalized on control. IDH, isocitrate dehydrogenase. SDH, succinate dehydrogenase. **(B,C)** Schematic summarizing key TCA metabolites and aminoacids significantly altered in RAW 264.7 macrophages after LPS (blue) or Silica (red) exposure. RAW 264.7 macrophages were exposed to vehicle, LPS (10 ng/ml), or silica (50 μg/cm^2) for 6 hours. Statistical analysis was performed on an average of 6 samples for each time and condition. The graph shows metabolites significantly differentially regulated by LPS or Silica. Metabolites with p-value < 0.05 and fold-change > 10% were deemed to be statistically significant.



Supplemental Figure 4. Intracellular enrichment of lactate. Changes in extracellular lactate atomic percent enrichment (APE%) at steady state determined by LC-HRMS. Atomic percent enrichment was calculated using the Mass isotopomer multi-ordinate spectral analysis (MIMOSA) method. Data are the mean ± SEM of 6 samples