Supplemental Information

Figure S1



Figure S1. Correlation between blood cell subtypes at baseline and LPS-stimulated cytokine response. (A) Correlation coefficient (Spearman r) between % baseline cell subtype distribution in and LPS-stimulated IL-6 and TNF- α levels in whole blood from n=13 individuals. Positive correlations are red and negative correlations are blue. (B) Spearman correlation along with linear regression lines showing direction of association between stimulated cytokines (IL-6 and TNF α) and distribution of cell subtypes.

Figure S2



Figure S2. Mitochondrial respiration inhibitors alter LPS-stimulated cytokine response. (A-C) Fold change of LPS-stimulated cytokine levels upon respiration inhibition (green bars) by Rotenone (Complex I), Antimycin A (Complex III) and Oligomycin (Complex V) relative to LPS only (blue bars). The cytokines are ranked from most- to least- suppressed by an inhibitor. Data are mean±SEM of n=19-20 individuals.

Figure S3

Α LPS +Oligo +Rot +AntiA +KCN +DEX 800 -⁶⁰⁰⁰] **r² 0.31** r² 0.30 r² 0.69 r² 0.00 r² 0.36 r² 0.26 P=0.04 P=0.05 P=0.93 P=0.0007 P=0.02 P=0.08 TNF-α (pg/mL) 4000 -0 0 0 | 0 40000 0 10000 20000 30000 40000 40000 0 IL-6 (pg/mL) Β +KCN +Rot +Anti A LPS +Oligo +DEX r²=0.58, P<0.0001 r²=0.72, P<0.0001 r²=0.75, P<0.0001 r²=0.65, r²=0.0004, 5000 r²=0.68, P<0.0001 P=0.93 P<0.0001 IL-1B (pg/mL) 400 0 400 0 300 0 500 0 400 0 IFN-γ (pg/mL) С LPS +Rot +Anti A +KCN +Oligo +DEX ²⁵ r²=0.37, P=0.01 r²=0.21, P=0.05 r²=0.00, 20 -r²=0.51, r²=0.43, r²=0.41, P=0.52 P=0.0009 P<0.0001 P=0.006 IL-13 (pg/mL) . . C 10000 0 MIP-1 α (pg/mL)

Figure S3. Mitochondrial respiration defects alter inter-cytokine associations in leukocytes. (A-C) Effect of mitochondrial respiration inhibition and DEX treatment on inter-cytokine correlations. The P values and r² are derived from Spearman rank correlation and linear regression respectively. Data presented are from n=19-20 and significant correlations are shown in bold.

Spearman rank correlation and linear regression between IL-6 and TNF- α

Figure S4



Figure S4. Linear regressions (Pearson r) between the age of participants in Cohort 2 and their baseline mitochondrial measures. Age does not correlate with mitochondrial enzyme activities of Complex I, II (SDH), IV (COX), mitochondrial content (CS), copy number (mtDNAcn) and mitochondrial health (MHI). n=37 except mtDNAcn (n=30).