

Figure S1

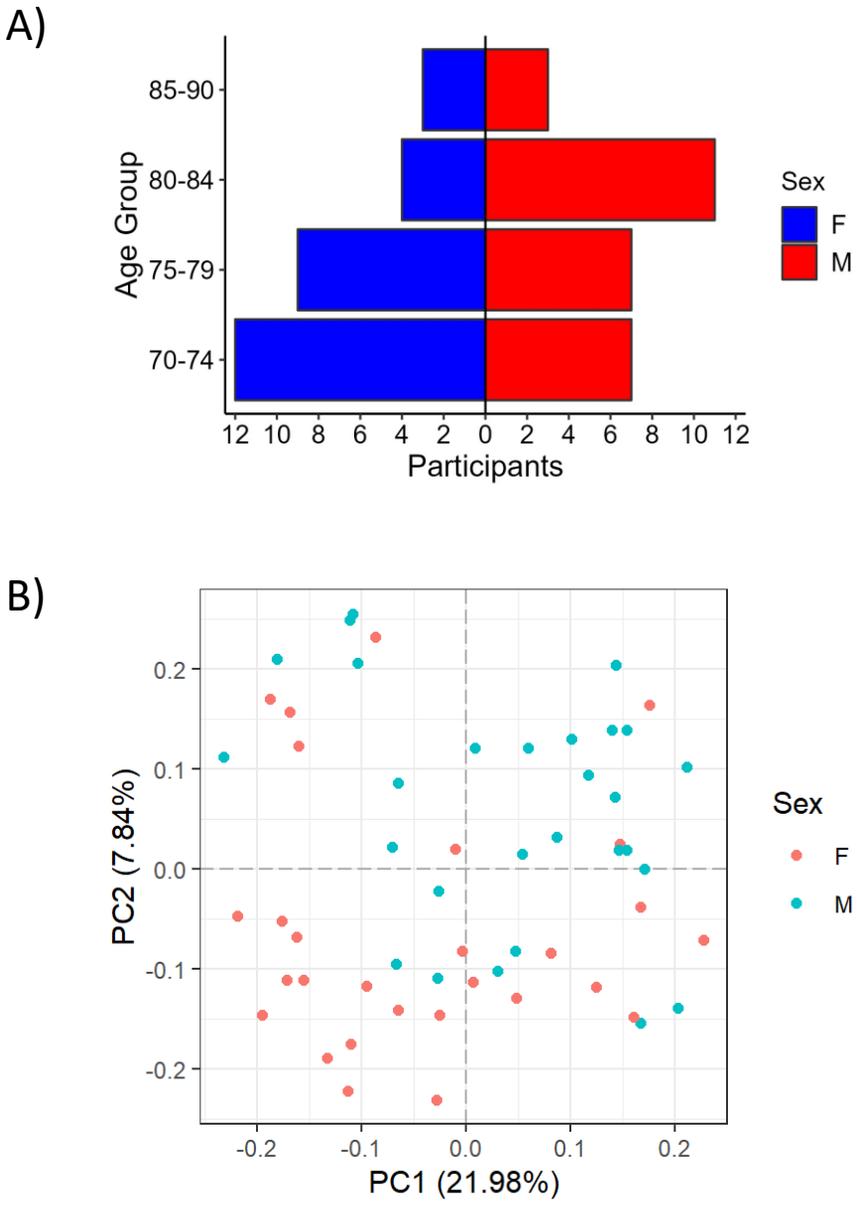
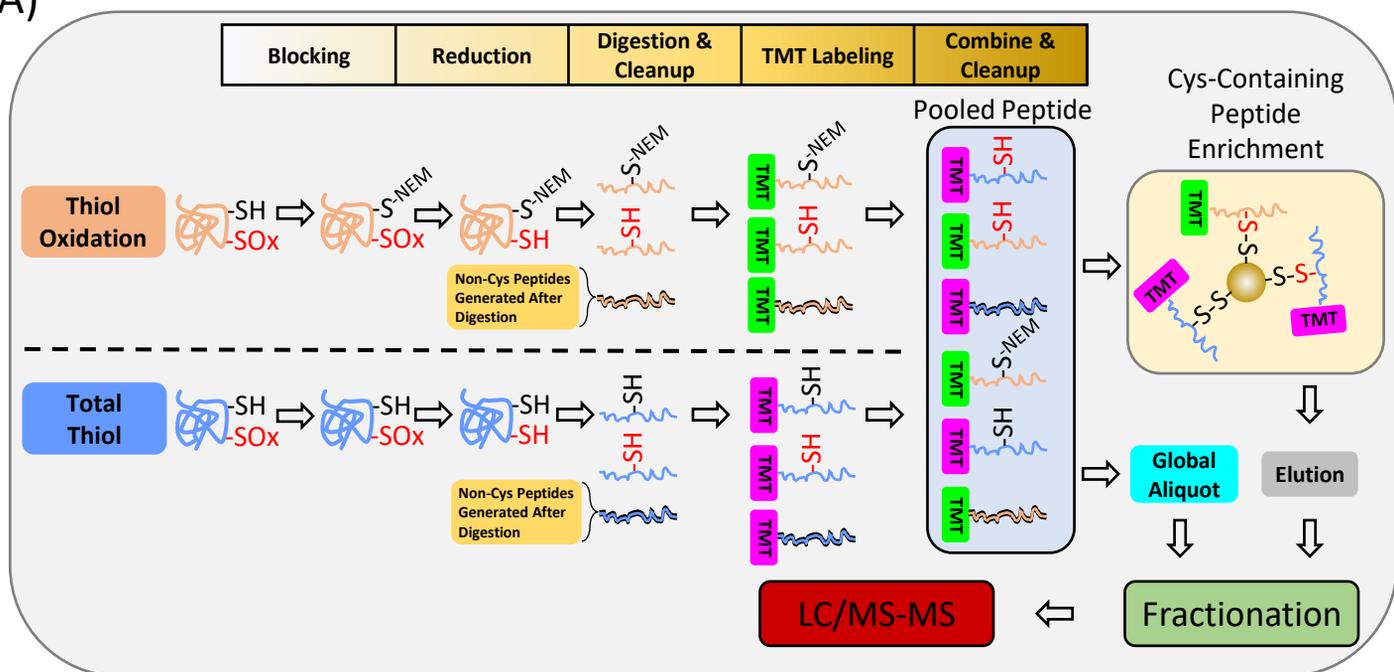


Figure S1. Additional participant characteristics. A) Pyramid plot representing age distribution of the cohort in this study for both sexes. B) Variation in muscle protein oxidation among participants as represented by principal component analysis (PCA) plot of redox proteomics data with each data point (participant) colored by sex.

Figure S2

A)

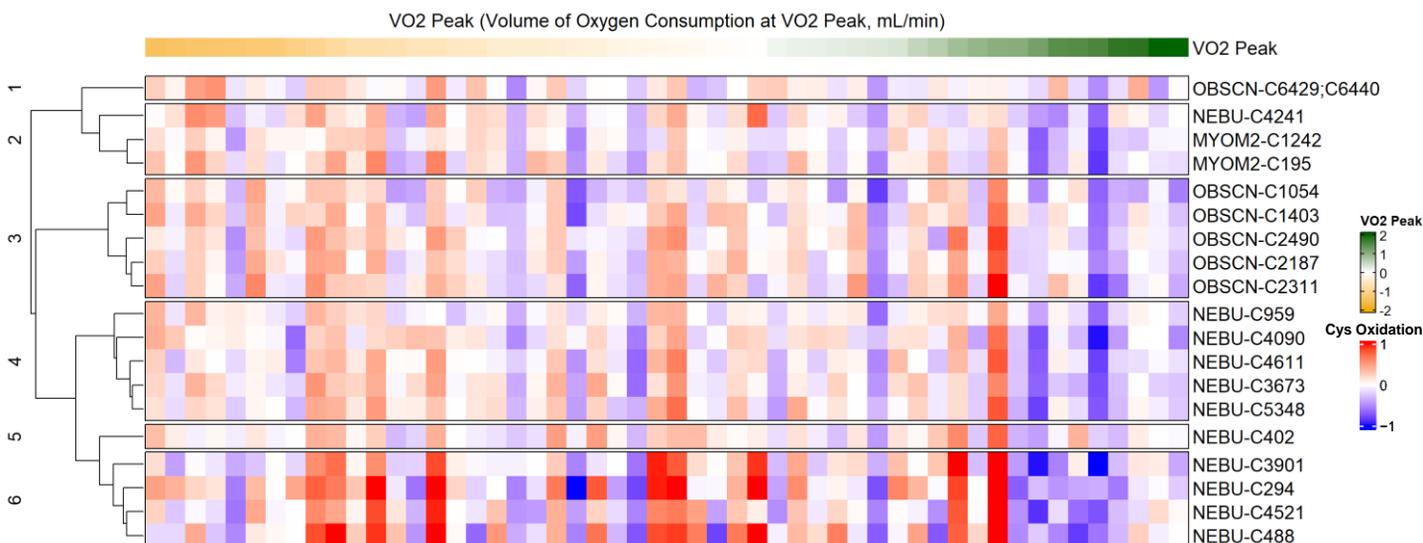


B)

126	127N	127C	128N	128C	129N	129C	130N	130C	131N	131C	132N	132C	133N	134C	135N
Thiol Oxidation (n=14)													Total Thiol (n=2)		

Figure S2. Integrated global and redox proteomics workflow. A) The RAC-TMT workflow (Guo et al., 2014) was modified to integrate both global and redox proteomics workflows into the same processing procedure from the same sample. The blocking and reduction strategies critical for measuring total oxidation of Cys sites were incorporated into a standard global proteomic processing workflow, ultimately allowing for both enrichment of oxidatively modified peptides and global proteomics from the same pool of peptide. The global proteomic data is used to calibrate the redox proteomics data in a similar manner as with phosphoproteomics data, to distinguish changes in Cys oxidation from changes in protein expression. Off-line reverse phase high pressure liquid chromatography fractionation of enriched redox peptides was implemented to increase coverage, as was recently demonstrated in one of our previous reports (Day et al., 2022). Total thiol channels were incorporated for a signal boosting strategy as described in (Day et al., 2022), as well as to provide enough peptide material for offline fractionation. B) Representative TMT18plex design. Muscle biopsy samples were randomly assigned different channels within a multiplex. A total of 4 plexes were generated to analyze 56 samples, where pooled samples were used to generate total thiol samples within each plex.

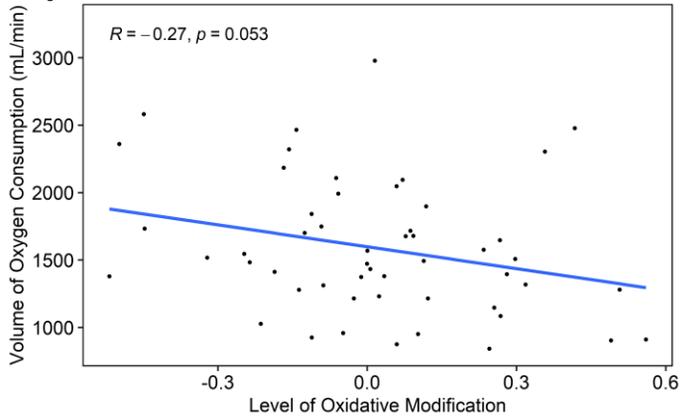
Figure S3



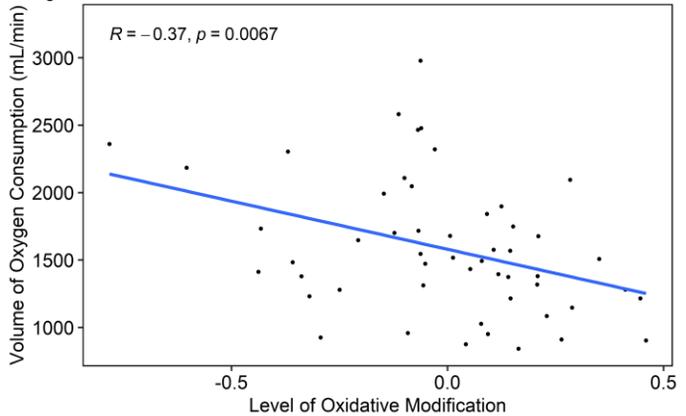
Figures S3-S10. Heatmaps and correlation plots of all Cys sites that are significantly associated with the four phenotypes investigated. For the heatmaps (**Figures S3, S5, S7, S9**), each row represents a Cys site with oxidation levels that are significantly associated with a phenotype, while each column represents a participant. Columns are ranked in ascending order from left to right based on phenotypic measurement (i.e., lower to higher performance), where the phenotypic values are represented by median-centered Z-scores in the row above each heatmap, while Cys oxidation levels were scaled by median-centering. Protein identities are in UniProt format. Sites passing an adjusted p value < 0.05 cutoff are denoted by '*'. For each cluster in a heatmap, Cys sites were plotted for correlation analysis (**Figures S4, S6, S8, S10**), where the mean level of oxidation across all Cys sites were plotted for each participant against their phenotypic measurement. *R* and *p* values are derived from Pearson correlation.

Figure S4

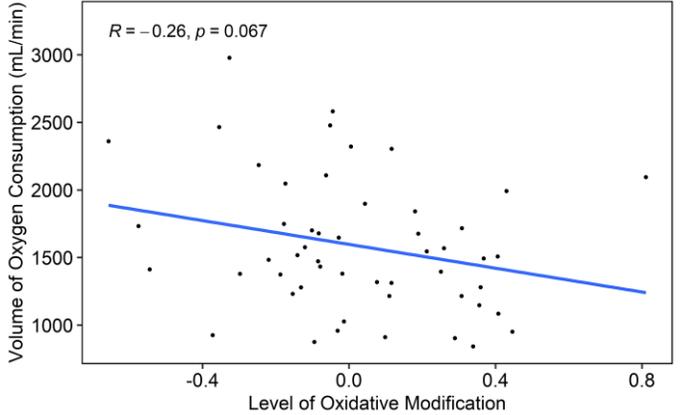
A) VO2 Peak, Cluster 1



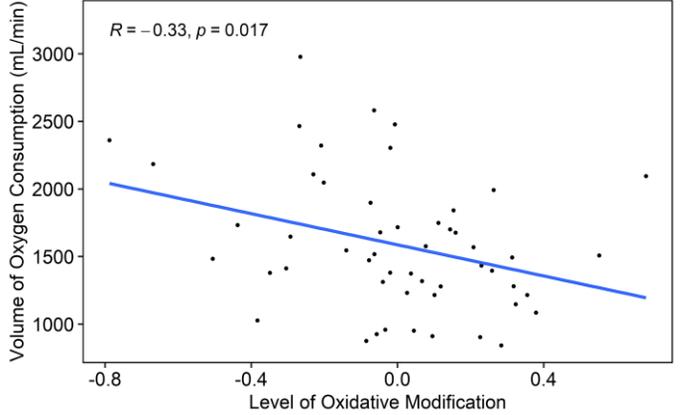
B) VO2 Peak, Cluster 2



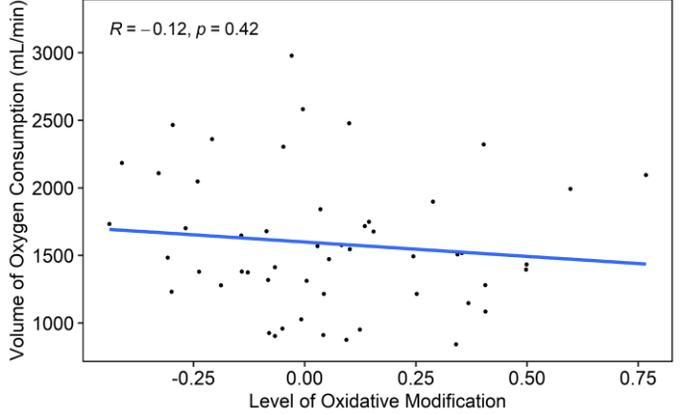
C) VO2 Peak, Cluster 3



D) VO2 Peak, Cluster 4



E) VO2 Peak, Cluster 5



F) VO2 Peak, Cluster 6

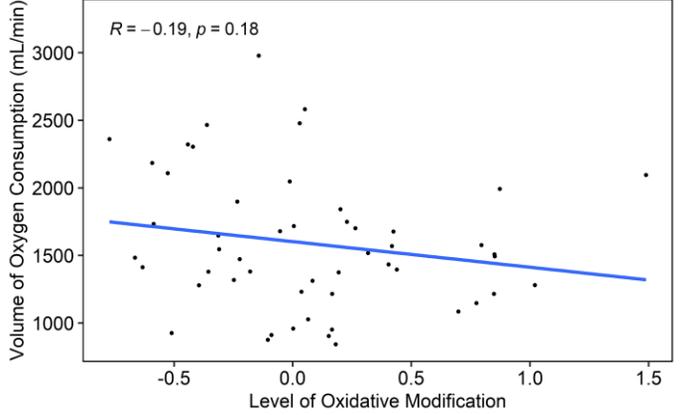


Figure S5

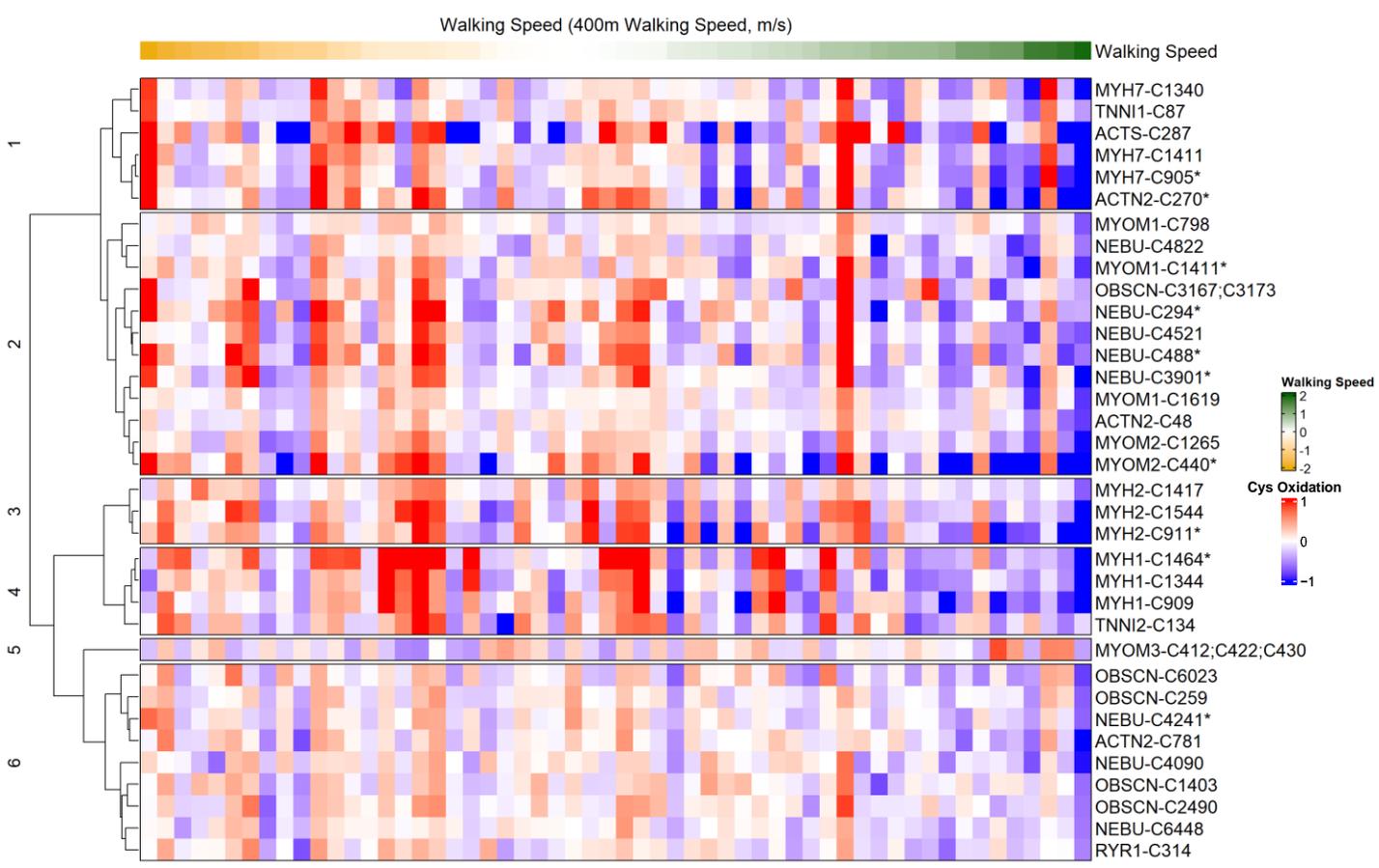
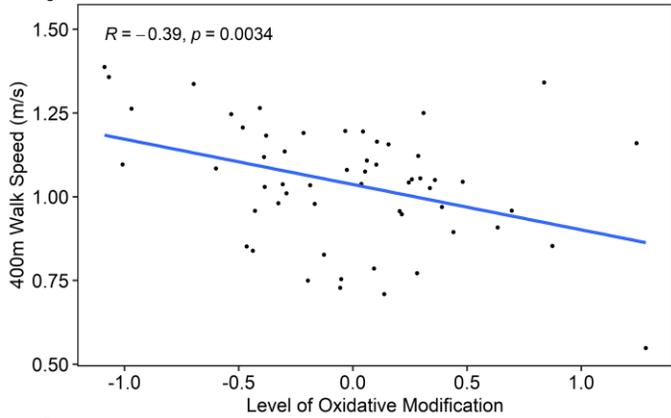
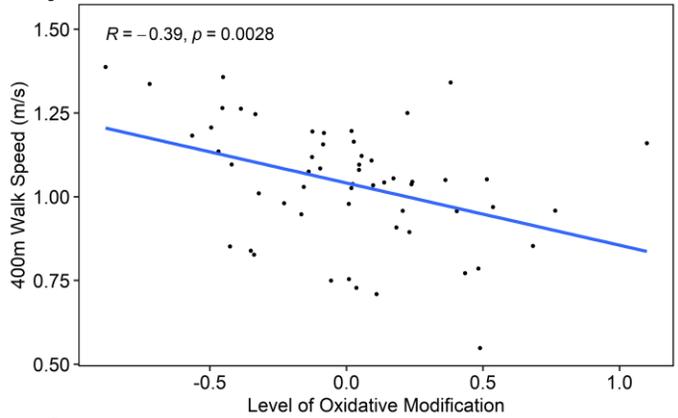


Figure S6

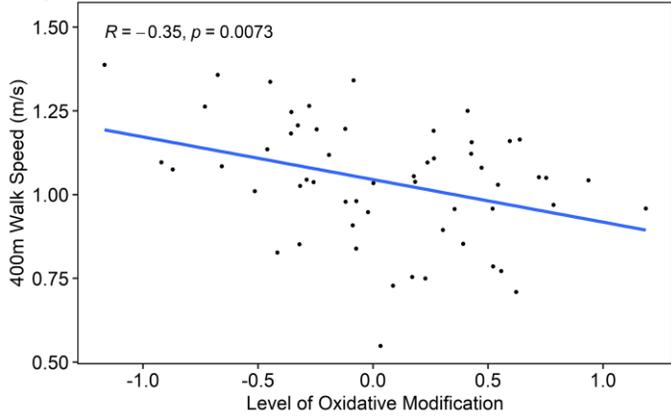
A) Walking Speed, Cluster 1



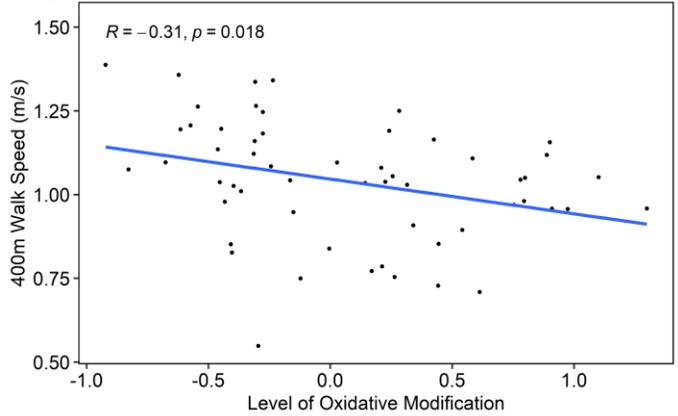
B) Walking Speed, Cluster 2



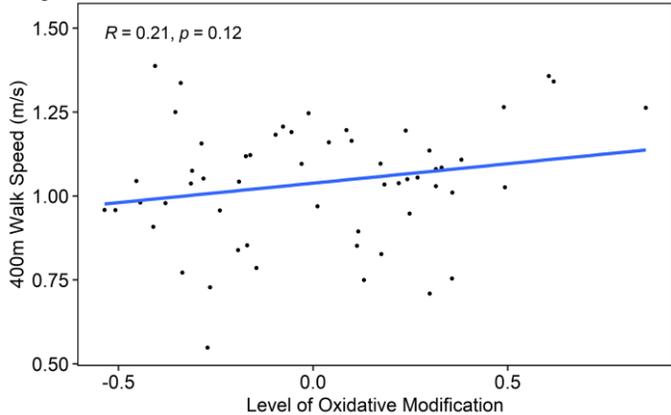
C) Walking Speed, Cluster 3



D) Walking Speed, Cluster 4



E) Walking Speed, Cluster 5



F) Walking Speed, Cluster 6

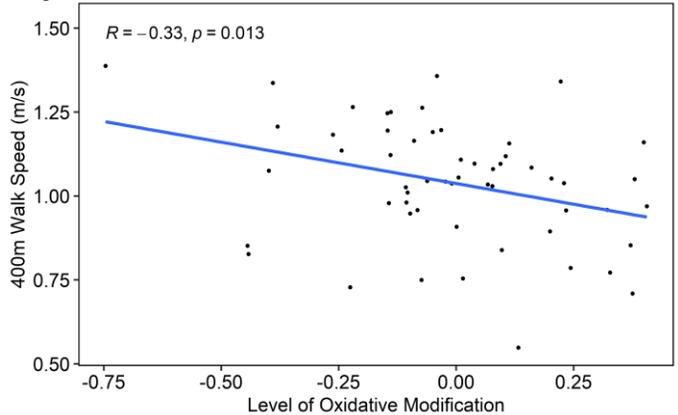


Figure S7

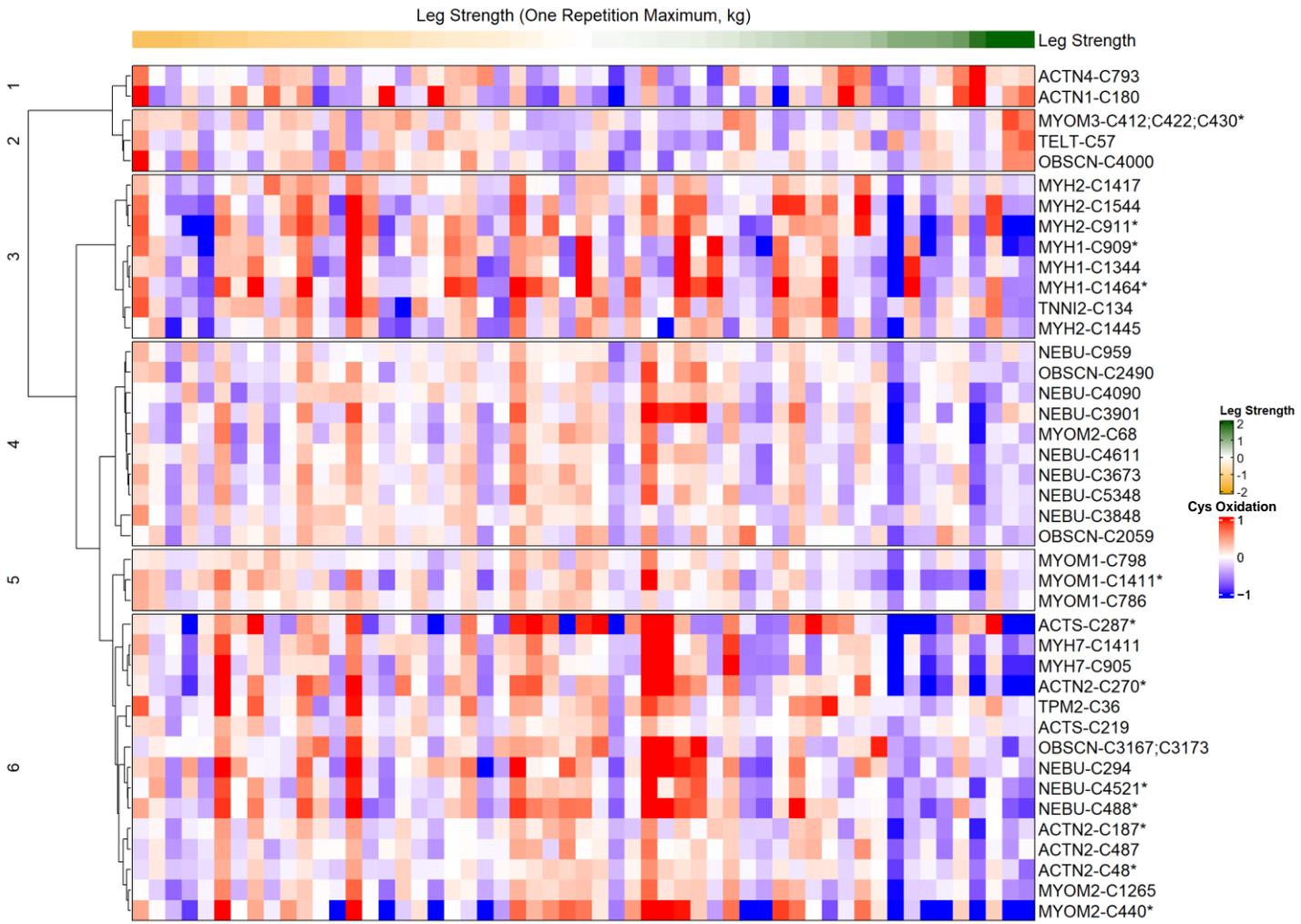
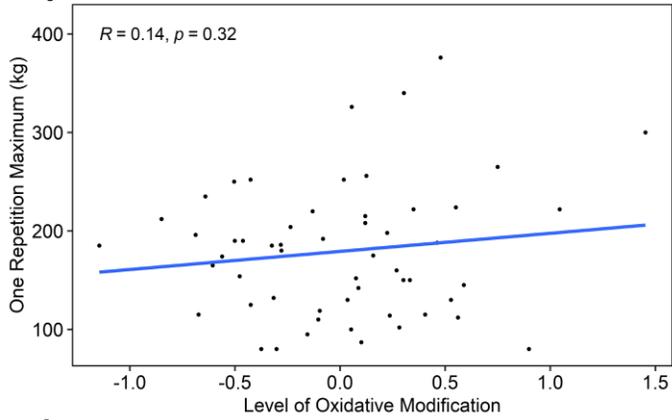
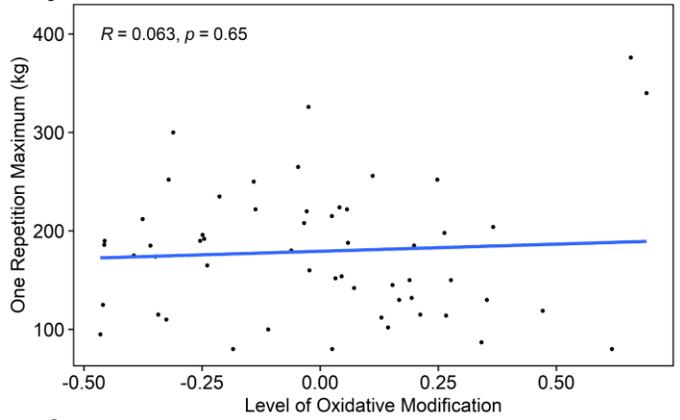


Figure S8

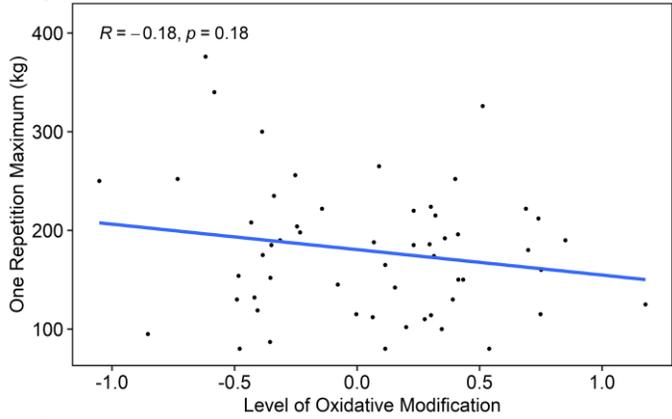
A) Leg Strength, Cluster 1



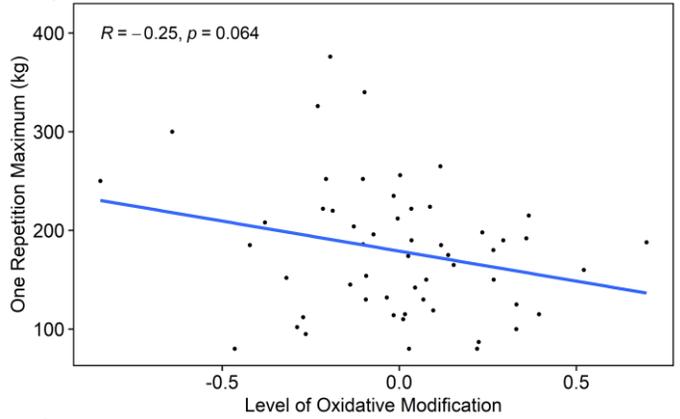
B) Leg Strength, Cluster 2



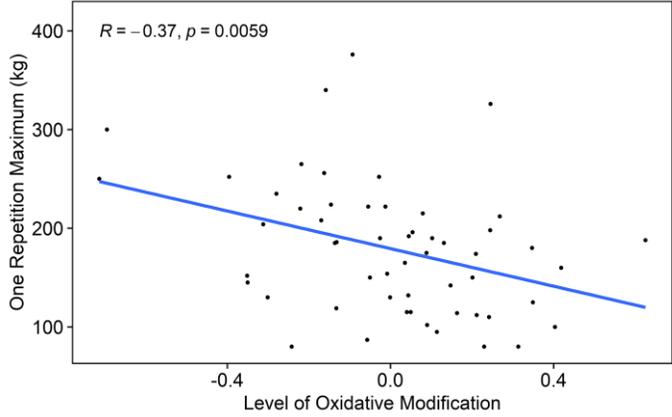
C) Leg Strength, Cluster 3



D) Leg Strength, Cluster 4



E) Leg Strength, Cluster 5



F) Leg Strength, Cluster 6

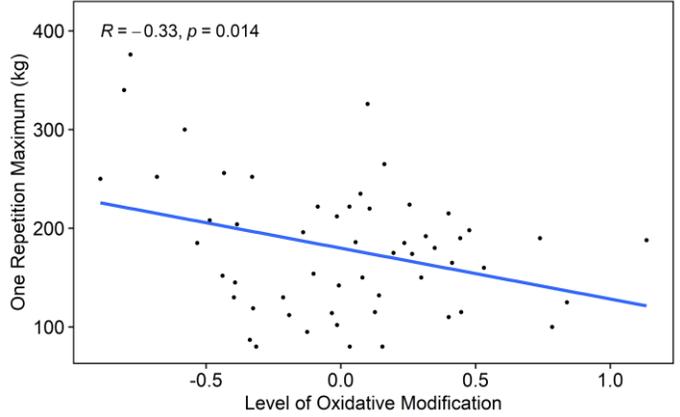


Figure S9

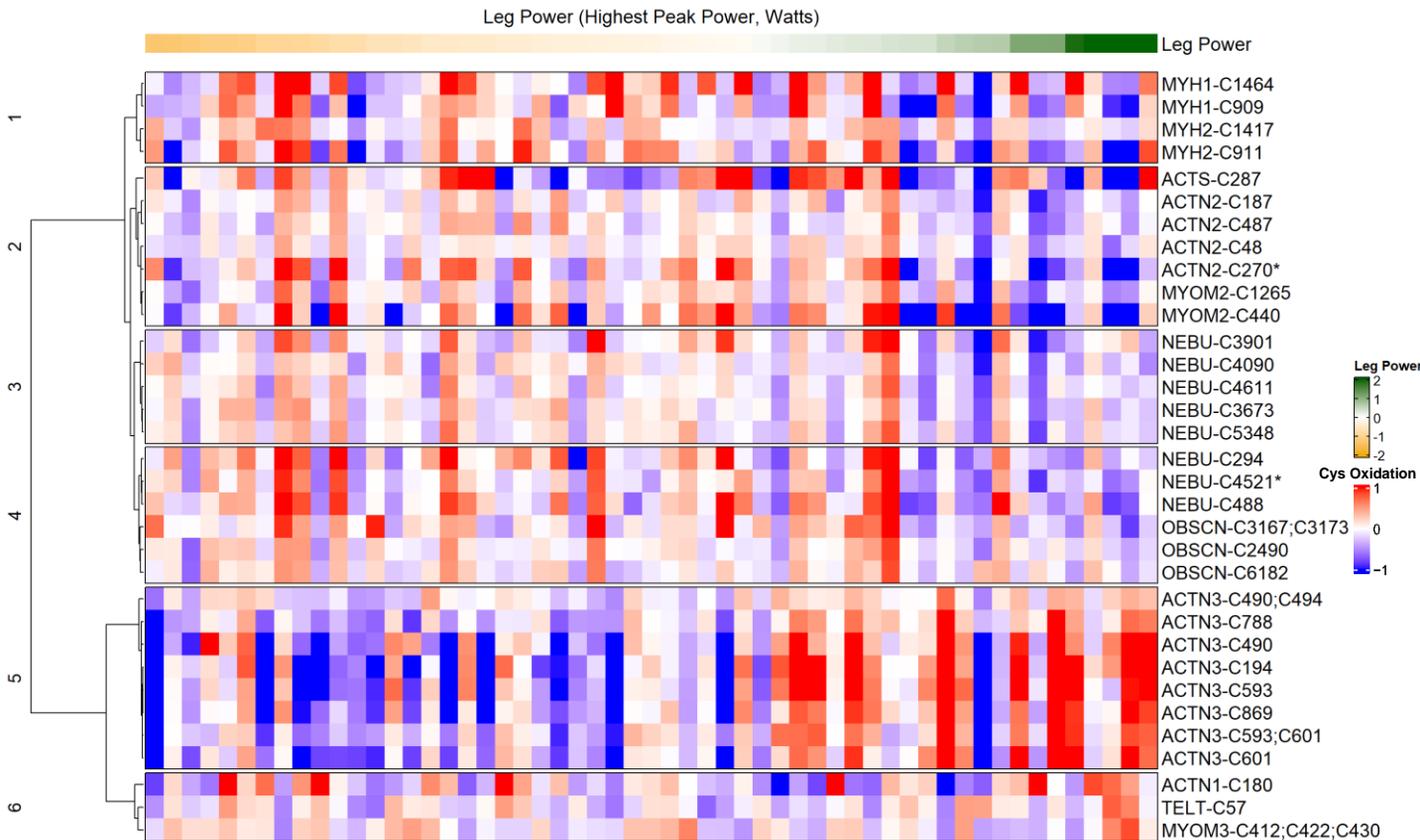
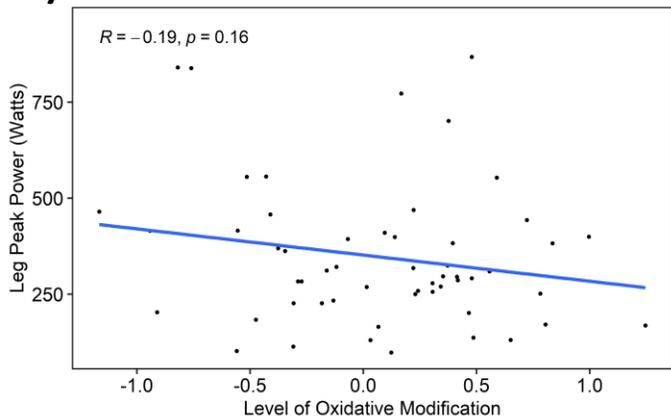
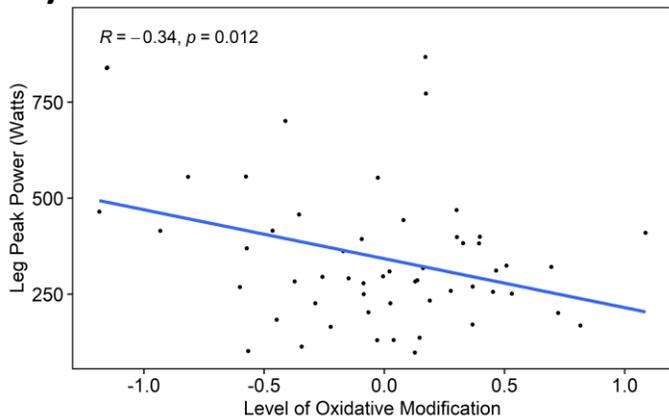


Figure S10

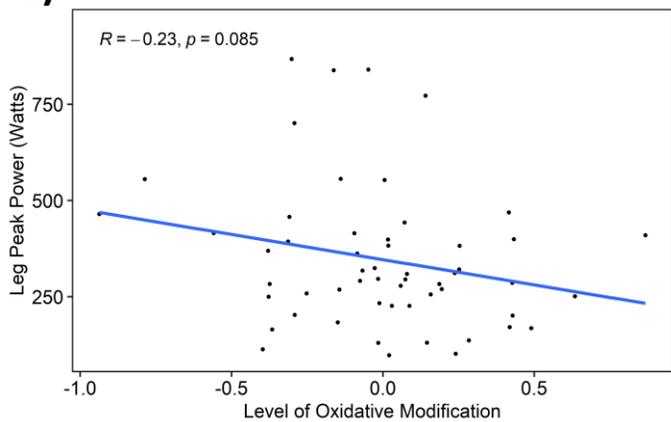
A) Leg Power, Cluster 1



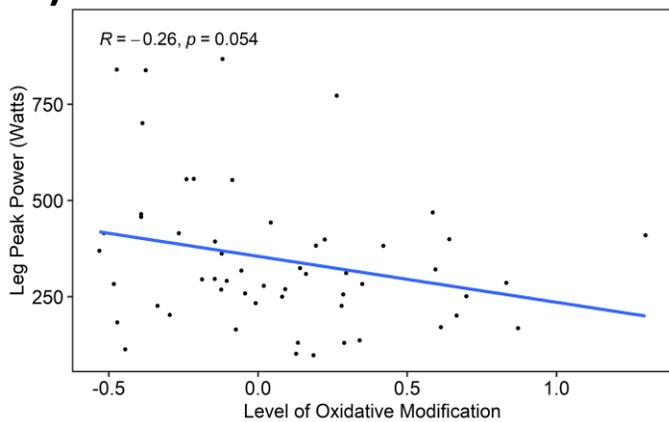
B) Leg Power, Cluster 2



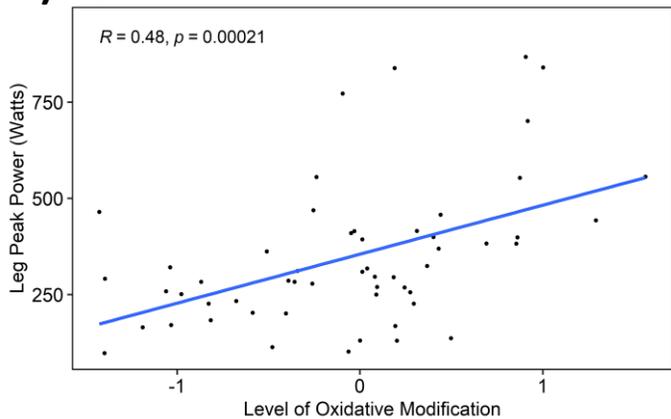
C) Leg Power, Cluster 3



D) Leg Power, Cluster 4



E) Leg Power, Cluster 5



F) Leg Power, Cluster 6

