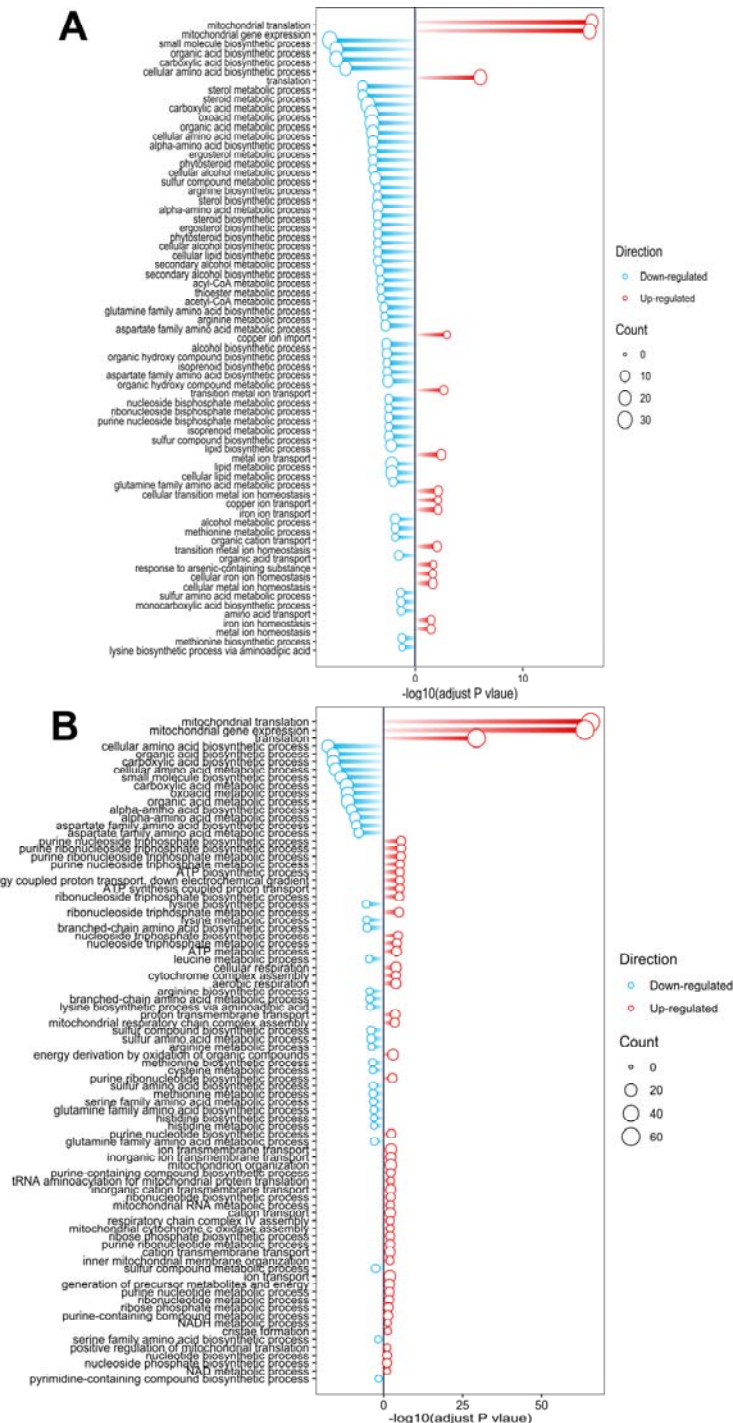
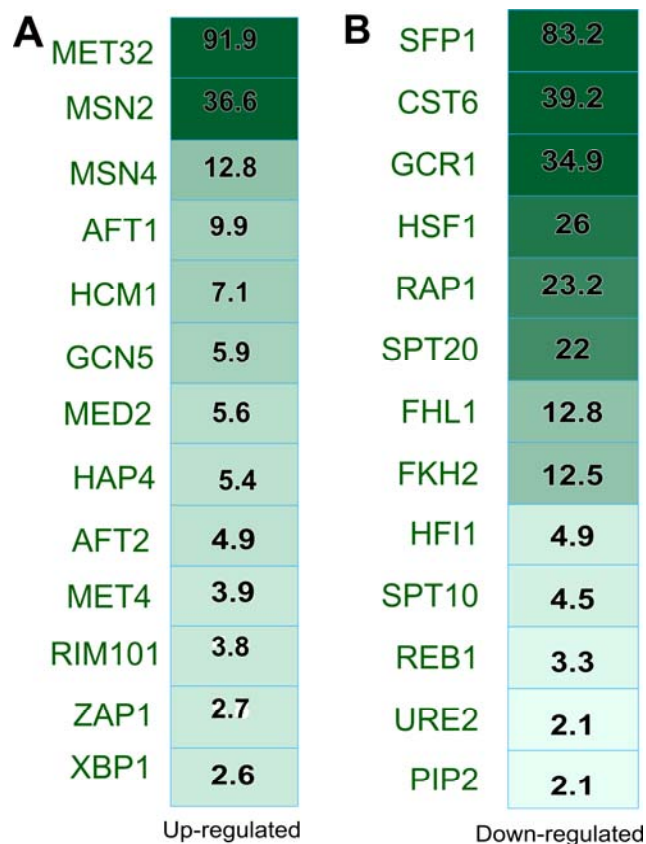


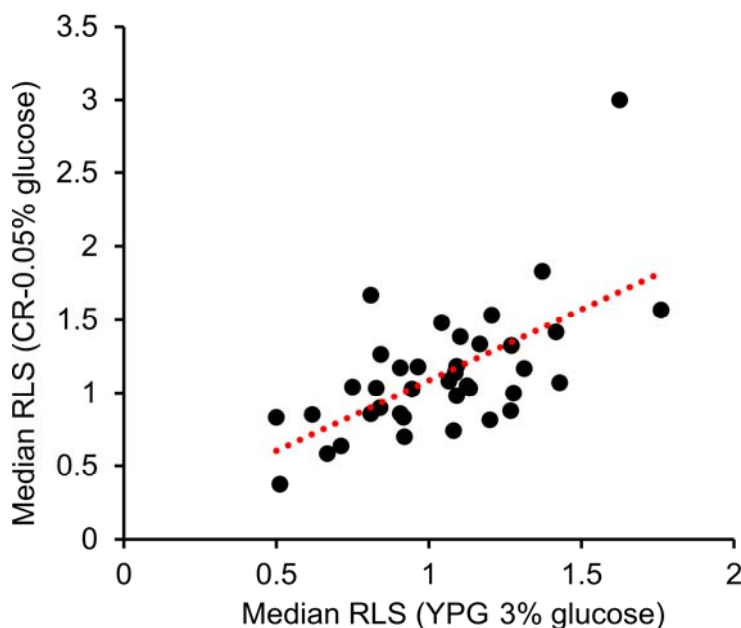
## Supplementary Figures



**Figure S1: GO term enrichment analyses:** The GO term (Molecular Function) analyses show significantly enriched terms for (A) positively responding versus non-responding and (B) positively responding versus negatively responding strains.



**Figure S2. Transcription factor enrichment analyses for non-responding strains analyzed under CR condition.** Significantly enriched TFs for (A) up- and (B) down-regulated DEGs obtained under CR conditions for non-responding strains. The color index and the number show the significance of the enrichment score ( $-\log_{10}$ , adjusted  $P$ -value).



**Figure S3. A positive correlation of median RLS phenotype between YPG and CR medium was observed.** A significant correlation was observed between median RLS in YPG and median RLS in CR, wherein glycerol-induced CR-induced respiration approximately equally extends the RLS of those strains we tested ( $R^2 = 0.62$ ,  $P_{adj} \text{ value} = 2.29 \times 10^{-4}$ ).

#### Supplementary Files:

**Supplementary file 1:** The file includes the strain list used in this study and their replicative lifespan analyzed under YPD, YPG, and CR conditions, along with the statistical significance of lifespan differences.

**Supplementary File 2:** Differentially expressed genes and metabolite abundances resulted from comparison of responding (POS) versus non-responding (NON) and negatively (NEG) responding comparisons. These -omics data were obtained under YPD conditions. The file also contains results from the regression analysis for the genes and metabolites whose transcript level/abundances correlate with CR-lifespan. The file also includes results from the GO term enrichment analysis associated with Figures 9 and 10.

**Supplementary File 3:** The file includes raw and normalized counts for RNA-seq data for selected responding and non-responding strains. Differentially expressed genes for each group resulting from comparison to the control (YPD) are also included.