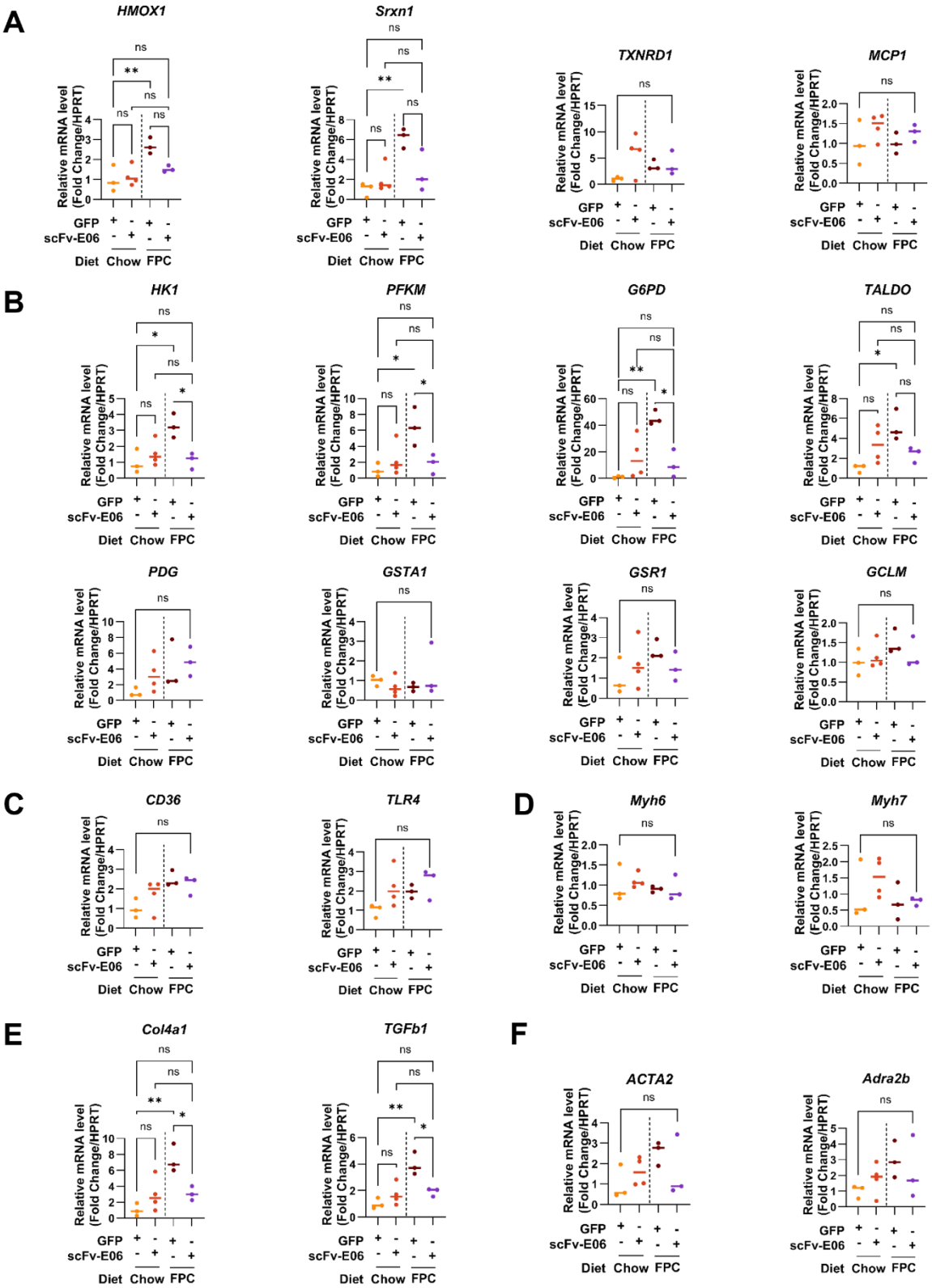
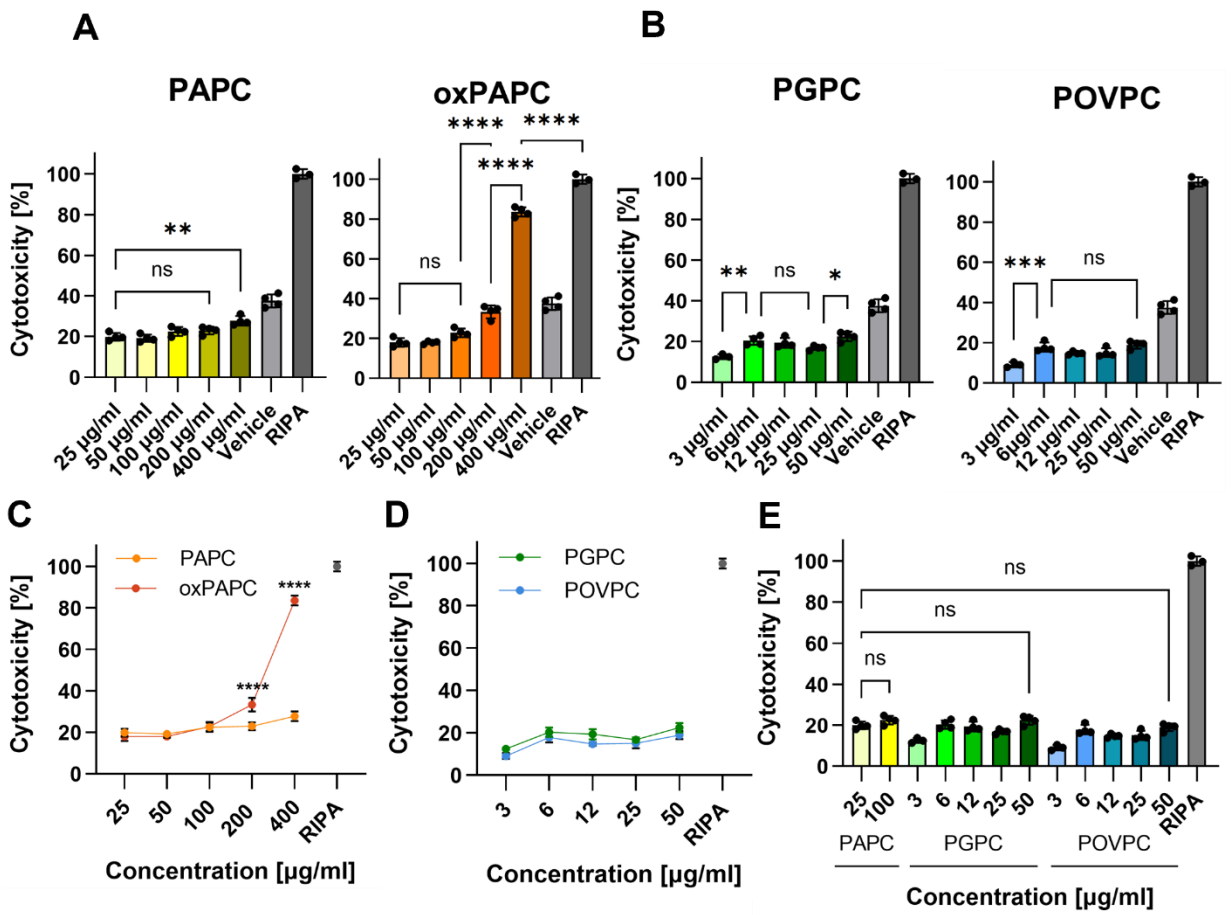
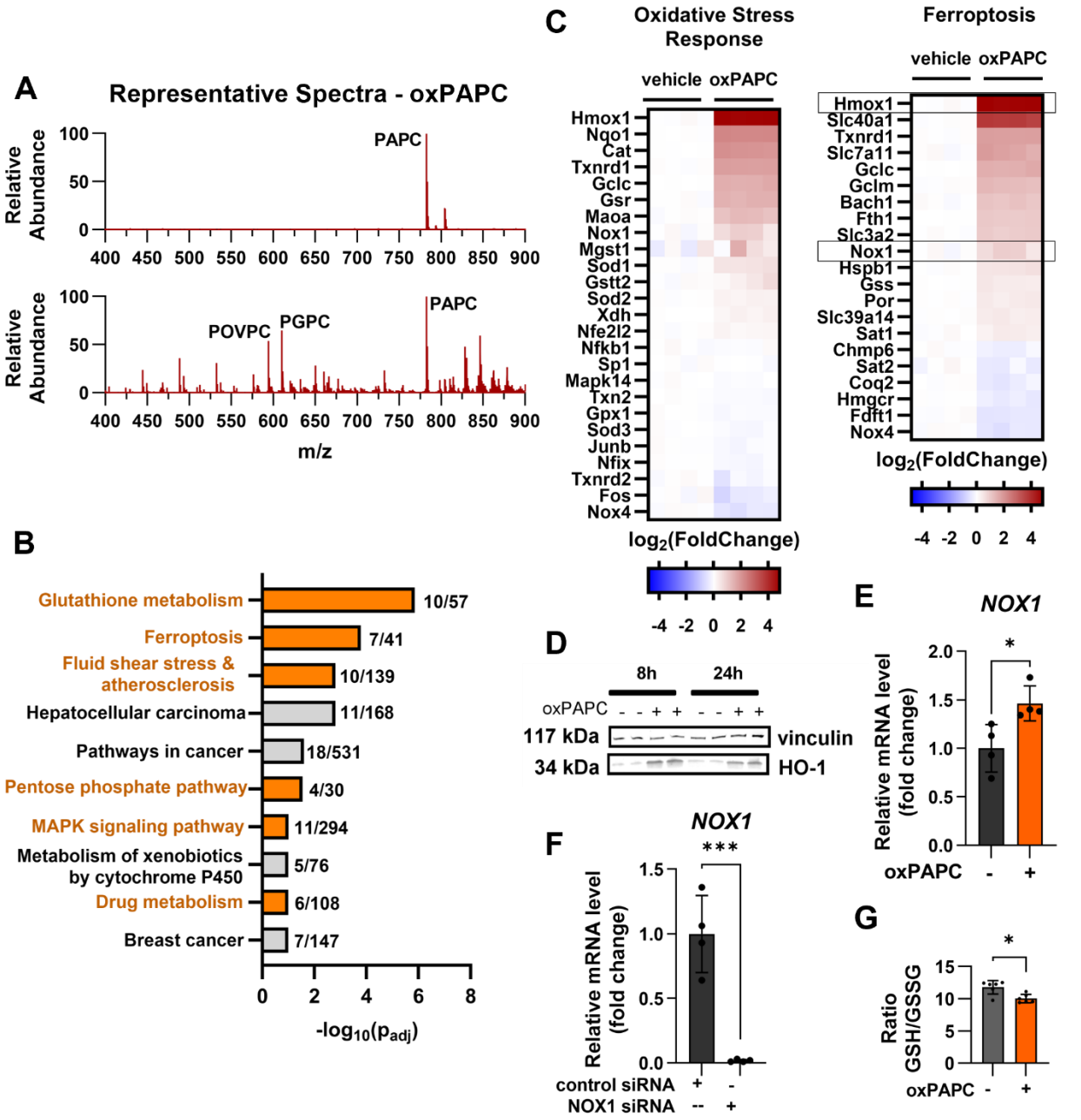


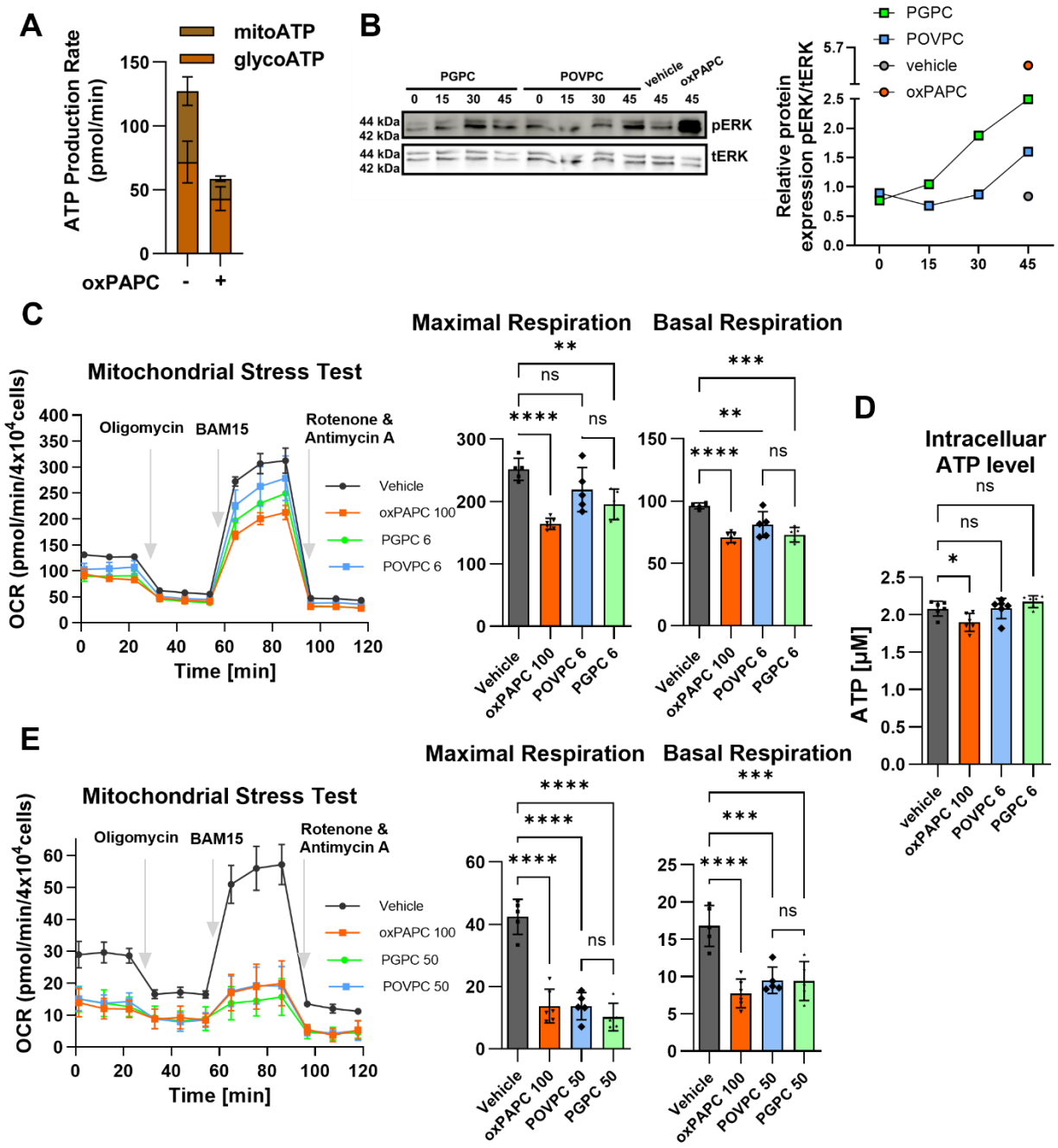
Supplemental Figure S1 Relative expression of chosen: **(A)** redox, **(B)** metabolic, **(C)** fatty acid, **(D)** cardiac damage, **(E)** fibrotic related and other **(F)** genes obtained using RT-qPCR in the hearts of GFP and scFv-E06 expressing mice on Chow and FCP diet. Quantification relative to *Hprt*. Statistical analysis: One-Way ANOVA with Tukey's Multiple Comparisons Test: *=p ≤ 0.05, **=p ≤ 0.01, N=3-4 (A-F).



Supplemental Figure S2 Impact of non-oxidized and various OxPC species on H9c2 viability following lipid exposure. Comparison of cell-mediated cytotoxicity in H9c2 cells as determined by the conventional LDH assay when treated for 6h with vehicle and **(A)** 25-400 µg/ml of PAPC and OxPAPC **(B)** 3-50 µg/ml of PGPC and POVPC. **(C)** Comparison of cytotoxicity induced after 6h exposure to non-oxidized and oxidized PAPC in the concentration range of 25-400 µg/ml. **(D)** Comparison of cytotoxicity induced after 6h treatment with two short-chain oxidized phospholipids PGPC and POVPC in the concentration range of 3-50 µg/ml. **(E)** Cytotoxicity caused by short-chain oxidized phospholipids (PGPC, POVPC, 3-50 µg/ml) compared to cytotoxicity induced by non-oxidized lipid (PAPC: 25 µg/ml, 100 µg/ml). Cytotoxicity is expressed as percentage of signal normalized to 100% lysis, obtained in control cells treated with RIPA. Error bars represent SD. Statistical analysis: One-Way ANOVA with Tukey's Multiple Comparisons Test: *=p ≤ 0.05, **=p ≤ 0.01, ****= p≤0,0001, N=3-5 (A-E). Data shown are representatives of 2 independent experiments.



Supplemental Figure S3 (A) Liquid chromatography–mass spectrometry (LC–MS) spectra of PAPC and OxPAPC after 8days of oxidation of PAPC. **(B)** 10 most correlated pathways with genes upregulated by OxPAPC in H9c2 cells. Source: KEGG Pathway 2021 Human in Enrich R. **(C)** Relative gene expression of pathway genes from „Oxidative Stress Response" and "Ferroptosis" in H9c2 cells treated with OxPAPC (6h, 100µg/ml). Source: Wiki Pathway 2023 Human. **(D)** Western Blott analysis showing the HO-1 protein expression of in H9c2 cells after treatment with 100µg/ml OxPAPC for 8h and 24h. **(E)** Nox1 gene expression levels in H9c2 cells after treatment with OxPAPC (6h, 100µg/ml). RT-qPCR quantification relative to Hprt. Error bars represent SD. N=4 (B,C). N=2 (D). Statistical analysis: Unpaired T-Test: **=p ≤ 0.01. N=4 (E, F), N=8 (G) Data shown are representatives of 3 independent experiments.

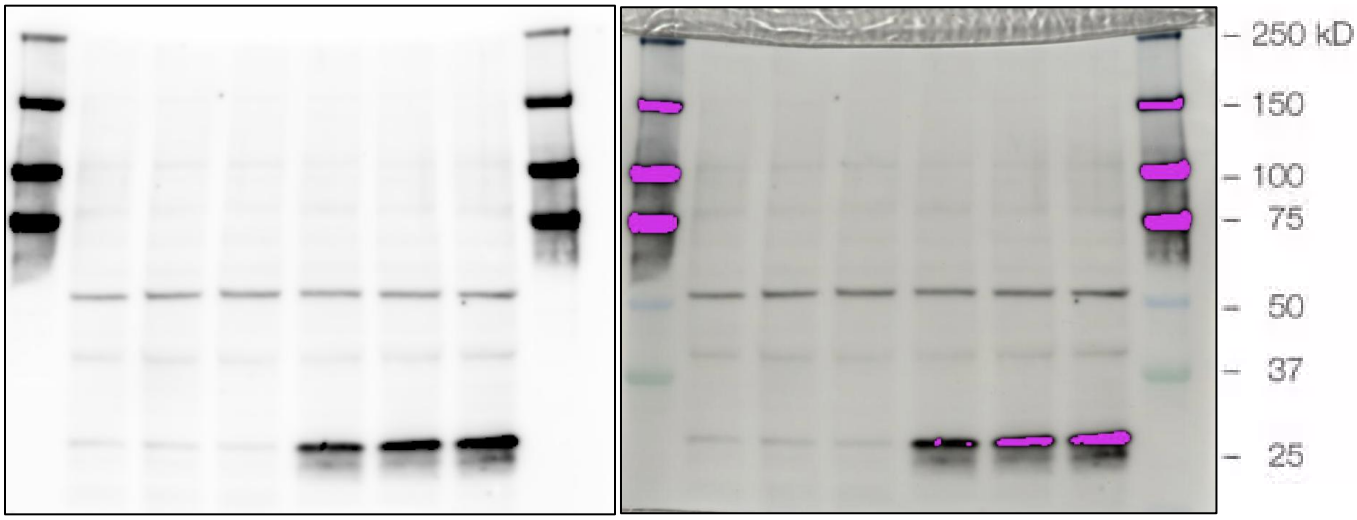


Supplemental Figure S4 (A) Total ATP production rate attributed to Glycolysis (glycoATP) and Oxidative Phosphorylation (mitoATP) in H9c2 cells treated with OxPAPC (6h, 100µg/ml). **(B)** Western blot analysis showing the kinetics of ERK 1/2 phosphorylation in H9c2 cells after treatment with PGPC and POVPC (6µg/ml) with a time course quantification of phosphorylated ERK 1/2 to total ERK 1/2 on the right. **(C)** Mitochondrial bioenergetics of H9c2 cells treated for 6h with 100µg/ml OxPAPC, 6µg/ml PGPC, 6µg/ml POVPC and quantification of basal and maximal oxygen consumption rate. **(D)** Intracellular ATP level after treatment for 6h with 100µg/ml OxPAPC, 6µg/ml PGPC, 6µg/ml POVPC. **(E)** Mitochondrial bioenergetics of H9c2 cells treated for 6h with 100µg/ml OxPAPC, 50µg/ml PGPC, 50µg/ml POVPC and quantification of basal and maximal oxygen consumption rate. Error bars represent SD. N=5 (A), N=1 (B). Statistical analysis: One-Way ANOVA with Tukey's Multiple Comparisons Test: N=5-6 (C, E), N=6 (D), *=p ≤ 0.05, **=p ≤ 0.01, ***= p≤0,001, ****= p≤0,0001. Data shown are representatives of 3 independent experiments.

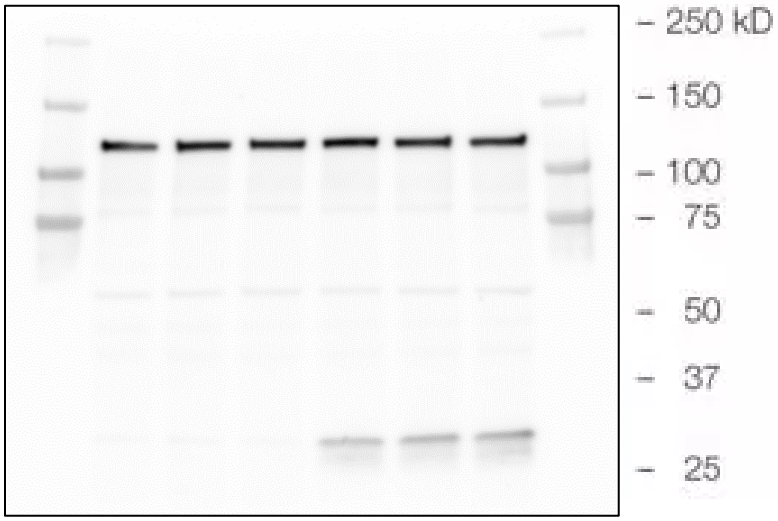
Supplemental Figure S5 Original Western Blots from:

- **For Figure 2E**

1) G6PD + HO-1

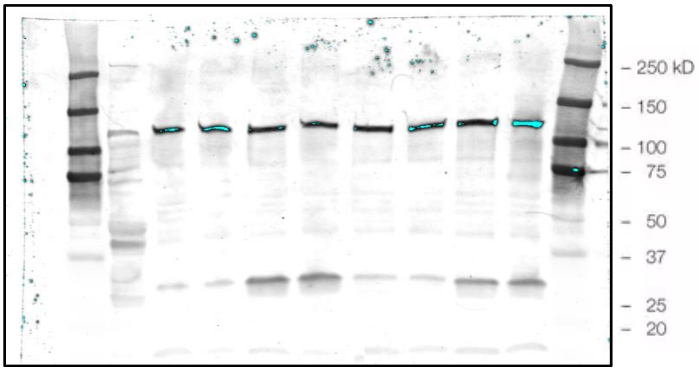


2) vinculin

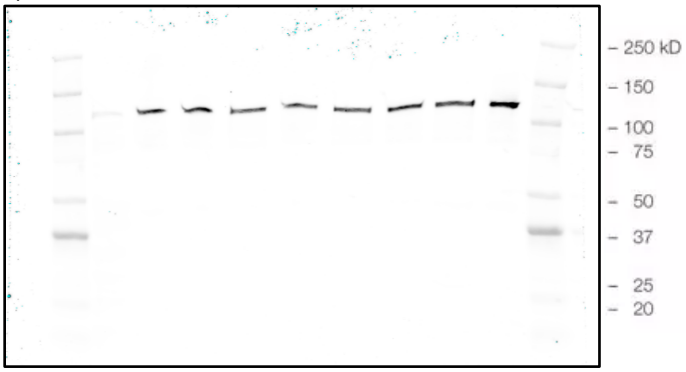


- **For Figure S3D**

1) HO-1

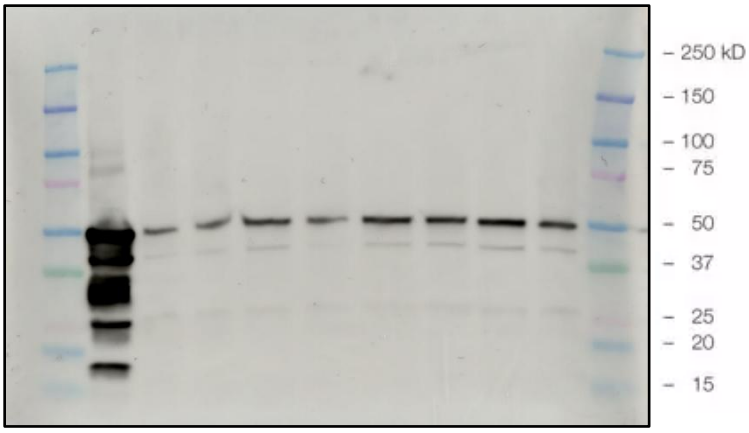


2) vinculin

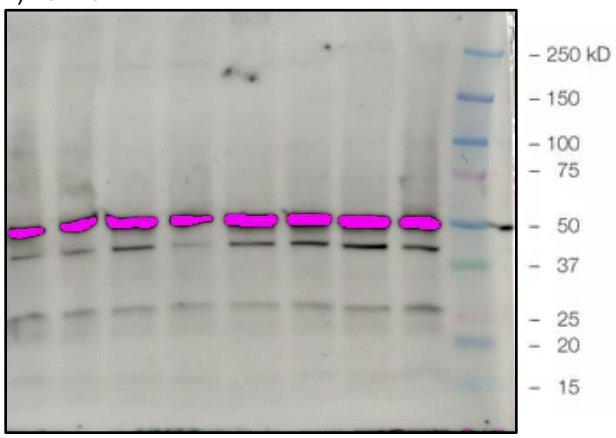


- **For Figure 5B:**

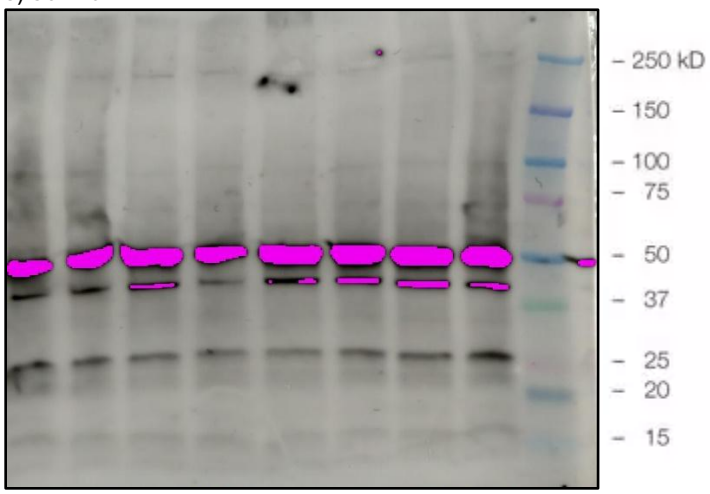
1) Positive control + 55kDa;



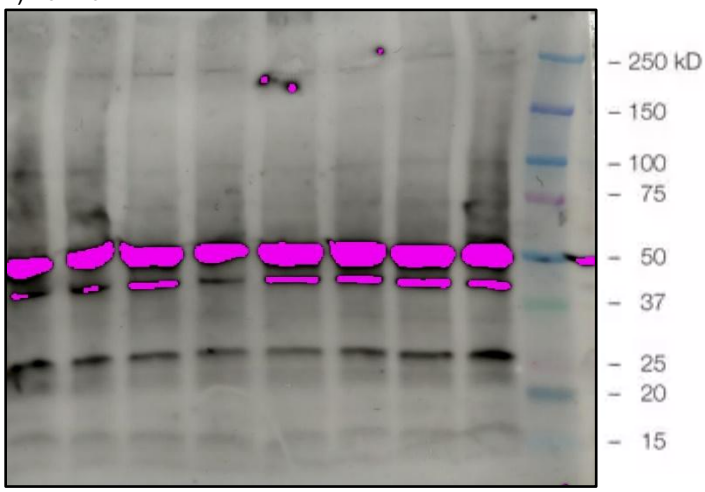
2) 48kDa



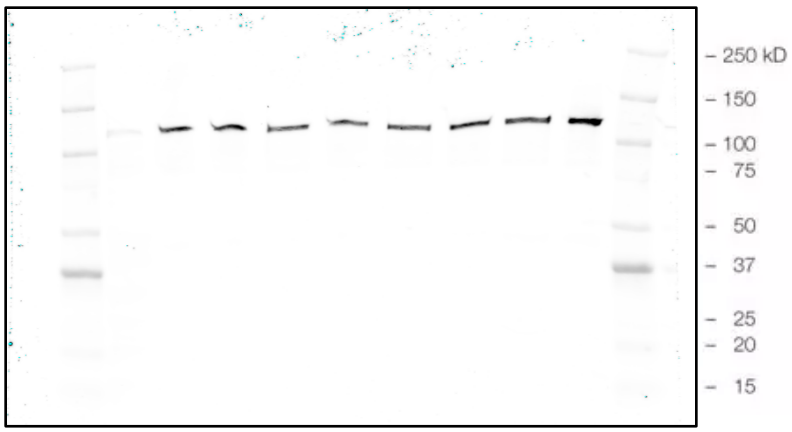
3) 30kDa



4) 20kDa

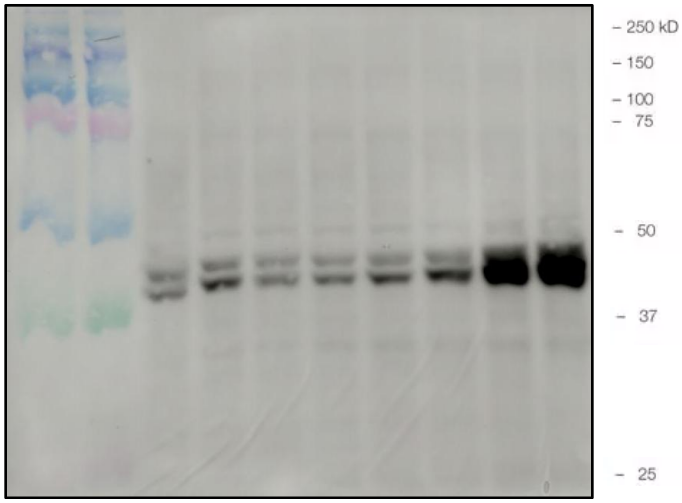


5) vinculin

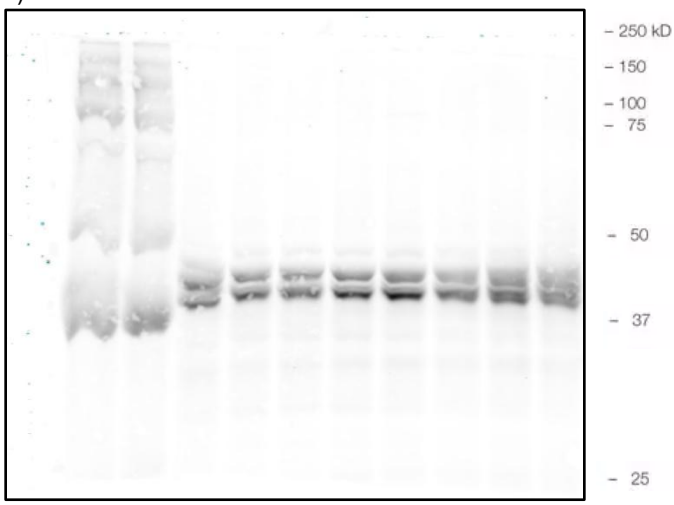


- **For Figure 5C:**

1) pERK 1/2

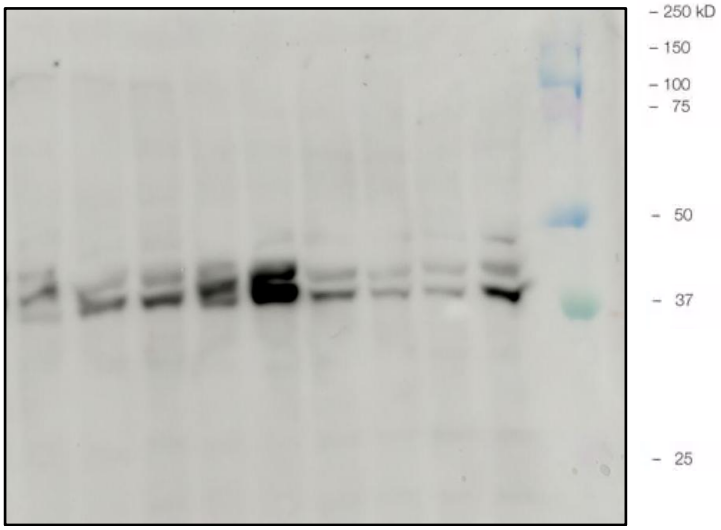


2) tERK 1/2

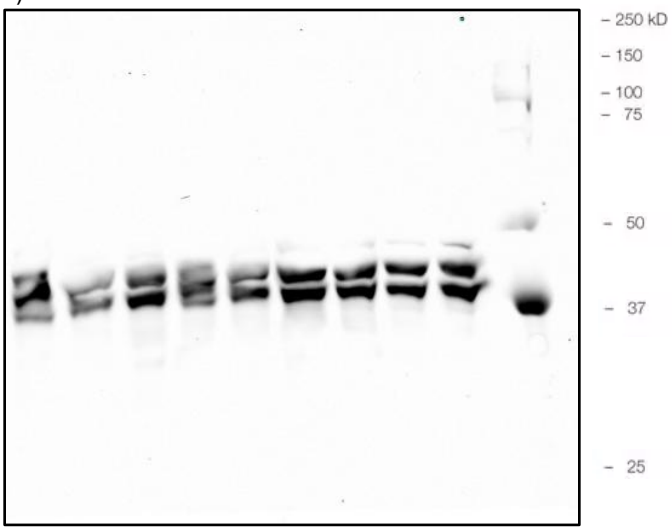


- **For Figure 5D**

1) pERK 1/2

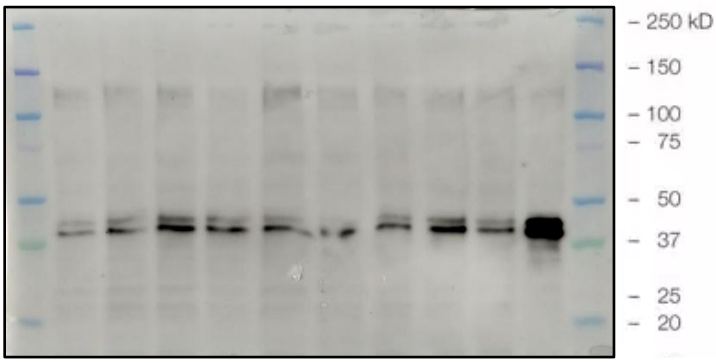


2) tERK 1/2



- **For Figure S4B**

1) pERK 1/2



2) tERK 1/2