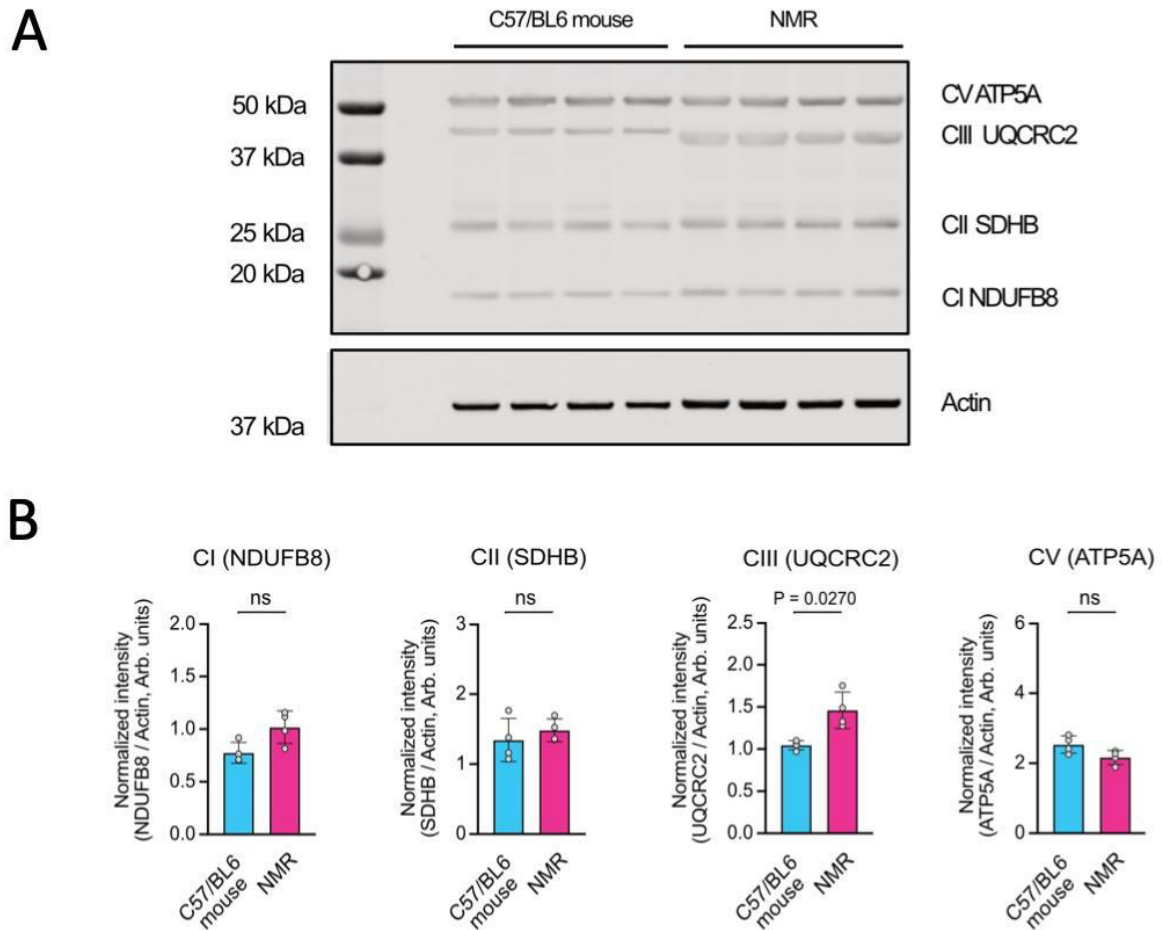


## Supplementary Table

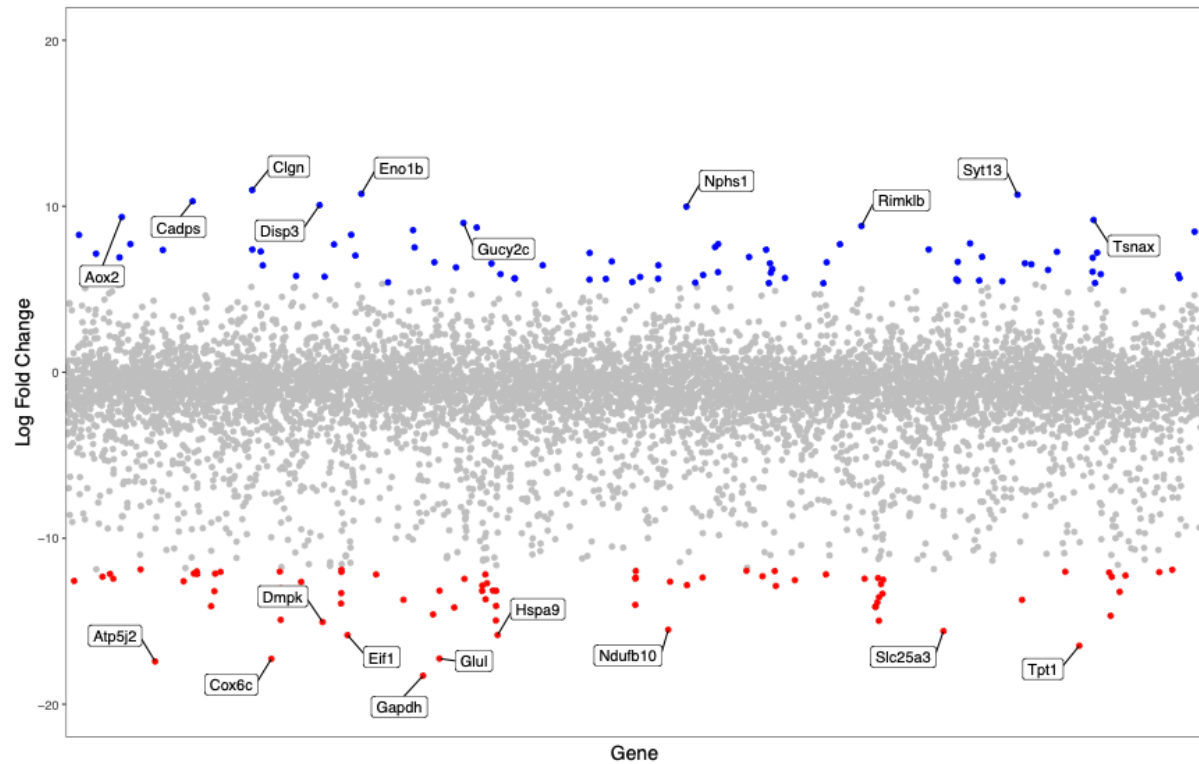
| Species                                  | Common name           | This study    |                 |                | Heart weight (mg) | Heart weight/body weight | Maximum lifespan (years) <sup>1</sup> | Soil Type                                           |
|------------------------------------------|-----------------------|---------------|-----------------|----------------|-------------------|--------------------------|---------------------------------------|-----------------------------------------------------|
|                                          |                       | Sample size   | Body weight (g) | Age (years)    |                   |                          |                                       |                                                     |
| <i>Heterocephalus glaber</i>             | Naked mole-rat        | n=14 (7m, 7f) | 32.9±4.8        | 5              | 178.0±33.6        | 4.4±0.6                  | >37                                   | Hard clays                                          |
| <i>Georchus capensis</i>                 | Cape mole-rat         | n=8 (2m, 6f)  | 154±16.9        | 5              | 571.7±63.1        | 3.3±0.2                  | 11                                    | Predominantly soft clays but sometimes loams        |
| <i>Bathyergus suillus</i>                | Cape-dune mole-rat    | n=7 (5m, 2f)  | 639±59.8        | 4-5            | 1642.5±219.0      | 2.8±0.3                  | >6                                    | Loose coarse sands                                  |
| <i>Cryptomys hottentotus hottentotus</i> | Common mole-rat       | n=8 (6m, 2f)  | 84.2±6.9        | 4-5            | 343.9±51.7        | 4.0±0.3                  | 11                                    | Hard clays and loams                                |
| <i>Cryptomys hottentotus pretoriae</i>   | Highveld mole-rat     | n=8 (3m, 5f)  | 102.7±11.1      | 4-5            | 559.8±50.9        | 4.7±0.3                  | 11                                    | Hard clays and loams                                |
| <i>Cryptomys hottentotus mahali</i>      | Mahali mole-rat       | n=5 (1m, 4f)  | 114.8±8.6       | 4              | N/A               | N/A                      | 11                                    | Hard clays and loams                                |
| <i>Cryptomys hottentotus natalensis</i>  | Natal mole-rat        | n=9 (3m, 6f)  | 82.3±6.7        | 4              | 469.9±13.2        | 4.3±0.04                 | 11                                    | Compacted thick clays                               |
| <i>Fukomys damarensis</i>                | Damaraland mole-rat   | n=11 (3m, 8f) | 124.6±8.2       | 6-7            | 583.3±32.6        | 4.3±0.3                  | 16                                    | Soft coarse sands and compacted fine kalahari sands |
| <i>Amblysomus hottentotus</i>            | Hottentot golden mole | n=3 (1m, 2f)  | 58.6±8.6        | Adult (>1year) | N/A               | N/A                      | >1                                    | Compacted thick clays                               |
| <i>Mus musculus</i>                      | C57/BL6 mouse         | n=5 (5m)      | 25.0±0.1        | 0.1            | 155.3±8.7         | 6.2±0.3                  | 2-3                                   | N/A                                                 |

**Table S1.** Morphological and life history characteristics of the taxa included in this study. m=male, f=female; N/A data not available.

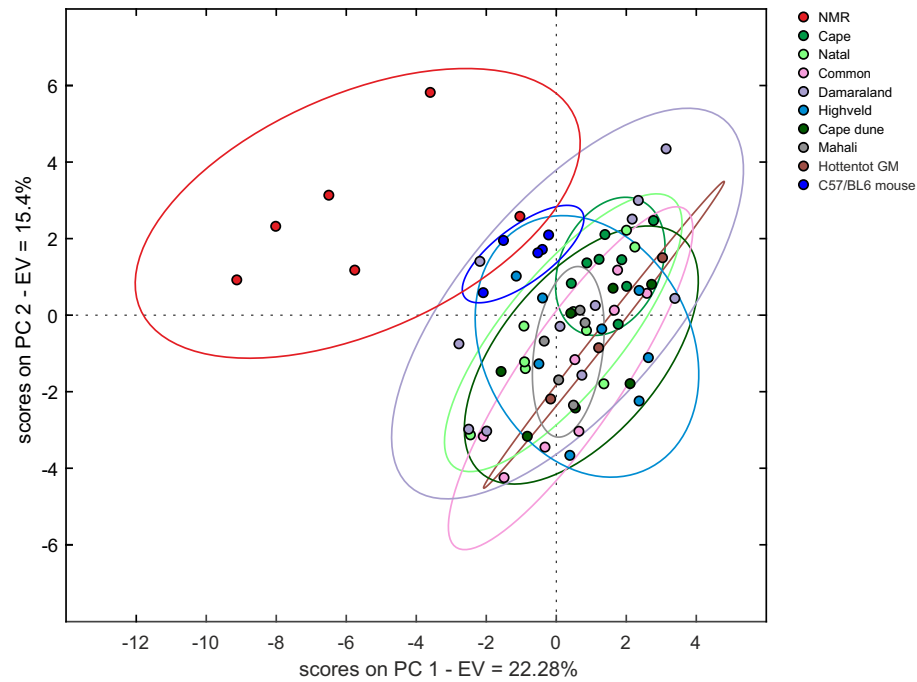
## Supplementary Figures



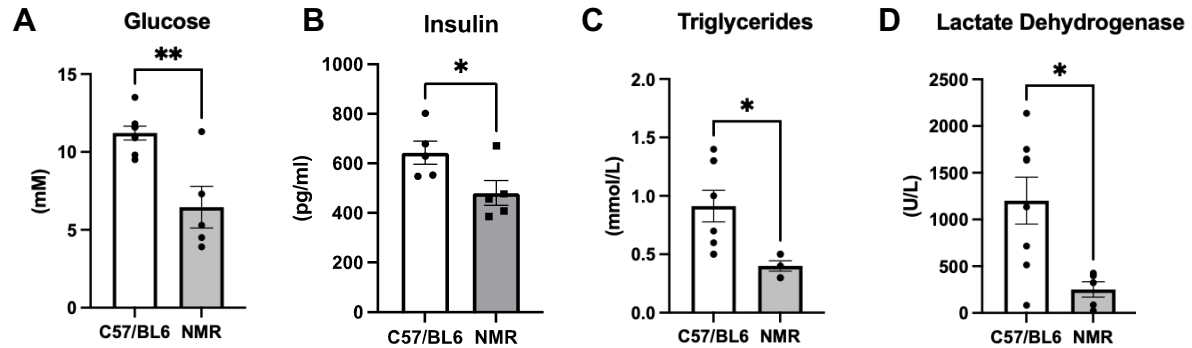
**Fig. S1.** Representative western blots ( $n = 4$  animals/group) for the assessment of protein expression of mitochondrial electron transport chain (ETC) complexes, lactate dehydrogenase (LDH) and monocarboxylate transporter 1 (MCT-1) (A) Western blot of indicative subunits (ATP5A, UQCRC2, SDHB and NDUFB8) of mitochondrial ETC protein complexes (Complex I, II, III, and V) isolated from C57/BL6 mice and NMR hearts. (B) Quantification of subunits of oxidative phosphorylation complexes in C57/BL6 and NMR hearts. All experimental groups contain 4 animals per group and western blot analysis was performed using several technical replicates; protein expression normalised to loading control (details on y axis). Statistical analysis was performed using unpaired two-tailed t test (with Welch's correction). Data mean $\pm$ SEM.



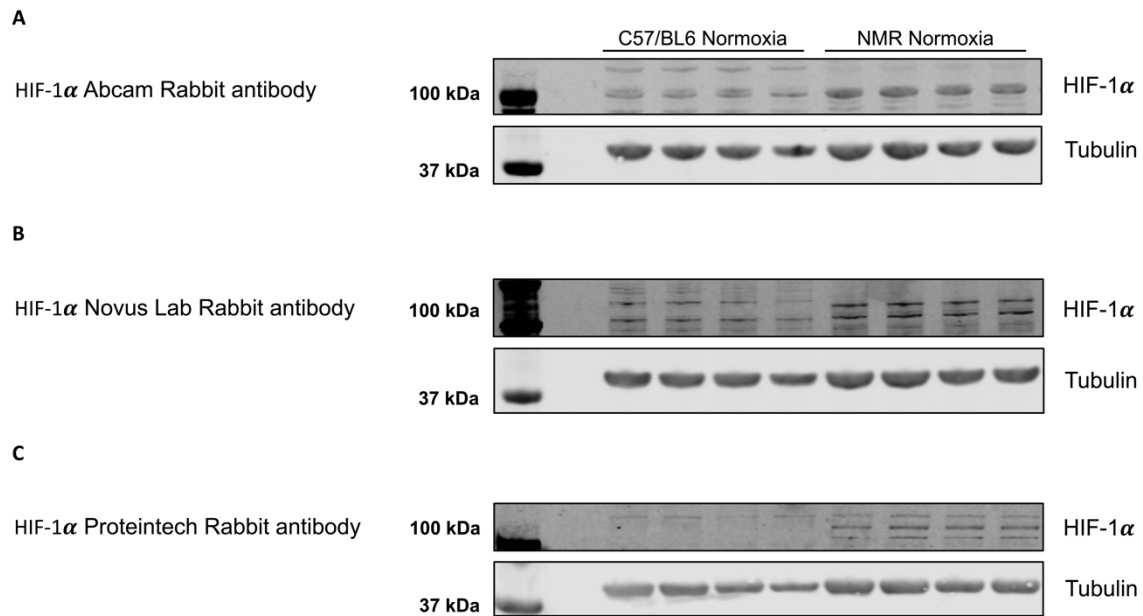
**Fig. S2.** Manhattan plot Log fold change gene expression NMR vs C57/BL6 Manhattan plot with top 1% gene expressed highlighted and top 10 genes labelled by name (blue for the NMR and red for the mouse). Note that of the top 20 expressed genes in the NMR, only FOUR are also expressed in the mouse and NONE of the top 12 in the NMR are also expressed in the mouse. The gene “clgn” has the highest logfold change but it is rank 1760 in genes ordered by expression (FPKM) in the NMR.



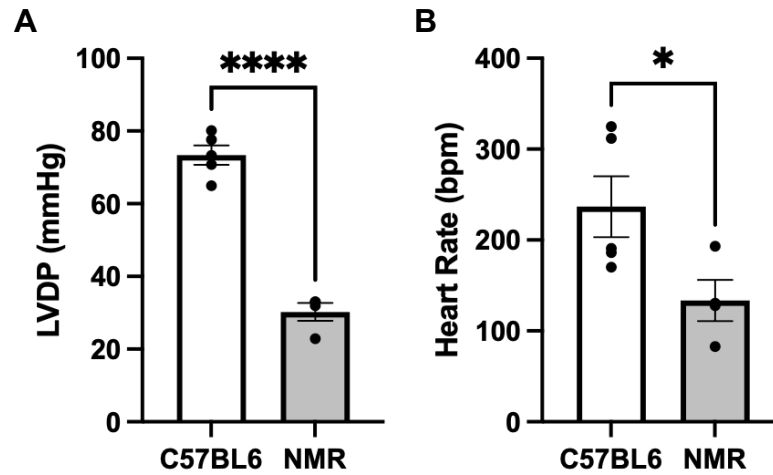
**Fig. S3.** Principal Component Analysis (PCA) of  $^1\text{H}$  nuclear magnetic resonance metabolomic data showing separation of the NMR metabolomics data compared to all other genera. NMR ( $n = 6$ ), Cape mole-rat ( $n = 8$ ), Natal mole-rat ( $n = 9$ ), Common mole-rat ( $n = 8$ ), Damaraland mole-rat ( $n = 11$ ), Highveld mole-rat ( $n = 8$ ), Cape dune mole-rat ( $n = 7$ ), Mahali mole-rat ( $n = 5$ ), Hottentot golden mole ( $n = 3$ ) and C57/BL6 mouse ( $n = 5$ ), where  $n$  correspond to biological repeats. Ellipses correspond to 90% confidence intervals.



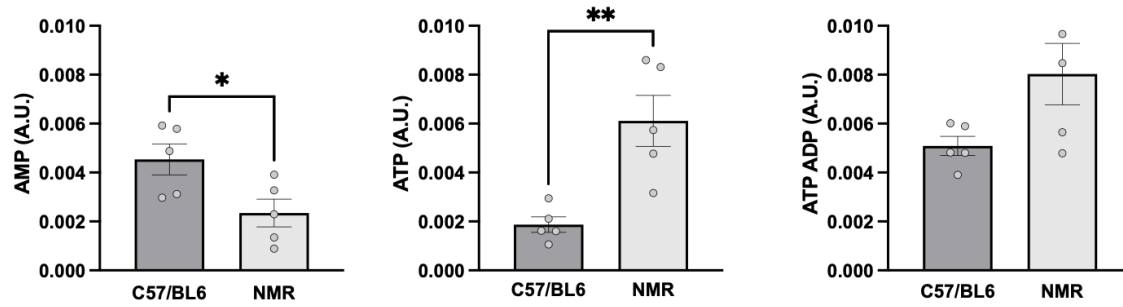
**Fig. S4.** Plasma metabolite concentrations of (A) glucose, (B) insulin, (C) triglycerides and (D) lactate dehydrogenase in NMR versus C57BL6 control mouse (glucose, triglycerides, lactate dehydrogenase showing reduced metabolite concentrations (NMR, n = 4 animals / group; C57BL6 n = 8 animals / group, Insulin n=5/group), data mean ± SEM, \*P<0.05, \*\* P<0.01 two-tailed t test. Glucose P=0.0019, insulin P=0.04, triglycerides P=0.014, lactate dehydrogenase P=0.014



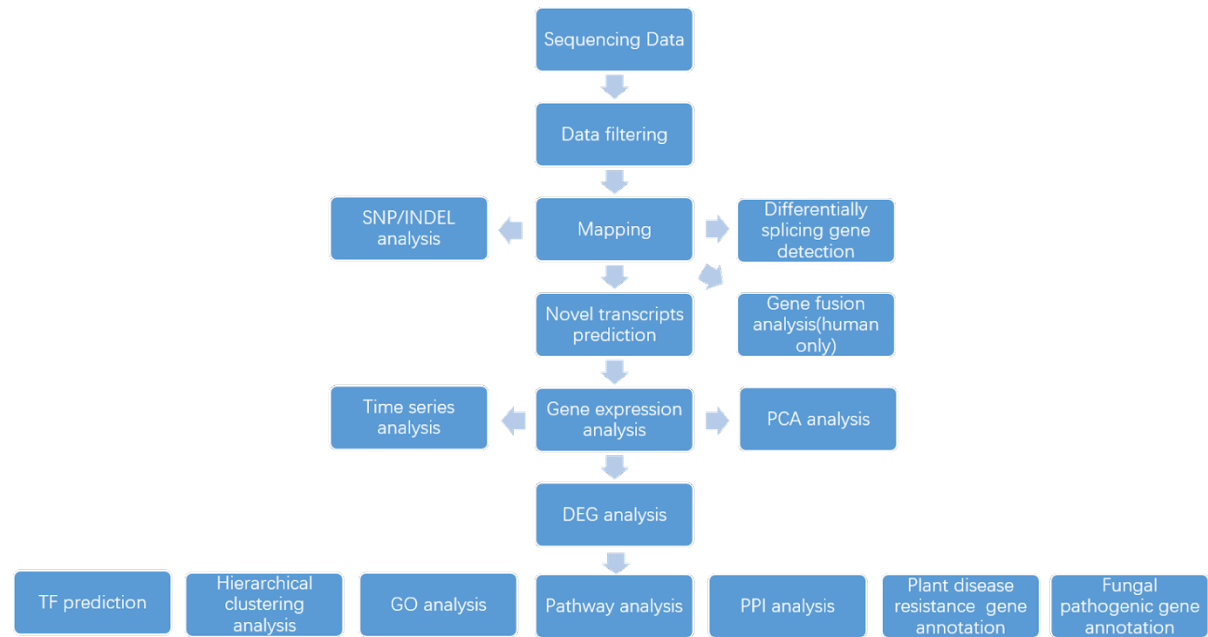
**Fig. S5.** Representative HIF-1 $\alpha$  western blots using three different antibodies against different HIF-1 $\alpha$  protein epitopes in cardiac tissue from C57/BL6 mouse and NMR (n = 4 animals / group). (A) Hif1 $\alpha$  Abcam rabbit Ab, (B) Hif1 $\alpha$  Novus lab rabbit Ab, (C) Hif1 $\alpha$  Proteintech rabbit Ab. Uncropped blots provided at the end of the document.



**Fig. S6.** *Ex vivo* cardiac function in Langedorff perfused hearts of NMR (n = 4 animals / group) and C57BL6 mouse (n = 5 animals / group), (A) left ventricular developed pressure (LVDP, mmHg) and (B) heart rate (HR, bpm), \*\*\* P=0.0001 \*P=0.047 vs control by two-tailed t test.



**Fig S7. Individual components of myocardial total adenine nucleotide pool in post-ischemia.** (n=5/group), Data mean + SEM, \* P<0.05 \*\* P<0.01 by two-tailed t test. AMP P=0.0328, ATP P=0.0045, ATPADP P=0.055



**Fig S8.** Summary of the bioinformatics workflow.

*Faulkes, Eykyn, Miljkovic et al.*

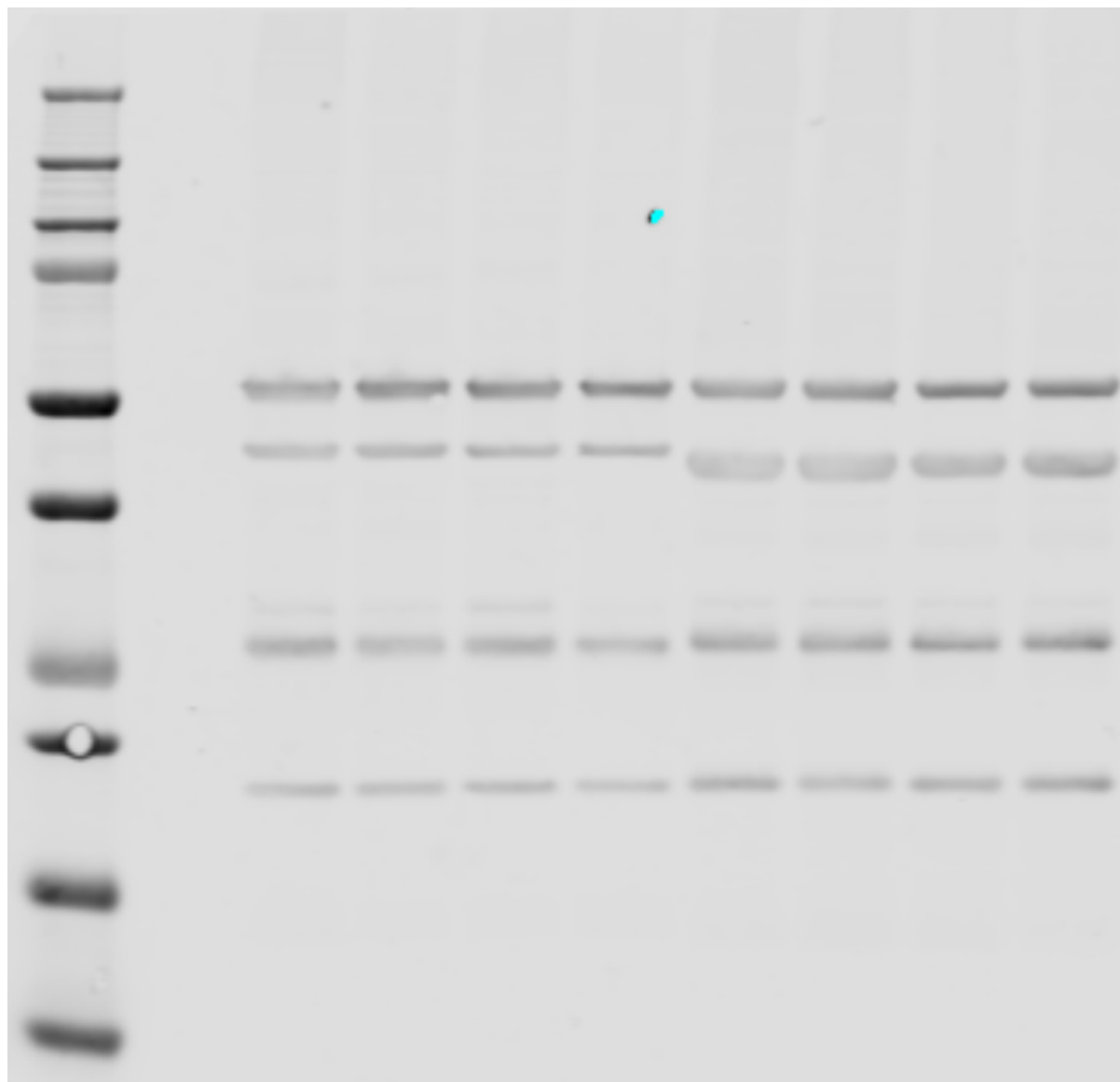
*“Naked mole rats have distinctive cardiometabolic and genetic adaptations to their underground low-oxygen lifestyles”*

### **Supplementary Reference**

1. Tacutu, Robi et al. “Human Ageing Genomic Resources: new and updated databases.” *Nucleic acids research* vol. 46,D1 (2018): D1083-D1090.  
doi:10.1093/nar/gkx1042

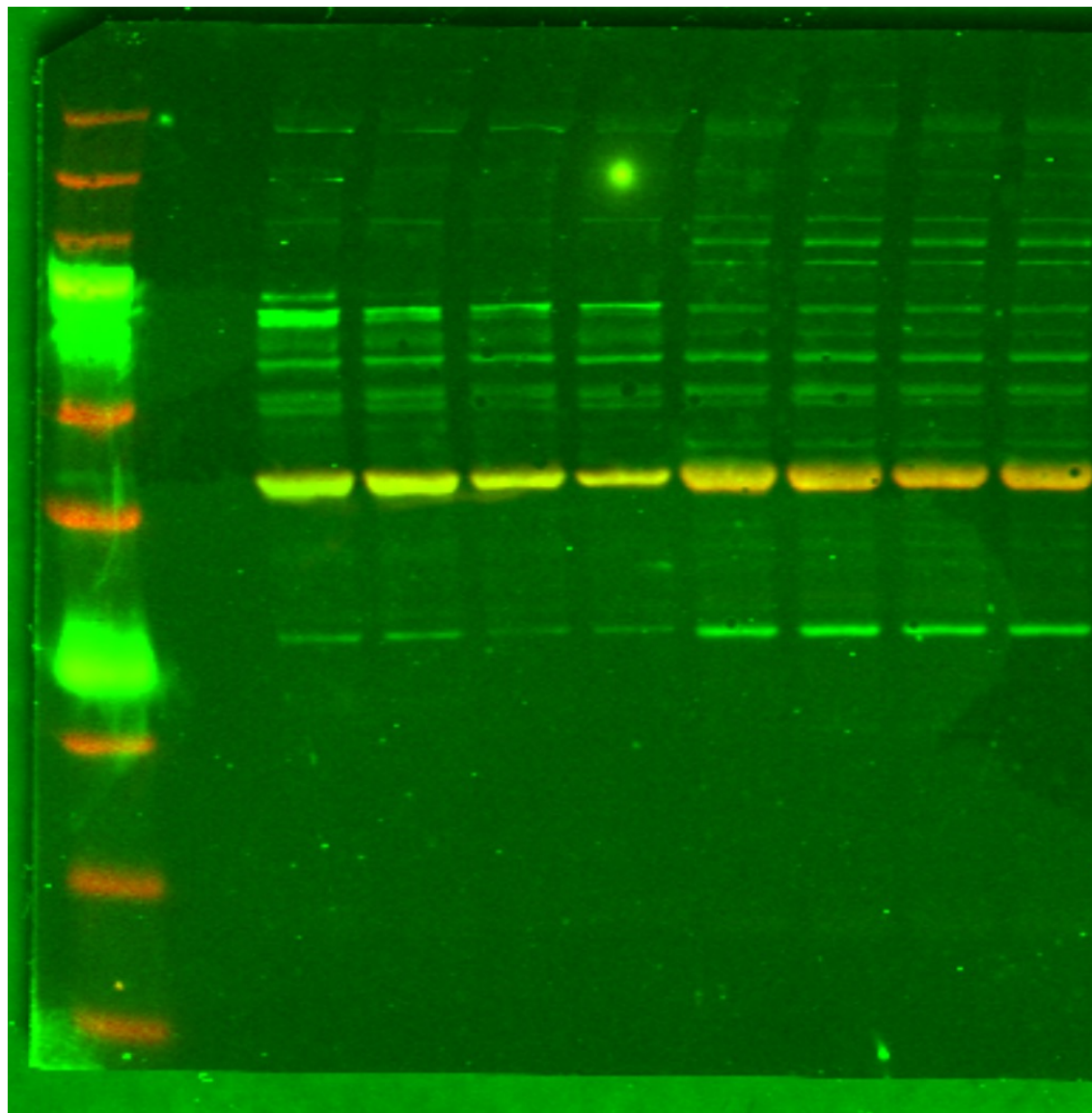
## Uncropped gels of blots supplied in Supplementary Figures

OXPHOS (Figure S1)

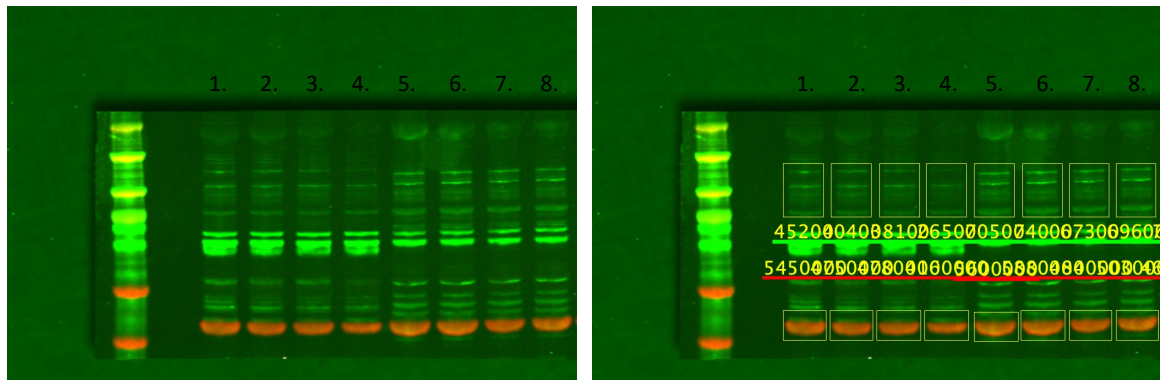


HIF1 $\alpha$  Proteintech Antibody (Figure S5)

1. 2. 3. 4. 5. 6. 7. 8.



# HIF1 $\alpha$ Abcam Antibody (Figure S5)



# HIF1 $\alpha$ Novus Lab Antibody (Figure S5)

