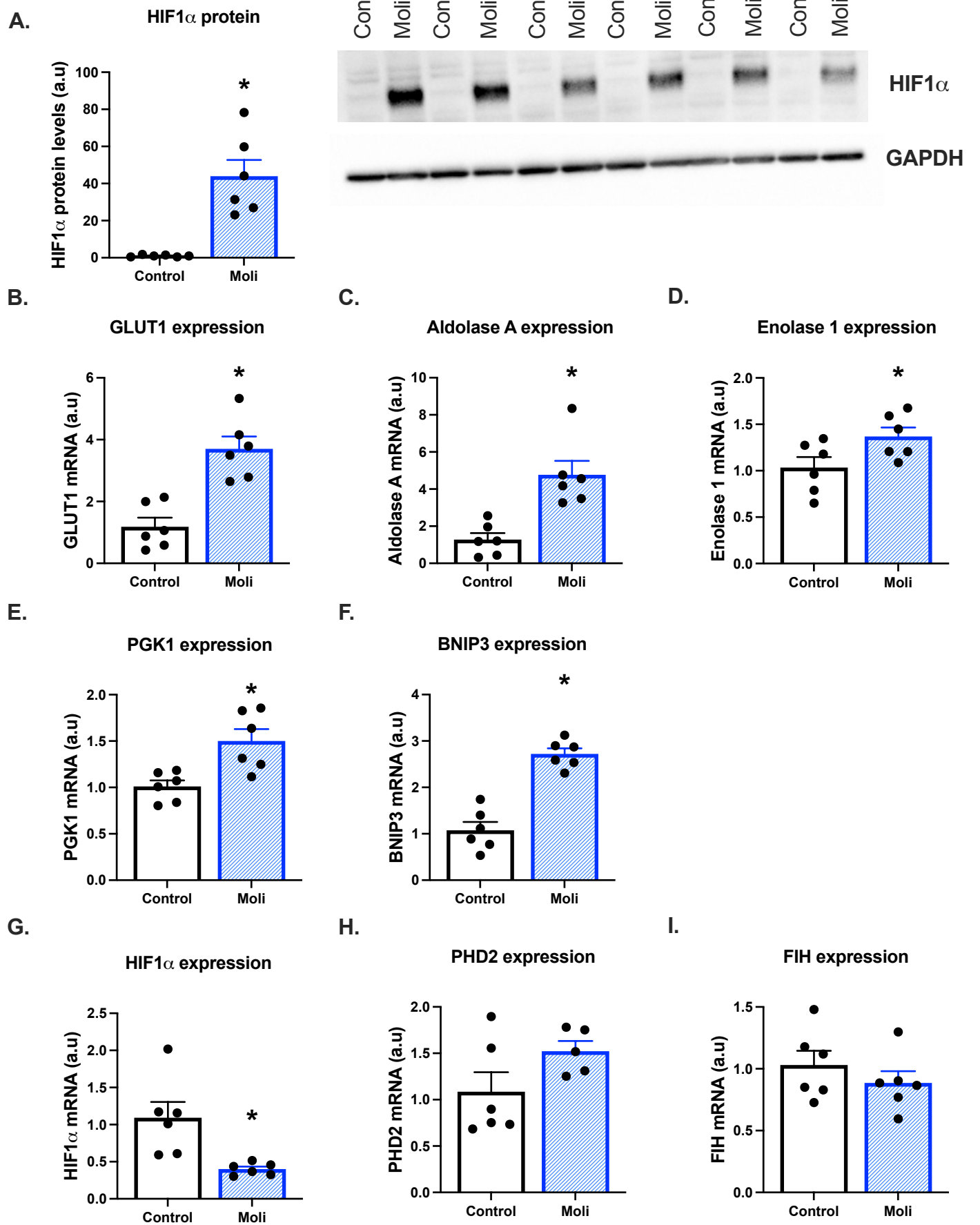


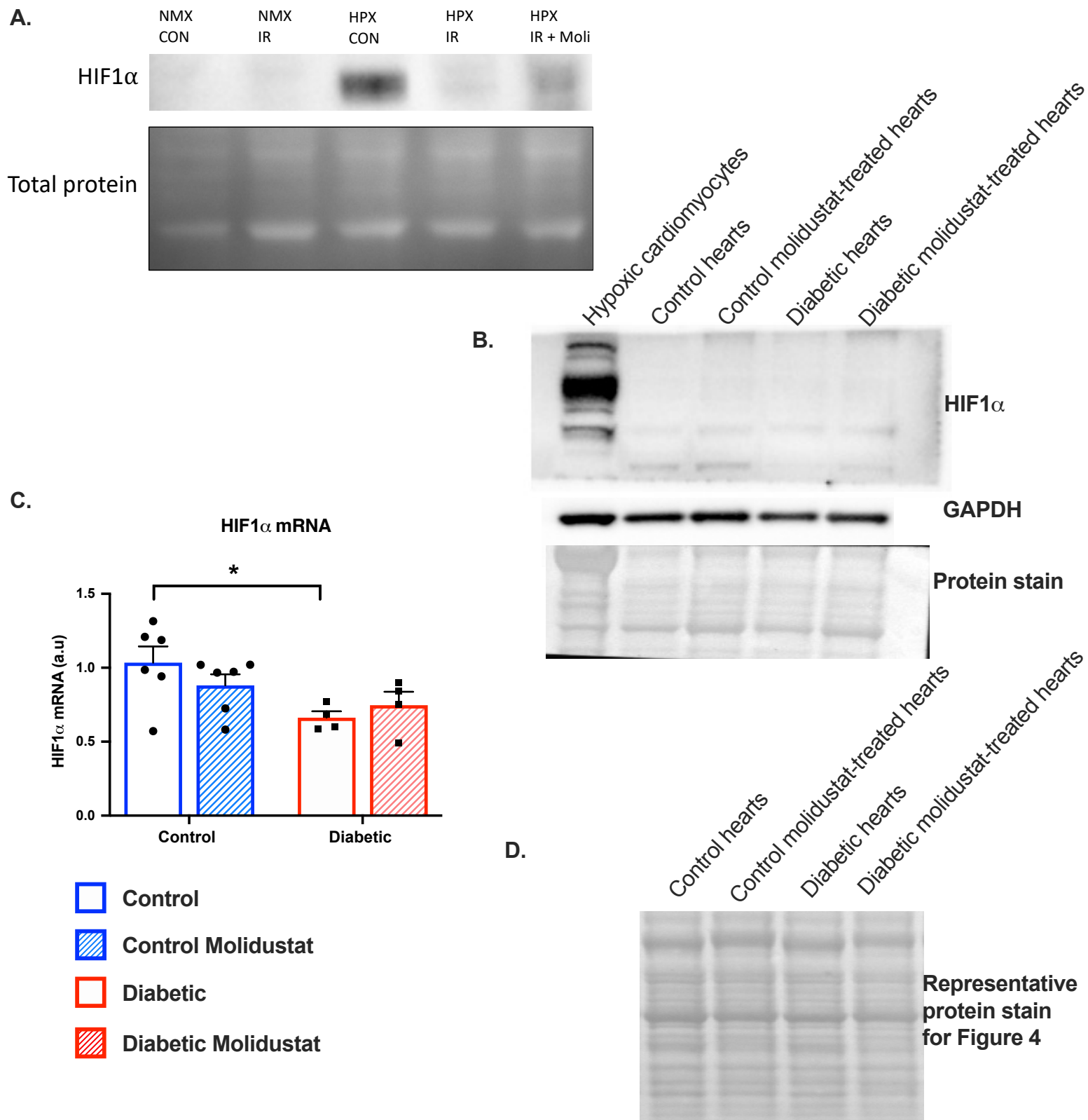
# Supp Figure 1



## Supplementary Figure 1 – Molidustat increases HIF signalling in M180 human cardiomyocytes.

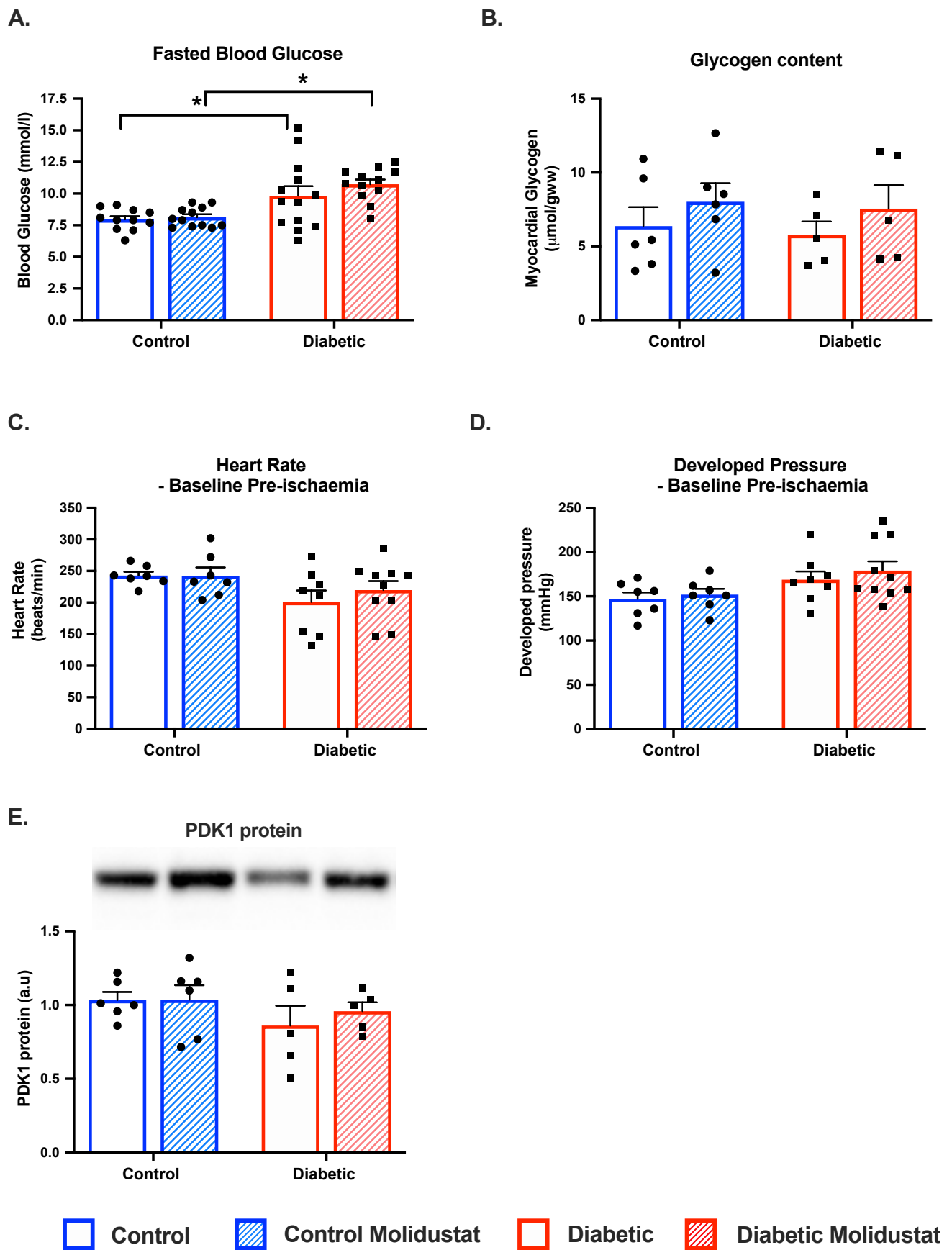
Hypoxia-Inducible Factor (HIF)1 $\alpha$  protein levels in control and molidustat-treated (Moli) human inducible pluripotent stem cell-derived cardiomyocytes (A). Expression of HIF1 $\alpha$  target genes in control and molidustat-treated cardiomyocytes, including glucose transporter 1 (GLUT1), aldolase A, enolase 1, phosphoglycerate kinase 1 (PGK1), bcl2/adenovirus E1B 19kDa interacting protein 3 (BNIP3), HIF1 $\alpha$  mRNA, prolyl hydroxylase domain (PHD)2, and factor inhibiting HIF (FIH) (B-I). \*  $p < 0.05$  vs. control.

## Supp Figure 2



### Supplementary Figure 2

Additional example blot for Figure 2 (A). HIF1 $\alpha$  protein levels were not detectable in control and diabetic hearts with and without molidustat treatment, due to the drug being metabolised out of the system during the 24 hours between the final molidustat dose and collection of the tissue. Blots contain hypoxic cardiomyocytes as a positive control, and GAPDH protein and ponceau protein stain as housekeeper (B). HIF1 $\alpha$  mRNA in control and diabetic hearts, with and without molidustat treatment (C). Representative ponceau protein stain as housekeeper for Figure 4 (D). \*  $p < 0.05$  vs. untreated control.



**Supplementary Figure 3**

Fasted blood glucose from control and diabetic rats with and without molidustat treatment (A). Myocardial glycogen concentration in control and diabetic hearts, with and without molidustat treatment (B). Heart rate and developed pressure during baseline perfusion prior to ischaemia, in control and diabetic hearts with and without molidustat treatment (C-D). Myocardial pyruvate dehydrogenase kinase 1 (PDK1) in control and diabetic hearts, with and without molidustat treatment (E). \*  $p < 0.05$  vs respective control group.

# Supp Table

**Supplementary Table. Primer sequences**

<b>Gene</b>	<b>Forward sequence</b>	<b>Reverse sequence</b>
<i>VEGFA</i>	CAAGCCAAGGCGGTGAGCCA	TCTGCCGGAGTCTCGCCCTC
<i>PHD2</i>	CAGAAGGCAAAGCCCAGTTTG	CCTCACACCTTTTTCACCTTGTA G
<i>BNIP3</i>	GAATTTCTGAAAGTTTTCTTCCA	TTGTCAGACGCCTTCCAATA
<i>GLUT1</i>	AAGCTGACGGGTCGCCTCATG	CTCTCCCCATAGCGGTGGACC
<i>Aldolase A</i>	GGGGCTTCAGGTTTCCCTA	GGTAGTAGCAAGTTCCTGCGG
<i>Enolase 1</i>	GCCCTGGTTAGCAAGAACT	GAATGGCGTTCGCACCAAAC
<i>PGK1</i>	GAATGGGAAGCTTTTGCCCG	GCAGTGTCTCCACCACCTATG
<i>FIH</i>	GCGCAGTTATAGCTTCCCGAC	GCACCACAGGCTCCTCATTCT
<i>HIF1<math>\alpha</math></i> (cells) (tissue)	CCACAGGACAGTACAGGATG GGCGAGAACGAGAAGAAAAATAGG	TCAAGTCGTGCTGAATAATACC GTGGCAACTGATGAGCAAGC
<i>SDHA</i>	TCCTTCCCCTGTGCATTACAA	CGTACAGACCAGGCACAATCTG
<i>UBC</i>	CCTGGTGCTCCGTCTTAGAG	TTTCCCAGCAAAGATCAACC