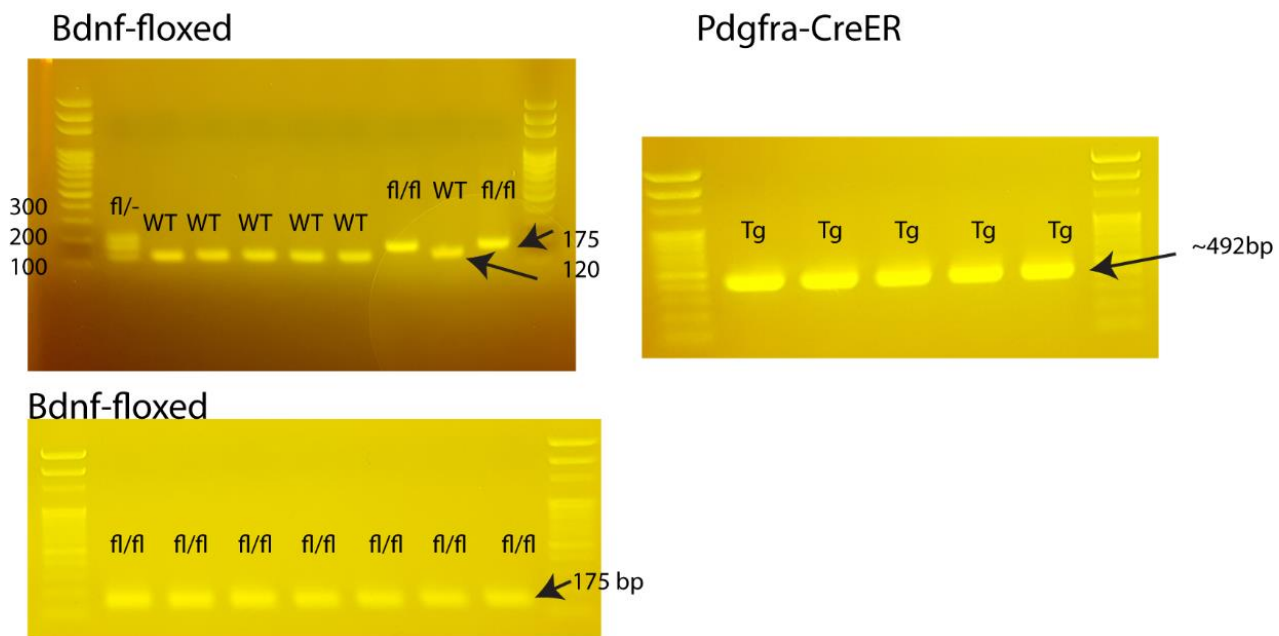


## **Aging-Induced Brain-Derived Neurotrophic Factor in Adipocyte Progenitors Contributes to Adipose Tissue Dysfunction**

**Hyun-Doo Song<sup>1,#</sup>, Sang Nam Kim<sup>2,#</sup>, Abhirup Saha<sup>2,#</sup>, Sang-Yeop Ahn<sup>1</sup>, Seun Akindehin<sup>1</sup>, Yeonho Son<sup>2</sup>, Yoon Keun Cho<sup>2</sup>, MinSu Kim<sup>2</sup>, Ji-Hyun Park<sup>2</sup>, Young-Suk Jung<sup>3</sup>, Yun-Hee Lee<sup>2\*</sup>**

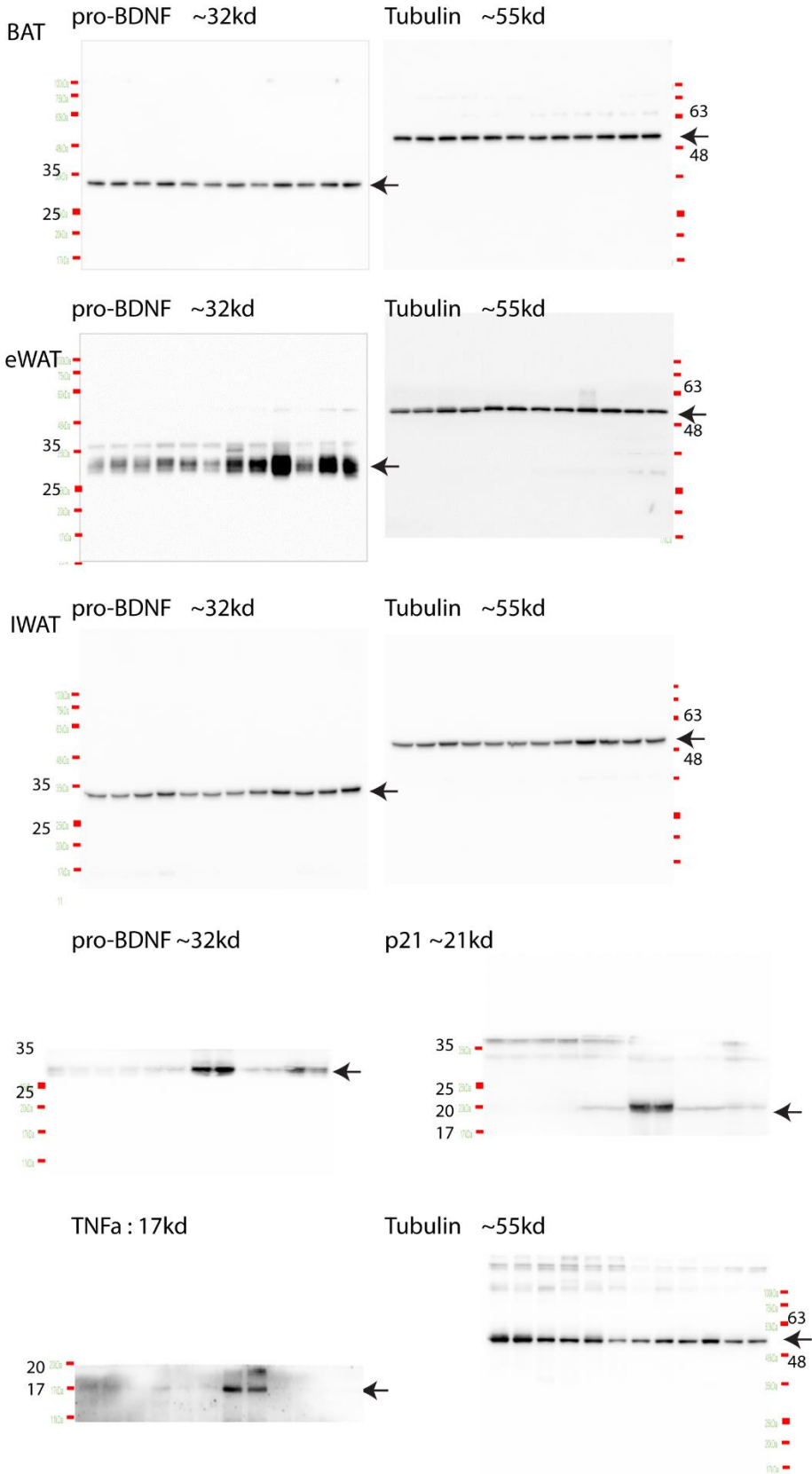
<sup>1</sup>College of Pharmacy, Yonsei University, Incheon, Republic of Korea. <sup>2</sup>College of Pharmacy and Research Institute of Pharmaceutical Sciences, Seoul National University, Seoul, Republic of Korea. <sup>3</sup>College of Pharmacy, Pusan National University, Busan, Republic of Korea.

# SUPPLEMENTARY DATA



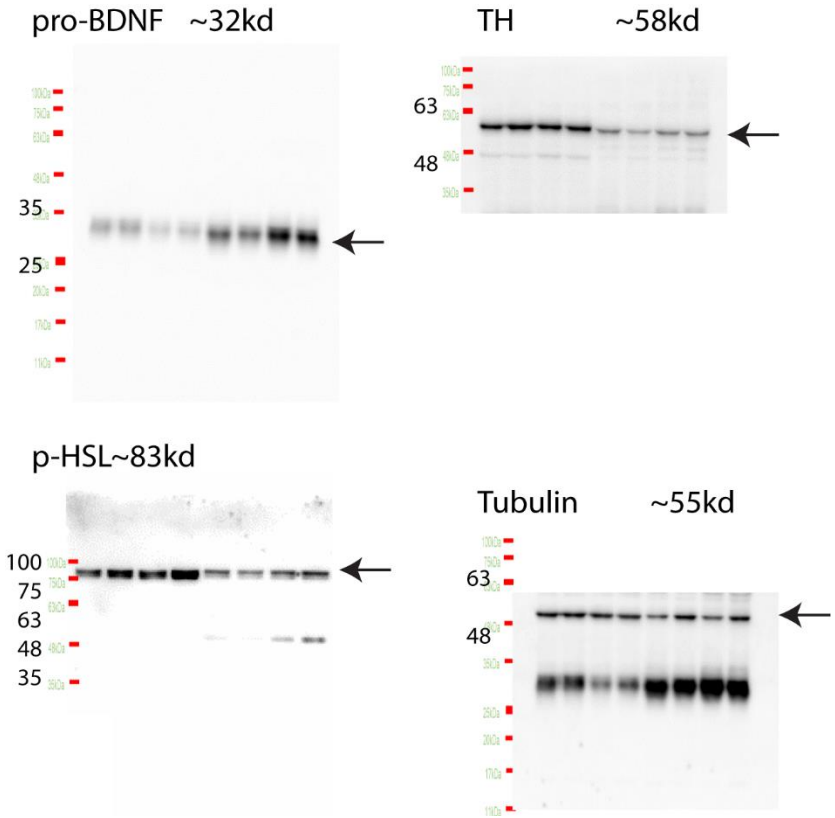
Supplementary Figure 1. Genotyping of BDNF floxed mice and Pdgfra\_CreERT2 mice.

# SUPPLEMENTARY DATA

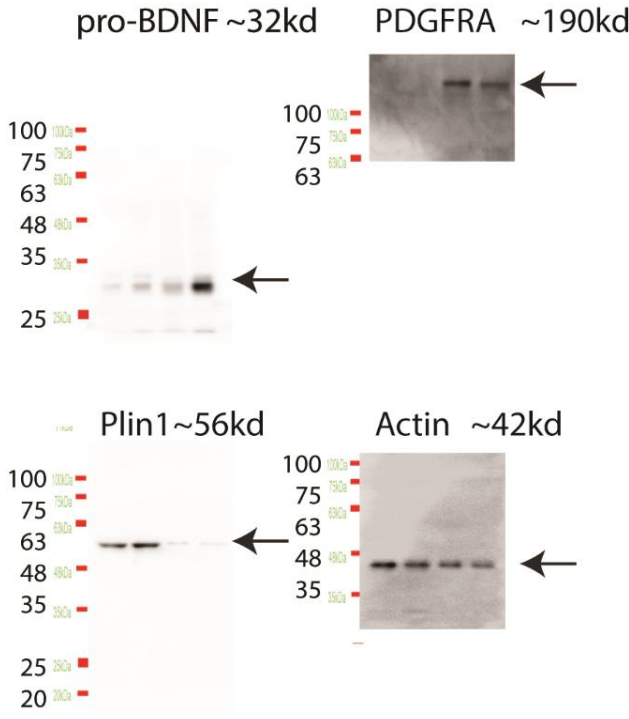


Supplementary Figure 2. Membrane images of western blot analyses used for Figure 1.

# SUPPLEMENTARY DATA

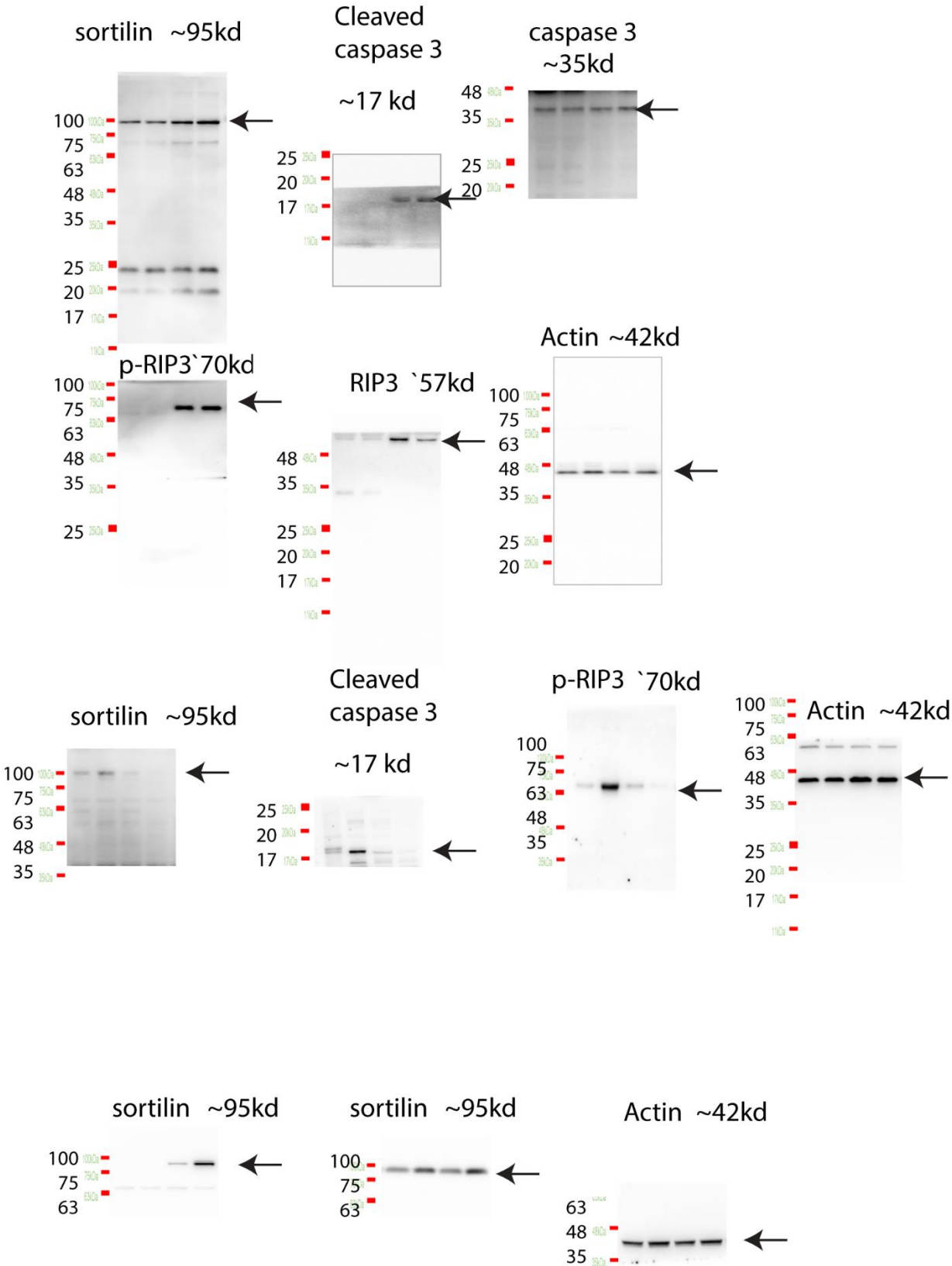


Supplementary Figure 3. Membrane images of western blot analyses used for Figure 2.



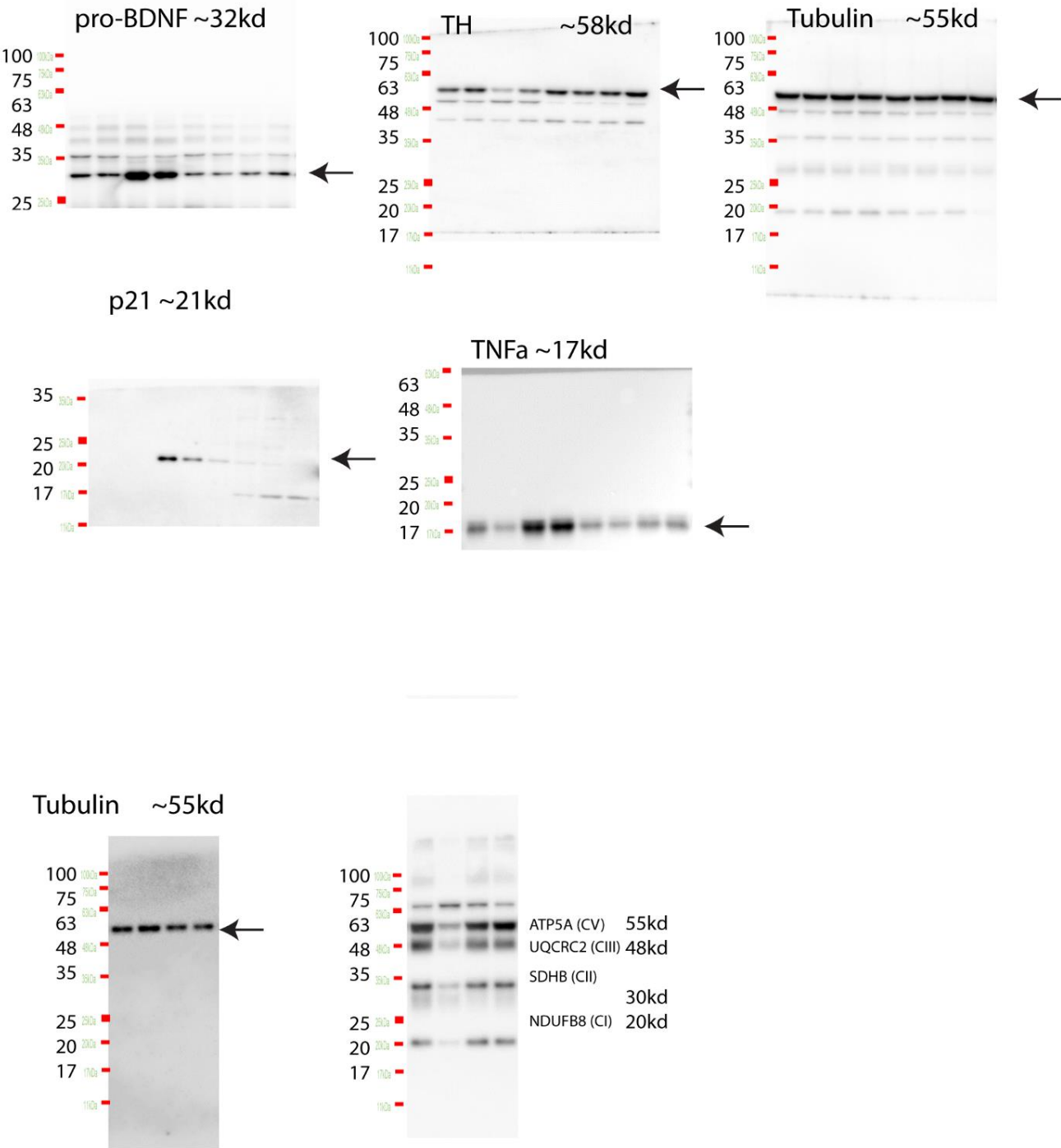
Supplementary Figure 4. Membrane images of western blot analyses used for Figure 3 and 4.

# SUPPLEMENTARY DATA



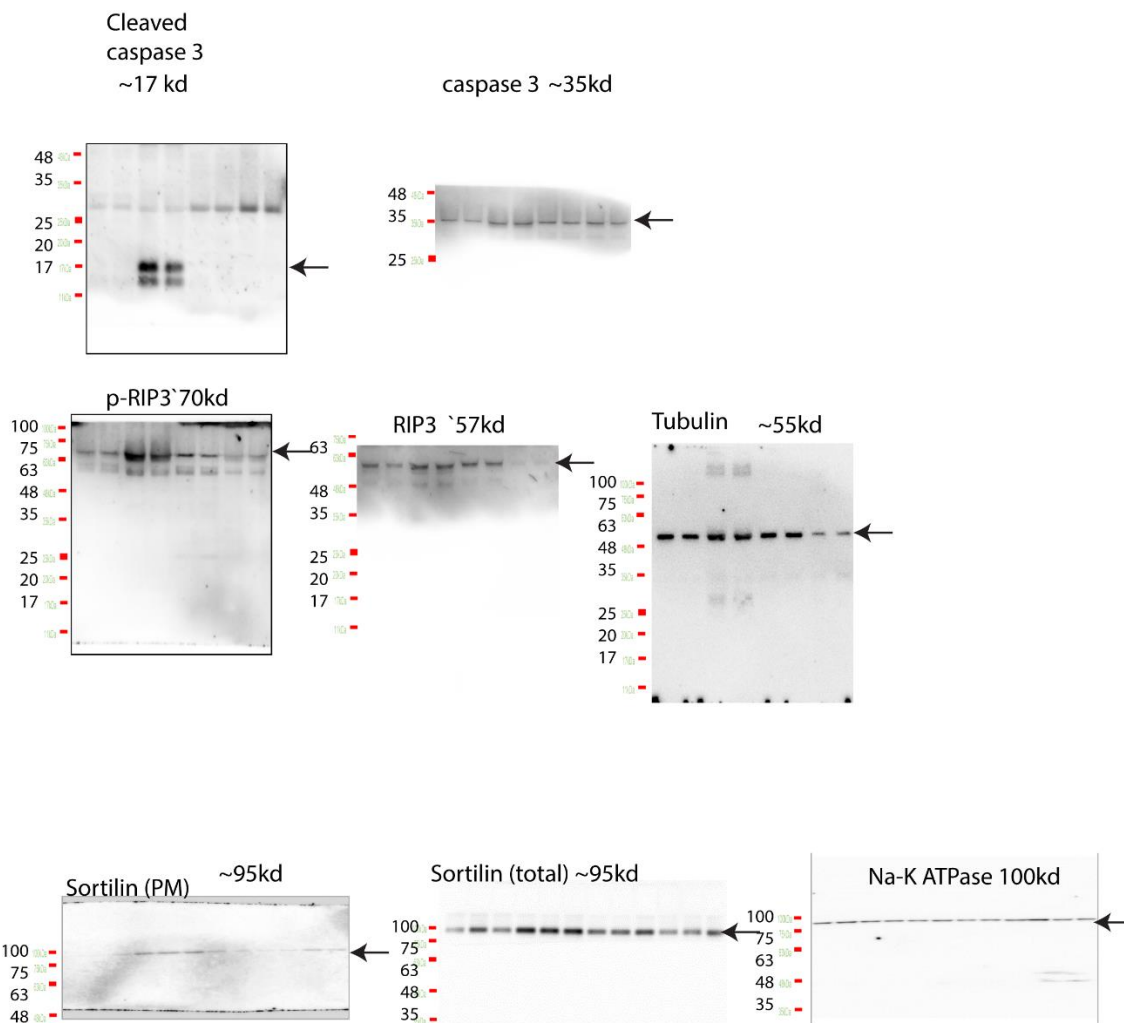
Supplementary Figure 5. Membrane images of western blot analyses used for Figure 5.

# SUPPLEMENTARY DATA

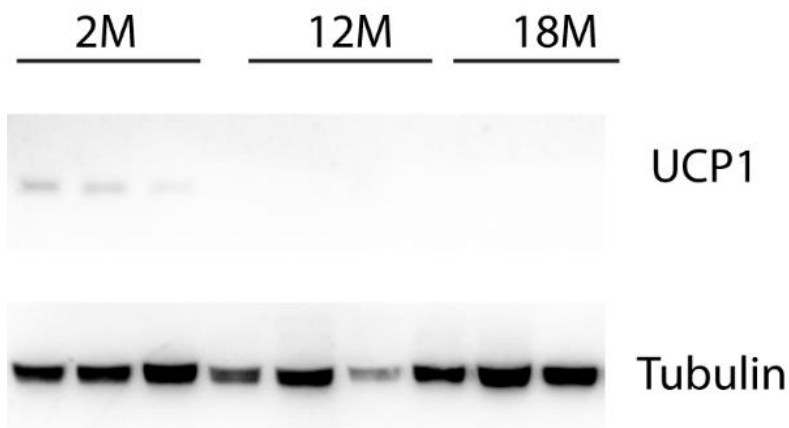


Supplementary Figure 6. Membrane images of western blot analyses used for Figure 6.

# SUPPLEMENTARY DATA

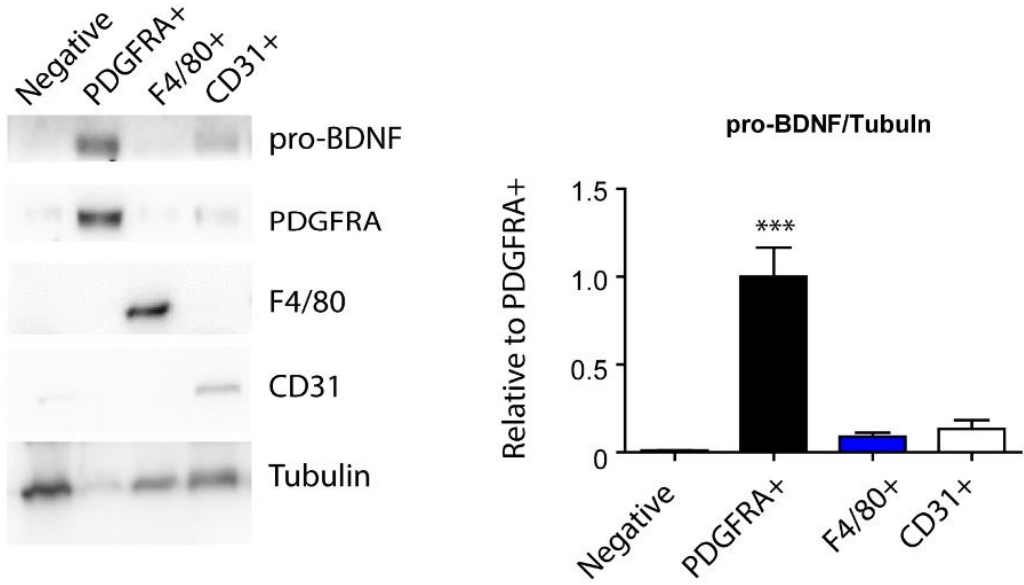


Supplementary Figure 7. Membrane images of western blot analyses used for Figure 7.

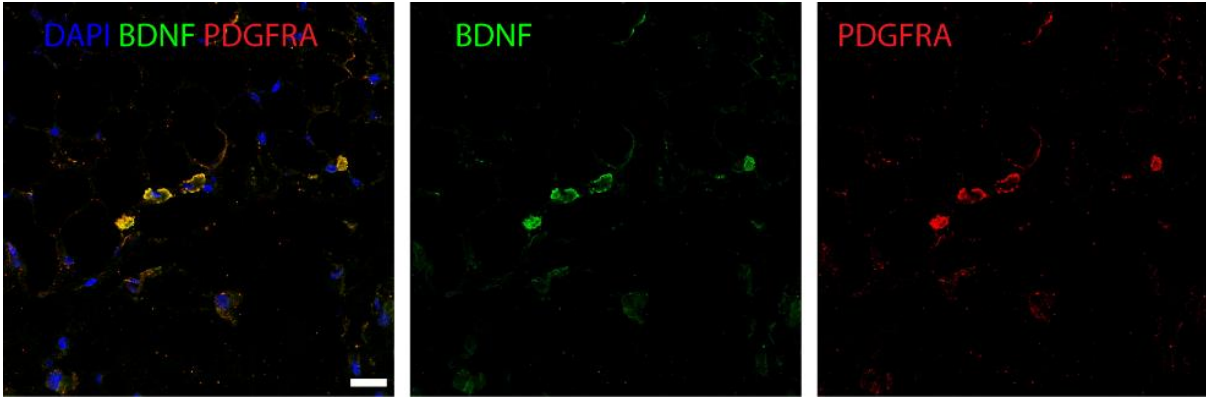


Supplementary Figure 8. Immunoblot analysis of UCP1 expression in eWAT of mice.

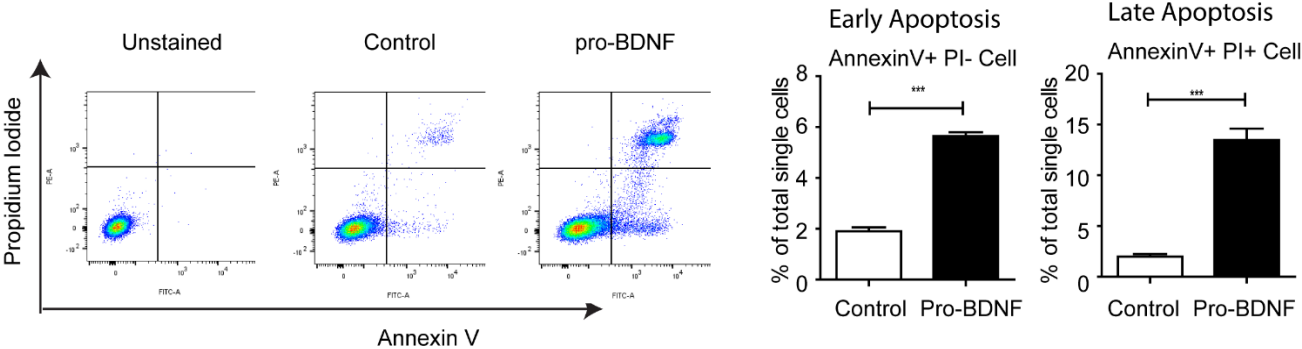
# SUPPLEMENTARY DATA



Supplementary Figure 9. Immunoblot analysis of pro-BDNF expression in stormovascular fractions of eWAT of 18-month-old WT mice. (n=3, t-test (comparison to levels in F4/80+ cells), \*\*\*p<0.001, Negative: F4/80-, CD31-, PDGFRA- stormovascular fraction).



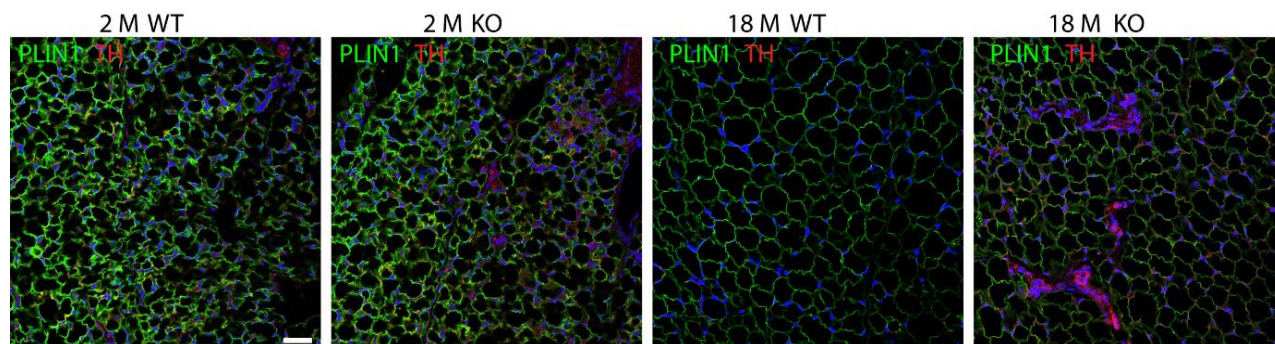
Supplementary Figure 10. Representative images of BDNF and PDGFRA+ expression in paraffin sections of eWAT of 18-month-old mice. Nuclei were counterstained with DAPI. Size bar = 20µm.



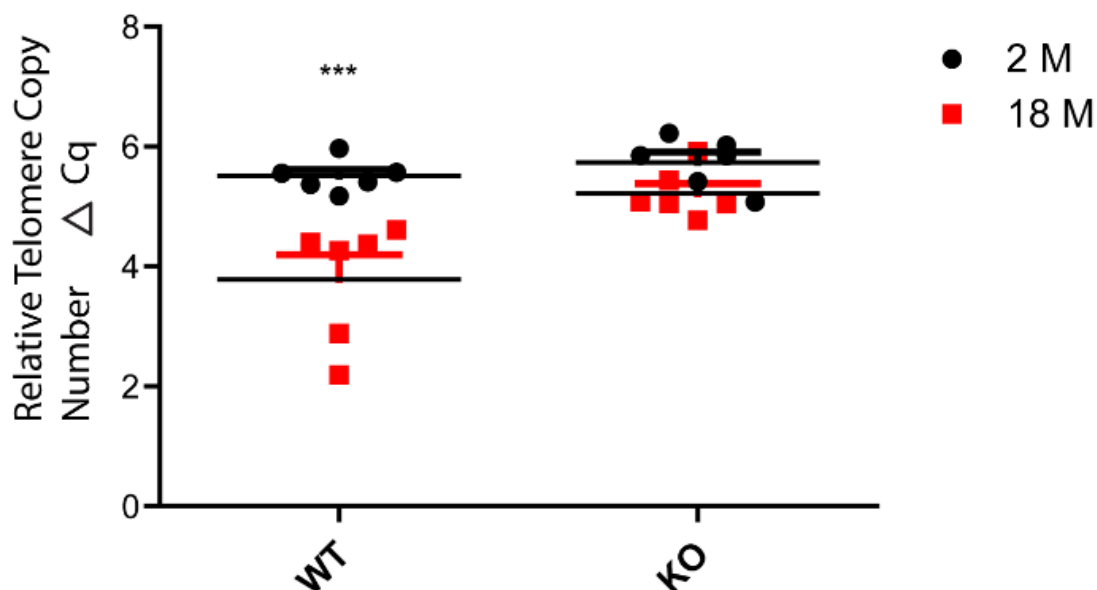
Supplementary Figure 11. Flow cytometric analysis of Annexin V/PI-stained, apoptotic cells after 24hrs of pro-BDNF treatment (10ng/ml) (n = 3, t-test, \*\*\*p<0.001).



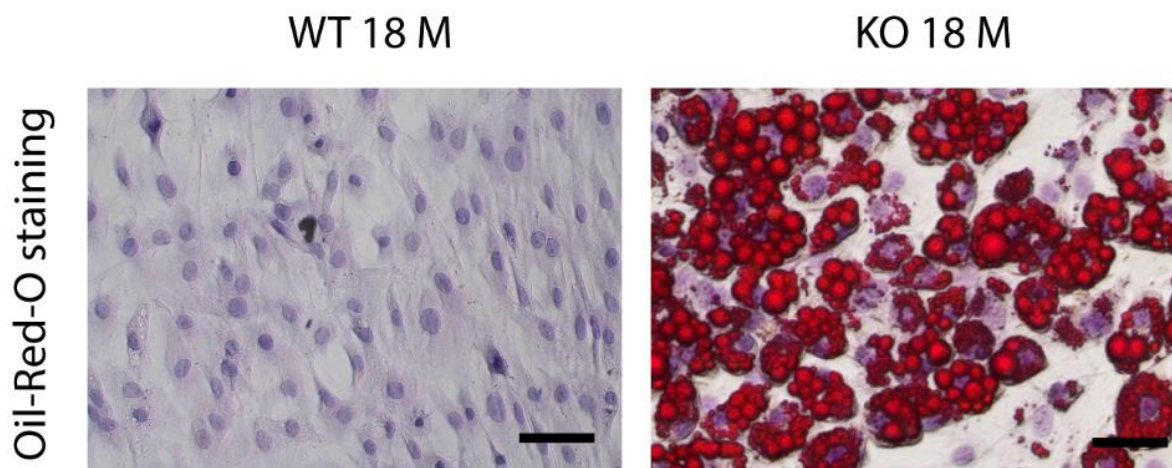
## SUPPLEMENTARY DATA



Supplementary Figure 12. Representative images of double staining for tyrosine hydroxylase (TH) and perilipin (PLIN1) in paraffin sections of eWAT of BDNF<sup>Pdgfra</sup>KO and WT mice. Nuclei were counterstained with DAPI (Size bar = 100 $\mu$ m).

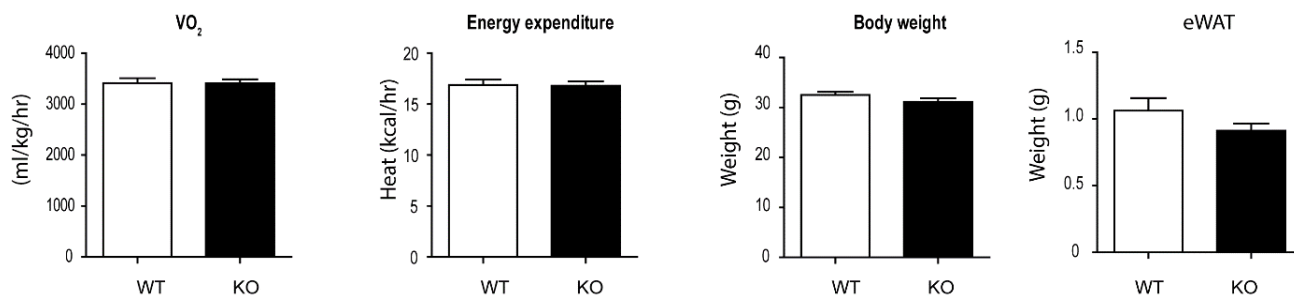


Supplementary Figure 13. Comparison of relative telomere copy number in eWAT between 2-month- and 18-month-old mice of BDNF<sup>Pdgfra</sup>KO mice and WT controls. (n = 6, t-test, \*\*\*p<0.001). *36B4* was used for a single copy gene control.

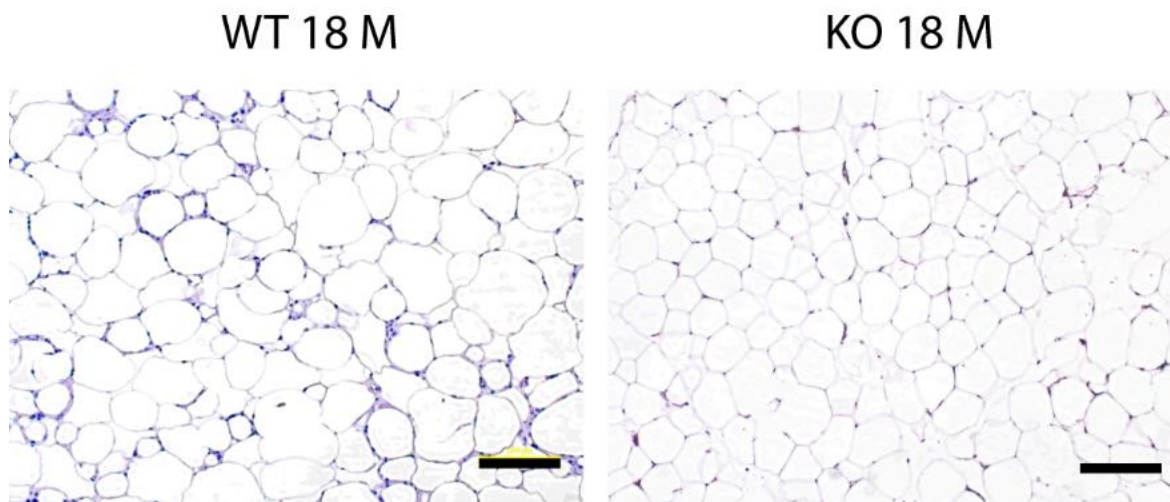


Supplementary Figure 14. Oil Red O staining of differentiated progenitor cells obtained from eWAT of BDNF<sup>Pdgfra</sup>KO mice and WT control mice (size bars = 25 $\mu$ m). Hematoxylin and eosin were used for counterstain.

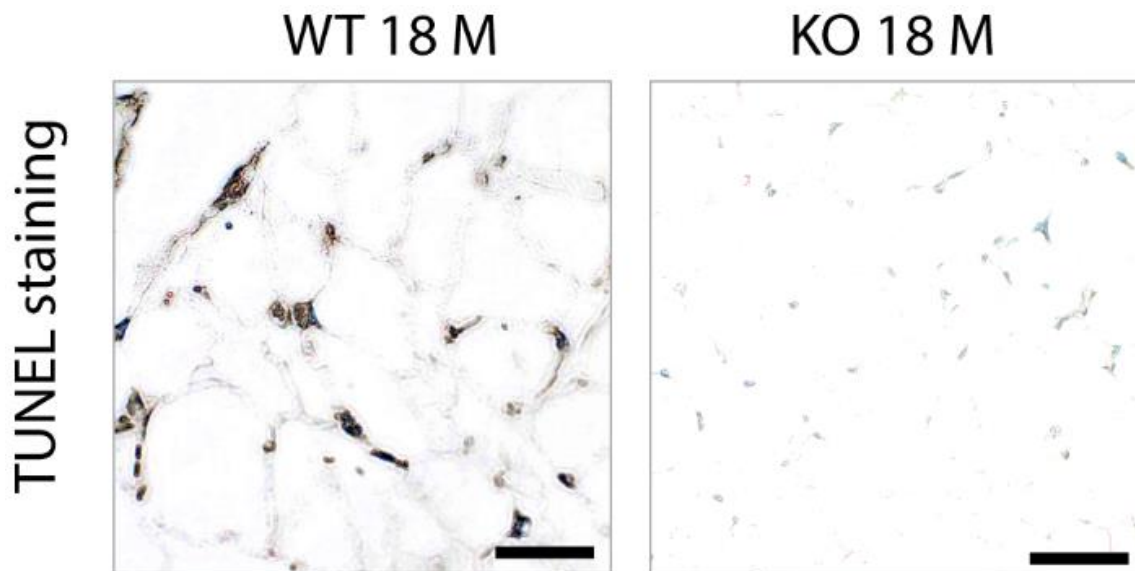
## SUPPLEMENTARY DATA



**Supplementary Figure 15.** Indirect calorimetry analysis, body weight and eWAT mass of 18-month-old BDNF<sup>Pdgfra</sup> KO mice and WT control mice. There was no statistical difference between KO and WT mice. ( $p = 0.968$  for VO<sub>2</sub>;  $p = 0.9008$  for Energy expenditure;  $p = 0.1843$  for Body weight;  $p = 0.1969$  for eWAT mass,  $n = 6$ ).

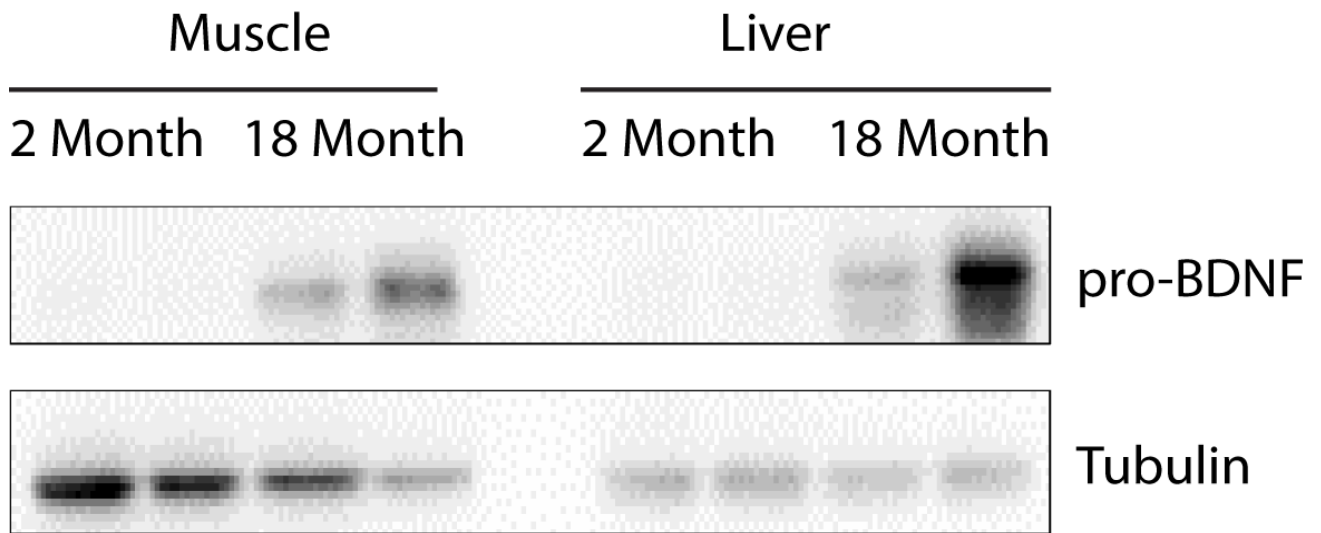


**Supplementary Figure 16.** Hematoxylin/eosin staining of paraffin sections of eWAT of 18-month-old BDNF<sup>Pdgfra</sup> KO mice and WT control mice. Size bars = 100 $\mu$ m.



**Supplementary Figure 17.** TUNEL staining of paraffin sections of eWAT of 18-month-old BDNF<sup>PDGFRA</sup> KO mice and control mice (Size bar = 50 $\mu$ m). Sections were counter-stained with Methyl Green.

## SUPPLEMENTARY DATA



Supplementary Figure 18. Immunoblot analysis of pro-BDNF expression in liver and quadriceps muscle of mice.