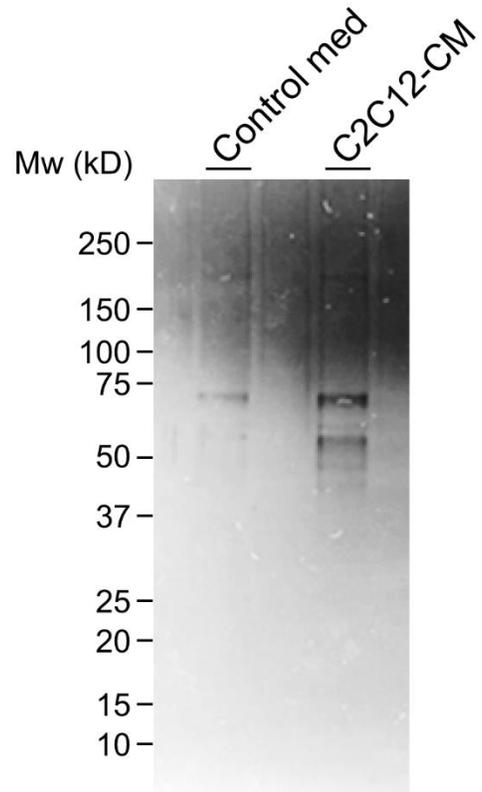
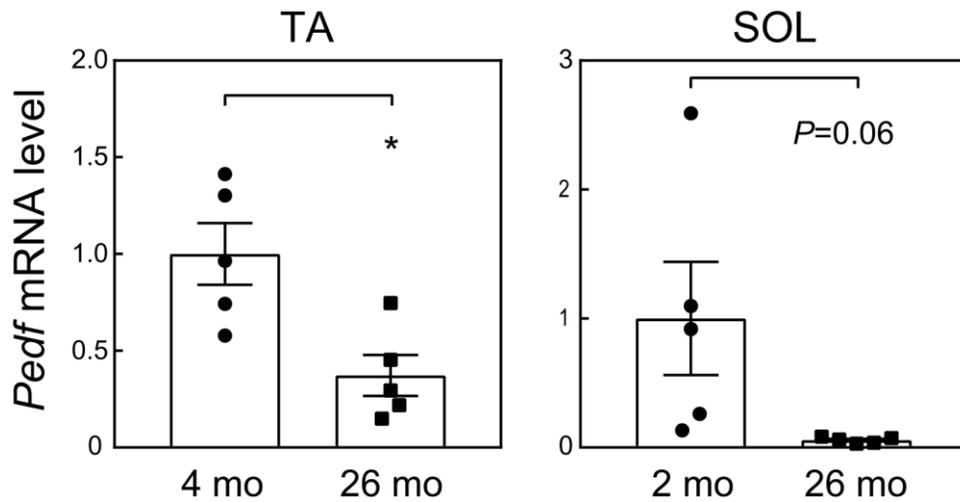


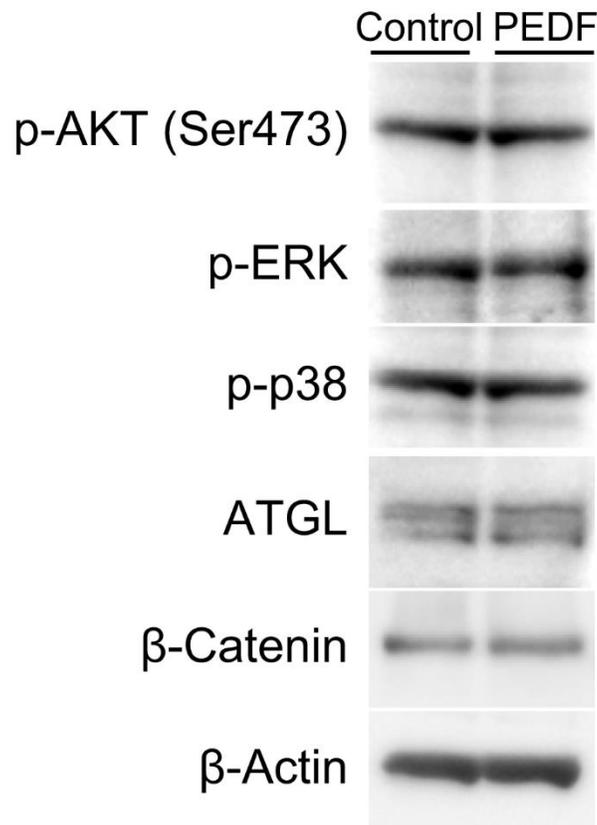
SUPPLEMENTARY FIGURES



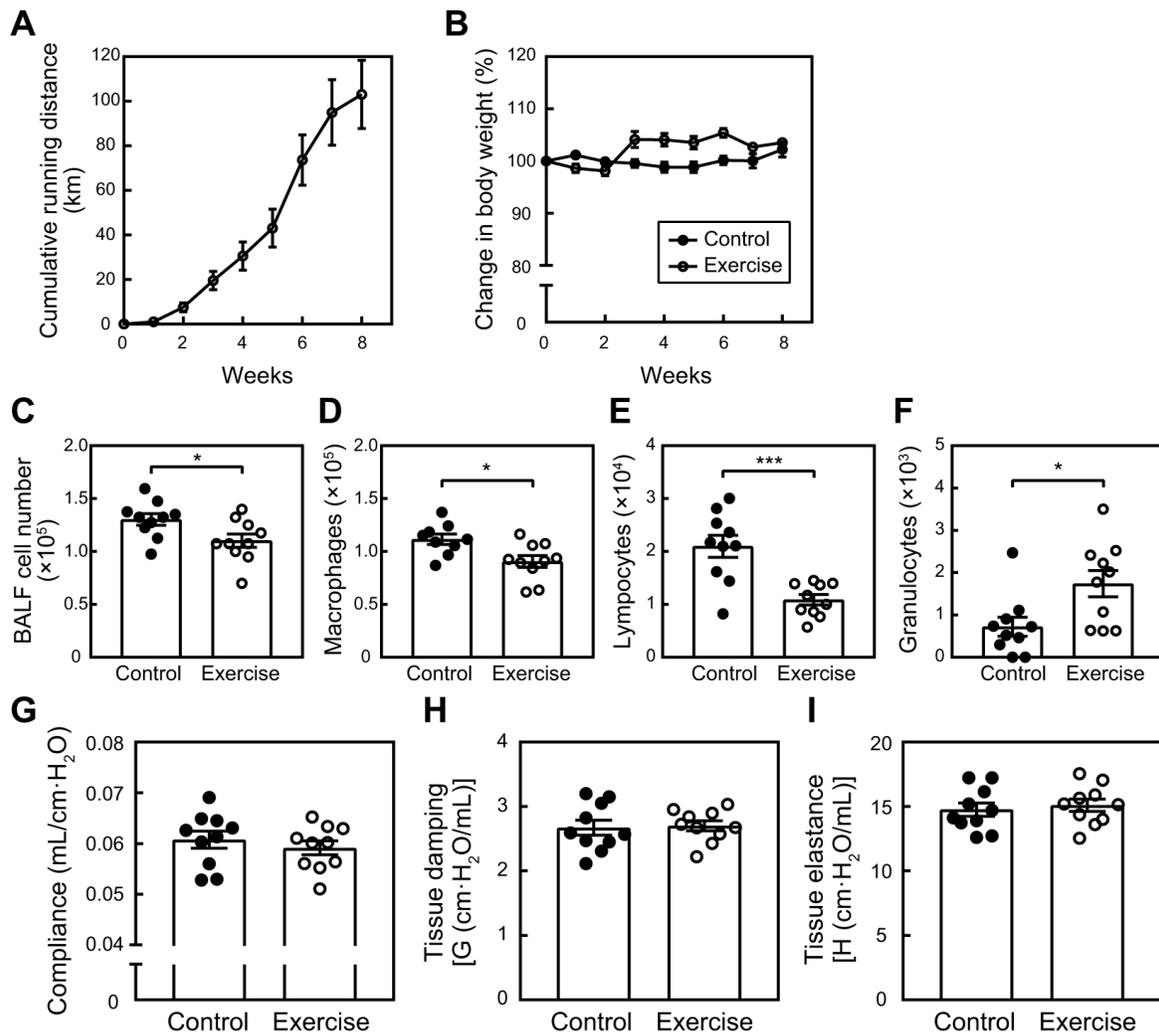
Supplementary Figure 1. Detection of proteins secreted by differentiated C2C12 cells. Equal volumes of control media and C2C12-CM were loaded onto SDS-PAGE. Proteins present in samples were detected using silver staining.



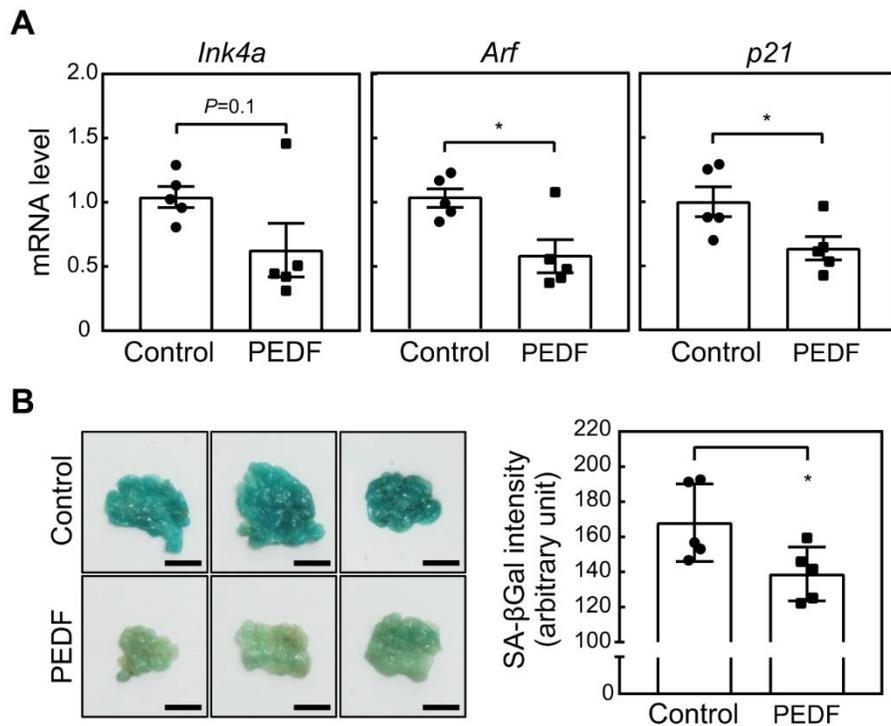
Supplementary Figure 2. *Pedf* expression is reduced in the skeletal muscle of aged animals. Total RNA was isolated from skeletal muscles (TA and SOL), and the expression of *Pedf* was analyzed by real-time PCR. Values were normalized to *Gapdh* in each sample. Values represent means \pm SEM. Data were analyzed by the Student's *t*-test (h). **P* < 0.05.



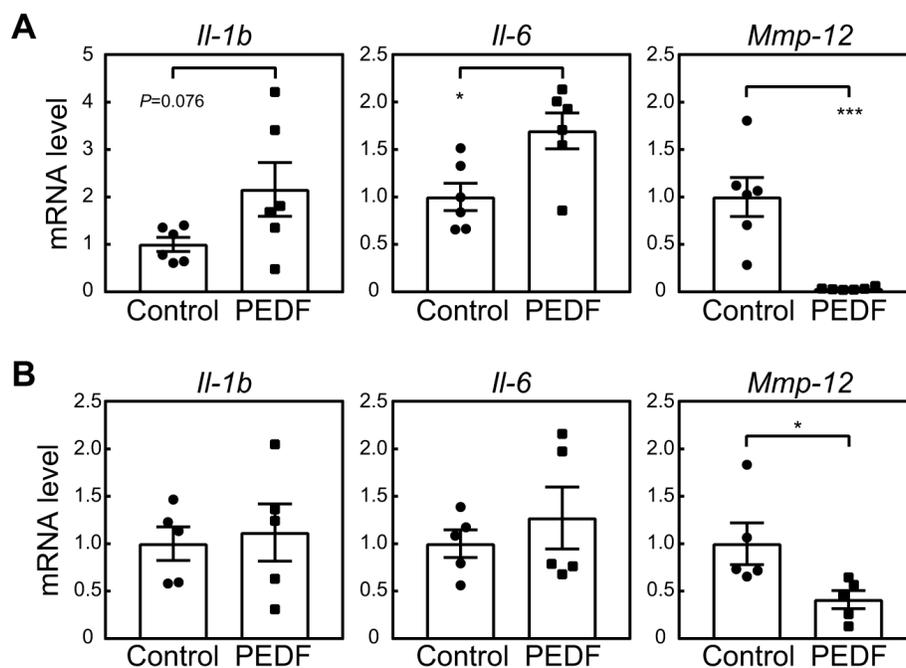
Supplementary Figure 3. Effects of PEDF on signaling molecules. MEFs were stimulated with PEDF for 24 hours. The phosphorylation or expression of the indicated proteins was analyzed by immunoblotting. β -Actin was used as a loading control.



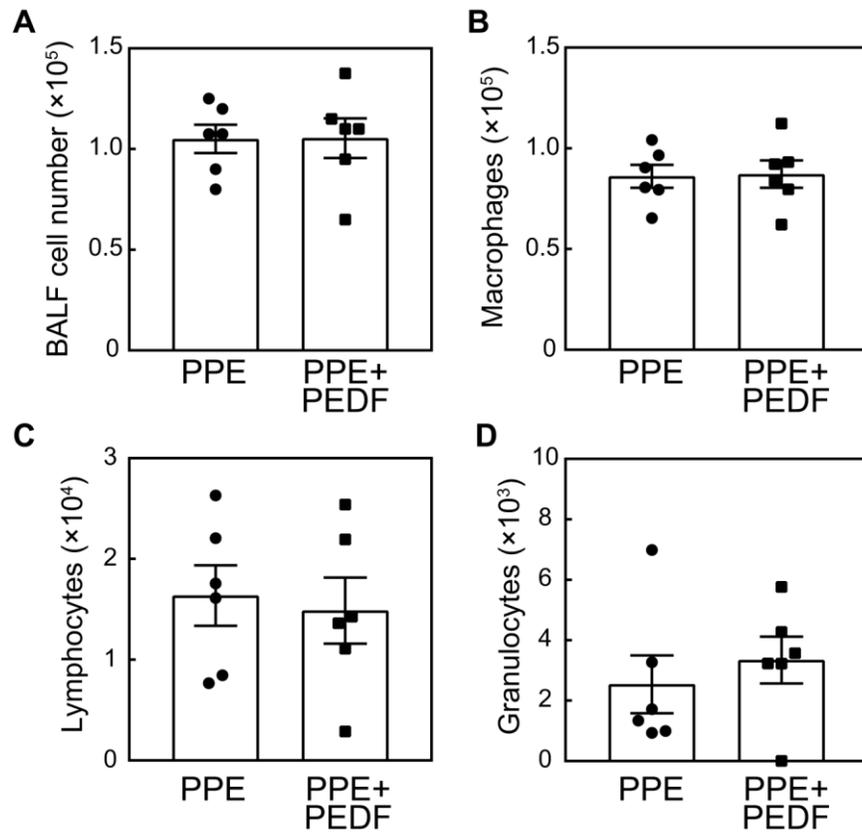
Supplementary Figure 4. Total running distance during voluntary exercise and its effects on body weight and lung parameters. (A) The cumulative running distance of mice in Figure 3. (B) Changes in body weights during voluntary exercise. (C) The number of total BALF cells was counted in each mouse. (D–F) BALF cells were analyzed by modified Giemsa staining. The number of macrophages (D), lymphocytes (E), and granulocytes (F) in each BALF sample was counted. (G–I) Mice were subjected to pulmonary function tests. Compliance (G), tissue damping (H), and tissue elastance (I) are shown. Values represent means \pm SEM. Data were analyzed by the Student's *t*-test. **P* < 0.05 and ****P* < 0.001.



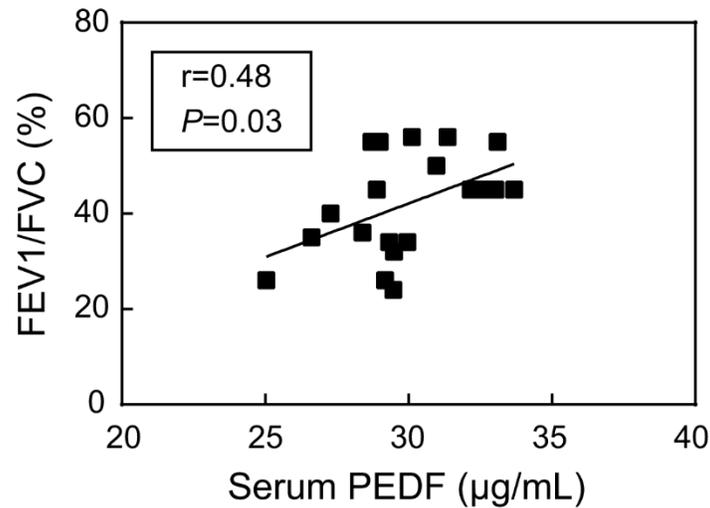
Supplementary Figure 5. PEDF suppresses cellular senescence in adipose tissue. (A) The expression of *Ink4a*, *Arf*, and *p21* in perigonadal adipose tissues was analyzed by real-time PCR. Values were normalized to *Gapdh* in each sample. (B) Left, Fat tissues were stained for SA-β-gal. Representative images are shown. Scale bar, 5 mm. Right, SA-β-gal intensity was analyzed in each sample. Values represent means ± SEM. Data were analyzed by the Student's *t*-test. * $P < 0.05$.



Supplementary Figure 6. Effects of PEDF on the expression of SASP-related factors. Total RNA was isolated from the lung (A) and adipose tissues (B) of mice in Figure 4, and the expression of the indicated genes was analyzed by real-time PCR. mRNA levels were normalized to *Gapdh* in each sample. Values represent means ± SEM. Data were analyzed by the Student's *t*-test. * $P < 0.05$ and *** $P < 0.001$.



Supplementary Figure 7. PEDF does not affect BALF cells. (A) BALF was prepared from mice in Figure 5, and the total cell number in BALF was counted. (B–D) BALF cells were analyzed by modified Giemsa staining. The numbers of macrophages (B), lymphocytes (C), and granulocytes (D) in each BALF sample were counted. Values represent means \pm SEM. Data were analyzed by the Student's *t*-test.



Supplementary Figure 8. Serum PEDF levels correlate with pulmonary function in patients with COPD. Detailed patient information is presented in Table S2. Pearson's correlation and a simple linear regression between serum PEDF levels and FEV1/FVC in patients with COPD ($n = 20$).