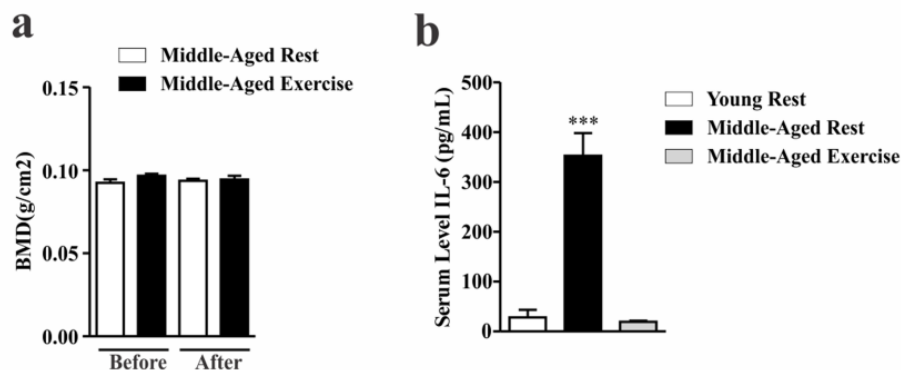
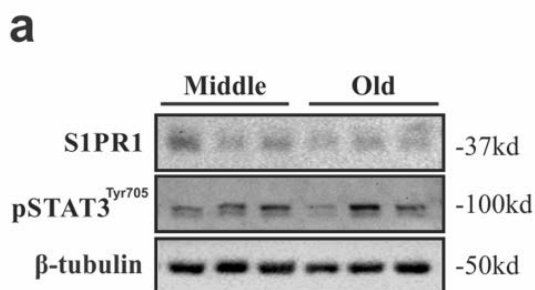


## SUPPLEMENTARY MATERIALS

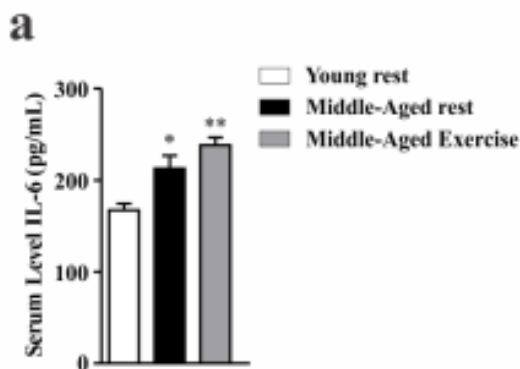


### Supplementary Figure S1. Serum IL-6 level and Bone Mineral Density after chronic exercise in middle-aged mice.

Dual energy X-ray absorptiometry analyses was performed to evaluate the bone Mineral Density (BMD) (a) (n=3 per group). Samples for analyses of serum IL-6 levels were collected after placing mice through the chronic exercise protocol for mice (b) (n=5-6 per group). One-way ANOVA was used for analyses where (b) \*\*\* p<0.0001 vs Young Rest and Middle-Aged Exercised.



**Supplementary Figure S2. Western blot analysis in the hypothalamus of old rats.** Western blot showing in the protein level of S1PR1 and STAT3 phosphorylation hypothalamus of Middle-Aged and old Wistar rats. (n=6 per group).



**Supplementary 3. Serum level of IL-6 in middle-aged rats after acute exercise.** Samples were collected following the acute protocol exercise for rats (n=4 per group). One-way ANOVA was performed to (a) \*\*p<0.05 vs young rest and \* p<0.05 vs young rest.