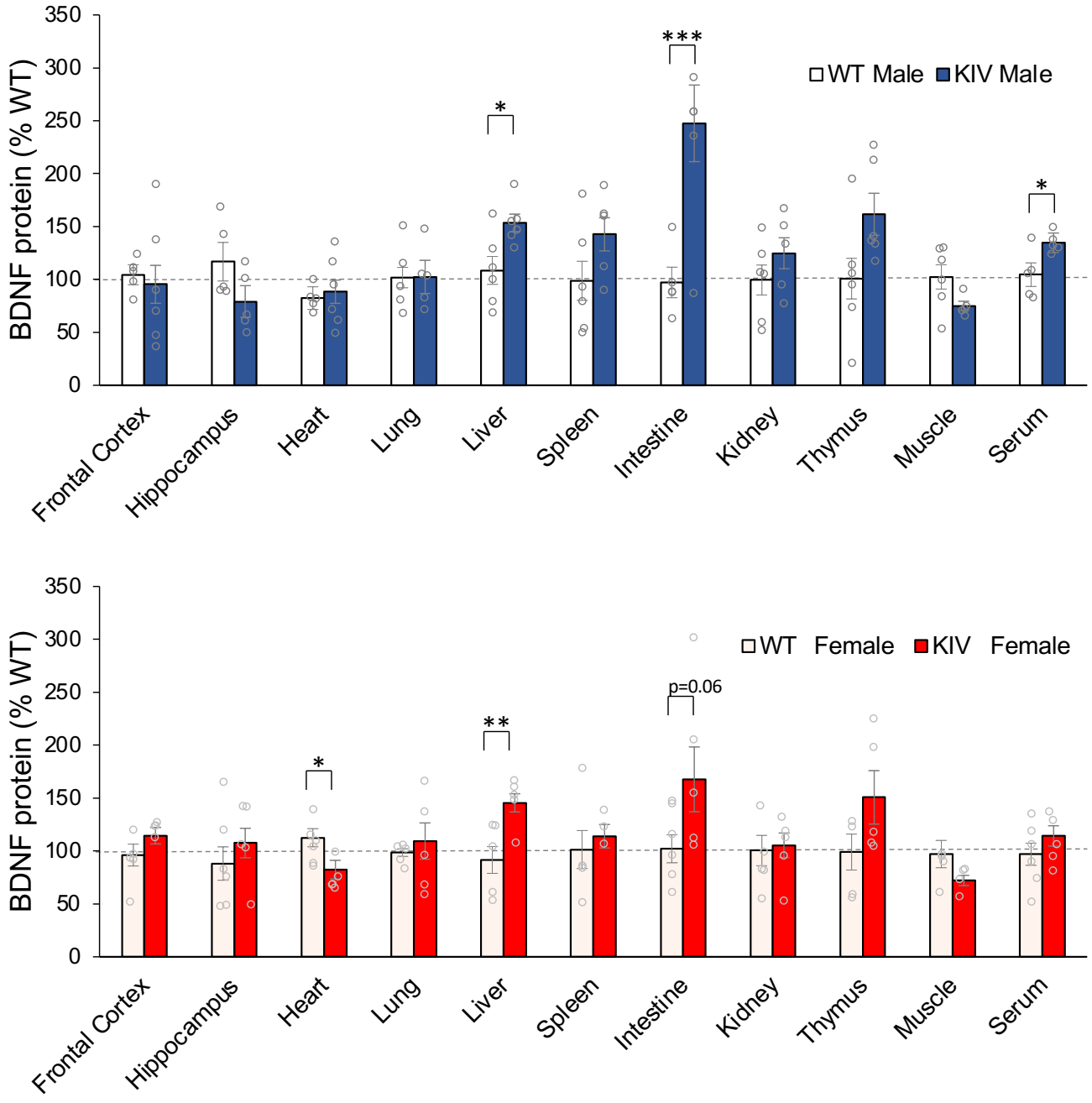
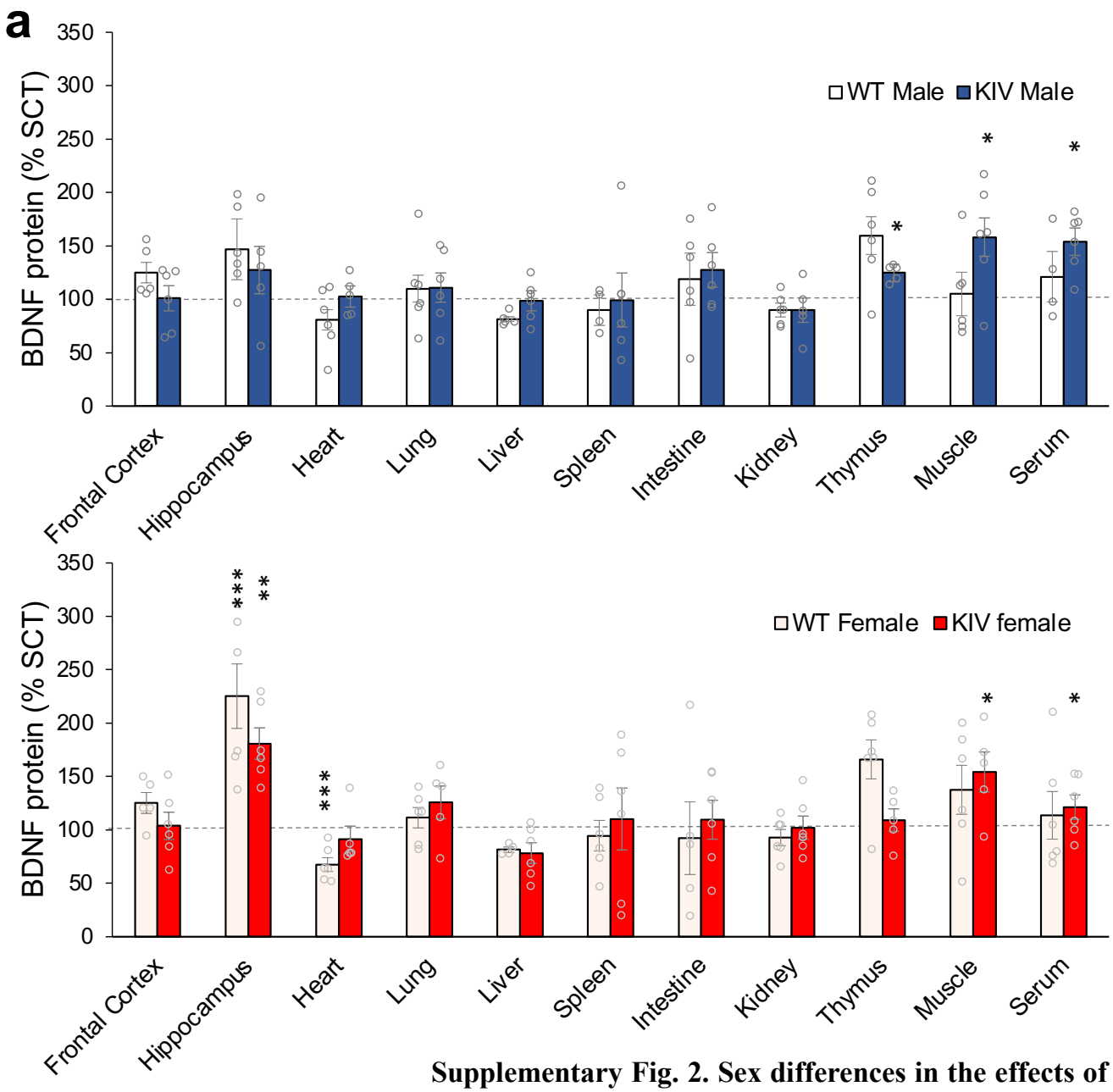
Supplementary Figure 1



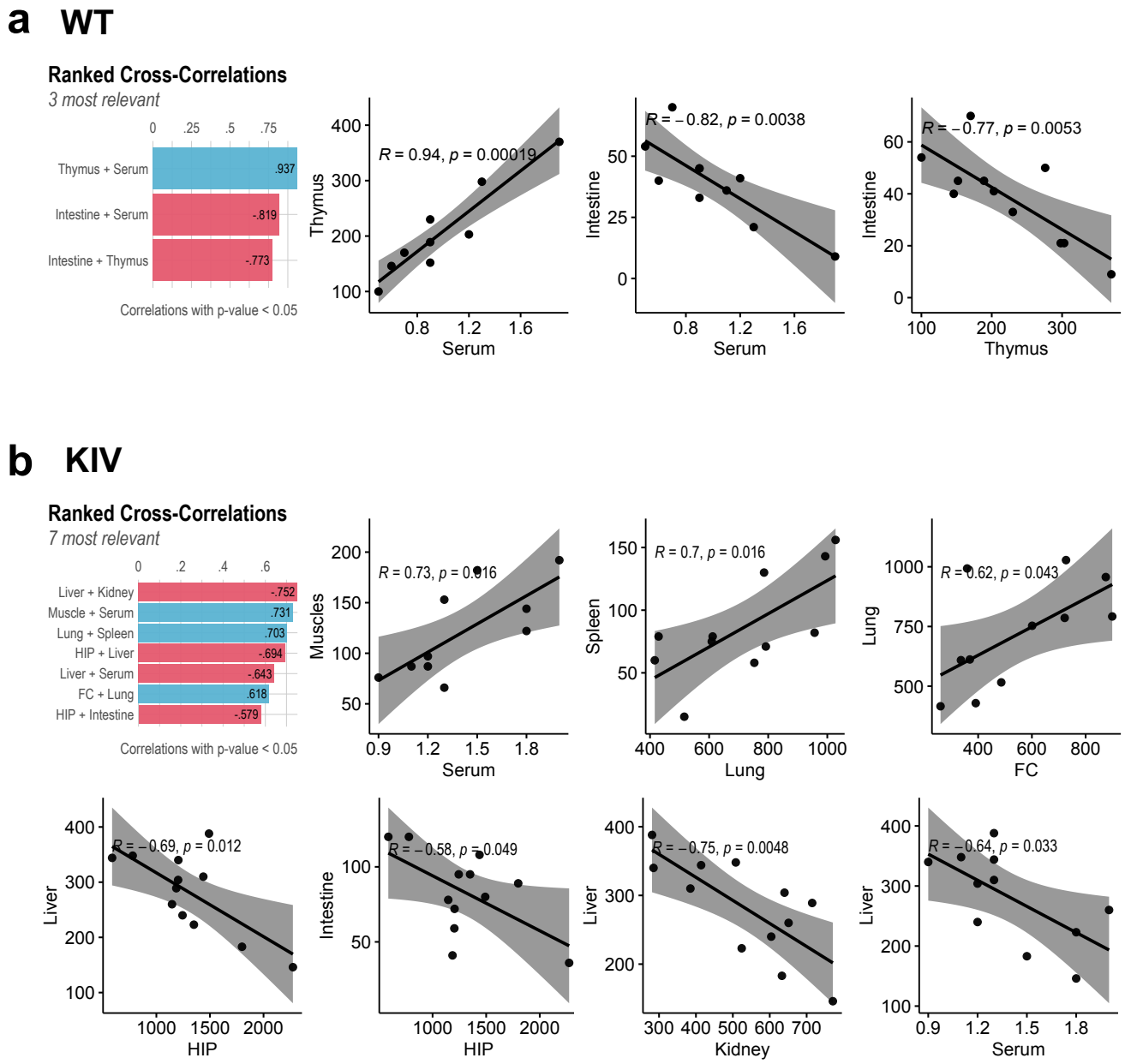
Supplementary Fig. 1. Sex effects on BDNF expression in standard control groups. Note that both males and females of promoter IV-BDNF deficient (KIV) mice showed similar pattern of BDNF expression levels across regions: significantly increased BDNF levels in the liver and intestine, a trend of increased BDNF levels in the thymus and serum and decreased BDNF levels in the muscle, when compared to WT mice. KIV female mice showed significantly decreased levels of BDNF in the heart. WT vs KIV: *p<0.05; **p<0.01; **p<0.001 by Student t-test. N=6 mice per group. BDNF levels (pg/mg total protein) were normalized to the mean of BDNF levels of each tissue of WT mice (% WT) and are shown as means ± S.E..

Supplementary Figure 2



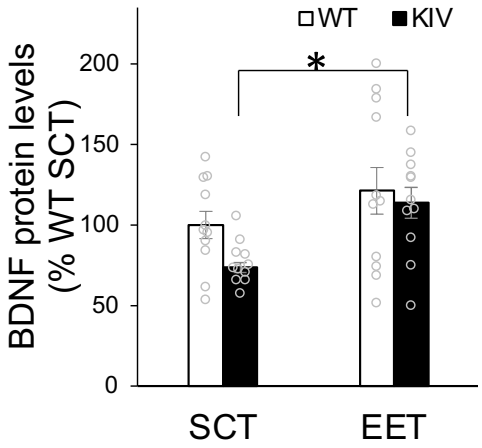
Supplementary Fig. 2. Sex differences in the effects of enriched environment treatment (EET) on BDNF. a. Males and females of both genotypes showed similar EET-induced changes in BDNF protein levels (% standard condition treatment: SCT). SCT vs EET: *p<0.05; **p<0.01; ***p<0.001 by Student's t-test. N=6 mice. group. **b.** There were no significant sex differences across the tissues except in the hippocampus, where WT females showed much higher EET-induced BDNF increases than WT males. Males vs females: *p<0.05 by Student's t-test. N=6 mice/group. BDNF levels (pg/mg total protein) were normalized to the mean of BDNF levels of each genotype with SCT (Means ± S.E.).

Supplementary Figure 3



Supplementary Fig. 3. Pearson's ranked cross-correlation in (a) WT and (b) KIV mice from both SCT and EET groups. BDNF levels in pg per mg total protein are plotted. N=12 mice per group. Data from ELISA measuring BDNF levels of 11 regions on a same plate were used to avoid variations due to different ELISA plates and different experimental handling. HIP: hippocampus; FC: frontal cortex.

Supplementary Figure 4



Supplementary Fig. 4. BDNF levels in muscle. KIV mice showed significantly reduced BDNF levels compared to WT mice, while EET increased (KIV-SCT versus KIV-EET, *p<0.05 by Bonferroni's comparison) and normalized (WT EET versus KIV EET p>0.05 by Student t-test). $F_{treatment}$ = 8.9, p<0.01 by Two-way ANOVA. N=12 mice per group.