

**Supplemental Figure 1.** 2-AG and AEA hydrolysis activity of tissue homogenates. 2-AG hydrolysis activities in whole-tissue homogenates of liver (A, B) and brain (C) from WT and *Cnr1*<sup>-/-</sup> adult female and/or mixed-sex neonatal mice. AEA hydrolysis activities in whole-tissue homogenates of brain (D, E) from WT and *Cnr1*<sup>-/-</sup> mice. Data are expressed as mean ± SD (n=3-5 mice per condition). \*p<0.05 for indicated comparison.

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**CES Activity**

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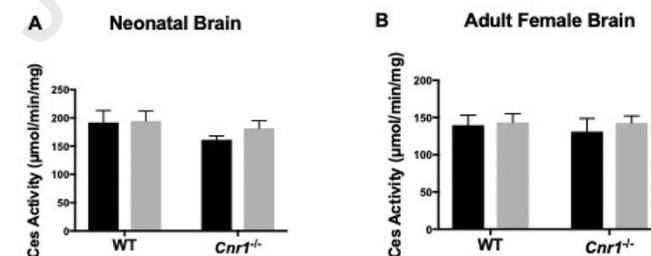
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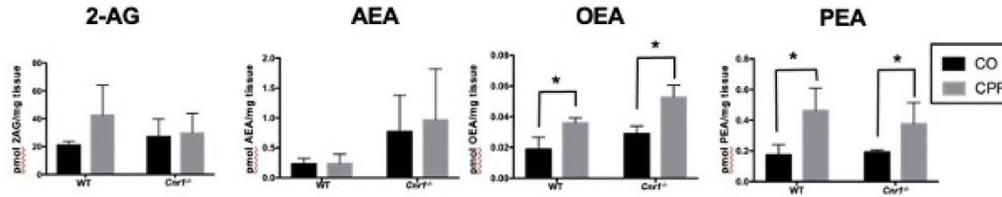
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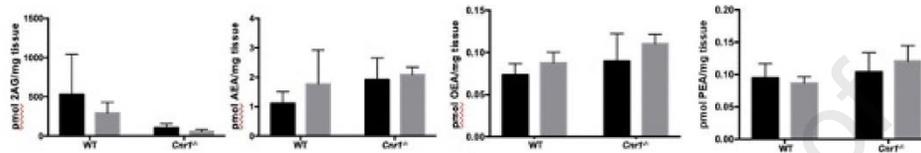


**Supplemental Figure 2.** Ces activity of tissue homogenates. Whole-tissue homogenates of brain from mixed-sex neonatal (A) and adult female (B) WT and *Cnr1*<sup>-/-</sup> mice. Data are presented as mean ± SD (n=3-5 mice per condition). None were

### A Neonatal Liver



### B Neonatal Brain

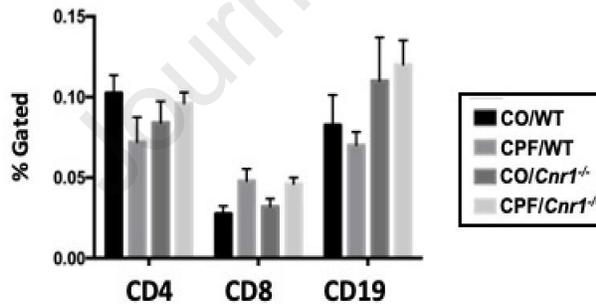


**Supplemental Figure 3.** eCB levels as measured by LC-MS/MS. A portion of the liver(A) and brain (B) from mixed-sex neonatal WT and *Cnr1*<sup>-/-</sup> mice was extracted for eCBs and quantified using deuterated standards (n=3-5). The resulting values were standardized by tissue weight. Data are expressed as mean ± SD, \*p<0.05 for indicated comparison.

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### Adult Female Liver



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**Supplemental Figure 4.** Adaptive immune cell phenotypes by flow cytometry. Cells from WT and *Cnr1*<sup>-/-</sup> adult female livers (n=3-5) were stained for extracellular markers to identify T helper cells (CD4), cytotoxic T cells (CD8), and B cells (CD19). Data are expressed as the mean of percent lymphocyte gated ± SD. None were significant within cell surface marker group.

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630 **Supplemental Table 1.** P values provided for treatment x genotype interactions.

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