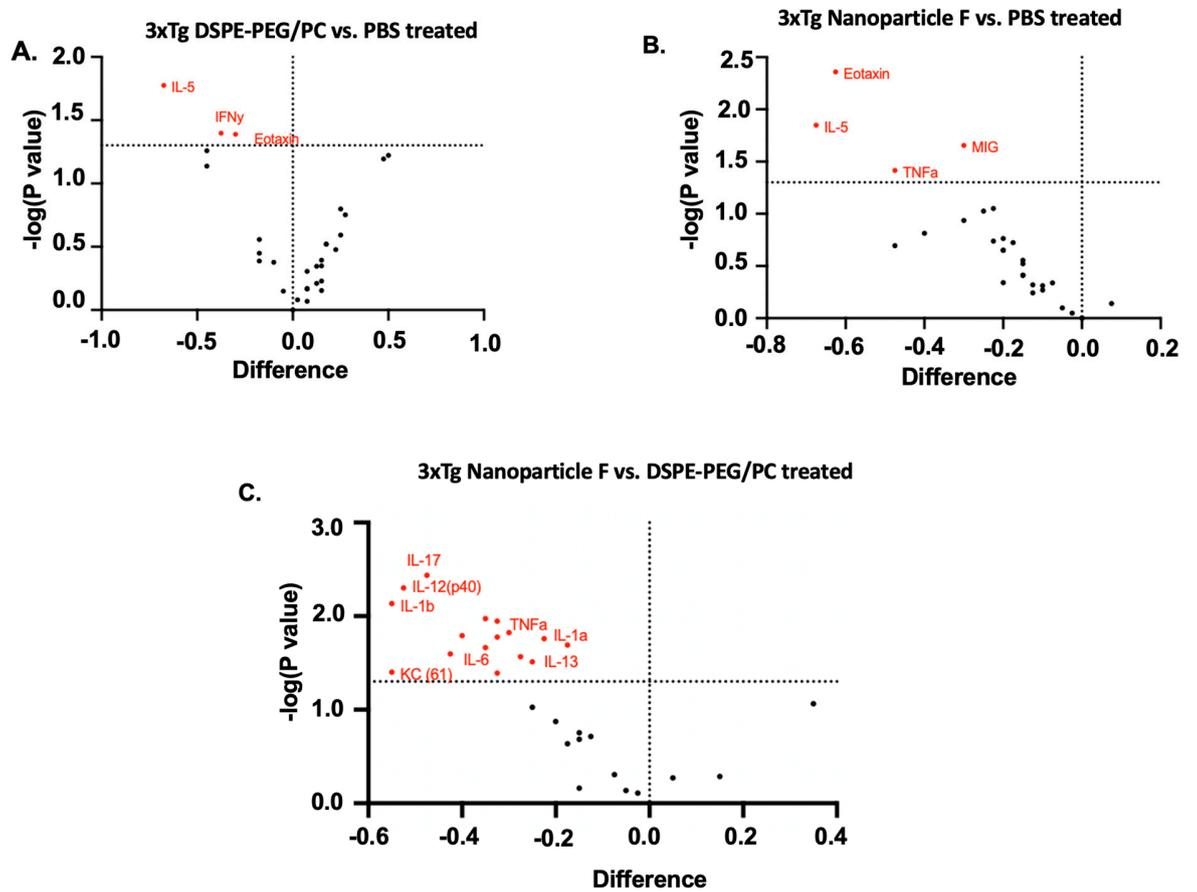


Figure S1. The oral gavage was performed to 8 WT male mice, at age 4-months old. Four mice were injected with nanoparticle alone, and the other four were injected with nanoparticle F. One *Acat1*<sup>-/-</sup> mouse served as the control. This study involved daily oral gavage administration of nanoparticle with or without F for 4 consecutive days, and measured ACAT activity 6 h after the final administration. Mice were sacrificed, ACAT enzyme activities were measured in forebrains, cerebellums/brain stems, adrenal glands, and livers isolated from the individual mouse.  $p < 0.001$  \*\*\*,  $p < 0.05$  \*.



**Figure S2. Brain cytokines differentiate upon treatment with DSPE-PEG/PC and nanoparticle F.** Volcano plot showing cytokines change upon (A) DSPE-PEG/PC treatment vs. PBS. (B) nanoparticle F vs. PBS. (C) nanoparticle F vs. DSPE-PEG/PC in 3xTg mice. Horizontal dashed line is determined at  $p = 0.05$ . Data points above the dash line are statically different at  $p < 0.05$  determined by unpaired student t-test.  $N = 4$  mice/group.