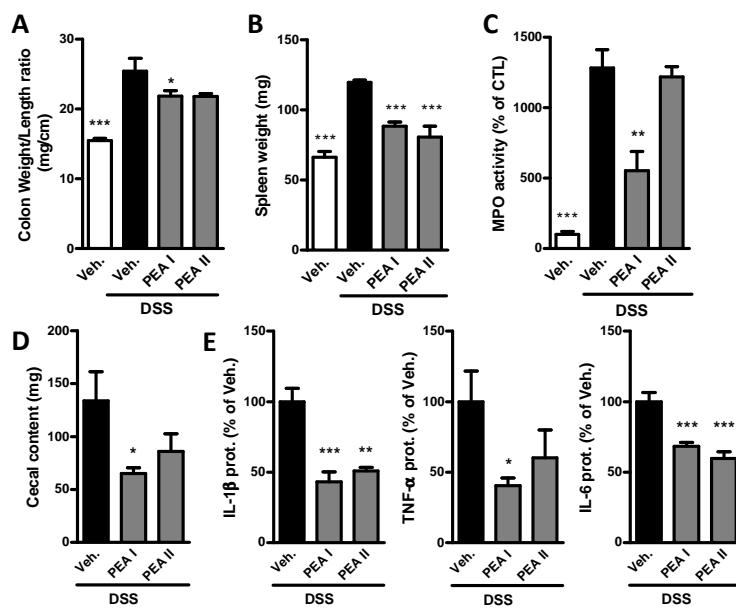


Supplemental figure 1: Effect of dextran sulfate sodium (DSS)-induced colitis on body weight loss and occult blood in the feces.

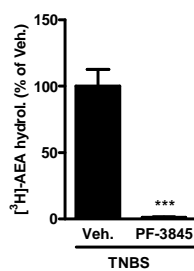
To induce colitis, 5% dextran sulfate sodium (DSS) was added to the drinking water. Mice were sacrificed on day 7. (A) Body weight of control mice (8 per group) and mice with DSS-induced colitis (8 per group). Mice receiving DSS start to lose weight on day 5 after addition of DSS to the drinking water.

(B) Occult blood in the feces of the DSS group as determined by the Hemocult® test over the course of 7 days. Occult blood in the feces is a sign of colon inflammation. On day 2, only one mouse is positive for Hemocult®, and starting on day 5, all eight mice are positive, indicating that the colitis is established.



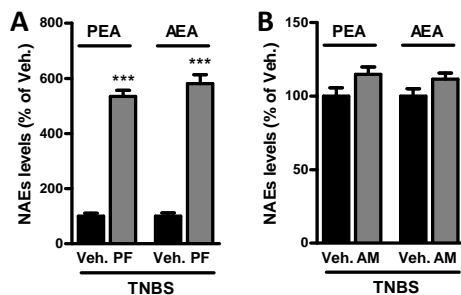
Supplemental figure 2: Beneficial effects of PEA administration on DSS-induced colitis.

Colitis is induced by addition of DSS (5%) to drinking water for 5 days, and mice are sacrificed on day 7. PEA (10mg/kg) was administered intraperitoneally to mice either starting on the day of DSS addition to drinking water or on day 5. Effects of PEA administration on (A) colon weight/length ratio, (B) spleen weight, (C) MPO activity, (D) feces weight in the cecum and (E) pro-inflammatory cytokines expression measured by ELISA. For E, results are expressed relatively to the DSS untreated group set at 100%. Results are expressed as mean ± SEM with n=8mice/group. * P<0.05; ** P<0.005; *** P<0.001 versus the DSS-untreated group.



Supplemental figure 3: PF-3845 administration in TNBS-induced colitis efficiently inhibits FAAH activity

FAAH activity measured in the particulate fraction of ileum homogenates obtained from mice with TNBS-induced colitis that received either vehicle (Veh.) or the FAAH inhibitor PF-3845 (10mg/kg). *** P<0.001 versus the TNBS untreated group.



Supplemental figure 4: Effect of PF-3845 and AM9053 administration on PEA and AEA levels in the brain of mice with TNBS-induced colitis.

(A) The FAAH inhibitor, PF-3845 administration (10mg/kg, PF) increases PEA and AEA levels in the cerebellum of mice with TNBS-induced colitis. (B) The NAAA inhibitor, AM9053 (10mg/kg b.i.d., AM) does not affect PEA or AEA levels in the cerebellum of mice with TNBS-induced colitis. Results are expressed as mean ± SEM with n=10 mice/group. *** P<0.001 versus the TNBS untreated group (set at 100%).