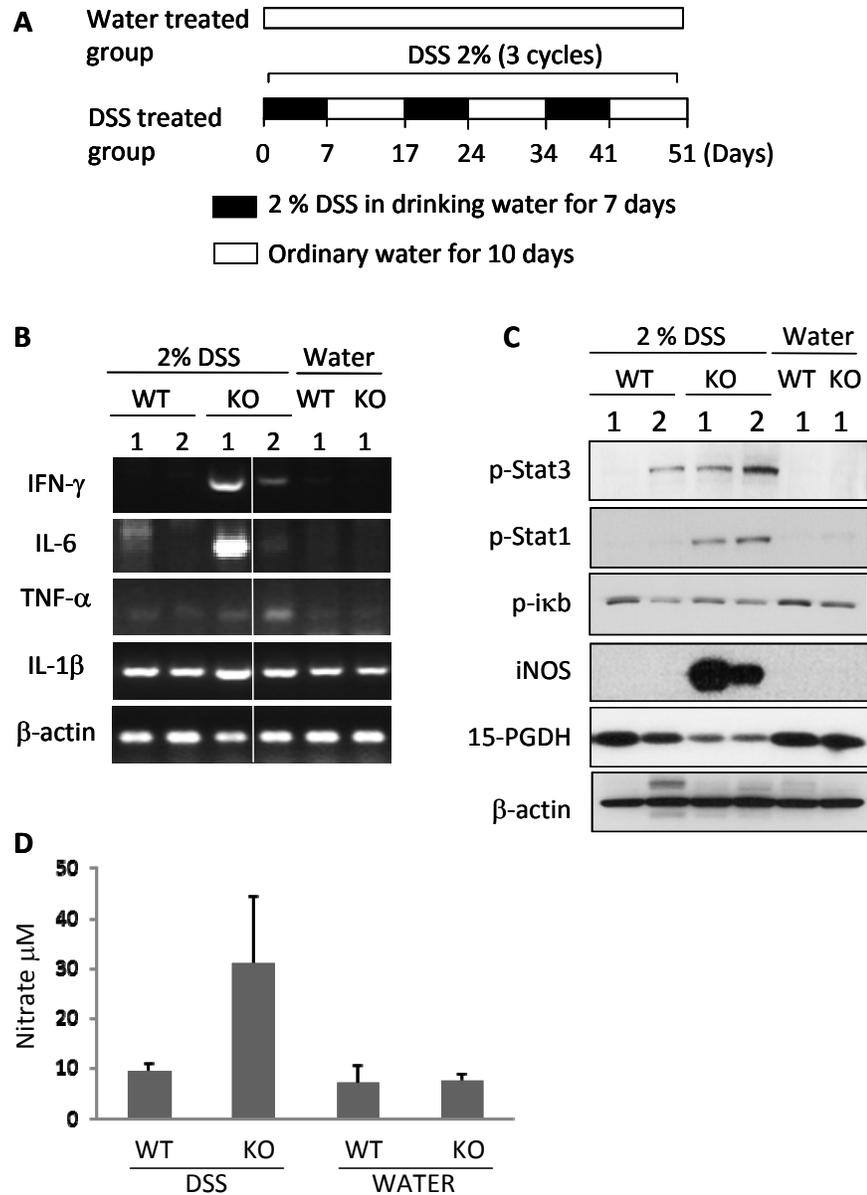
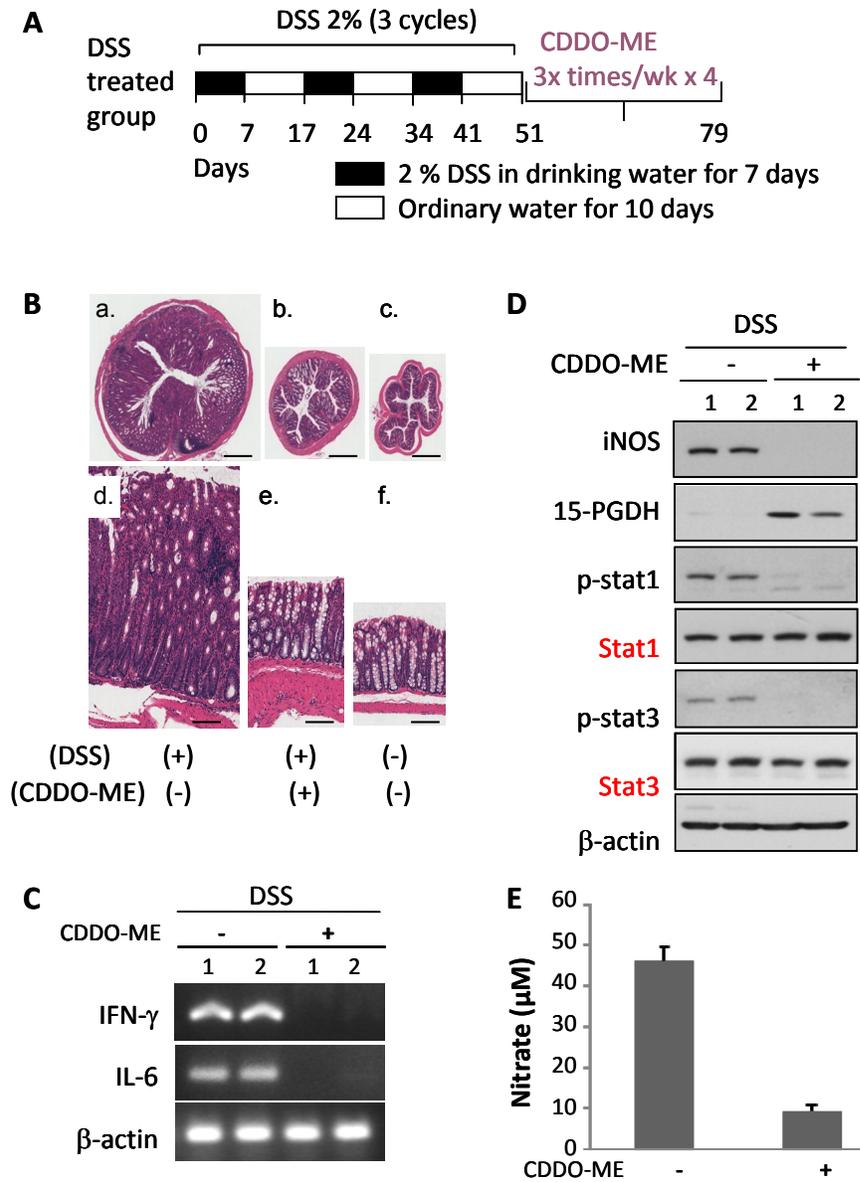


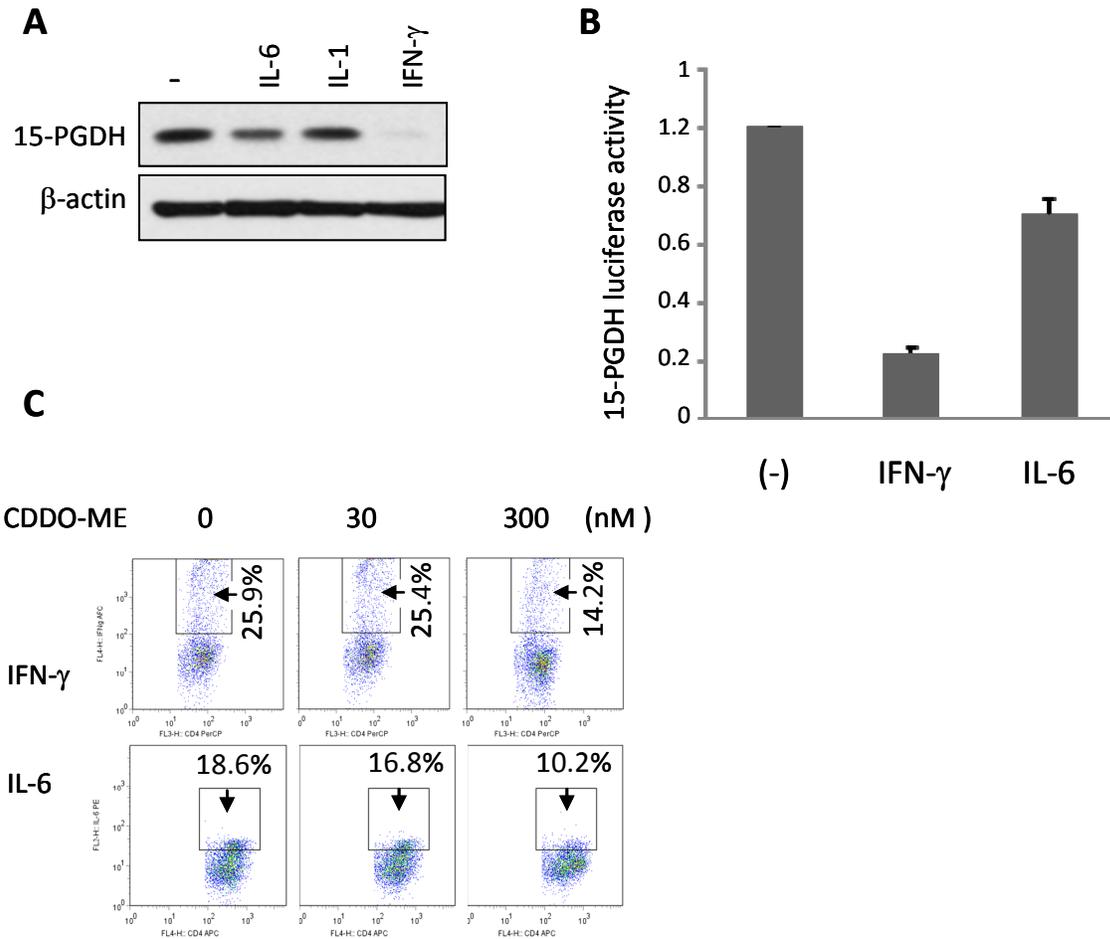
## Supplemental data



**Supplemental Figure 1.** The DSS-induced model of colitis. A) Experimental design of DSS-induced colitis in mice. 2% DSS in drinking water is given to mice for 7 days and then mice are permitted to consume regular drinking water for 10 days. The cycle is repeated 3 times (over 3 months) and then each mouse is sacrificed. B) pro-inflammatory cytokines, IFN- $\gamma$ , IL-6, TNF- $\alpha$ , and IL-1 $\beta$  are measured by RT-PCR in WT and KO mice following DSS treatment, with those receiving water alone serving as control mice (all non-contiguous lanes were run on the same gel). C) Expression of p-Stat1, p-Stat3, p-I $\kappa$ B, iNOS and 15-PGDH were determined in colon epithelia of WT and KO mice following treatment with/without DSS. D) Concentration of nitrate in serum was measured (n=4-6).



**Supplemental Figure 2.** CDDO-Me suppresses DSS-induced colitis. A) Experimental design/protocol for CDDO-Me administration in  $Smad4^{Tko}$  mice on study. After 3 cycles of DSS treatment, 250 ng of CDDO-Me was given by gavage 3 times/week for 4 weeks. The vehicle is sesame oil. B) H & E staining of colon sections of mice receiving either sesame oil (a and d) or CDDO-Me (b and e). C) Expression of mRNA for IFN- $\gamma$  and IL-6 in colon mucosa of sesame oil or CDDO-Me treated mice was measured by RT-PCR analysis. D) Protein expression of iNOS, 15-PGDH, p-Stat1, p-Stat3 and  $\beta$ -actin was measured by Western blot analysis of colon epithelial cell scrapings. E) Nitrate concentration in serum of CDDO-Me treated or untreated  $Smad4^{Tko}$  (KO) mice (n=4-6).



**Supplemental Figure 3.** CDDO-Me blocks suppression of 15-PGDH by inflammatory mediators. A) FET cells were treated pro-inflammatory cytokines including IL-6 (20 ng/ml), IL-1 (5 ng/ml) and IFN- $\gamma$  (20 ng/ml) for 24 hrs and harvested for Western Blot analysis to determine effects of these inflammatory cytokines on 15-PGDH protein expression. B) Both IFN- $\gamma$  and IL-6 suppress 15-PGDH promoter luciferase activity. pGL3 and 15-PGDH promoter activity in FET cells following stimulation with IFN- $\gamma$  (20 ng/ml) or IL-6 (20 ng/ml) for 24 hrs. A dual luciferase assay was performed. Results are representative of three different experiments. Bars, S.E. C) CDDO-Me suppresses the production of INF- $\gamma$  and IL-6 from T-cells. Spleen lymphocytes from WT mice were activated with anti-CD3/CD28 in the presence or absence of CDDO-Me for 24 hrs. INF- $\gamma$  and IL-6 production from activated lymphocytes were measured by intracellular staining and FACS analysis.