

**Figure S1.** Experimental plan and colitis induction (**A**) Representative scheme showing our experimental protocol. Vehicle group received no treatment and served as internal control. All other mice groups were administered dextran sulfate sodium (DSS 4% w/v, MW 36,000 to 50,000, Sigma Aldrich, Italy) in drinking water for six consecutive days (starting from day 1). Starting from day 2, mice were randomly divided into the following groups (n = 10 each): (1) no further treatment (DSS 4%); (2) pLP+ palmitate (0.0003 µg/Kg), (3) pNAPE-LP + palmitate (0.0003 µg/Kg) (4) palmitate alone (0.0003 µg/Kg) (5) pNAPE-LP + palmitate (0.0003 µg/Kg) with the selective PPAR $\alpha$  antagonist MK886 (10 mg/Kg) and (6) pNAPE-LP + palmitate (0.0003 µg/Kg) with the selective PPAR $\alpha$  antagonist GW966 (1 mg/Kg), respectively. All treatments were given daily from day 2 until day 6 by intragastric gavage, while PPAR $\alpha$  and PPAR $\gamma$  antagonists were administered intraperito-neally from day 2 to day 6. (**B**) Kinetic of colitis induction showing DAI measurements from day 0 to 7 in DSS-treated mice.