**Supplemental data**

***Fig S1: Lack of direct inhibitory effect of teriflunomide on emopamil binding protein (EBP)***

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***EBP Biochemical Assay Procedure***

Teriflunomide (20 nL/well, 0.1% DMSO final), and an internal positive quality control for the assay, were dispensed to the 384-well assay plates (Corning #3575) in a dose-response manner using the ECHO555 (Labcyte). Two duplicate plates were stamped with two replicate 10-point dose responses for each compound on each plate. The following concentrations of compounds were included: 9.99, 3.746, 1.249, 0.3842, 0.1441, 0.04803, 0.01496, 0.005611, 0.001561, and 0.0006242 uM.

20 ug/ml EBP microsomes isolated from Sf9 insect cells expressing human EBP were added to the assay plates with compounds using a multichannel pipette. The plates were sealed with a foil seal and then spun down for 30 – 60 seconds at 1000 rpm in a benchtop Eppendorf centrifuge at room temperature. The compounds and microsomes were incubated in the plates for 15 minutes at 37°C. Then, 10 ul/well of 15 uM (final) zymostenol-d7 substrate (Avanti, #700117P) in the assay buffer (50 mM Tris-HCL, 2 mM magnesium chloride, 1 mM EDTA, 2 mM beta-mercaptoethanol, 0.1% Tween-80, 5% glycerol, pH 7.5) were added to the plates with a multichannel pipette or Multidrop to initiate a reaction. The plates were sealed with a foil seal. Again, the plates were spun down for 30 – 60 seconds at 1000 rpm at room temperature. The plates were incubated at 37°C for 2 hours. After the 2 hour incubation, the reactions were treated with 70 uL of stop/extraction solution (50% methanol, 50% acetonitrile, 5 mM ammonium formate, 0.2% formic acid; Multidrop). The plates were covered with a plastic lid immediately after the solvent was added to prevent evaporation. Next, the plates were spun down at 2300 rpm for 5 minutes at room temperature in a benchtop Eppendorf centrifuge. Using the Apricot iPipette with 125 ul tips (Apricot Designs, #125-384K-EZL-NS), 70 ul of reaction mixtures were transferred to 384-well Waters plates (Waters, #186002631). The plates were heat sealed for 3.2 – 3.5 seconds at 160-163°C. Then, the plates were spun one final time at 1500 rpm for 2 – 3 minutes at room temperature. The plates were analyzed on the Vanquish 6500+ LC/MS system for zymostenol-d7 and lathosterol-d7 product. Data was analyzed and the IC50 values were calculated (ActivityBase, Citrix).