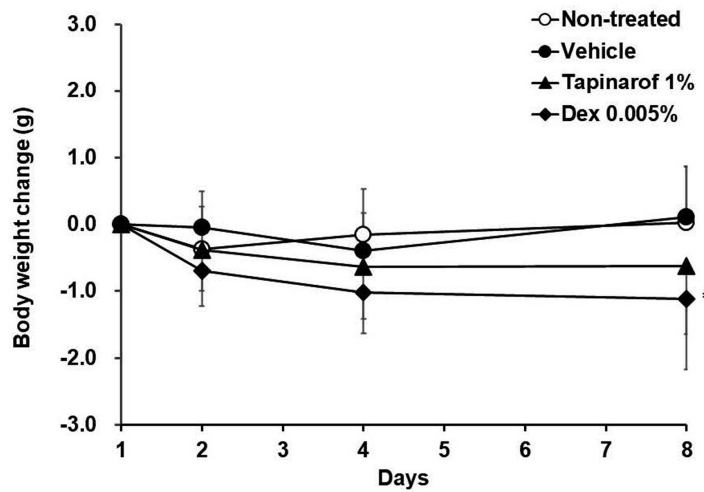


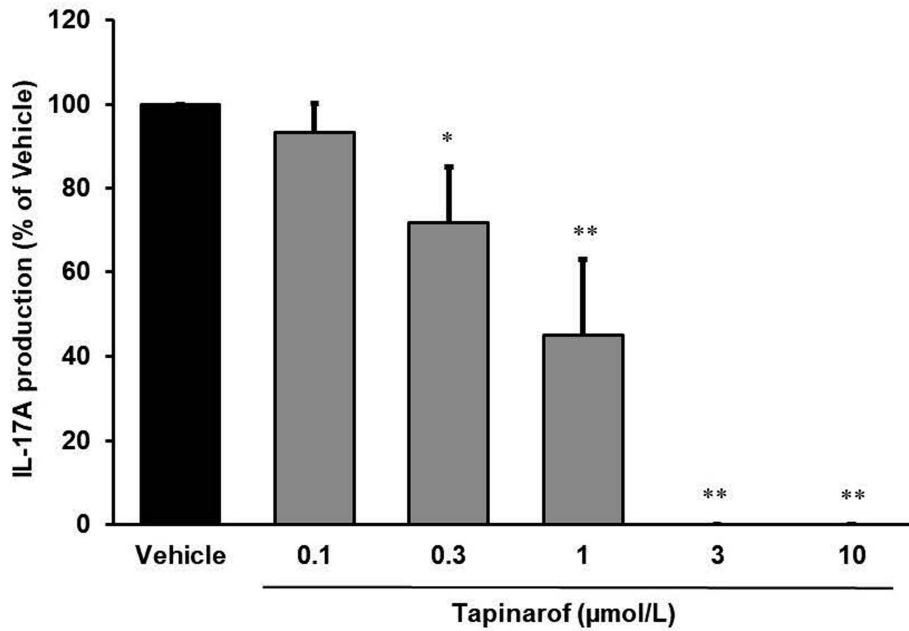
Supplementary Figure S1. Effects of Tapinarof on Acanthosis and Crust on the Ear Skin in IL-23-Induced Psoriasis-Like Dermatitis in Mice

A) Representative photomicrographs of HE-stained ear skin samples with the features of acanthosis. Group names are presented on each panel. Sham, normal ear skin; vehicle, slight acanthosis; 0.01%, 0.1%, 1% tapinarof, very slight acanthosis; and 0.005% Dex, no abnormality. Bar = 50 μm . (B) Representative photomicrographs of HE-stained ear skin samples with the features of crust. Group names are presented on each panel. Sham, normal ear skin; vehicle, slight crust; 0.01%, 0.1%, 1% tapinarof, very slight crust; and 0.005% Dex, no abnormality. Bar = 100 μm .



Supplementary Figure S2. Effects of Topical Administration of Tapinarof on Body Weight in Normal Mice

(A) Vehicle (EtOH), 1% tapinarof or 0.005% Dex were administered topically once daily to both sides of the left ear for 7 days. Body weight changes were assessed on Days 1, 2, 4, and 8. Data are represented as the change from baseline. The results are shown as the mean and SD (n = 8 or 10). Significant difference; *, p < 0.05; 0.005% Dex vs. vehicle (Tukey multiple comparison test).



Supplementary Figure S3. Effect of Tapinarof on IL-17A Production in Human PBMCs

ELISA kit was used to measure the IL-17A level in the supernatant of human PBMCs that were stimulated with PHA-L/PMA, either with or without tapinarof. Data are shown as mean + SD (n = 4). One-tailed significant difference versus vehicle control group; *: p < 0.025, **: p < 0.005 (Shirley-Williams test).

Supplementary Method

IL-17A measurement in human peripheral blood mononuclear cells (PBMCs)

Cryopreserved human PBMCs (STEMCELL Technologies Inc. Vancouver, BC, Canada) were thawed and suspended in RPMI-1640 medium (Thermo Fisher Scientific Inc.) containing 10% fetal bovine serum, 100 IU/mL penicillin G, and 100 µg/mL streptomycin. The cells were plated at 2×10^5 cells/well in a 96-well plate and stimulated with 0.5 ng/mL phorbol 12-myristate 13-acetate (PMA) (Sigma-Aldrich, Co., St. Louis, MO, USA) and 1.0 µg/mL phytohemagglutinin-L (PHA-L) (Roche Diagnostics GmbH, Mannheim, Germany) for 2 days in the presence or absence of tapinarof at 37°C in 5% CO₂. The supernatants were collected, and IL-17A was measured with the Human IL-17A ELISA Kit (Diacclone SAS, Besançon, France).