

SUPPLEMENTAL FIGURE LEGENDS

Supplemental figure S1. Increased Vldlr in brains of mice lacking LXRs.

Immunoblot analysis of total brain lysates from 15 week old male C57Bl/6 wildtype and *Lxrαβ*^(-/-) mice (n=3 mice/group).

Supplemental figure S2. Ligand activated LXR requires Idol to reduce the level of the Vldlr.

(A) 3T3-Vldlr cells were transfected with a control siRNA or siRNAs targeting Idol and subsequently treated with 1 μM GW3965 for an additional 24 h. Total cell lysates were blotted as indicated. (B) Expression of *Abca1*, *Idol*, and *Vldlr* in these cells was analyzed (n=2). Bars and errors represent the mean ± S.D.

Supplemental figure S3. Evolutionary conservation of IDOL.

The sequences of IDOL proteins from the indicated species were aligned using clustalW. The following accession numbers were used: Dm (NP_61168), Ag (XP_551203), Tc (XP_975394), Am (XP_396349), Nv (XP_001633631), Dr (NP_956277), XI (NP_001085668), Tg (XP_002188133), Gg (NP_001012579), Oa (XP_001520686), Md (XP_001367101), Cf (XP_545352), Ss (XP_001929111), Bt (NP_001095723), Ec (XP_001493202), Mm (NP_722484), Pt (XP_518252), Hs (NP_037394), Mmul (XP_001094408).

Supplemental figure S4. IDOL does not inhibit the IMD pathway.

(A) Immunoblot analysis of lysates from control *Drosophila* S2 cells, S2 cells that constitutively express IDOL and S2 cells that constitutively express IDOL (mut). Each cell line was treated with PGN for the indicated periods and probed for P-dJNK and total dJNK. (B) qPCR analysis of the expression of the IMD-responsive transcript attacin (*att*) in control *Drosophila* S2 cells, S2 cells that constitutively express IDOL and S2 cells that constitutively express IDOL (mut). Cells were treated with PGN for six hours where indicated. Att expression levels in untreated control S2 cells were assigned a value of 1 and all other values are reported relative to this value.

Supplemental figure S5. Disrupting lysosomal function inhibits the LXR-mediated reduction of Vldlr.

3T3-Vldlr cells were treated with or without 1 μM GW3965 for 16 h. Cells were subsequently cultured in the absence or presence of 10 mM ammonium chloride or 25 μM chloroquine for an additional 24 h. Total cell lysates were blotted as indicated.

Supplemental figure S6. Densitometric analysis of protein levels in LXR ligand treated primary neurons.

Primary rat neurons were treated with 1 μM GW3965 for 24 h. Total cell lysates were blotted and quantified by densitometry (n=4-6). Bars and errors represent the mean ± S.D. * p< 0.05

