Supplementary figures

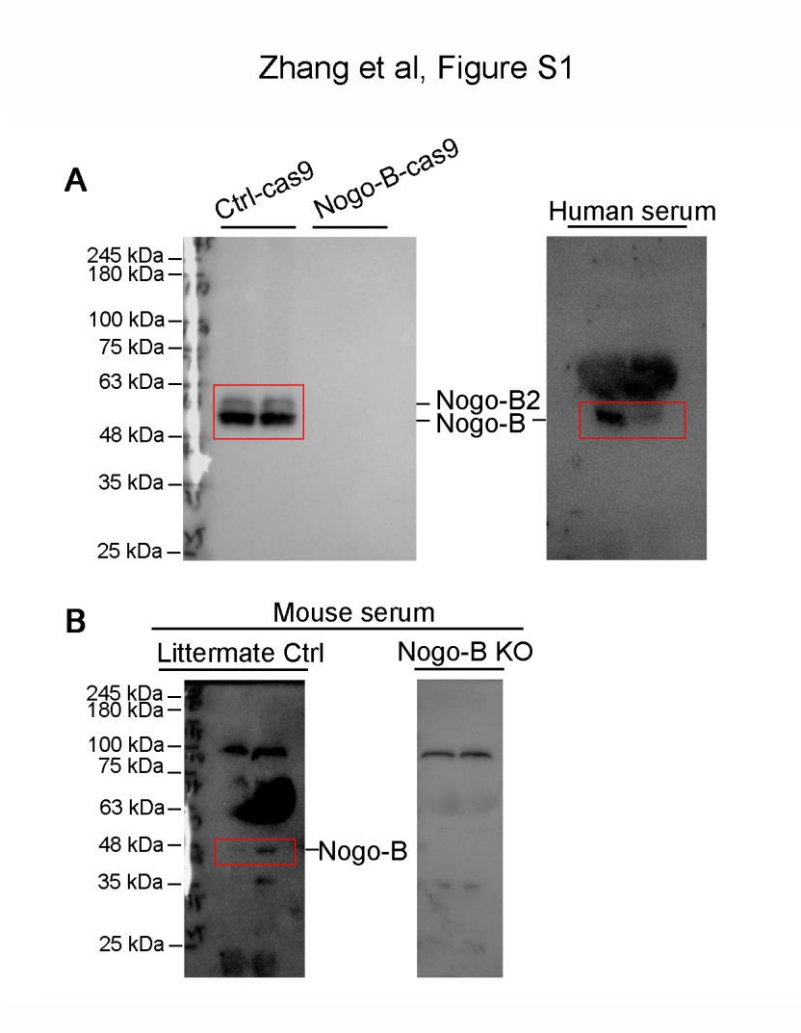

Figure S1. Expression of Nogo family members in HepG2 cells, human and mouse serum

A: total cellular proteins were extracted from Ctrl-cas9 and Nogo-B-cas9 HepG2 cells. Expression of Nogo family members in HepG2 cells and human serum was determined by Western blot; B: serum samples were colleted from littermate control and Nogo-B KO mice, followed by determination of Nogo family member protein expression by Western blot. Both Nogo-B2 and Nogo-B can be determined in HepG2 cells, while only Nogo-B was detectable in both human and mouse serum.

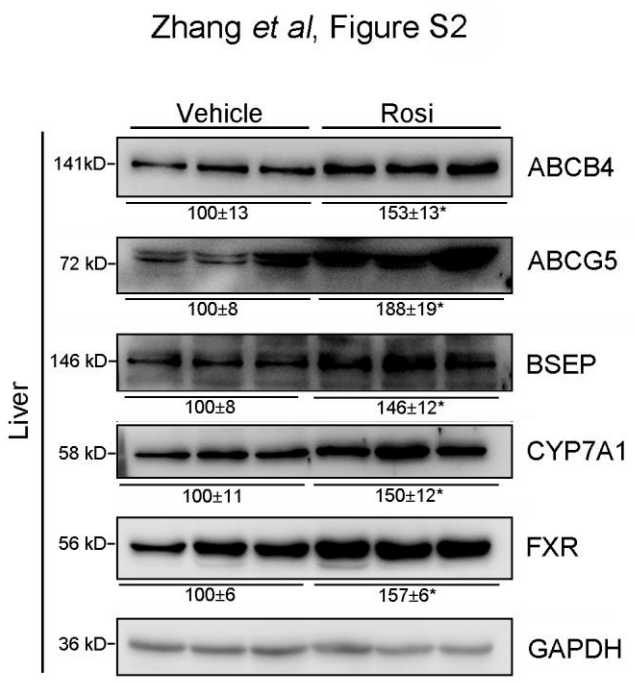

Figure S2. Rosiglitazone induces expression of molecules for bile homeostasis in mouse liver.

Total proteins were extracted from a piece of mouse liver after treatment as indicated in Figure 1A. Expression of ABCB4, ABCG5, BSEP, CYP7A1 and FXR protein was determined by Western blot with quantification of band density. *p<0.05 *vs.* Vehicle, n=6.

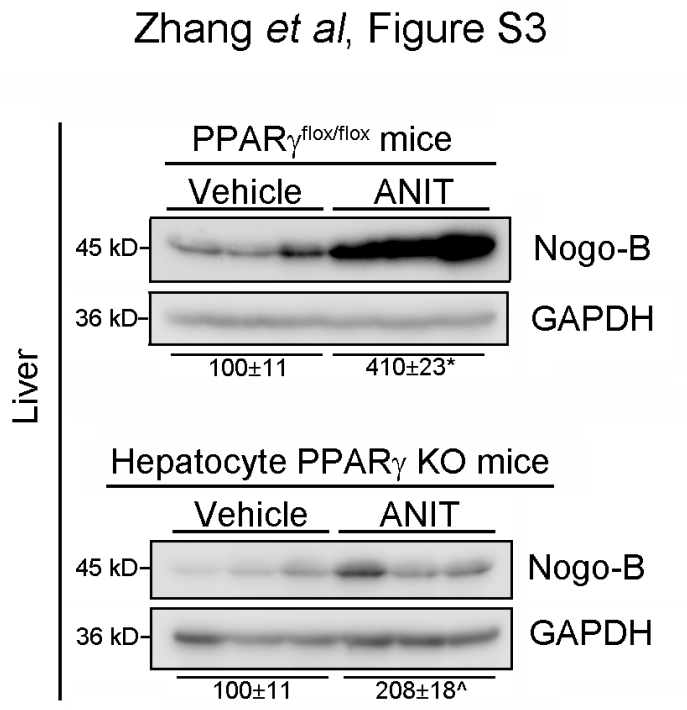

Figure S3. ANIT induces Nogo-B expression in PPARγ$^{fl/fl}$ and hepatocyte PPARγ KO mouse liver.

Total proteins were extracted from a piece of liver of PPARγ$^{fl/fl}$ and hepatocyte PPARγ KO mice after ANIT treatment as indicated in Figure 3A. Expression of Nogo-B in the liver was determined by Western blot with quantification of band density. *,^p<0.05 *vs*. Vehicle in corresponding type of mice, n=5 for Vehicle groups, n=7 for ANIT groups.

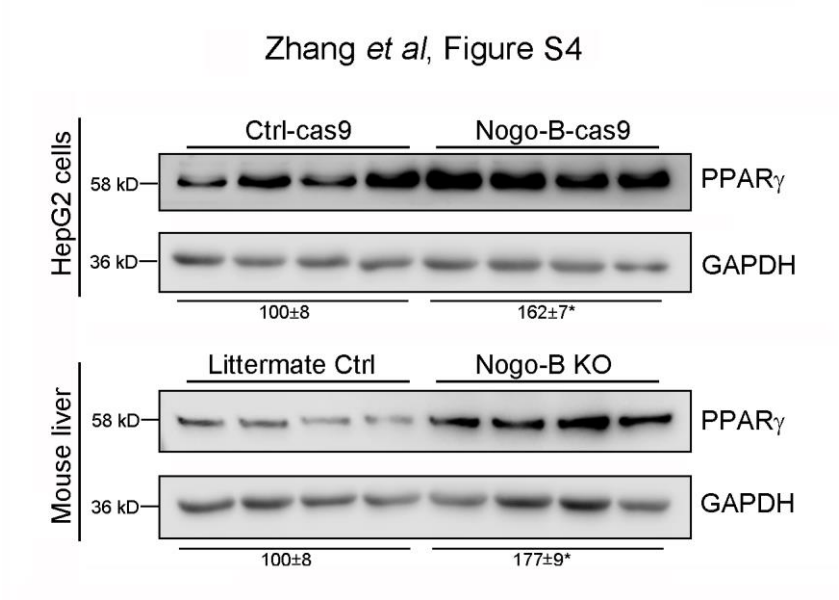

Figure S4. Nogo-B deficiency induces PPARγ protein expression in HepG2 cells and mouse liver.

Total proteins were extracted from Ctrl-cas9 and Nogo-B-cas9 HepG2 cells, or a piece of liver of littermate control and Nogo-B KO mice, followed by determination of PPARγ protein expression by Western blot with quantification of band density. *p<0.05 *vs.* Ctrl-cas9 cells or littermate control mice, n=6.

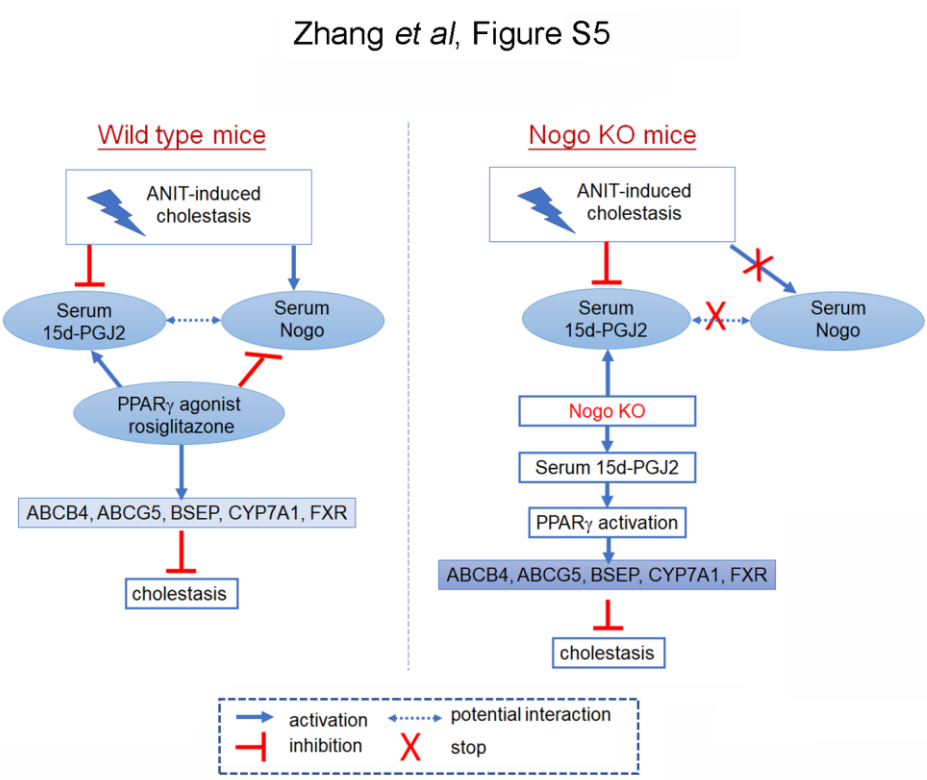

Figure S5. The model depicts anti-intrahepatic cholestasis properties of rosiglitazone and Nogo-B deficiency.
In wild type mice, ANIT induces intrahepatic cholestasis by inhibiting expression of molecules for bile homeostasis, which is associated with reduction of 15d-PGJ_2 and increase of Nogo in circulation. Treatment of cholestatic mice with rosiglitazone activates PPARγ to correct ANIT-inhibited hepatic expression of molecules for bile homeostasis and circulating 15d-PGJ_2 and Nogo, thereby reducing intrahepatic cholestasis. In Nogo KO mice, lack of Nogo-B expression in the liver enhances 15d-PGJ_2 production to activate PPARγ, therefore, the basal expression of molecules for bile homeostasis is activated which results in that Nogo KO mice are resistant to intrahepatic cholestasis naturally.