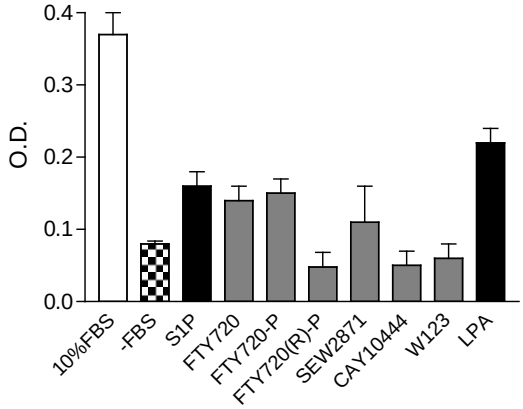
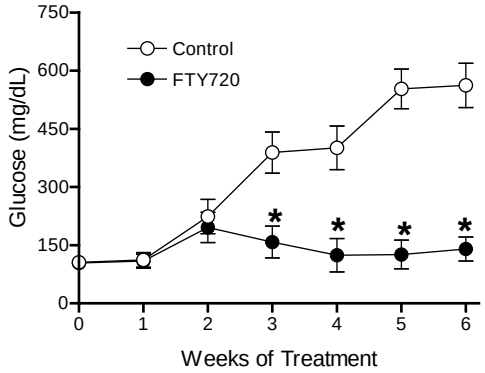
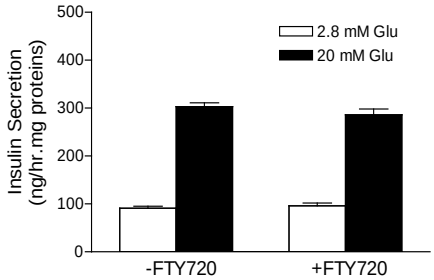


Supplementary Fig. 1. Lysophospholipid-induced cell proliferation. INS-1 cells were cultured in the RPMI 1640 medium. The same numbers of INS-1 cells were plated in the 96-well plate in the medium of RPMI for overnight, washed with PBS, and continuously cultured in the Hanks' balanced salt solution (HBSS) containing 2 mM glucose and 0.5% FBS for overnight. Then the cells were treated with LP analogs in the fresh HBSS medium for 24 hours. Then the treated cells were subjected to analysis by a Cell Proliferation Assay Kit (XTT) according to the manufacturer's instruction (Roche). The absorbance (A492 nm–A690 nm) was measured by a microplate reader. S1P, FTY720, and FTY720-P: 0.1 μM; FTY720(R)-P: 0.01 μM; Cay, 10 μM; W123: 20 μM; SEW2871: 0.1 μM; LPA, 10 μM.



Supplementary Fig. 2. Fasting glucose levels. Five-week-old female db/db mice (BKS.Cq-*m+/+Leprdb*) were purchased from Jackson Laboratories (Bar Harbor, Me., USA). After a week housing, FTY720 (10 mg/kg) was intraperitoneally injected into db/db mice daily (6 weeks old). The fasting glucose levels were measured at the end of each week. *$p < 0.001$. Some mice developed ankylenteron in the injection area. Therefore, after 6 weeks treatments, all mice with injection of FTY720 were sacrificed.



Supplementary Fig. 3. FTY720 does not affect glucose-stimulated insulin secretion by normal islets *ex vivo*. Islets were isolated from 8 weeks old normal C57/BL6 mice and treated with or without 0.2 μM FTY720 in the culture medium without FBA for 24 hours. Then the islets were stimulated with glucose and secreted insulin was measured using a Ultra Sensitive Mouse Insulin ELISA Kit (Crystal Chem Inc., Downers Grove, IL) and total proteins of islets were measured.