Figure S1. Immunohistochemical staining of (A) negative controls and (B) positive controls of insulin, Ki-67 and S1PR1-3 in tissue. Magnification, x400; scale bar, 100 μm. S1PR, S1P receptor.
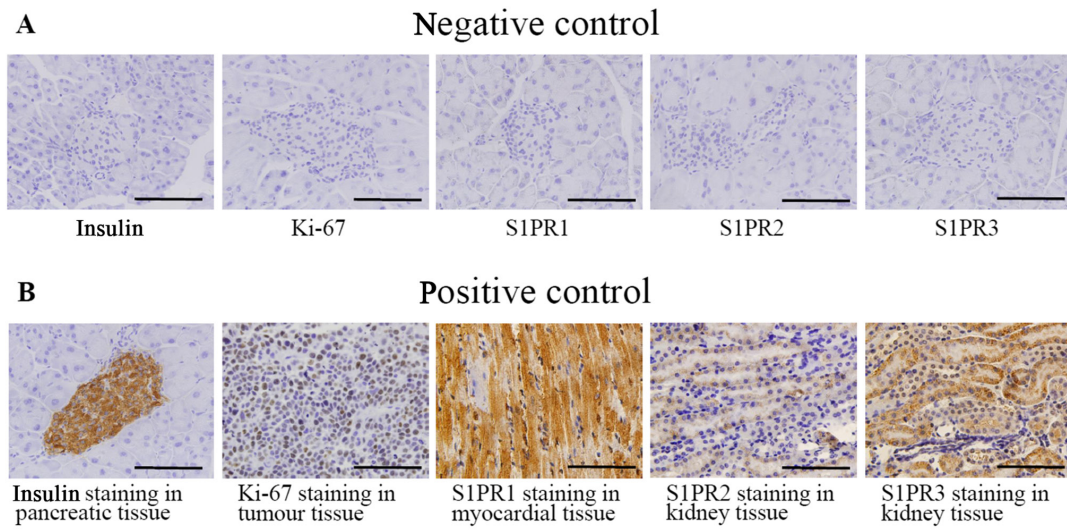
A Negative control

| Insulin | Ki-67 | S1PR1 | S1PR2 | S1PR3 |

B Positive control

| Insulin staining in pancreatic tissue | Ki-67 staining in tumour tissue | S1PR1 staining in myocardial tissue | S1PR2 staining in kidney tissue | S1PR3 staining in kidney tissue |

Table SI. Effect of S1P on mouse fasting blood glucose.

Group	n	0 w	1 w	2 w	3 w
NC	10	6.85±1.02	7.49±0.52	7.45±0.68	8.03±0.47
DC	8	16.11±4.05[a]	15.19±4.73[a]	16.39±5.22[a]	17.26±4.27[a]
S1P	9	16.03±4.32[a]	14.48±5.44[a]	14.76±4.90[a]	16.01±4.26[a]

Values are presented as the mean ± standard deviation. Parametric one-way analysis of variance followed by Least Significant Difference post hoc test was performed for the comparison of the groups. [a]$P<0.01$ vs. NC. NC, normal control; DC, diabetic control; S1P, sphingosine-1-phosphate.

Table SII. Proliferation rate of islet cells in all groups.

Group	n	Proliferation rate (%)
NC	10	0.71 (0.51, 1.02)
DC	8	0 (0, 0.39)[a]
S1P	9	0.65 (0, 1.18)[b]

Values are expressed as the median (interquartiles). Statistical analysis was performed using the Kruskal-Wallis H test. [a]P<0.01 vs. NC; [b]P<0.05 vs. DC. NC, normal control; DC, diabetic control; S1P, sphingosine-1-phosphate.

Table SIII. Apoptosis rate of islet cells in all groups.

Group	n	Apoptosis rate (%)
NC	10	21.98±2.85
DC	8	30.43±3.15[a]
S1P	9	27.52±2.23[a,b]

Values are expressed as the mean ± standard deviation. Parametric one-way analysis of variance followed by Least Significant Difference post hoc test was performed for comparison of the groups. [a]$P<0.01$ vs. NC; [b]$P<0.05$ vs. DC. NC, normal control; DC, diabetic control; S1P, sphingosine-1-phosphate.

Table SIV. IOD/area of S1PR1, S1PR2 and S1PR3 in all groups.

Group	n	IOD/area of S1PR1	IOD/area of S1PR2	IOD/area of S1PR3
NC	10	0.0914±0.0139	0.0356±0.0147	0.0813±0.0250
DC	8	0.1296±0.0181[b]	0.0499±0.0130[a]	0.0779±0.0234
S1P	9	01308±0.0108[b]	0.0495±0.0133[a]	0.0943±0.0178

Values are expressed as the mean ± standard deviation. Parametric one-way analysis of variance followed by Least Significant Difference post hoc test was performed for the comparison of the groups. [a]$P<0.05$ and [b]$P<0.01$ vs. NC. NC, normal control; DC, diabetic control; S1P, sphingosine-1-phosphate; S1PR, S1P receptor; IOD, integrated optical density.