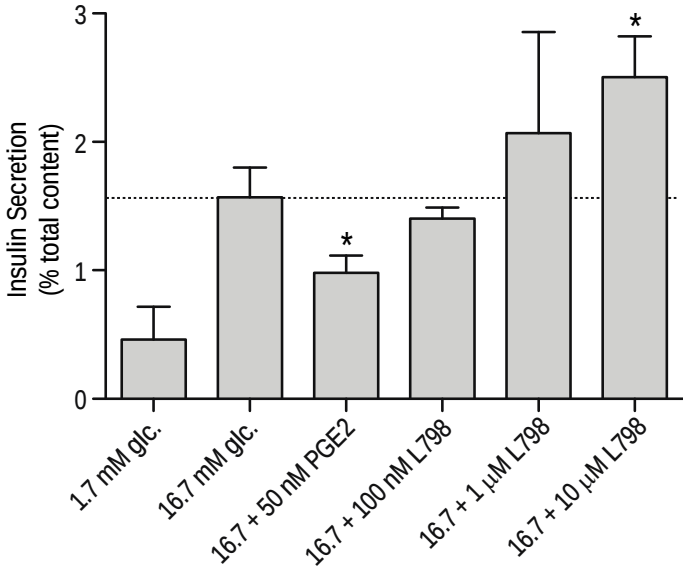
SUPPLEMENTARY DATA

**Supplementary Table 1.** Donor Demographics for human islet samples used in GSIS assays in Figure 3. If a value is missing, it was not known.

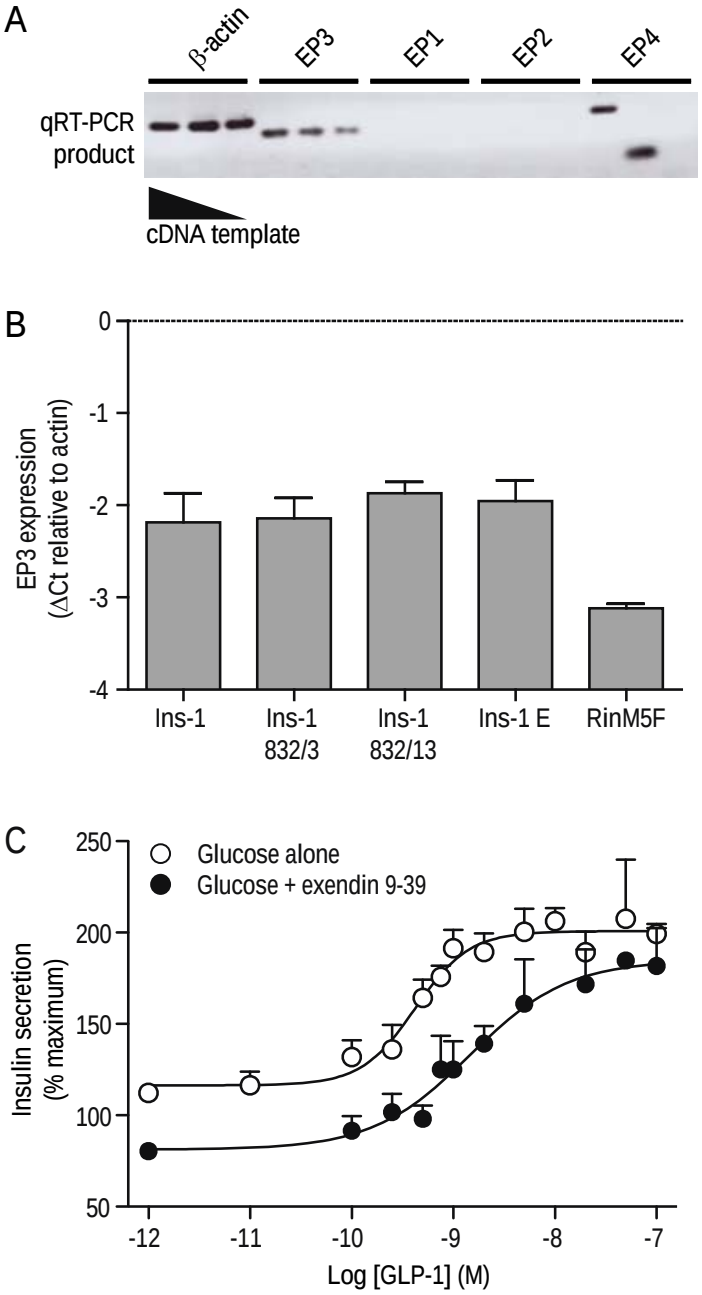
| Sample name | BMI | Age | Sex | Race | Cold Ischemia (min) | Time to shipment (hours) | Purity | Viability | Batch Type | Type Of Islets | Institution | Shipped | Delivered |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ND1 | 34.4 | 48 | M | White | | 69 | 80% | 99% | Most Pure | Cultured | University of Minnesota | 11/3/10 | 11/4/10 |
| ND2 | 30 | 64 | | | 841 | 118 | 85% | 95% | Most Pure | Cultured | The Scharp/Lacy Institute | 11/17/10 | 11/18/10 |
| ND3 | 33.1 | 49 | F | White | 258 | 26 | 92% | 99% | Most Pure | Cultured | University of Minnesota | 12/10/10 | 12/11/10 |
| ND4 | 27.4 | 39 | M | White | | | 98% | 99% | Most Pure | Cultured | Massachusetts General Hospital | 2/22/11 | 2/23/11 |
| ND5-xylitol | 28.8 | 20 | M | White | 308 | 24.5 | 90% | 95% | Most Pure | Cultured | The Scharp/Lacy Institute | 3/1/11 | 3/2/11 |
| ND6-xylitol | 31.6 | 51 | F | White | 308 | 95 | 90% | 96% | Most Pure | Cultured | University of Pennsylvania | 3/7/11 | 3/8/11 |
| ND7-xylitol | 23.2 | 61 | | | | 36 | 90% | 97% | Most Pure | Cultured | University of Illinois | 3/10/11 | 3/11/11 |
| T2D1 | 38 | 54 | M | | | | 80% | 95% | Most Pure | Cultured Confirmed Type II Diabetic Donor | The Scharp/Lacy Institute | 1/14/11 | 1/15/11 |
| T2D2 | 50 | 52 | M | White | | | 80% | 92% | Most Pure | Cultured Confirmed Type II Diabetic Donor | The Scharp/Lacy Institute | 2/14/11 | 2/15/11 |
| T2D3 | 34 | 66 | M | White | | | 95% | 99% | Most Pure | Cultured Confirmed Type II Diabetic Donor | Massachusetts General Hospital | 2/14/11 | 2/15/11 |
| T2D4 | 33.5 | 44 | M | Hispanic | | | 80% | 95% | Most Pure | Cultured Confirmed Type II Diabetic Donor | The Scharp/Lacy Institute | 5/10/11 | 5/11/11 |
| **t-test (ND vs T2D):** | **0.03** | **0.44** | | | | | | | | | | | |
| **Mean ND:** | **30** | **47** | | | | | | | | | | | |
| **Mean T2D:** | **39** | **54** | | | | | | | | | | | |

**Supplementary Figure 1.** The EP3 antagonist, L-798,106, causes a dose-dependent increase in GSIS in islets isolated from diabetic BTBR mice. Increasing the concentration of L-798,106 100-fold, from 100 nM to 10 μM, elicits a significant potentiation of GSIS. The 10 μM or 20 μM concentration was chosen for all further experiments. (n=3; *, $p<0.05$).



SUPPLEMENTARY DATA

**Supplementary Figure 2.** The EP3 receptor is expressed in Ins-1 832/3 cells, which are highly responsive to cAMP stimulation. (A) EP3 qRT-PCR product is expressed in all PCR reactions in a 100X cDNA dilution series, from 20 ng to 0.2 ng input cDNA. The $G\alpha_s$-coupled EP4 is also expressed in these reactions, but only at the highest concentration of cDNA, whereas the PCR product in the 2 ng reaction is primer dimer. (B) EP3 mRNA is expressed at similar levels in all Ins-1-derived rat insulinoma cell lines, being slightly reduced in the RinM5F rat insulinoma cell line. (C) The Ins-1 (832/3) cell line is highly responsive to cAMP agonists like GLP-1 to promote GSIS. GSIS assays were performed in the presence of 11 mM glucose with increasing concentrations of GLP-1. The GSIS effect in 11 mM glucose alone was set at 100 percent; GLP-1 potentiated the effect of glucose by another 100%. In this experiment, the ability of GLP-1 to compete with 70 nM Exendin 9-39, an inverse agonist of the GLP-1 receptor, was also tested. Exendin 9-39 acts as a competitive antagonist by shifting the EC50 to the right, while having little effect on the maximal effect of GLP-1.



SUPPLEMENTARY DATA

**Supplementary Figure 3.** The expression patterns of the EP receptor family and PGE2 synthetic enzymes are similar in the mouse α-cell-derived line, αTC1, and β-cell-derived line, Min6, as compared to isolated mouse islets. Copy DNA was generated from RNA samples derived from the indicated cell lines and subjected to qRT-PCR analysis with primers specific for β-actin or the indicated genes. Ct values were normalized to β-actin and to a control RNA sample that had not been subjected to cDNA synthesis (no-RT control). All primer sets except those for EP2 elicited a significant amplification above control in all samples. The ΔCt values for isolated lean mouse islets is shown in black bars as a comparison. The gene expression patterns are all similar for lean islets, Min6 cells, and αTC1 cells. Technical replicates were performed in duplicate, and the values for each primer set were averaged before subtracting from the average of the β-actin values for that sample.