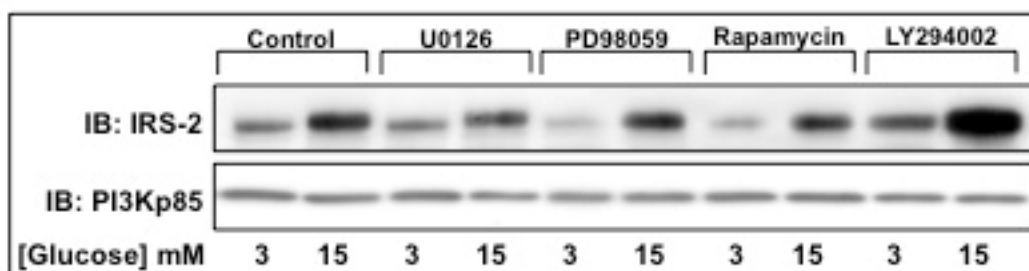


## SUPPLEMENTARY DATA

**Supplementary Table 1. Sequences of PCR primer sets used in this study.**

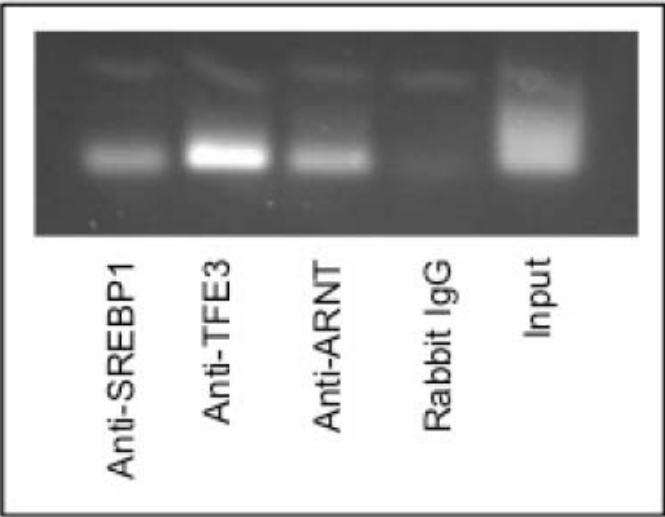
| Gene        | Forward Primer                   | Reverse Primer                   |
|-------------|----------------------------------|----------------------------------|
| RAT IRS-2   | 5' -CCCCAGTGTCCCATCCT- 3'        | 5' -TTTCCTGAGAGAGACGTTTTCCA- 3'  |
| RAT SREBP1c | 5' -AGCGCTACCGTTCCTCTATC- 3'     | 5' -GCGCAAGACAGCAGATTTAT- 3'     |
| RAT FoxO1   | 5' -CACCTTGCTATTCGTTTGC- 3'      | 5' -CTGTCCTGAAGTGTCTGC- 3'       |
| RAT FoxO3a  | 5' -CGGCTCACTTTGTCCCAGAT- 3'     | 5' -TCTTGCCAGTCCCTTCGTTC- 3'     |
| RAT FoxO4   | 5' -AGGCTCCTACACTTCTGTACTGG- 3'  | 5' -CTTCAGTAGGAGATGCAAGCACAG- 3' |
| RAT ARNT    | 5' -CTGCAGGTAACCAGTTCTCCTAAC- 3' | 5' -CACCTGCTGAAAGCTGTCTCTTAG- 3' |
| RAT TFE3    | 5' -CCATCTCAGTGATTGGTGTGTC- 3'   | 5' -GTAGCGTGTAGGGTTCTCTAGGTG- 3' |
| RAT p85PI3K | 5' -GAGAGGAAGACATCGACCTACACT- 3' | 5' -CCTCTCCCAGTAGTTTCATTG- 3'    |

**Supplementary Figure 1. The effect of IRS-2 signal transduction inhibitors on glucose-induced increase in IRS-2 protein levels in rat islets.** Isolated rat islets were incubated at basal 3mM or stimulatory 15mM glucose for 6h in the presence or absence of U0126 (10μM), PD98059 (50μM), rapamycin (10nM) or LY294002 (5μM) or as indicated. IRS-2 and PI3K(p85) (as a loading control) protein levels were then analyzed by immunoblotting. An example immunoblot is shown.

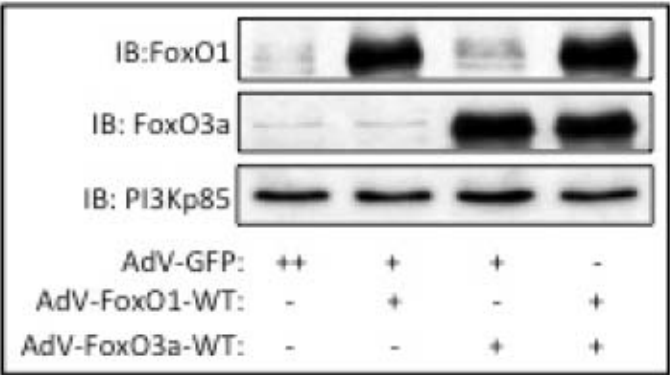


SUPPLEMENTARY DATA

**Supplementary Figure 2. The transcription factors ARNT, SREBP1c and TFE3 specifically bind to the IRS-2 promoter in HepG2 cells.** It has been previously shown that the antibodies to SREBP-1c, TFE3, FoxO1 and FoxO3a used for ChIP assays in this study can be readily used for IRS-2 promoter ChIP assays in other cell types (1 -3), including hepatocytes. The ARNT antibody used was the same as previously described (4). Nonetheless, since we were unable to show that ARNT, SREPB1c and TFE3 associated with the IRS-2 promoter in  $\beta$ -cells (Fig. 3), positive control experiments were conducted in the HepG2 cell lysates to indicate that the antibodies for ARNT, SREPB1c and TFE3 could be used in ChIP assays in our hands to demonstrate an interaction with the IRS-2 promoter in an alternative cell type. An example electrophoretic analysis from a ChIP assay is shown where clearly SREPB1c, TFE3 and ARNT can be seen to associate with the IRS-2 promoter in HepG2 cells above the IgG control.

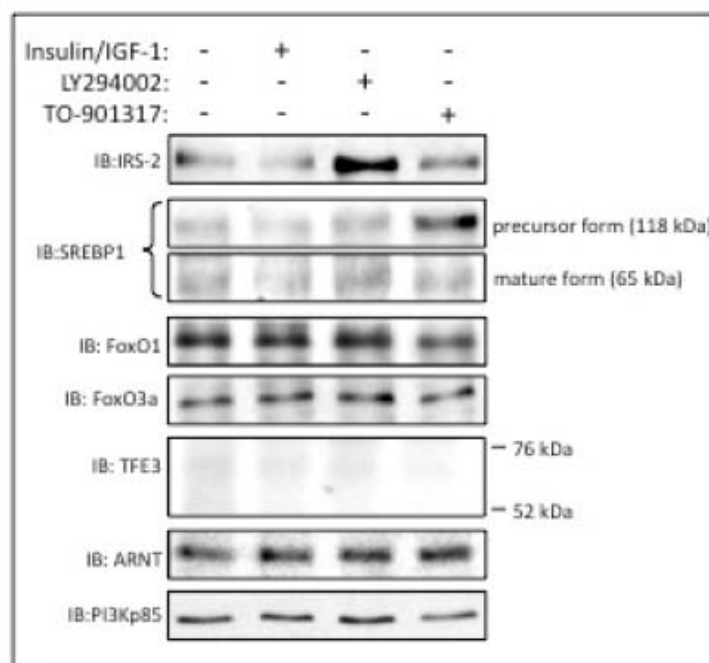


**Supplementary Figure 3. Comparable levels of adenoviral mediated FoxO1 and FoxO3a expression in INS-1 cells.** In order to indicate that equivalent expression of FoxO1 and FoxO3a could be obtained with a similar titer and dose of adenoviral vector, INS-1 cells were infected with Adv-GFP (control), Adv-FoxO1-WT or Adv-FoxO3a-WT as indicated and cells analyzed for FoxO1 , FoxO3a and PI3K(p85) (as a loading control) protein expression by immunoblotting. An example immunoblot analysis is shown. Note also that there is negligible cross-reactivity between FoxO1 and FoxO3a antibodies used in this analysis.



## SUPPLEMENTARY DATA

**Supplementary Figure 4. SREBP1 expression is induced but not activated by an LXR agonist in isolated rat islets and does not affect IRS-2 expression.** In order to indicate that SREBP1 expression could be regulated and detected in pancreatic islets, isolated rat islets were incubated for 6 hours at basal 3 mM glucose  $\pm$  insulin (100 nM)/IGF-1 (10 nM), LY294002 (50  $\mu$ M) or the LXR agonist, TO901317 (1  $\mu$ M). The protein expression levels of IRS-2, SREBP-1 (precursor and proteolyzed activated forms), FoxO1, FoxO3a, TFE3, ARNT and PI3Kp85 (control) were measured in parallel by immunoblotting. An example immunoblot analysis is shown.



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