

# Supporting Information

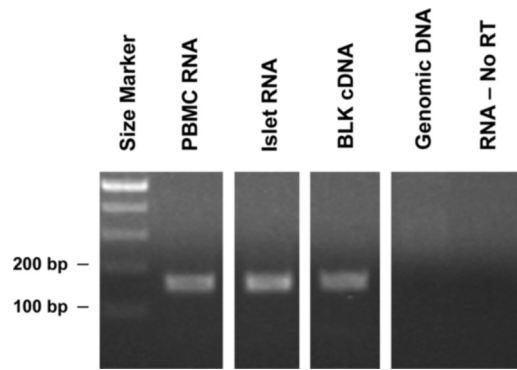
Borowiec et al. 10.1073/pnas.0906474106

## SI Text

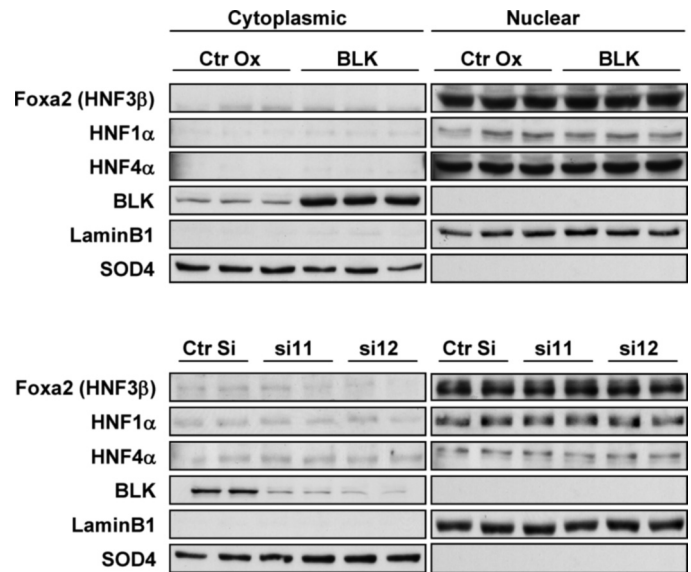
**Primers Used to Amplify the DNA Fragments for Luciferase Reported Studies.** The fragment spanning positions 11,369,157 (960 bp) was amplified with primers GCTTACGGTACCCACCTTCTTC-CCATCCCATC and CCATTGCTCGAGGAAACCAAGTCT-CAATCCTAAGATGTG, the fragments spanning positions 11,459,364 and 11,459,531 (527 bp) with primers GGTTAG-GATCCGTAAGGTGTTTCAGGACTGGTAAGCGAC and CCATTGTCGACGCGCCCATCGTCACCCG, and the fragment spanning position 11,468,050 (707 bp) with primers GGTT-TAGGATCCGAGGCTGACAGGGGCTGATGG and CCAT-TACAGCTGGTCCCCATTCCTTTGCGTATTG.

**Antibodies for Western Blotting.** Rabbit polyclonal anti-Akt, anti-phospho Akt (S473) and anti-BLK antibodies were purchased from Cell Signaling Technology; rabbit polyclonal anti-HNF4 $\alpha$ , anti-HNF1 $\alpha$ , HNF3 $\beta$ , anti-Glut2, anti-GCK, anti-IR $\beta$ , and anti-IGF1R $\beta$  as well as goat polyclonal anti-Kir6.2 and anti-SUR1 were obtained from Santa Cruz Biotechnology; rabbit polyclonal anti-Pdx1 was from Chemicon International; rabbit polyclonal anti-IRS1 and anti-IRS2 were obtained from Upstate; mouse monoclonal anti-Nkx6.1 was obtained from the Developmental Studies Hybridoma Bank (University of Iowa); mouse monoclonal anti- $\alpha$ -tubulin, anti-laminB1, and anti-SOD4 were purchased from Abcam.



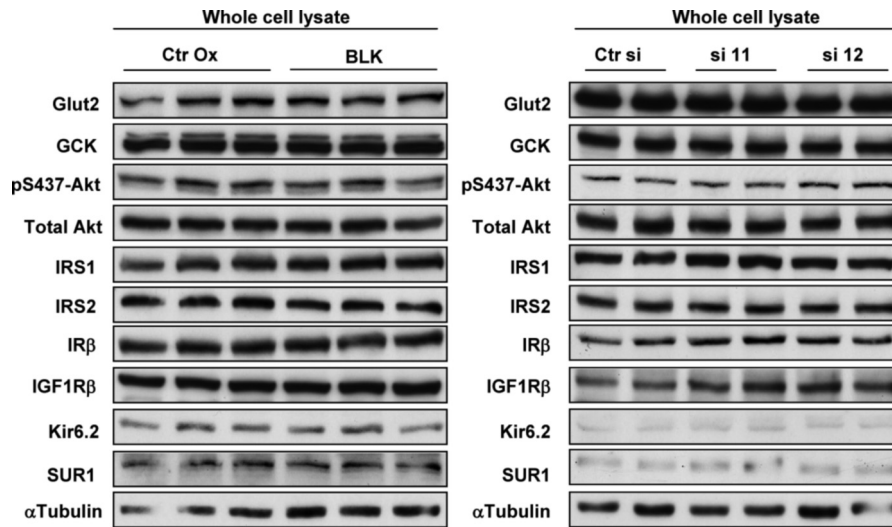


**Fig. S2.** RT-PCR amplification of BLK from pancreatic islets. Reverse transcription-PCR was performed starting from total RNA extracted from purified peripheral blood mononuclear cells (PBMC) and pancreatic islets. cDNA was synthesized from 1  $\mu$ g total RNA by reverse transcription using random hexamers as primers and standard conditions. PCR was performed from cDNA using primers GCAGATGCTGAAGGGGAGAAG (exon 4) and GCAGATGCTGAAGGGGAGAAG (exon 6) for 35 cycles with an annealing temperature of 61°C. The expected PCR product size was 177 bp. BLK cDNA served as a positive control; genomic DNA and an RT preparation from which the reverse transcriptase was omitted from the reaction served as negative controls.



**Fig. S3.**  $\beta$ -cell expression of HNF-3 $\beta$ , HNF-1 $\alpha$ , and HNF-4 $\alpha$  in MIN6  $\beta$ -cells in relation to BLK overexpression or knock-down. Western blot analysis was performed on cytosolic and nuclear fractions prepared from MIN6  $\beta$ -cells using antibodies specific for each factor. Lamin B1 and SOD4 were used as markers of the nuclear and cytosolic fractions, respectively, to control for purity and gel loading.





**Fig. S5.**  $\beta$ -cell expression of proteins involved in insulin signaling and glucose sensing in MIN6  $\beta$ -cells in relation to BLK overexpression or knockdown. Western blotting analysis of proteins involved in insulin signaling and glucose sensing was performed on whole-cell lysates prepared from MIN6  $\beta$ -cells expressing control, BLK (overexpression), BLK si11, and BLKsi12 (knockdown).



**Table S1. Summary of mutation screening at 8p23**

Gene	Symbol	Size, Kb	Exons	Kb sequenced		Sequence differences
				Coding	Noncoding	
RefSeq						
Acyl-malonyl condensing enzyme	<i>AMAC1L2</i>	2	1	1.0	2.1	19
B lymphoid tyrosine kinase	<i>BLK</i>	71	13	4.0	80.0	31
Cathepsin B	<i>CTSB</i>	35	12	1.0	21.0	29
Deubiquitinating enzyme 3	<i>DUB3</i>	3	1	2.7	1.9	10
Farnesyl-diphosphate farnesyltransferase 1	<i>FDFT1</i>	38	8	2.5	16.0	19
GATA-binding protein 4	<i>GATA4</i>	67	8	1.3	77.0	29
L-threonine 3-dehydrogenase	<i>TDH</i>	31	8	2.3	12.0	12
Methionine sulfoxide reductase A	<i>MSRA</i>	400	7	2.6	48.0	3
Myotubularin-related protein 9	<i>MTMR9</i>	46	10	7.4	12.0	23
Nei-like 2	<i>NEIL2</i>	28	5	3.1	9.2	5
PIN2-interacting protein 1	<i>PINX</i>	81	7	1.8	9.0	11
Protein phosphatase 1 regulatory subunit 3b*	<i>PPP1R3B</i>	12	3	0.9	4.1	20
Retinitis pigmentosa 1-like 1	<i>RP1L1</i>	114	6	8.7	24.0	6
SRY-box 7	<i>SOX7</i>	6	2	3.3	3.8	13
Tankyrase 1*	<i>TNKS</i>	220	27	4.0	176.0	22
Other mRNAs						
AA909882	-	5	3	1.1	1.4	3
AJ291676	-	3	1	0.8	1.2	-
AJ301563	-	3	5	0.8	1.2	2
AK055863	-	10	3	1.4	2.8	13
AK124536	-	4	1	2.3	3.4	3
BC043573	-	3	3	1.2	1.3	4
BC065837	-	26	6	1.5	2.7	8
BM803853	-	1	1	1.0	1.2	1
C8orf12	-	50	4	1.2	1.8	12
C8orf13	-	42	3	2.1	1.2	8
C8orf14	-	6	3	1.9	3.0	9
C8orf15	-	8	2	1.7	2.4	8
C8orf16	-	12	2	1.2	4.7	2
C8orf21	-	300	4	1.9	23.0	11
C8orf49	-	4	1	1.9	1.3	3
C8orf5	-	6	1	1.8	2.4	5
C8orf6	-	6	1	1.4	1.6	9
C8orf7	-	6	2	1.4	2.4	-
C8orf8	-	20	2	1.3	3.4	4
UNQ9391	-	16	5	2.1	7.8	16
Intergenic regions						
BLK-C8orf14	-	11	-	-	9.0	15
C8orf14-GATA4	-	110	-	-	80.0	22
<b>Total</b>		<b>1,696</b>	<b>171</b>	<b>76.6</b>	<b>655.3</b>	<b>410</b>

\*Functional candidate genes placed outside the critical interval.