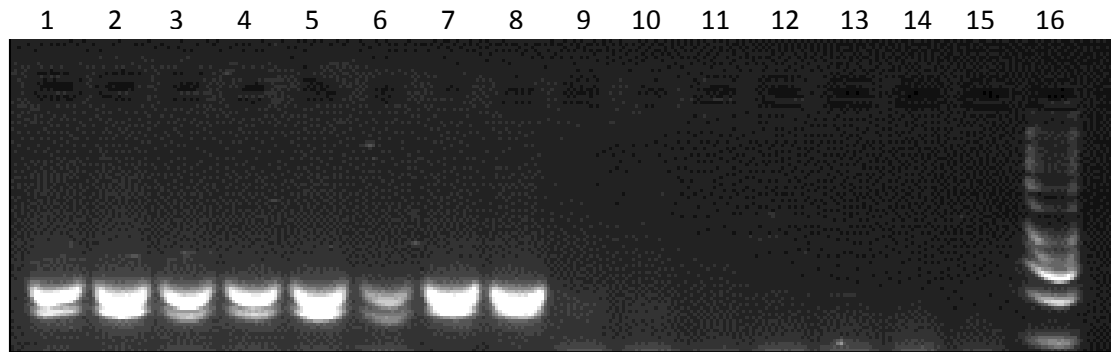
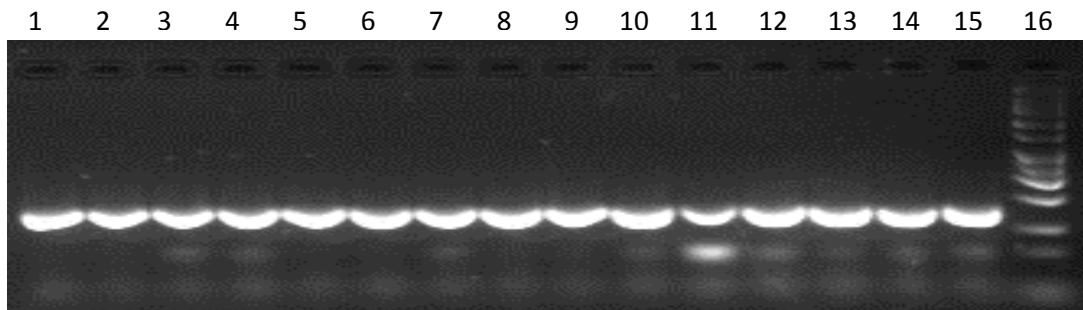


cRNA PCR on *Tpcn2*



cRNA PCR on GAPDH



Lane	Genotype	Tissue cRNA is from
1	Wild Type	Kidney
2	Wild Type	Kidney
3	Wild Type	Retroperitoneal Fat
4	Wild Type	Retroperitoneal Fat
5	Wild Type	Heart
6	Wild Type	Heart
7	Wild Type	Liver
8	Wild Type	Liver
9	Knockout	Kidney
10	Knockout	Kidney
11	Knockout	Retroperitoneal Fat
12	Knockout	Heart
13	Knockout	Heart
14	Knockout	Liver
15	Knockout	Liver
16	Size Standard	

Figure S1 PCR on RNA from multiple tissues in wild-type and knock-out *Tpcn2* mice. Results confirm that the knock-out mice do not transcribe *Tpcn2*.

File S1

**** List of MAGIC (Meta-Analysis of Glucose and Insulin-Related traits) Consortium investigators**

File S1 is available for download as a pdf at <http://www.genetics.org/lookup/suppl/doi:10.1534/genetics.114.162982/-/DC1>.

Files S2-S5

Available for download as Excel files at <http://www.genetics.org/lookup/suppl/doi:10.1534/genetics.114.162982/-/DC1>

File S2 Phenotype data used for the cluster analysis

File S3 HS genotype data for 18 SNPs within the 3.1 Mb QTL on rat chromosome 1

File S4 Quantitative rt-PCR data for *Tpcn2* and GAPDH in 120 HS rats

File S5 Glucose and insulin levels during the IPGTT in *Tpcn2* knock-out, heterozygous and wild-type mice

Table S1 Association between *Tpcn2* SNPs and diabetic traits in humans

SNP	Location (Mb)	Functional location	Fasting Insulin		HOMA_IR	
			Unadjusted p-value (effect)	BH adjusted p-value	Unadjusted p-value (effect)	BH adjusted p-value
rs2376554	Chr 11:68811445	upstream				
rs749363	Chr. 11:68812024	upstream				
rs7932947	Chr. 11:68812781	upstream				
rs55918435	Chr. 11:68813015	upstream				
rs35678276	Chr. 11:68814544	upstream				
rs59234009	Chr. 11:68814545	upstream				
rs56932042	Chr. 11:68814568	upstream				
rs10792010	Chr. 11:68814887	upstream				
rs3018679	Chr. 11:68814894	upstream				
rs59427626	Chr. 11:68815258	upstream				
rs35443329	Chr. 11:68815437	upstream				
rs10750836	Chr. 11:68815523	upstream	0.5689	0.5689	0.6327	0.6643
rs12790685	Chr. 11:68815948	upstream				
rs12791187	Chr. 11:68815949	upstream				
rs4930642	Chr. 11:68816370	UTR 5'				
rs4453241	Chr. 11:68816825	intron				
rs11823877	Chr. 11:68819011	intron				
rs11228458	Chr. 11:68819204	intron				
rs11604251	Chr. 11:68820429	intron	0.0073	0.0511*	0.6643	0.6643
rs10792012	Chr. 11:68820569	intron	0.5117	0.5689	0.6216	0.6643
rs6591367	Chr. 11:68821947	intron				
rs7127082	Chr. 11:68822023	intron	0.02475	0.0937	0.0392	0.2415
rs7942690	Chr. 11:68823940	intron	0.5004	0.5689	0.6251	0.6643
rs3019776	Chr. 11:68826155	intron	0.5221	0.5689	0.2321	0.6499
rs7930211	Chr. 11:68827717	intron				
rs11228469	Chr. 11:68829638	intron	0.0868	0.2430	0.1142	0.3997
rs3829236	Chr. 11:68838028	intron	0.3042	0.5689	0.3242	0.6643
rs4930263	Chr. 11:68847005	intron				
rs2290418	Chr. 11:68847687	intron				
rs2376558	Chr. 11:68851414	missense				
rs753559	Chr. 11:68851605	intron	0.02676	0.0937	0.03936	0.2415
rs3750967	Chr. 11:68855112	intron	0.4648	0.5689	0.5844	0.6643
rs1060435	Chr. 11:68855595	UTR 3'	0.2497	0.5689	0.507	0.6643

rs4930265	Chr. 11:68855954	UTR 3'	0.5297	0.5689	0.5493	0.6643
rs3018681	Chr. 11:68856224	UTR 3'				
rs3168115	Chr. 11:68858090	downstream	0.5077	0.5689	0.5037	0.6643
rs10736671	Chr. 11:68858907	downstream	0.0038	0.0511*	0.05174	0.2415
rs3018673	Chr. 11:68859608	downstream				
rs7930709	Chr. 11:68860223	downstream				

39 human SNPs within or near *Tpcn2* were used to determine association with diabetes and related traits. DIAGRAM assessed association between 11 SNPs (in italics) and diabetes while MAGIC assessed association between 14 SNPs (in bold) and fasting glucose, fasting insulin and the homeostatic model assessment of insulin resistance (HOMA_IR). Associations between 14 SNPs and fasting insulin and HOMA_IR, as assessed by MAGIC, are listed above. Multiple comparisons were adjusted for using the Benjamini and Hochberg FDR method (BH). No significant associations were found between the SNPs and diabetes or fasting glucose. Associations could not be determined for SNPs that are not in bold because of insufficient data. * p = 0.051 after adjusting for multiple corrections.

Table S2 Phenotypic differences between glucose intolerant and normal glucose HS rats

Trait	Normal Glucose HS (mean \pm SD)	Glucose Intolerant HS (mean \pm SD)
Glucose_AUC	9061.0 \pm 209.1	13,458.9 \pm 1,035.5***
Insulin_AUC	204.3 \pm 63.3	311.3 \pm 106.7***
Fasting glucose (mg/dL)	77.5 \pm 6.6	90.3 \pm 6.7***
Fasting insulin (ng/ml)	1.1 \pm 0.5	1.8 \pm 1.2**
Fasting c-peptide (pg/ml)	1505.8 \pm 479.8	1808.0 \pm 367.8*
Fasting cholesterol (mg/dL)	100.1 \pm 46.8	125.5 \pm 56.0
Fasting triglycerides (mg/dL)	72.3 \pm 20.1	86.2 \pm 12.2**
QUICKI (1/(logI0 + logG0))	0.54 \pm 0.06	0.48 \pm 0.08**
Body Weight (g)	314.4 \pm 25.8	349.1 \pm 33.5***
Retroperitoneal fat pad weight (g)	0.014 \pm 0.004	0.014 \pm 0.005
Epidydimal fat pad weight (g)	0.015 \pm 0.005	0.016 \pm 0.005

***p < 0.0001, **p < 0.01, *p < 0.05, see manuscript for full statistics

Tables S3-S6

Available for download as .docx files at <http://www.genetics.org/lookup/suppl/doi:10.1534/genetics.114.162982/-/DC1>

Table S3 Differentially Expressed Genes between Glucose Intolerant and Normal Glucose HS rats (Genome-wide)

Table S4 Mean expression levels for all probes within the 3.1 Mb chromosome 1 region

Table S5 Significance of association ($-\log_{10}P$) between 18 SNPs within the 3.1 Mb QTL on rat chromosome 1 and all traits that map to this locus

Table S6 Correlations between probes within the chromosome 1 region and six diabetic traits

Table S7 Phenotypic differences in *Tpcn2* knock-out, heterozygote and wild-type mice

Trait	Wild-type (mean \pm SD)	Heterozygotes (mean \pm SD)	Knock-out (mean \pm SD)
Glucose_AUC	22,917.5 \pm 4,384.2	21,811.2 \pm 1,609.2	20,700.0 \pm 3,660.1
Insulin_AUC	165.4 \pm 13.4	147.2 \pm 35.8	126.2 \pm 6.4**
Fasting glucose (mg/dL)	111.0 \pm 12.0	116.3 \pm 15.5	96.2 \pm 9.6*
Fasting insulin (ng/ml)	1.04 \pm 0.22	1.03 \pm 0.51	0.80 \pm 0.25
QUICKI (1/(logI0 + logG0))	0.49 \pm 0.02	0.49 \pm 0.04	0.54 \pm 0.04
Body Weight (g)	25.3 \pm 2.1	24.3 \pm 2.4	27.0 \pm 3.6

**p = 0.031 (wild-type mice differ from knock-out mice based on a Tukey-post-hoc based after an ANOVA between all three genotypes), *p = 0.048 (t-test between wild-type and knock-out mice only)