ESM Table 1. Characteristics summary of the murine models.

Diabetes Status	**Non-diabetic control**	**T1DM-like model**	**Non-diabetic control**	**T2DM-like model**
Mouse model	**DBA2J**	**DBA2J-STZ**	**BKS *db*/+**	**BKS *db*/*db***
DPN studies: Wiggin *et al.* 2008 Endocrinology [10]; Pande *et al.* 2011 Diabetes[11]				
Terminal age (week)	34	34	24	24
Metabolic Parameters:				
Body Weight (g)	29.7 ± 3.9	23.5 ± 1.7	29.6 ± 1.6	51.8 ± 4.4
Fasting Glucose (mmol/L)	6.7 ± 1.0	25.1 ± 9.0	8.2 ± 1.9	28.0 ± 4.4
% Glycosylated Hemoglobin	5.8 ± 0.9	14.2 ± 1.7	7.1 ± 0.6	12.3 ± 0.52
Neuropathy Measures:				
Hindpaw latency (s)	6.3 ± 1.0	11.1 ± 0.8	2.7 ± 0.6	4.0 ± 1.1
Motor Nerve Conduction Velocity (m/s)	45.5 ± 3.9	34.4 ± 7.1	48.3 ± 4.2	30.2 ± 10.4
Sensory Nerve Conduction Velocity (m/s)	23.7 ± 3.5	20.3 ± 3.2	20.6 ± 5.0	15.7 ± 5.5
IENF Density (fibers/m^2)	-	-	39.8 ± 3.1	27.2 ± 2.8
DN study: Hodgin *et al.* 2013 Diabetes [13]				
Terminal age (week)	22	22	24	24
Metabolic Parameters:				
Body Weight (g)	28 ± 1	22 ± 1	31 ± 1	50 ± 1
Fasting Glucose (mmol/L)	7.7 ± 0.3	30.9 ± 1.3	7.7 ± 0.3	31.3 ± 0.3
% Glycosylated Hemoglobin	-	-	-	-
Nephropathy Measures:				
Albumin/Creatinine Ratio	79 ± 11	916 ± 420	36± 2	426± 48

This table summarizes the characteristics of the murine models used in the current study, which are reported in our published papers (Wiggin *et al*. 2008 Endocrinology, Pande *et al*. 2011 Diabetes, Hodgin *et al*. 2013 Diabetes). We used the same microarray raw data as in the published papers, with the exception of the Pande *et al*. 2011 Diabetes paper for type 2 diabetes DPN study (*db*/*db*-SCN). While the published paper (Pande *et al.* 2011 Diabetes) included two batches of microarray data sets (n=7 for *db*/+ and n=6 for *db*/*db* group), our current study only used one batch of microarray data (n=5 for *db*/+ and n=6 for *db*/*db*) for type 2 diabetes DPN (*db*/*db*-SCN). This discrepancy was unavoidable because the batch-effect cannot be properly addressed in ChipInspector, which was used in the current study to identify differentially expressed genes. DN, diabetic nephropathy; DPN; diabetic peripheral neuropathy; IENF, intraepidermal nerve fiber; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus

ESM Table 2. Significant signaling pathways of the whole DEG sets.

Significant signaling pathways were identified by GeneRanker (Genomatix Software GmbH, http://www.genomatix.de) using a false discovery rate (FDR) < 0.05 as the significance cutoff. The values in the columns 3-6 are the FDR, indicating the statistical significance level. Pathways found significant in at least two DEG sets are given in this table.

Pathway terms	**# of significant pathways**	**STZ-Glom**	***db/db*-Glom**	**STZ-SCN**	***db/db*-SCN**
		32	**28**	**69**	**58**
Reelin signaling pathway	4	0.032	0.006	0.006	0.003
AKT(PKB)-Bad signaling (IL-7 signaling(JAK1 JAK3 STAT5))	3	0.025	0.005		<0.001
AKT(PKB)-Bad signaling (EPO signaling pathway(JAK2 STAT1 STAT3 STAT5))	3	0.032	0.003		<0.001
Gene expression (VEGF signaling pathway)	3	0.032	0.003		<0.001
Angiopoietin receptor Tie2-mediated signaling	3	0.020	<0.001		0.004
IL6-mediated signaling events	3	<0.001	0.020	0.016	
Filopodium formation (Integrin signaling pathway)	3		0.008	0.032	0.040
thrombin signaling and protease-activated receptors	3		0.025	0.010	0.032
inhibition of matrix metalloproteinases	3	0.040	0.010		0.013
Beta1 integrin cell surface interactions	2	<0.001	<0.001		
Thromboxane A2 receptor signaling	2	<0.001	0.002		
Plasma membrane estrogen receptor signaling	2			<0.001	0.040
regulators of bone mineralization	2		0.001		0.040
KitReceptor	2	0.010	0.002		
Integrin family cell surface interactions	2	0.003	0.032		
Regulation of RAC1 activity	2		0.010	0.003	
VEGFR3 signaling in lymphatic endothelium	2		0.004		0.040
EGFR1	2		0.040	0.005	
igf-1 signaling pathway	2			0.006	0.005
IGF1 pathway	2			0.010	0.032
AndrogenReceptor	2			0.010	0.013
bioactive peptide induced signaling pathway	2		0.025		0.013
Urokinase-type plasminogen activator (uPA) and uPAR-mediated signaling	2	0.013	0.040		
sumoylation by ranbp2 regulates transcriptional repression	2			0.016	0.040
Integrins in angiogenesis	2	0.016			0.016
Ephrin B reverse signaling	2	0.016	0.025		
regulation of pgc-1a	2		0.020		0.025
E-cadherin signaling events	2	0.025		0.032	
Regulation of p38-alpha and p38-beta	2	0.025	0.032		
Regulation of glucocorticoid receptor	2			0.050	0.032
Endothelins	2		0.032	0.040	

ESM Table 3. Canonical pathways (type 1 diabetes DN vs type 1 diabetes DPN).

Significant pathways (Benjamini-Hochberg adjusted P-values <0.05) were identified by GeneRanker (Genomatix) from the four DEG subsets (concordant, discordant, and the two unique sets). The numbers in columns 3-6 are the P-values. The Set-Count column indicates the number of DEG sets which have the corresponding pathway significantly enriched.

Names	Set-Count	STZ-Glom-Only	Concordant	Discordant	STZ-SCN-Only
foxa2 and foxa3 transcription factor networks	2	0.015	0.004		
lissencephaly gene (lis1) in neuronal migration and development	2		0.023	0.01	
kitreceptor	2	0.028		0.002	
g alpha s gdp-gtp exchange signaling (gpcr adenosine a2a receptor signaling pathway)	2			0.01	0.044
il6-mediated signaling events	2	0.005		0.023	
tumor suppressor arf inhibits ribosomal biogenesis	2			0.025	0.042
validated targets of c-myc transcriptional repression	2			0.046	0
circadian rhythm pathway	1		0.021		
il-3 signaling pathway(jak1 jak2 stat5) (il-3 signaling(jak1 jak2 stat5))	1		0.029		
posttranslational regulation of adherens junction stability and dissassembly	1		0.03		
srebp control of lipid synthesis	1		0.038		
alpha6beta4integrin	1		0.04		
eicosanoid metabolism	1		0.043		
shp2 signaling	1		0.043		
lpa4-mediated signaling events	1			0.002	
il2 signaling events mediated by pi3k	1			0.01	
reelin signaling pathway	1			0.01	
apoptotic signaling in response to dna damage	1			0.011	
a4b1 and a4b7 integrin signaling	1			0.012	
west nile virus	1			0.017	
canonical wnt signaling pathway	1			0.027	
il2 signaling events mediated by stat5	1			0.031	
regulation of nuclear smad2/3 signaling	1			0.033	
p38 mapk signaling pathway	1			0.034	
integrins in angiogenesis	1			0.037	
syndecan-4-mediated signaling events	1			0.038	
angiopoietin receptor tie2-mediated signaling	1			0.04	
filopodium formation (integrin signaling pathway)	1			0.045	
role of mitochondria in apoptotic signaling	1			0.048	
thromboxane a2 receptor signaling	1	0.002			
amb2 integrin signaling	1	0.003			
urokinase-type plasminogen activator (upa) and upar-mediated signaling	1	0.008			
glypican 1 network	1	0.011			
jak_stat_molecularvariation_2	1	0.012			
intrinsic prothrombin activation pathway	1	0.013			
ephrinb-ephb pathway	1	0.016			
il-10 signaling pathway(jak1 tyk2 stat3) (il-10 signaling(jak1 tyk2 stat3))	1	0.018			
alpha-synuclein signaling	1	0.018			
antigen processing and presentation	1	0.02			
integrin family cell surface interactions	1	0.02			
vegf and vegfr signaling network	1	0.02			
cxcr3-mediated signaling events	1	0.023			
ephrin b reverse signaling	1	0.029			
regulation of p38-alpha and p38-beta	1	0.033			
arf6 signaling events	1	0.037			
s1p3 pathway	1	0.037			
s1p1 pathway	1	0.044			
bone remodeling	1	0.045			
signaling pathway from g-protein families	1				0
chromatin remodeling by hswi/snf atp-dependent complexes	1				0
thrombin signaling and protease-activated receptors	1				0
nuclear receptors coordinate the activities of chromatin remodeling complexes and coactivators to facilitate initiation of transcription in carcinoma cells	1				0
p53 pathway	1				0.001
tgfbr	1				0.002
cxcr4 signaling pathway	1				0.002
how progesterone initiates the oocyte maturation	1				0.002
overview of telomerase rna component gene hterc transcriptional regulation	1				0.002

Names	Set-Count	STZ-Glom-Only	Concordant	Discordant	STZ-SCN-Only
bmp receptor signaling	1				0.002
plasma membrane estrogen receptor signaling	1				0.002
tgf-beta receptor signaling	1				0.002
regulation of spermatogenesis by crem	1				0.003
cell proliferation (pdgf signaling pathway)	1				0.003
carm1 and regulation of the estrogen receptor	1				0.005
the information processing pathway at the ifn beta enhancer	1				0.005
phospholipase c signaling pathway	1				0.005
s1p2 pathway	1				0.005
regulation of eif-4e and p70s6 kinase	1				0.007
nfat and hypertrophy of the heart	1				0.007
id	1				0.008
signaling events activated by hepatocyte growth factor receptor (c-met)	1				0.009
androgenreceptor	1				0.01
coregulation of androgen receptor activity	1				0.01
foxo family signaling	1				0.011
phospholipids as signalling intermediaries	1				0.013
regulation of androgen receptor activity	1				0.013
cell adhesion (hgf signaling pathway)	1				0.015
mtor signaling pathway	1				0.017
trk receptor signaling mediated by pi3k and plc-gamma	1				0.017
notch	1				0.018
p75(ntr)-mediated signaling	1				0.018
ccr3 signaling in eosinophils	1				0.019
regulation of c-myc	1				0.019
role of pi3k subunit p85 in regulation of actin organization and cell migration	1				0.02
cystic fibrosis transmembrane conductance regulator (cftr) and beta 2 adrenergic receptor (b2ar) pathway	1				0.02
signaling events mediated by hdac class ii	1				0.02
influence of ras and rho proteins on g1 to s transition	1				0.021
p53 signaling pathway	1				0.022
akt(pkb) activation signaling (insulin receptor signaling (mammal))	1				0.022
polyadenylation of mrna	1				0.023
segmentation clock	1				0.025
dicer pathway	1				0.026
reversal of insulin resistance by leptin	1				0.027
trefoil factors initiate mucosal healing	1				0.027
endothelins	1				0.027
notch signaling pathway	1				0.028
pkc-catalyzed phosphorylation of inhibitory phosphoprotein of myosin phosphatase	1				0.029
s1p4 pathway	1				0.029
yaci and bcma stimulation of b cell immune responses	1				0.031
corticosteroids and cardioprotection	1				0.033
pdgf signaling pathway	1				0.033
hedgehog signaling events mediated by gli proteins	1				0.033
pdgfr-alpha signaling pathway	1				0.033
rho-selective guanine exchange factor akap13 mediates stress fiber formation	1				0.034
generation of amyloid b-peptide by ps1	1				0.036
akt signaling pathway	1				0.039
class i pi3k signaling events mediated by akt	1				0.039
regulation of ck1/cdk5 by type 1 glutamate receptors	1				0.043
s1p5 pathway	1				0.043
ctcf: first multivalent nuclear factor	1				0.044
transcription factor creb and its extracellular signals	1				0.047
erk and pi-3 kinase are necessary for collagen binding in corneal epithelia	1				0.048
bcr signaling pathway	1				0.048
ras signaling pathway	1				0.049
akt(pkb) activation signaling (insulin receptor signaling)	1				0.049

ESM Table 4. Canonical pathways (type 2 diabetes DN vs type 2 diabetes DPN).

Significant pathways (Benjamini-Hochberg adjusted P-values <0.05) were identified by GeneRanker (Genomatix) from the four DEG subsets (concordant, discordant, and the two unique sets). The numbers in columns 3-6 are the P-values. The Set-Count column indicates the number of DEG sets which have the corresponding pathway significantly enriched.

Names	Set-Count	*db/db*-Glom-only	Concordant	Discordant	*db/db*-SCN-only
cdk regulation of dna replication	2		0		0.026
p73 transcription factor network	2		0.018		0.034
sphingosine 1-phosphate (s1p) pathway	2		0.047		0.033
angiopoietin receptor tie2-mediated signaling	2		0.049	0.014	
akt(pkb)-bad signaling (epo signaling pathway(jak2 stat1 stat3 stat5))	2			0.001	0.005
akt(pkb)-bad signaling (il-7 signaling(jak1 jak3 stat5))	2			0.002	0.001
gene expression (vegf signaling pathway)	2			0.003	0.006
cd40l signaling pathway	1		0		
signal dependent regulation of myogenesis by corepressor mitr	1		0.002		
mapkinase signaling pathway	1		0.003		
regulation of retinoblastoma protein	1		0.008		
nf-kb signaling pathway	1		0.009		
e2f transcription factor network	1		0.009		
p38 mapk signaling pathway	1		0.009		
regulation of pgc-1a	1		0.01		
aurora c signaling	1		0.014		
urokinase-type plasminogen activator (upa) and upar-mediated signaling	1		0.018		
tnf receptor signaling pathway	1		0.027		
thrombin signaling and protease-activated receptors	1		0.031		
gata3 participate in activating the th2 cytokine genes expression	1		0.032		
plk1 signaling events	1		0.036		
nfkb activation by nontypeable hemophilus influenzae	1		0.042		
shp2 signaling	1		0.043		
regulation of nuclear smad2/3 signaling	1		0.044		
platelet amyloid precursor protein pathway	1		0.046		
signaling events mediated by hdac class ii	1		0.046		
tgfbr	1		0.047		
bioactive peptide induced signaling pathway	1			0.001	
retinoic acid receptors-mediated signaling	1			0.001	
reelin signaling pathway	1			0.002	
thromboxane a2 receptor signaling	1			0.002	
ion channels and their functional role in vascular endothelium	1			0.004	
integrin signaling pathway	1			0.005	
trka receptor signaling pathway	1			0.005	
transcription factor creb and its extracellular signals	1			0.007	
the igf-1 receptor and longevity	1			0.013	
inhibition of matrix metalloproteinases	1			0.018	
phospholipase c delta in phospholipid associated cell signaling	1			0.021	
ephrin b reverse signaling	1			0.021	
regulation of eif-4e and p70s6 kinase	1			0.024	
cytokine receptor degradation signaling	1			0.027	
canonical wnt signaling pathway	1			0.027	
il6-mediated signaling events	1			0.028	
osteopontin-mediated events	1			0.028	
regulators of bone mineralization	1			0.03	
regulation of nuclear smad2/3 signaling	1			0.033	
egf signaling pathway	1			0.034	
cystic fibrosis transmembrane conductance regulator (cftr) and beta 2 adrenergic receptor (b2ar) pathway	1			0.035	
syndecan-4-mediated signaling events	1			0.038	
inhibition of cellular proliferation by gleevec	1			0.045	
activation of pkc through g-protein coupled receptors	1			0.045	
beta1 integrin cell surface interactions	1	0			
regulation of rac1 activity	1	0.002			
tgf-beta receptor signaling	1	0.002			
regulation of rhoa activity	1	0.003			
kitreceptor	1	0.013			
tpo signaling pathway(jak2 stat3) (tpo signaling(jak2 stat3))	1	0.03			
role of erbb2 in signal transduction and oncology	1	0.032			

Names	Set-Count	*db/db*-Glom-only	Concordant	Discordant	*db/db*-SCN-only
prion pathway	1	0.033			
glypican 2 network	1	0.033			
bmp2 signaling pathway(through tak1) (bmp2 signaling(through tak1))	1	0.036			
lpa4-mediated signaling events	1				0
s1p4 pathway	1				0.004
ras signaling pathway	1				0.006
glypican 3 network	1				0.006
s1p5 pathway	1				0.007
aurora a signaling	1				0.009
eukaryotic protein translation	1				0.01
aurora b signaling	1				0.013
insulin pathway	1				0.013
s1p2 pathway	1				0.013
antigen processing and presentation	1				0.014
lpa receptor mediated events	1				0.015
agrin in postsynaptic differentiation	1				0.016
erk and pi-3 kinase are necessary for collagen binding in corneal epithelia	1				0.017
sonic hedgehog receptor ptc1 regulates cell cycle	1				0.019
nongenotropic androgen signaling	1				0.019
validated nuclear estrogen receptor alpha network	1				0.019
validated nuclear estrogen receptor alpha network	1				0.019
erbb2/erbb3 signaling events	1				0.019
regulation of bad phosphorylation	1				0.021
integrins in angiogenesis	1				0.022
reversal of insulin resistance by leptin	1				0.023
cdc25 and chk1 regulatory pathway in response to dna damage	1				0.025
fgf signaling pathway	1				0.027
insulin signaling pathway	1				0.035
role of ran in mitotic spindle regulation	1				0.038
g alpha s gdp-gtp exchange signaling (gpcr adenosine a2a receptor signaling pathway)	1				0.038
p38 signaling mediated by mapkap kinases	1				0.038
repression of pain sensation by the transcriptional regulator dream	1				0.04
endothelins	1				0.04
estrogen responsive protein efp controls cell cycle and breast tumors growth	1				0.044
e-cadherin signaling events	1				0.045
signaling events mediated by focal adhesion kinase	1				0.045
ikk-nf-kappab cascade (cd4 t cell receptor signaling)	1				0.046
cdc42 signaling events	1				0.046
cell cycle: g2/m checkpoint	1				0.047
sumoylation by ranbp2 regulates transcriptional repression	1				0.047
igf-1 signaling pathway	1				0.049
neurotrophic factor-mediated trk receptor signaling	1				0.049

ESM Table 5. The 20 most up-regulated genes and 20 most down-regulated genes that are concordantly dysregulated in type 1 diabetes DN and type 2 diabetes DN.

The fold-changes (FC) by diabetes are highlighted in red (up-regulated) and green (down-regulated).

Gene ID	Symbol	Description	STZ-Glom FC	*db/db*-Glom FC	Average FC
13119	Cyp4a14	cytochrome P450, family 4, subfamily a, polypeptide 14	11.96	9.25	10.61
16819	Lcn2	lipocalin 2	1.87	11.79	6.83
76074	Gbp8	guanylate-binding protein 8	6.82	6.68	6.75
100034251	Wfdc17	WAP four-disulfide core domain 17	3.14	7.36	5.25
20715	Serpina3g	serine (or cysteine) peptidase inhibitor, clade A, member 3G	3.92	5.70	4.81
14289	Fpr2	formyl peptide receptor 2	2.60	6.88	4.74
12655	Chil3	chitinase-like 3	1.82	7.31	4.56
20568	Slpi	secretory leukocyte peptidase inhibitor	2.64	5.86	4.25
68774	Ms4a6d	membrane-spanning 4-domains, subfamily A, member 6D	2.16	5.94	4.05
229214	Qrfpr	pyroglutamylated RFamide peptide receptor	2.11	5.51	3.81
11801	Cd5l	CD5 antigen-like	1.48	5.82	3.65
15439	Hp	haptoglobin	1.48	5.35	3.42
13924	Ptprv	protein tyrosine phosphatase, receptor type, V	1.95	4.82	3.38
17384	Mmp10	matrix metallopeptidase 10	1.48	5.28	3.38
380794	Ighg	Immunoglobulin heavy chain (gamma polypeptide)	1.30	5.37	3.34
57875	Angptl4	angiopoietin-like 4	1.82	4.13	2.97
20310	Cxcl2	chemokine (C-X-C motif) ligand 2	1.42	4.44	2.93
211187	Lrtm2	leucine-rich repeats and transmembrane domains 2	1.46	4.32	2.89
246256	Fcgr4	Fc receptor, IgG, low affinity IV	2.11	3.66	2.88
64380	Ms4a4c	membrane-spanning 4-domains, subfamily A, member 4C	3.04	2.69	2.87
20216	Acsm3	acyl-CoA synthetase medium-chain family member 3	-1.74	-3.16	-2.45
27204	Syn3	synapsin III	-1.68	-3.26	-2.47
12425	Cckar	cholecystokinin A receptor	-2.48	-2.51	-2.50
70059	Degs2	degenerative spermatocyte homolog 2 (Drosophila), lipid desaturase	-1.71	-3.39	-2.55
171284	Timd2	T cell immunoglobulin and mucin domain containing 2	-1.88	-3.23	-2.55
69836	Pla2g12b	phospholipase A2, group XIIB	-1.60	-3.51	-2.55
105387	Akr1c14	aldo-keto reductase family 1, member C14	-2.01	-3.14	-2.58
74087	Slc7a13	solute carrier family 7 member 13	-1.14	-4.06	-2.60
380997	Cyp2d12	cytochrome P450, family 2, subfamily d, polypeptide 12	-2.16	-3.10	-2.63
69787	Anxa13	annexin A13	-2.23	-3.07	-2.65
70370	Fbln7	fibulin 7	-1.66	-3.69	-2.67
234564	Ces1f	carboxylesterase 1F	-1.92	-3.46	-2.69
12350	Car3	carbonic anhydrase 3	-2.09	-3.38	-2.73
230459	Cyp2j13	cytochrome P450, family 2, subfamily j, polypeptide 13	-1.90	-3.60	-2.75
17242	Mdk	midkine	-1.92	-4.08	-3.00
11818	Apoh	apolipoprotein H	-3.61	-2.45	-3.03
54612	Sfrp5	secreted frizzled-related sequence protein 5	-2.45	-3.86	-3.15
22139	Ttr	transthyretin	-5.82	-3.01	-4.41
28248	Slco1a1	solute carrier organic anion transporter family, member 1a1	-2.58	-8.63	-5.61
108114	Slc22a7	solute carrier family 22 (organic anion transporter), member 7	-2.89	-8.82	-5.85

ESM Table 6. Canonical pathways (type 1 diabetes DN vs type 2 diabetes DN).

Significant pathways (Benjamini-Hochberg adjusted P-values <0.05) were identified by GeneRanker (Genomatix) from the four DEG subsets (concordant, discordant, and the two unique sets). The numbers in columns 3-6 are the P-values. The Set-Count column indicates the number of DEG sets which have the corresponding pathway significantly enriched.

Names	**Set-Count**	**STZ-Glom-only**	**Concordant**	**Discordant**	***db/db*-Glom-only**
foxa2 and foxa3 transcription factor networks	3	0.023	0.021	0.004	
il6-mediated signaling events	2	0.032	0		
thromboxane a2 receptor signaling	2	0.024	0.02		
regulation of rac1 activity	2			0.048	0.024
g alpha s gdp-gtp exchange signaling (gpcr adenosine a2a receptor signaling pathway)	2	0			0.005
lpa4-mediated signaling events	2	0.001			0.002
lpa receptor mediated events	2	0.018			0.01
integrin family cell surface interactions	1		0		
kitreceptor	1		0.001		
beta1 integrin cell surface interactions	1		0.001		
jak_stat_molecularvariation_2	1		0.002		
angiopoietin receptor tie2-mediated signaling	1		0.002		
urokinase-type plasminogen activator (upa) and upar-mediated signaling	1		0.002		
ifn alpha signaling pathway	1		0.003		
inhibition of matrix metalloproteinases	1		0.005		
il-6 signaling pathway(jak1 jak2 stat3) (il-6 signaling(jak1 jak2 stat3))	1		0.005		
cbl mediated ligand-induced downregulation of egf receptors pathway	1		0.01		
th2 cell proliferation (il-4 signaling(jak1 jak3 stat6))	1		0.013		
vegfr3 signaling in lymphatic endothelium	1		0.015		
ephrin b reverse signaling	1		0.016		
il4-mediated signaling events	1		0.017		
phospholipase c delta in phospholipid associated cell signaling	1		0.018		
syndecan-4-mediated signaling events	1		0.019		
extrinsic prothrombin activation pathway	1		0.024		
il 4 signaling pathway	1		0.024		
alpha6beta4integrin	1		0.026		
hif-1-alpha transcription factor network	1		0.027		
glypican 1 network	1		0.028		
signaling events mediated by tcptp	1		0.029		
circadian rhythm pathway	1		0.034		
cystic fibrosis transmembrane conductance regulator (cftr) and beta 2 adrenergic receptor (b2ar) pathway	1		0.035		
multi-drug resistance factors	1		0.04		
stat3 signaling pathway	1		0.04		
il2 signaling events mediated by pi3k	1		0.041		
signaling events mediated by ptp1b	1		0.042		
vegf and vegfr signaling network	1		0.045		
il 6 signaling pathway	1		0.046		
rxr and rar heterodimerization with other nuclear receptor	1		0.048		
stabilization and expansion of the e-cadherin adherens junction	1			0.008	
bmp2 signaling pathway(through smad) (tgf-beta_bmp diagram(molecularvariation))	1			0.011	
lissencephaly gene (lis1) in neuronal migration and development	1			0.035	
e-cadherin signaling in the nascent adherens junction	1			0.041	
antigen processing and presentation	1	0.002			
cell to cell adhesion signaling	1	0.007			
sumoylation by ranbp2 regulates transcriptional repression	1	0.007			
sumoylation by ranbp2 regulates transcriptional repression	1	0.008			
integrins in angiogenesis	1	0.012			
e-cadherin signaling events	1	0.015			
cycling of ran in nucleocytoplasmic transport	1	0.019			
regulation of bad phosphorylation	1	0.03			
il-10 signaling pathway(jak1 tyk2 stat3) (il-10 signaling(jak1 tyk2 stat3))	1	0.03			
insulin pathway	1	0.03			
arf6 signaling events	1	0.04			
arf6 trafficking events	1	0.044			
endothelins	1				0

Names	**Set-Count**	**STZ-Glom-only**	**Concordant**	**Discordant**	***db/db*-Glom-only**
integrin signaling pathway	1				0.003
regulation of rhoa activity	1				0.003
regulators of bone mineralization	1				0.011
thrombin signaling and protease-activated receptors	1				0.012
tumor suppressor arf inhibits ribosomal biogenesis	1				0.013
chaperones modulate interferon signaling pathway	1				0.016
akt signaling pathway	1				0.018
tnf alpha/nf-kb	1				0.019
gene expression (vegf signaling pathway)	1				0.021
influence of ras and rho proteins on g1 to s transition	1				0.022
androgenreceptor	1				0.024
akt(pkb)-bad signaling (il-7 signaling(jak1 jak3 stat5))	1				0.024
akt(pkb)-bad signaling (epo signaling pathway(jak2 stat1 stat3 stat5))	1				0.025
trefoil factors initiate mucosal healing	1				0.036
signaling events mediated by the hedgehog family	1				0.037
regulation of androgen receptor activity	1				0.039
ucalpain and friends in cell spread	1				0.04
cd40l signaling pathway	1				0.044
canonical nf-kappab pathway	1				0.044

ESM Table 7. The 20 most up-regulated genes and 20 most down-regulated genes that are concordantly dysregulated in type 1 diabetes DPN and type 2 diabetes DPN.

The fold-changes (FC) by diabetes are highlighted in red (up-regulated) and green (down-regulated).

Gene ID	Symbol	Description	STZ-SCN FC	*db/db*-SCN FC	Average FC
29818	Hspb7	heat shock protein family, member 7 (cardiovascular)	1.83	4.26	3.04
217946	Cdca7l	cell division cycle associated 7 like	1.41	4.66	3.04
71886	2310002L09Rik	RIKEN cDNA 2310002L09 gene	1.35	4.72	3.04
66790	Grtp1	GH regulated TBC protein 1	1.44	4.05	2.75
68453	Gpihbp1	GPI-anchored HDL-binding protein 1	2.45	2.68	2.56
57875	Angptl4	angiopoietin-like 4	1.56	3.39	2.47
16997	Ltbp2	latent transforming growth factor beta binding protein 2	2.06	2.88	2.47
232599	Gm4876	predicted gene 4876	1.64	3.07	2.35
75590	Dusp9	dual specificity phosphatase 9	1.39	3.20	2.29
12984	Csf2rb2	colony stimulating factor 2 receptor, beta 2, low-affinity (granulocyte-macrophage)	2.62	1.91	2.26
239126	C1qtnf9	C1q and tumor necrosis factor related protein 9	2.62	1.79	2.21
76843	Dtl	denticleless homolog (Drosophila)	1.33	3.07	2.20
67177	Cdt1	chromatin licensing and DNA replication factor 1	1.48	2.68	2.08
60527	Fads3	fatty acid desaturase 3	1.51	2.54	2.02
14229	Fkbp5	FK506 binding protein 5	1.86	2.11	1.98
53608	Map3k6	mitogen-activated protein kinase kinase kinase 6	2.01	1.88	1.95
17919	Myo5b	myosin VB	1.76	2.14	1.95
15259	Hipk3	homeodomain interacting protein kinase 3	1.75	2.14	1.95
228790	Asxl1	additional sex combs like 1	2.01	1.79	1.90
207728	Pde2a	phosphodiesterase 2A, cGMP-stimulated	1.79	1.99	1.89
268890	Lsamp	limbic system-associated membrane protein	-3.28	-4.08	-3.68
17755	Map1b	microtubule-associated protein 1B	-3.03	-4.45	-3.74
15444	Hpca	hippocalcin	-4.23	-3.58	-3.91
72902	Spock3	sparc/osteonectin, cwcv and kazal-like domains proteoglycan 3	-3.56	-5.46	-4.51
29859	Sult4a1	sulfotransferase family 4A, member 1	-4.89	-4.23	-4.56
17758	Map4	microtubule-associated protein 4	-4.03	-5.24	-4.63
15572	Elavl4	ELAV (embryonic lethal, abnormal vision, Drosophila)-like 4 (Hu antigen D)	-3.71	-5.65	-4.68
75276	Ppp1r1c	protein phosphatase 1, regulatory (inhibitor) subunit 1C	-3.71	-5.94	-4.82
15569	Elavl2	ELAV (embryonic lethal, abnormal vision, Drosophila)-like 2 (Hu antigen B)	-2.84	-6.89	-4.87
69480	Ttc9	tetratricopeptide repeat domain 9	-3.63	-6.36	-5.00
20983	Syt4	synaptotagmin IV	-3.31	-6.75	-5.03
20614	Snap25	synaptosomal-associated protein 25	-2.53	-8.17	-5.35
78283	Map7d2	MAP7 domain containing 2	-3.56	-7.55	-5.56
16392	Isl1	ISL1 transcription factor, LIM/homeodomain	-5.70	-5.54	-5.62
72003	Synpr	synaptoporin	-4.20	-7.31	-5.75
22771	Zic1	zinc finger protein of the cerebellum 1	-9.34	-6.23	-7.78
18039	Nefl	neurofilament, light polypeptide	-3.51	-12.38	-7.94
21333	Tac1	tachykinin 1	-6.63	-9.99	-8.31
24046	Scn11a	sodium channel, voltage-gated, type XI, alpha	-6.63	-11.96	-9.30
22152	Tubb3	tubulin, beta 3 class III	-7.62	-13.64	-10.63

ESM Table 8. Canonical pathways (type 1 diabetes DPN vs type 2 diabetes DPN).

Significant pathways (Benjamini-Hochberg adjusted P-values <0.05) were identified by GeneRanker (Genomatix) from the four DEG subsets (concordant, discordant, and the two unique sets). The numbers in columns 3-6 are the P-values. The Set-Count column indicates the number of DEG sets which have the corresponding pathway significantly enriched.

Names	**Set-Count**	**STZ-SCN-only**	**Concordant**	**Discordant**	***db/db*-SCN-only**
akt(pkb)-bad signaling (il-7 signaling(jak1 jak3 stat5))	2		0.005		0
akt(pkb)-bad signaling (epo signaling pathway(jak2 stat1 stat3 stat5))	2		0.006		0
gene expression (vegf signaling pathway)	2		0.006		0
lissencephaly gene (lis1) in neuronal migration and development	2		0.013	0.023	
reversal of insulin resistance by leptin	2	0.012	0.018		
igf-1 signaling pathway	2		0.031	0.027	
coregulation of androgen receptor activity	2		0.033	0.009	
validated targets of c-myc transcriptional repression	2	0.004		0.009	
thrombin signaling and protease-activated receptors	2	0.046		0.013	
regulation of eif-4e and p70s6 kinase	2	0.036		0.041	
skeletal muscle hypertrophy is regulated via akt-mtor pathway	2	0.021		0.044	
validated nuclear estrogen receptor alpha network	2	0.019			0.004
validated nuclear estrogen receptor alpha network	2	0.019			0.004
regulation of bad phosphorylation	1		0.003		
keratinocyte differentiation	1		0.007		
erk cascade (igf1 signaling pathway)	1		0.01		
notch	1		0.021		
cytosolic calcium ion concentration elevation (through ip3 receptor) (gpcr groupi metabotropic glutamate receptor signaling pathway)	1		0.023		
fc epsilon receptor i signaling in mast cells	1		0.024		
fgf signaling pathway	1		0.024		
regulation of glucocorticoid receptor	1		0.024		
reelin signaling pathway	1		0.027		
cytokine receptor degradation signaling	1		0.028		
erbb2/erbb3 signaling events	1		0.029		
il2 signaling events mediated by pi3k	1		0.029		
transcription factor creb and its extracellular signals	1		0.031		
egf signaling pathway	1		0.031		
mcalpain and friends in cell motility	1		0.034		
rxr and rar heterodimerization with other nuclear receptor	1		0.038		
inhibition of cellular proliferation by gleevec	1		0.041		
ifn-gamma pathway	1		0.041		
mechanisms of transcriptional repression by dna methylation	1		0.041		
neuroregulin receptor degredation protein-1 controls erbb3 receptor recycling	1		0.045		
il2-mediated signaling events	1		0.046		
role of erk5 in neuronal survival pathway	1			0.001	
dicer pathway	1			0.003	
influence of ras and rho proteins on g1 to s transition	1			0.003	
nongenotropic androgen signaling	1			0.003	
tumor suppressor arf inhibits ribosomal biogenesis	1			0.005	
eukaryotic protein translation	1			0.006	
angiopoietin receptor tie2-mediated signaling	1			0.006	
signaling events mediated by focal adhesion kinase	1			0.008	
alpha4 beta1 integrin signaling events	1			0.008	
paxillin-independent events mediated by a4b1 and a4b7	1			0.009	
signal dependent regulation of myogenesis by corepressor mitr	1			0.011	
androgenreceptor	1			0.013	
role of parkin in ubiquitin-proteasomal pathway	1			0.013	
hypoxia-inducible factor in the cardivascular system	1			0.014	
human cytomegalovirus and map kinase pathways	1			0.015	
vegfr3 signaling in lymphatic endothelium	1			0.016	
signaling events activated by hepatocyte growth factor receptor (c-met)	1			0.016	
egfr1	1			0.017	
vegfr1 specific signals	1			0.021	
sprouty regulation of tyrosine kinase signals	1			0.026	
igf1 pathway	1			0.028	
fc-epsilon receptor i signaling in mast cells	1			0.029	
cyclins and cell cycle regulation	1			0.03	

Names	**Set-Count**	**STZ-SCN-only**	**Concordant**	**Discordant**	***db/db*-SCN-only**
control of skeletal myogenesis by hdac and calcium/calmodulin-dependent kinase (camk)	1			0.031	
cell proliferation (pdgf signaling pathway)	1			0.032	
s1p4 pathway	1			0.034	
bcr signaling pathway	1			0.036	
il6-mediated signaling events	1			0.036	
urokinase-type plasminogen activator (upa) and upar-mediated signaling	1			0.036	
pten dependent cell cycle arrest and apoptosis	1			0.038	
pkc-catalyzed phosphorylation of inhibitory phosphoprotein of myosin phosphatase	1			0.042	
mtor signaling pathway	1			0.045	
overview of telomerase rna component gene hterc transcriptional regulation	1			0.046	
b cell survival pathway	1			0.048	
trefoil factors initiate mucosal healing	1			0.049	
regulation of spermatogenesis by crem	1	0.001			
regulation of nuclear smad2/3 signaling	1	0.003			
cystic fibrosis transmembrane conductance regulator (cftr) and beta 2 adrenergic receptor (b2ar) pathway	1	0.004			
tgfbr	1	0.006			
plasma membrane estrogen receptor signaling	1	0.007			
alpha6beta4integrin	1	0.009			
canonical wnt signaling pathway	1	0.01			
chrebp regulation by carbohydrates and camp	1	0.012			
chromatin remodeling by hswi/snf atp-dependent complexes	1	0.013			
regulation of c-myc	1	0.013			
nuclear receptors coordinate the activities of chromatin remodeling complexes and coactivators to facilitate initiation of transcription in carcinoma cells	1	0.014			
regulation of telomerase	1	0.018			
ccr3 signaling in eosinophils	1	0.019			
the information processing pathway at the ifn beta enhancer	1	0.019			
validated transcriptional targets of ap1 family members fra1 and fra2	1	0.021			
tgf-beta receptor signaling	1	0.022			
multi-step regulation of transcription by pitx2	1	0.026			
p53 pathway	1	0.026			
activation of csk by camp-dependent protein kinase inhibits signaling through the t cell receptor	1	0.027			
phospholipids as signalling intermediaries	1	0.028			
how progesterone initiates the oocyte maturation	1	0.028			
foxo family signaling	1	0.028			
signaling pathway from g-protein families	1	0.03			
foxa2 and foxa3 transcription factor networks	1	0.03			
integrin-linked kinase signaling	1	0.03			
yaci and bcma stimulation of b cell immune responses	1	0.031			
bmp receptor signaling	1	0.031			
telomeres telomerase cellular aging and immortality	1	0.033			
segmentation clock	1	0.042			
beta catenin degradation signaling (canonical) (canonical wnt signaling pathway diagram)	1	0.042			
regulation of rac1 activity	1	0.044			
wnt signaling pathway	1	0.046			
signaling without wnt (mammal) (mammalian wnt signaling pathway diagram)	1	0.048			
plk1 signaling events	1				0.001
cdk regulation of dna replication	1				0.003
antigen processing and presentation	1				0.003
integrin signaling pathway	1				0.005
p73 transcription factor network	1				0.006
deregulation of cdk5 in alzheimers disease	1				0.009
regulation of p38-alpha and p38-beta	1				0.009
cdc42 signaling events	1				0.01
role of ran in mitotic spindle regulation	1				0.012
aurora a signaling	1				0.012
foxm1 transcription factor network	1				0.014
nephrin/neph1 signaling in the kidney podocyte	1				0.019
sphingosine 1-phosphate (s1p) pathway	1				0.022
lpa4-mediated signaling events	1				0.027
trk receptor signaling mediated by the mapk pathway	1				0.027
integrins in angiogenesis	1				0.029
cdc25 and chk1 regulatory pathway in response to dna damage	1				0.034
s1p1 pathway	1				0.043
aurora b signaling	1				0.045
neurotrophic factor-mediated trk receptor signaling	1				0.046
insulin pathway	1				0.047
role of erbb2 in signal transduction and oncology	0				
il-2 receptor beta chain in t cell activation	0				

Names	**Set-Count**	**STZ-SCN-only**	**Concordant**	**Discordant**	***db/db*-SCN-only**
insulin signaling pathway	0				
the igf-1 receptor and longevity	0				
nerve growth factor pathway (ngf)	0				
pdgf signaling pathway	0				
ras signaling pathway	0				
trka receptor signaling pathway	0				
ikk-nf-kappab cascade (cd4 t cell receptor signaling)	0				
g alpha s gdp-gtp exchange signaling (gpcr adenosine a2a receptor signaling pathway)	0				
il-6 signaling pathway(jak1 jak2 stat3) (il-6 signaling(jak1 jak2 stat3))	0				
akt(pkb) activation signaling (insulin receptor signaling)	0				
posttranslational regulation of adherens junction stability and dissassembly	0				
osteopontin-mediated events	0				
glypican 3 network	0				
gmcsf-mediated signaling events	0				
il2 signaling events mediated by stat5	0				
n-cadherin signaling events	0				
signaling events regulated by ret tyrosine kinase	0				
s1p2 pathway	0				
s1p3 pathway	0				