

Supplemental material

Supplementary Table 1. Primary and secondary antibodies used in immunofluorescence

Primary antibodies				
Antigen	Species	Manufacturer	Catalog#	Working dilution
Insulin	Rabbit	Proteintech	15848-1-AP	1:1000
Insulin	Rabbit	Santa Cruz Biotechnology	H-86	1:250
Insulin	Guinea pig	Dako	IR002	1:1
Ki67	Rabbit	Cell Signaling Technology	D3B5	1:200
MafA	Rabbit	BETHYL	IHC-00352	1:50
Nkx6.1	Rabbit	Cell Signaling Technology	D8O4R	1:200
Tom20	Rabbit	Cell Signaling Technology	D8T4N	1:200
Secondary antibodies				
Antigen	Species	Fluorescent dye	Catalog#	Manufacturer

Guinea pig IgG	Goat	Alexa Fluor 488	A11073	Life Technologies
Rabbit IgG	Goat	Alexa Fluor 488	A11008	Life Technologies
Rabbit IgG	Goat	Alexa Fluor 594	A11012	Life Technologies

Supplementary Table 2. The primer sequences used for real-time quantitative PCR

Gene (Forward/Reverse)	Sequence
<i>Gapdh</i> forward	GGCCCCTCTGGAAAGCTGTGGTGT
<i>Gapdh</i> reverse	GTTGGGGGCCCAGTTGGGATAGG
<i>Ki67</i> forward	CTGCCTGCGAAGAGAGCATC
<i>Ki67</i> reverse	AGCTCCACTTCGCCTTTTGG
<i>Ccna2</i> forward	TCCTTGCTTTTGACTTGGCT
<i>Ccna2</i> reverse	ATGACTCAGGCCAGCTCTGT
<i>Ccnb1</i> forward	TGGCCTCACAAAGCACATGA
<i>Ccnb1</i> reverse	GCTGTGCCAGCGTGCTAATC
<i>Ccnd1</i> forward	TAGGCCCTCAGCCTCACTC
<i>Ccnd1</i> reverse	CCACCCCTGGGATAAAGCAC
<i>Ccnd2</i> forward	AAGCCTGCCAGGAGCAAA
<i>Ccnd2</i> reverse	ATCCGGCGTTATGCTGCTCT
<i>Ccnd3</i> forward	CCAGCGTGTCCTGCAGAGTT
<i>Ccnd3</i> reverse	CCTTTTGCACGCACTGGAAG
<i>Nkx6.1</i> forward	CTGCACAGTATGGCCGAGATG
<i>Nkx6.1</i> reverse	CCGGGTTATGTGAGCCCAA
<i>Mafa</i> forward	CTTCAGCAAGGAGGAGGTCATC
<i>Mafa</i> reverse	GCGTAGCCGCGGTTCTT
<i>Pdx1</i> forward	CTCCGGACATCTCCCCATAC
<i>Pdx1</i> reverse	ACGGGTCCTCTTGTTTTCCT
<i>Ins1</i> forward	GACCAGCTATAATCAGAGACC
<i>Ins1</i> reverse	AGTTGCAGTAGTTCTCCAGCTG
<i>Ins2</i> forward	AGCCCTAAGTGATCCGCTACAA
<i>Ins2</i> reverse	AGTTGCAGTAGTTCTCCAGCTG
<i>Neurog3</i> forward	CCAAGAGCGAGTTGGCACT
<i>Neurog3</i> reverse	CGGGCCATAGAAGCTGTGG
<i>Aldh1a</i> forward	ATCAACAACGACTGGCACGAA
<i>Aldh1a</i> reverse	CACATCGGGCTTATCTCCTTC
<i>Atf3</i> forward	CAGACCCCTGGAGATGTCAGT
<i>Atf3</i> reverse	TTCTTGTTTCGACTTTCCTGGA
<i>Cyba</i> forward	TGCCAGTGTGATCTATCTGCT
<i>Cyba</i> reverse	TCGGCTTCTTTCGGACCTCT
<i>Cybb</i> forward	AGCTATGAGGTGGTGATGTTAGTGG

<i>Cybb</i> reverse	CACAATATTTGTACCAGACAGACTTGAG
<i>Ncf1</i> forward	ACACCTTCATTGCGCCATATTGC
<i>Ncf1</i> reverse	CCTGCCACTTAACCAGGAACA
<i>Chop</i> forward	CACCACACCTGAAAGCAGAA
<i>Chop</i> reverse	GGTGAAAGGCAGGGACTCA
<i>Casp3</i> forward	ATGGAGAACAACAAAACCTCAGT
<i>Casp3</i> reverse	TTGCTCCCATGTATGGTCTTTAC
<i>Pcx</i> forward	CTGAAGTTCCAAACAGTTCGAGG
<i>Pcx</i> reverse	CGCACGAAACACTCGGATG
<i>Aldob</i> forward	CATTGCCAGCATCTGTCAGC
<i>Aldob</i> reverse	TCATGGTCTCCGTCAGGAA
<i>Pfkfb3</i> forward	AGAACTTCCACTCTCCCACCC
<i>Pfkfb3</i> reverse	AGGGTAGTGCCCATTTGTTGAA

Supplementary Table 3. The expression levels of genes that were derived from the pathway analysis

Ratio>1.5

PathwayName	Gene Symbol	Average value (test: <i>Gck</i> ^{+/-} db/db)	Average value (control: <i>Gck</i> ^{+/+} db/db)	Ratio (test/control)	P-value
Mm_Amino_Acid_metabolism_WP662_71177	<i>Hnmt</i>	347.632125	152.2555333	2.283215049	0.033691103
	<i>Hadh</i>	78763.6	34672.5	2.271644675	0.00014307
	<i>Hibadh</i>	6141.03625	3812.089333	1.61093713	0.001269935
	<i>Ddc</i>	19383.9175	12433.97333	1.558947971	5.68E-06
	<i>Pycr1</i>	9032.9185	5095.820333	1.772613222	8.26E-06
	<i>Auh</i>	2639.04675	1489.584333	1.771666559	0.001263633
	<i>Mut</i>	1815.274	1100.152767	1.650019938	0.032195054
	<i>Pcx</i>	198.300625	75.55101333	2.624724888	0.007169447
Mm_GPCRs_Class_B_Secretin-like_WP456_69131	<i>Adgrl3</i>	304.4685	184.0100667	1.654629584	0.035386165
	<i>Gipr</i>	988.566125	552.5489333	1.789101499	0.019487163
	<i>Glp1r</i>	151594.3	81222.03333	1.866418431	0.002077917
Mm_Ptfla_related_regulatory_pathway_WP201_69113	<i>Pdx1</i>	889.402875	477.7243	1.861749287	0.010752779
	<i>Nkx6-1</i>	4710.87225	2027.207333	2.323823603	0.000846666
Mm_G1_to_S_cell_cycle_control_WP413_84705	<i>E2f1</i>	137.998295	77.32614667	1.784626558	0.042186002
	<i>Ccnd2</i>	21602.7125	13166.48333	1.640735187	0.029020869
	<i>Cdc45</i>	131.001925	53.31039	2.457343212	0.030840887
	<i>Cdkn1a</i>	2763.967	993.9763667	2.78071702	0.002967721
Mm_G_Protein_Signaling_Pathways_WP232_89955	<i>Pde7a</i>	291.9717	188.6763667	1.547473619	0.021738645

	<i>Pde4b</i>	3889.847	2521.726667	1.542533158	0.046963153
	<i>Gng12</i>	90266.3125	55975.44667	1.612605488	0.025064981
	<i>Akap13</i>	478.29825	288.5759667	1.657443118	0.024128225
	<i>Akap5</i>	20.6755775	13.68572	1.51074094	0.001626769
Mm_Non-odorant_GPCRs_WP1396_69993	<i>Adgrb3</i>	1191.78975	706.4209667	1.687081508	0.007799991
	<i>P2ry1</i>	6651.711	3256.601667	2.04253135	0.000890103
	<i>Gabbr2</i>	9370.19725	5152.217	1.818672865	0.023692258
	<i>Adgrl3</i>	304.4685	184.0100667	1.654629584	0.035386165
	<i>Gipr</i>	988.566125	552.5489333	1.789101499	0.019487163
	<i>Ackr2</i>	60.84691	28.91527	2.104317546	0.002327293
	<i>Sstr3</i>	9617.47325	5262.054	1.82770326	0.032049576
	<i>Glp1r</i>	151594.3	81222.03333	1.866418431	0.002077917
	<i>Mc5r</i>	17.22025	9.63859	1.786594305	0.010042421
	<i>Adra2a</i>	3420.55575	1672.067	2.045704957	0.004504519
Mm_Metapathway_biotransformation_WP1251_69747	<i>Hnmt</i>	347.632125	152.2555333	2.283215049	0.033691103
	<i>Akr1b10</i>	618.694475	331.1804667	1.868149052	0.001908686
	<i>Chst11</i>	4333.1485	2833.848333	1.529068599	0.012752632
	<i>Gal3st1</i>	256.4241	160.1561667	1.601087897	0.004776445
	<i>Gpx2</i>	492.436075	247.419	1.990292075	0.00502907
	<i>Hs3st6</i>	235.5686	88.11595667	2.673393207	0.002099471

Ratio<0.67

PathwayName	Gene Symbol	Average value (test: <i>Gck^{+/-} db/db</i>)	Average value (control: <i>Gck^{+/+} db/db</i>)	Ratio (test/control)	P-value
Mm_Cytoplasmic_Ribosomal_Proteins_WP163_78425	<i>Rpl37a</i>	2139.58675	3298.377667	0.648678522	0.041030326
	<i>Rpl7</i>	15691.635	27774.49667	0.564965594	0.001271937
	<i>Rpl7a</i>	5401.72275	8333.442	0.648198277	0.002193117
	<i>Rpl35</i>	18785.615	29824.13	0.629879732	0.006999332
	<i>Rps3a1</i>	7601.53075	13726.52333	0.553784128	0.001198088
	<i>Rpl34</i>	11655.78	19427.68333	0.599957277	0.000965261
	<i>Rps20</i>	5238.35425	9910.484667	0.528566909	0.001344429
	<i>Rps8</i>	32415.0025	50708.32667	0.639244176	0.006245172
	<i>Rpl9</i>	9029.38925	15624.08667	0.577914693	0.000998786
	<i>Rpl37rt</i>	4908.989	7757.416	0.632812395	0.038993619
	<i>Rps5</i>	834.554425	1412.028333	0.591032351	0.007701656
	<i>Rps19</i>	860.29375	1692.115667	0.508413087	0.034261181
	<i>Rps16</i>	3658.11025	5601.506333	0.653058308	0.020218778
	<i>Rpl27a</i>	699.01585	1084.2073	0.644725275	0.043752632
	<i>Rplp2</i>	5474.607	9044.800333	0.605276711	0.002068296
	<i>Rps11</i>	11292.276	18465.84333	0.611522355	0.010928454
	<i>Rps13</i>	2662.765	4445.625667	0.598962936	0.02350522
	<i>Rps15a</i>	2396.2435	4705.18	0.509277753	0.004984506
	<i>Rpl13</i>	1047.1354	1840.193	0.569035639	0.003348844

	<i>Rps25</i>	9728.64475	14587.56	0.666913778	0.005115276
	<i>Rpl36a</i>	2430.02375	4613.496333	0.526720642	0.001472341
	<i>Rpl39</i>	6793.6915	10362.129	0.655626995	0.032896507
	<i>Rps4x</i>	3758.1055	6999.447333	0.536914605	0.007735063
	<i>Rps12</i>	19251.8525	30788.40333	0.625295579	0.007490412
	<i>Rpl26</i>	27343.2925	51906.02	0.52678461	0.000147361
	<i>Rps27a</i>	3307.49175	5386.617667	0.614020143	0.008014311
	<i>Rpl23a</i>	2532.525	4295.69	0.589550224	0.000808677
	<i>Rps7</i>	19918.15	31037.38	0.641747145	0.001317775
	<i>Rpl37</i>	8059.096	12539.02333	0.64272119	0.010495203
	<i>Rpl3</i>	29375.7225	48913.36333	0.600566399	0.004517845
	<i>Rpl35a</i>	520.100125	858.7334667	0.60565955	0.004753296
	<i>Rps28</i>	12453.625	21054.65	0.591490478	0.014349745
	<i>Rps14</i>	5758.791	8734.200667	0.659338069	0.001876575
	<i>Fau</i>	5026.19925	8451.427667	0.594715999	0.005361187
Mm_Focal_Adhesion_WP85_82887	<i>Col3a1</i>	326.099725	3478.643667	0.093743354	0.000491964
	<i>Lamb3</i>	6.6191925	11.55468667	0.57285781	0.013320847
	<i>Col5a2</i>	20.040275	35.89594	0.558288068	0.029293837
	<i>Fn1</i>	35.0263875	607.7869933	0.05762938	0.030387613
	<i>Lamc1</i>	276.1241	467.9596	0.590059697	0.000317157
	<i>Col5a1</i>	8.18205	19.6147	0.417138677	0.000719352
	<i>Lamc3</i>	31.3503525	67.87056	0.461913862	0.046603314
	<i>Pdgfc</i>	23.3219575	93.67722	0.24896082	5.90E-05
	<i>Jun</i>	950.163675	2867.254333	0.331384511	0.034334835

<i>Hgf</i>	27.1695	58.35599333	0.465581998	0.005642612
<i>Pdgfra</i>	24.722745	49.64476333	0.497993008	0.001644464
<i>Spp1</i>	3003.63575	29620.42667	0.101404203	0.004556873
<i>Pxn</i>	113.1230625	201.3696667	0.561768137	0.013849378
<i>Actb</i>	92874.8975	151511.9	0.612987478	0.004902507
<i>Colla2</i>	98.95484	964.4898333	0.102598116	0.001109313
<i>Cav2</i>	48.0455575	114.5031367	0.419600361	0.01651268
<i>Cav1</i>	33.041455	53.37377	0.619057919	0.007974994
<i>Met</i>	498.0858	972.3606333	0.512243897	0.004144254
<i>Vwf</i>	87.52641	281.8331333	0.310561107	0.02399348
<i>Itgam</i>	22.63767	42.04191	0.538454842	0.011538641
<i>Dock1</i>	343.2434	561.4304667	0.611372949	0.018769646
<i>Col4a2</i>	149.598975	248.8547	0.601149888	0.003779064
<i>Pdgfd</i>	133.3755225	392.3055667	0.339978664	0.001825636
<i>Lamb2</i>	180.7027	464.8498667	0.388733466	0.004751886
<i>Figf</i>	60.7189275	118.8654533	0.510820645	0.017878475
<i>Flna</i>	1913.239	8263.932333	0.23151678	0.000895542
<i>Lama4</i>	295.62555	527.1579	0.560791273	0.046260794
<i>Igfl</i>	185.5764	1552.777433	0.119512556	0.002938087
<i>Lama2</i>	108.9375325	397.5324667	0.274034303	8.59E-05
<i>Col6a2</i>	101.2813775	273.4747	0.370350082	0.010717393
<i>Vtn</i>	589.036225	2251.151667	0.261659947	0.000630694
<i>Colla1</i>	193.3673	1547.431667	0.124960154	0.000121359
<i>ErbB2</i>	11.0547875	33.71550667	0.327884365	0.000193152

	<i>Itgb4</i>	31.9832075	71.04363	0.450191066	0.002481815
	<i>Rhob</i>	116.44297	213.6732	0.544958235	0.017788003
	<i>Itgb8</i>	400.79445	759.4512333	0.527742181	0.040237815
	<i>Shc3</i>	49.975155	93.23714333	0.536000495	0.034901654
	<i>Mylk</i>	89.8487425	338.5928667	0.26535923	0.00103148
	<i>Lama3</i>	208.004075	451.7060667	0.460485458	0.021773403
	<i>Pdgfrb</i>	400.01485	893.8316667	0.44752817	0.010281689
Mm_PodNet-protein-protein_interactions_in_the_podocyte_WP2310_82879	<i>Sulf1</i>	32.1025725	76.06706	0.422029884	0.012032786
	<i>Cfh</i>	1524.45775	6894.653667	0.221107227	0.001744584
	<i>Lamc1</i>	276.1241	467.9596	0.590059697	0.000317157
	<i>Tgfb2</i>	38.414105	76.54238333	0.501867114	0.028102025
	<i>Olfm1</i>	180.92065	392.8322	0.460554532	0.019978975
	<i>Angptl2</i>	23.31332	40.80357667	0.571354815	0.000251307
	<i>Notch2</i>	37.3756075	99.10491667	0.377131718	0.011464067
	<i>Cyr61</i>	836.261425	3447.838	0.242546612	0.011006223
	<i>Hspg2</i>	216.628825	426.8094667	0.507553937	0.001490151
	<i>Pdpn</i>	43.299375	106.5801367	0.406261207	0.009832608
	<i>Agrn</i>	116.2691825	223.1902333	0.520942072	0.020137847
	<i>Spp1</i>	3003.63575	29620.42667	0.101404203	0.004556873
	<i>Pxn</i>	113.1230625	201.3696667	0.561768137	0.013849378
	<i>Slc29a4</i>	623.63525	1052.802133	0.59235751	0.015002089
	<i>Arpc1b</i>	471.65085	961.9741	0.490294749	0.009200175
	<i>Actb</i>	92874.8975	151511.9	0.612987478	0.004902507
	<i>Smurf1</i>	155.4138	253.9444	0.61199932	0.005311685

<i>Met</i>	498.0858	972.3606333	0.512243897	0.004144254
<i>Cxcl12</i>	141.9617	583.5046667	0.243291456	0.000808209
<i>Plaur</i>	46.1354675	134.2371867	0.343686192	0.004363717
<i>Tgfb1</i>	172.230425	365.4635333	0.471265692	0.002123612
<i>Cd151</i>	2039.922	4364.061	0.467436638	1.05E-05
<i>Bcam</i>	282.532575	964.9272333	0.292801949	7.41E-05
<i>Fcgrt</i>	77.5623225	222.8515333	0.348044823	0.002479283
<i>Nr2f2</i>	396.749	1727.796467	0.229627162	0.002148058
<i>Sh2d4a</i>	18.83314	73.66236667	0.255668408	0.003364604
<i>Nrp1</i>	202.763175	356.0331333	0.569506476	0.006079936
<i>Palld</i>	115.1482775	195.4604333	0.589112976	0.03167828
<i>Myo1e</i>	318.794375	551.6008	0.577944004	0.013217954
<i>Lamb2</i>	180.7027	464.8498667	0.388733466	0.004751886
<i>Tagln</i>	235.52925	727.0724667	0.323941919	0.006492889
<i>Smad3</i>	86.73054	149.1512333	0.581493951	0.004335903
<i>Tgfbr2</i>	212.5581	346.3352667	0.613735073	0.015917667
<i>Ctgf</i>	335.24885	1247.872267	0.268656383	0.002735711
<i>Igfl</i>	185.5764	1552.777433	0.119512556	0.002938087
<i>Tcf21</i>	23.9863025	48.16696333	0.497982452	0.028456607
<i>Coll8a1</i>	56.5854875	125.4698333	0.450988783	0.007384802
<i>Myh10</i>	182.896325	302.1116	0.605393255	0.023187448
<i>Itgb4</i>	31.9832075	71.04363	0.450191066	0.002481815
<i>Wwc1</i>	40.109065	104.5829367	0.383514427	0.001082614
<i>Cxcl16</i>	197.9695	564.8711	0.350468452	0.005438866

	<i>Egln3</i>	59.1285275	433.1805667	0.136498569	0.000266898
	<i>Tgfb3</i>	126.7735	260.4992	0.486656005	0.002228968
	<i>Nid1</i>	525.1724	1118.360267	0.469591433	0.000463279
	<i>Dbn1</i>	61.7646625	142.2334333	0.434248552	0.003197544
	<i>Ctsl</i>	5221.62225	8314.422	0.628019873	0.014594389
	<i>Scel</i>	1373.3152	2170.505333	0.632716805	0.043048156
	<i>Bmp4</i>	20.8116275	46.56906333	0.446898134	0.008932982
	<i>Lgals1</i>	120.1296	527.6775667	0.227657205	0.000525071
	<i>Angpt1</i>	24.2376675	48.63081333	0.498401442	0.014243486
	<i>Igsf5</i>	1894.81625	3166.090333	0.598471948	0.029880387
	<i>Crim1</i>	341.426725	766.9369333	0.44518227	0.003041619
	<i>Epas1</i>	3306.0545	5852.216333	0.564923494	0.002255754
	<i>Ezr</i>	468.631675	1625.428333	0.288312727	0.001098085
	<i>Notch3</i>	37.683475	92.42969	0.407698814	0.002838127
	<i>Plce1</i>	117.1150625	278.8296	0.42002378	0.005062133
Mm_XPodNet_-protein-	<i>Sulf1</i>	32.1025725	76.06706	0.422029884	0.012032786
protein_interactions_in_the_podocyte_expanded_by_STRING_WP2309_82878	<i>Nrp2</i>	54.1929	132.4797	0.409065691	0.006362543
	<i>Fn1</i>	35.0263875	607.7869933	0.05762938	0.030387613
	<i>Cfh</i>	1524.45775	6894.653667	0.221107227	0.001744584
	<i>Lamc1</i>	276.1241	467.9596	0.590059697	0.000317157
	<i>Tgfb2</i>	38.414105	76.54238333	0.501867114	0.028102025
	<i>Vim</i>	839.006275	5155.641	0.162735589	0.00492182
	<i>Olfm1</i>	180.92065	392.8322	0.460554532	0.019978975
	<i>Lamc3</i>	31.3503525	67.87056	0.461913862	0.046603314

<i>Angptl2</i>	23.31332	40.80357667	0.571354815	0.000251307
<i>Enkur</i>	19.414645	32.80255	0.591863895	0.017529259
<i>Zeb2</i>	77.193385	219.4029333	0.351833879	0.005647433
<i>Eng</i>	5011.766	9582.146333	0.52303167	0.009098857
<i>Notch2</i>	37.3756075	99.10491667	0.377131718	0.011464067
<i>Ngf</i>	161.286725	309.6286667	0.520903722	0.004524949
<i>Csfl</i>	490.016125	960.1109333	0.510374487	0.000317365
<i>Cyr61</i>	836.261425	3447.838	0.242546612	0.011006223
<i>Lyn</i>	427.572675	1068.103367	0.400310202	0.037134753
<i>Nr4a3</i>	30.954005	154.50463	0.200343543	0.022139649
<i>Hspg2</i>	216.628825	426.8094667	0.507553937	0.001490151
<i>Pdpn</i>	43.299375	106.5801367	0.406261207	0.009832608
<i>Agrn</i>	116.2691825	223.1902333	0.520942072	0.020137847
<i>Cdk6</i>	151.4389	253.8985	0.596454489	0.010418369
<i>Ptpn13</i>	851.17575	1311.900333	0.648811292	0.021880418
<i>Spp1</i>	3003.63575	29620.42667	0.101404203	0.004556873
<i>Pxn</i>	113.1230625	201.3696667	0.561768137	0.013849378
<i>Slc29a4</i>	623.63525	1052.802133	0.59235751	0.015002089
<i>Arpc1b</i>	471.65085	961.9741	0.490294749	0.009200175
<i>Eln</i>	65.7795825	180.913	0.363597876	0.024602447
<i>Cldn4</i>	825.069575	1412.263667	0.584217802	0.036567609
<i>Actb</i>	92874.8975	151511.9	0.612987478	0.004902507
<i>Smurf1</i>	155.4138	253.9444	0.61199932	0.005311685
<i>Cav1</i>	33.041455	53.37377	0.619057919	0.007974994

<i>Met</i>	498.0858	972.3606333	0.512243897	0.004144254
<i>Fbln2</i>	62.622485	128.2571867	0.488257123	0.010488495
<i>Bhlhe40</i>	799.024175	3761.526667	0.212420181	7.39E-05
<i>Cxcl12</i>	141.9617	583.5046667	0.243291456	0.000808209
<i>Vwf</i>	87.52641	281.8331333	0.310561107	0.02399348
<i>Plaur</i>	46.1354675	134.2371867	0.343686192	0.004363717
<i>Tgfb1</i>	172.230425	365.4635333	0.471265692	0.002123612
<i>Gab2</i>	271.12415	411.2243667	0.659309545	0.029938969
<i>Arrb1</i>	114.4340725	218.9162667	0.522729874	0.038342838
<i>Htra1</i>	20.28432	40.07706333	0.506132893	0.033111589
<i>Cd151</i>	2039.922	4364.061	0.467436638	1.05E-05
<i>Cdc42ep5</i>	19.1857475	29.71843	0.645584154	0.032252553
<i>Bcam</i>	282.532575	964.9272333	0.292801949	7.41E-05
<i>Zfp36</i>	286.78275	1173.418467	0.244399384	0.01588454
<i>Fcgrt</i>	77.5623225	222.8515333	0.348044823	0.002479283
<i>Nr2f2</i>	396.749	1727.796467	0.229627162	0.002148058
<i>Nrip3</i>	94.52475	230.1133667	0.410774704	0.017706169
<i>Sh2d4a</i>	18.83314	73.66236667	0.255668408	0.003364604
<i>Cdh5</i>	1655.719	2825.671	0.585956044	0.00543529
<i>Sntb2</i>	146.772025	221.4332	0.662827548	0.000327571
<i>Plcg2</i>	40.5245975	61.07198333	0.663554633	0.033891134
<i>Nrp1</i>	202.763175	356.0331333	0.569506476	0.006079936
<i>Palld</i>	115.1482775	195.4604333	0.589112976	0.03167828
<i>Gab1</i>	93.04781	198.0040667	0.469928783	0.02170104

<i>Anxa2</i>	173.37005	747.8007667	0.231839893	5.19E-05
<i>Myo1e</i>	318.794375	551.6008	0.577944004	0.013217954
<i>Lamb2</i>	180.7027	464.8498667	0.388733466	0.004751886
<i>Tagln</i>	235.52925	727.0724667	0.323941919	0.006492889
<i>Smad3</i>	86.73054	149.1512333	0.581493951	0.004335903
<i>Rab8b</i>	1915.4045	3444.444	0.556085249	0.013971467
<i>Tgfbr2</i>	212.5581	346.3352667	0.613735073	0.015917667
<i>Trf</i>	127.44395	1156.071233	0.110238839	0.028067544
<i>L1cam</i>	82.6725625	216.8988333	0.381157248	0.020205943
<i>Ctgf</i>	335.24885	1247.872267	0.268656383	0.002735711
<i>Gjal</i>	271.023325	703.2965667	0.385361365	0.001799194
<i>Igfl</i>	185.5764	1552.777433	0.119512556	0.002938087
<i>Cdk17</i>	349.631525	549.7546	0.635977443	0.038997677
<i>Tcf21</i>	23.9863025	48.16696333	0.497982452	0.028456607
<i>Lama2</i>	108.9375325	397.5324667	0.274034303	8.59E-05
<i>Hkl</i>	84.9669275	289.7776667	0.293214203	0.002618936
<i>Col18a1</i>	56.5854875	125.4698333	0.450988783	0.007384802
<i>Syt1</i>	249.65415	815.0466	0.306306596	0.007822806
<i>Gnb2l1</i>	13900.6525	22980.77333	0.604881842	0.005913472
<i>Myh10</i>	182.896325	302.1116	0.605393255	0.023187448
<i>Tax1bp3</i>	370.243075	558.8700667	0.66248507	0.002460236
<i>Vtn</i>	589.036225	2251.151667	0.261659947	0.000630694
<i>Itgb4</i>	31.9832075	71.04363	0.450191066	0.002481815
<i>Wwc1</i>	40.109065	104.5829367	0.383514427	0.001082614

<i>Cxcl16</i>	197.9695	564.8711	0.350468452	0.005438866
<i>Abcc3</i>	148.44305	366.3747	0.405167305	3.66E-05
<i>Pecam1</i>	1932.546	3347.473333	0.57731483	0.015736265
<i>Dock4</i>	272.29515	441.0449	0.617386461	0.03426011
<i>Egln3</i>	59.1285275	433.1805667	0.136498569	0.000266898
<i>Tgfb3</i>	126.7735	260.4992	0.486656005	0.002228968
<i>Nid1</i>	525.1724	1118.360267	0.469591433	0.000463279
<i>Actn2</i>	28.7756675	139.40474	0.206418143	0.001313398
<i>Dbn1</i>	61.7646625	142.2334333	0.434248552	0.003197544
<i>Ctsl</i>	5221.62225	8314.422	0.628019873	0.014594389
<i>Scel</i>	1373.3152	2170.505333	0.632716805	0.043048156
<i>Bmp4</i>	20.8116275	46.56906333	0.446898134	0.008932982
<i>Ajuba</i>	26.55721	85.82232	0.309444093	0.000841255
<i>Sorbs3</i>	148.9443	283.3580333	0.525639941	0.005905825
<i>Cdc42ep1</i>	66.8877975	138.6352333	0.482473293	0.000518442
<i>Lgals1</i>	120.1296	527.6775667	0.227657205	0.000525071
<i>Angpt1</i>	24.2376675	48.63081333	0.498401442	0.014243486
<i>Plec</i>	285.84015	473.1458333	0.604126952	0.015857587
<i>Cldn8</i>	16.89709	44.4503	0.380134442	0.000669562
<i>Igsf5</i>	1894.81625	3166.090333	0.598471948	0.029880387
<i>Ltbpl</i>	30.51057	80.22275333	0.380323147	0.004515528
<i>Crim1</i>	341.426725	766.9369333	0.44518227	0.003041619
<i>Epas1</i>	3306.0545	5852.216333	0.564923494	0.002255754
<i>Ezr</i>	468.631675	1625.428333	0.288312727	0.001098085

	<i>Notch3</i>	37.683475	92.42969	0.407698814	0.002838127
	<i>Pdgfrb</i>	400.01485	893.8316667	0.44752817	0.010281689
	<i>Csflr</i>	88.406155	263.3199333	0.33573666	0.005290299
	<i>Rin1</i>	14.1628825	22.20940667	0.637697473	0.001335313
	<i>Ffar4</i>	47.1836425	80.31835	0.587457816	0.039582994
	<i>Plce1</i>	117.1150625	278.8296	0.42002378	0.005062133
	<i>Sorbs1</i>	672.992725	1504.442333	0.447337003	0.009214168
	<i>Blnk</i>	26.8696975	72.92096333	0.368476996	0.026666741
Mm_Prostaglandin_Synthesis_and_Regulation_WP374_69204	<i>Hsd11b1</i>	132.952815	385.3149333	0.345049733	0.013450618
	<i>Ptgs1</i>	76.2559025	243.3698667	0.313333378	0.004732459
	<i>SI00a6</i>	23.2272925	84.45539	0.275024395	0.004501011
	<i>SI00a10</i>	1463.435	2917.734667	0.501565484	0.022618669
	<i>Ptger3</i>	32.6654625	409.4368333	0.079781446	6.17E-05
	<i>Anxa3</i>	157.829225	561.0061333	0.281332441	0.000174098
	<i>Tbxas1</i>	25.15005	45.13677	0.557196494	0.034487258
	<i>Hpgd</i>	64.2974075	185.5881333	0.346452148	0.012379314
	<i>Anxa2</i>	173.37005	747.8007667	0.231839893	5.19E-05
	<i>Ednrb</i>	2684.9895	5889.460667	0.455897348	0.001914478
	<i>Anxa1</i>	40.81987	126.2498233	0.323326155	0.049898577
Mm_Endochondral_Ossification_WP1270_87973	<i>Ddr2</i>	38.9604875	129.4284667	0.301019463	0.001073084
	<i>Tgfb2</i>	38.414105	76.54238333	0.501867114	0.028102025
	<i>Fgfr3</i>	42.134605	258.0517667	0.163279661	0.00197107
	<i>Spp1</i>	3003.63575	29620.42667	0.101404203	0.004556873
	<i>Mgp</i>	1123.9309	5824.687667	0.192959857	0.001566508

	<i>Tgfb1</i>	172.230425	365.4635333	0.471265692	0.002123612
	<i>Serpinh1</i>	239.08935	717.9896	0.332998347	5.73E-05
	<i>Sox6</i>	19.3012925	39.57107667	0.487762632	0.023496758
	<i>Fgfr1</i>	32.8912025	74.04085333	0.444230462	0.004923827
	<i>Timp3</i>	949.175	1525.720333	0.62211598	0.015876356
	<i>Igf1</i>	185.5764	1552.777433	0.119512556	0.002938087
	<i>Enpp1</i>	104.132685	242.9446667	0.42862717	0.00708508
	<i>Sox9</i>	59.449575	242.679	0.244972062	0.004226726
	<i>Mef2c</i>	1455.98875	3166.981	0.459740286	0.047085674
	<i>Ctsl</i>	5221.62225	8314.422	0.628019873	0.014594389
	<i>Slc38a2</i>	20283.7725	34474.61333	0.588368383	0.008978424
Mm_Complement_Activation_Classical_Pathway_WP200_72061	<i>Clqb</i>	112.6643	180.2585667	0.625014955	0.028655717
	<i>Clqc</i>	41.6008625	93.15491667	0.446577207	0.01723451
	<i>Clra</i>	83.4978725	265.4218667	0.314585507	0.029629821
	<i>Clsl</i>	207.250225	557.3640667	0.371839947	0.007369744
	<i>C7</i>	157.964565	402.2963333	0.392657233	0.037783103
	<i>Maspl</i>	39.2921275	133.4244467	0.294489717	0.007003271
	<i>C4b</i>	39.97345	116.0005667	0.344597024	0.023438414
Mm_Spinal_Cord_Injury_WP2432_87679	<i>Selp</i>	32.314285	94.40940333	0.342278246	0.015221083
	<i>Fcgr2b</i>	41.166975	174.843	0.23545109	0.003661907
	<i>Vim</i>	839.006275	5155.641	0.162735589	0.00492182
	<i>Rhoc</i>	464.71365	735.0998	0.632177631	0.025502295
	<i>Tlr4</i>	46.4875025	82.52730667	0.563298433	0.02321352
	<i>Tgfb1</i>	172.230425	365.4635333	0.471265692	0.002123612

	<i>Rgma</i>	40.8127425	72.19470333	0.565314914	0.002078039
	<i>Zfp36</i>	286.78275	1173.418467	0.244399384	0.01588454
	<i>Pirb</i>	57.7231525	109.05524	0.529301962	0.045006507
	<i>Mmp12</i>	92.7276125	317.8057667	0.291774481	0.025074631
	<i>Icam1</i>	28.05433	51.33745333	0.546469063	0.022766703
	<i>Gjal</i>	271.023325	703.2965667	0.385361365	0.001799194
	<i>Sox9</i>	59.449575	242.679	0.244972062	0.004226726
	<i>Rhob</i>	116.44297	213.6732	0.544958235	0.017788003
	<i>Rtn4r</i>	14.581325	22.41890333	0.650403134	0.021542628
	<i>Egr1</i>	2982.07575	9096.248	0.327835801	0.049672302
	<i>Aqp4</i>	1047.788725	6970.607333	0.15031527	0.000357011
	<i>Sema6a</i>	204.9183	441.1739333	0.464484151	0.016905262
	<i>Anxa1</i>	40.81987	126.2498233	0.323326155	0.049898577
Mm_Complement_and_Coagulation_Cascades_WP449_71733	<i>Cfh</i>	1524.45775	6894.653667	0.221107227	0.001744584
	<i>Tfpi</i>	110.79045	307.4441333	0.360359617	0.000638669
	<i>Serping1</i>	14695.7445	30927.50333	0.475167502	0.023970877
	<i>Clqb</i>	112.6643	180.2585667	0.625014955	0.028655717
	<i>Clqc</i>	41.6008625	93.15491667	0.446577207	0.01723451
	<i>Clra</i>	83.4978725	265.4218667	0.314585507	0.029629821
	<i>Vwf</i>	87.52641	281.8331333	0.310561107	0.02399348
	<i>Clsl</i>	207.250225	557.3640667	0.371839947	0.007369744
	<i>Plaur</i>	46.1354675	134.2371867	0.343686192	0.004363717
	<i>C7</i>	157.964565	402.2963333	0.392657233	0.037783103
	<i>Pros1</i>	72.265575	179.3809333	0.40286096	0.001131909

	<i>Masp1</i>	39.2921275	133.4244467	0.294489717	0.007003271
	<i>C4b</i>	39.97345	116.0005667	0.344597024	0.023438414
	<i>Cfb</i>	11.51019	27.03415333	0.425764767	0.000612751
Mm_Macrophage_markers_WP2271_69962	<i>Cd52</i>	56.147335	153.92037	0.364781705	0.038106291
	<i>Cd163</i>	19.988915	36.11256667	0.553516874	0.012764355
	<i>Lyz2</i>	253.955825	3170.484	0.080100018	0.002855792
	<i>Cd68</i>	126.1940475	314.5799333	0.401150977	0.025679705
	<i>Cd14</i>	18.55365	80.2196	0.231285746	0.004969535
Mm_TYROBP_Causal_Network_WP3625_90841	<i>Dpyd</i>	29.1266125	43.92146	0.663152193	0.007918875
	<i>Clqc</i>	41.6008625	93.15491667	0.446577207	0.01723451
	<i>Spp1</i>	3003.63575	29620.42667	0.101404203	0.004556873
	<i>Tyrobp</i>	27.26938	57.28381667	0.476039859	0.007274133
	<i>Kcne3</i>	53.7096925	250.4577333	0.214446133	0.000336572
	<i>Itgam</i>	22.63767	42.04191	0.538454842	0.011538641
	<i>Igsf6</i>	20.6900025	47.04756	0.439767812	0.009876198
	<i>Elf4</i>	36.1456175	90.56087667	0.399130605	0.008639425
	<i>Cxcl16</i>	197.9695	564.8711	0.350468452	0.005438866
	<i>Npc2</i>	1092.132375	1893.487333	0.576783565	0.022403876
	<i>Lhfpl2</i>	27.13682	42.50462	0.638444009	0.021543541
	<i>Slc7a7</i>	55.8654225	87.03153667	0.641898611	0.006032498
	<i>Zfp36l2</i>	778.835175	1574.773333	0.4945697	0.020605066
Mm_Focal_Adhesion-PI3K-Akt-mTOR-signaling_pathway_WP2841_89989	<i>Col3a1</i>	326.099725	3478.643667	0.093743354	0.000491964
	<i>Lamb3</i>	6.6191925	11.55468667	0.57285781	0.013320847
	<i>Col5a2</i>	20.040275	35.89594	0.558288068	0.029293837

<i>Fnl</i>	35.0263875	607.7869933	0.05762938	0.030387613
<i>Lamc1</i>	276.1241	467.9596	0.590059697	0.000317157
<i>Col5a1</i>	8.18205	19.6147	0.417138677	0.000719352
<i>Lamc3</i>	31.3503525	67.87056	0.461913862	0.046603314
<i>Pfkfb3</i>	53.326055	391.1625667	0.136327091	0.000361581
<i>Pdgfc</i>	23.3219575	93.67722	0.24896082	5.90E-05
<i>Ngf</i>	161.286725	309.6286667	0.520903722	0.004524949
<i>Csf1</i>	490.016125	960.1109333	0.510374487	0.000317365
<i>Slc2a1</i>	627.8459	1069.8136	0.586874106	0.016112861
<i>Hgf</i>	27.1695	58.35599333	0.465581998	0.005642612
<i>Fgfr3</i>	42.134605	258.0517667	0.163279661	0.00197107
<i>Pdgfra</i>	24.722745	49.64476333	0.497993008	0.001644464
<i>Spp1</i>	3003.63575	29620.42667	0.101404203	0.004556873
<i>Ppargc1a</i>	164.4451	599.9447333	0.274100414	0.010033555
<i>Colla2</i>	98.95484	964.4898333	0.102598116	0.001109313
<i>Met</i>	498.0858	972.3606333	0.512243897	0.004144254
<i>Vwf</i>	87.52641	281.8331333	0.310561107	0.02399348
<i>Itgam</i>	22.63767	42.04191	0.538454842	0.011538641
<i>Fgfr2</i>	41.53819	99.78233667	0.416288006	0.009120717
<i>Col4a2</i>	149.598975	248.8547	0.601149888	0.003779064
<i>Fgfr1</i>	32.8912025	74.04085333	0.444230462	0.004923827
<i>Pdgfd</i>	133.3755225	392.3055667	0.339978664	0.001825636
<i>Lamb2</i>	180.7027	464.8498667	0.388733466	0.004751886
<i>Figf</i>	60.7189275	118.8654533	0.510820645	0.017878475

	<i>Lama4</i>	295.62555	527.1579	0.560791273	0.046260794
	<i>Igfl</i>	185.5764	1552.777433	0.119512556	0.002938087
	<i>Kitl</i>	579.38455	1204.362233	0.481071669	0.015710689
	<i>Lama2</i>	108.9375325	397.5324667	0.274034303	8.59E-05
	<i>Col6a2</i>	101.2813775	273.4747	0.370350082	0.010717393
	<i>Vtn</i>	589.036225	2251.151667	0.261659947	0.000630694
	<i>Colla1</i>	193.3673	1547.431667	0.124960154	0.000121359
	<i>Itgb4</i>	31.9832075	71.04363	0.450191066	0.002481815
	<i>Itgb8</i>	400.79445	759.4512333	0.527742181	0.040237815
	<i>Fgfr4</i>	12.3935275	20.70385	0.5986098	0.011933838
	<i>Osmr</i>	73.2079075	149.7408	0.488897532	0.004530251
	<i>Angpt1</i>	24.2376675	48.63081333	0.498401442	0.014243486
	<i>Epas1</i>	3306.0545	5852.216333	0.564923494	0.002255754
	<i>Lama3</i>	208.004075	451.7060667	0.460485458	0.021773403
	<i>Pdgfrb</i>	400.01485	893.8316667	0.44752817	0.010281689
	<i>Csflr</i>	88.406155	263.3199333	0.33573666	0.005290299
	<i>Ppp2r2b</i>	40.14104	92.52508	0.43383956	0.004607635
Mm_Oxidative_Stress_WP412_89965	<i>Cat</i>	796.6019	2646.369	0.301016941	0.000585539
	<i>Mgst1</i>	83.856195	1273.3054	0.065857095	0.000468062
	<i>Hmox1</i>	131.23145	287.3418333	0.456708473	0.036457211
	<i>Mtl</i>	118329.3375	187821.3667	0.630009991	0.049223099
	<i>Nfix</i>	2348.8075	4300.999	0.546107428	0.01055731
	<i>Junb</i>	168.2739	635.3924	0.264834612	0.022890086
	<i>Cyba</i>	83.6466425	137.6863	0.607516089	0.01177478

Mm_Alpha6-Beta4_Integrin_Signaling_Pathway_WP488_72049	<i>Lamb3</i>	6.6191925	11.55468667	0.57285781	0.013320847
	<i>Lamc1</i>	276.1241	467.9596	0.590059697	0.000317157
	<i>Vim</i>	839.006275	5155.641	0.162735589	0.00492182
	<i>Met</i>	498.0858	972.3606333	0.512243897	0.004144254
	<i>Cd151</i>	2039.922	4364.061	0.467436638	1.05E-05
	<i>Lamb2</i>	180.7027	464.8498667	0.388733466	0.004751886
	<i>Smad3</i>	86.73054	149.1512333	0.581493951	0.004335903
	<i>Ar</i>	15.8150275	42.60934333	0.371163371	0.001942655
	<i>Lama2</i>	108.9375325	397.5324667	0.274034303	8.59E-05
	<i>ErbB2</i>	11.0547875	33.71550667	0.327884365	0.000193152
	<i>Itgb4</i>	31.9832075	71.04363	0.450191066	0.002481815
	<i>Plec</i>	285.84015	473.1458333	0.604126952	0.015857587
	<i>Lama3</i>	208.004075	451.7060667	0.460485458	0.021773403
Mm_Striated_Muscle_Contraction_WP216_87693	<i>Des</i>	34.7486725	72.49361	0.479334282	0.047635859
	<i>Vim</i>	839.006275	5155.641	0.162735589	0.00492182
	<i>Myl9</i>	231.853275	508.6976667	0.455778137	0.005564108
	<i>Tpm3</i>	11691.14725	17678.73667	0.661311239	0.003690043
	<i>Tpm2</i>	65.5363225	117.9875	0.555451404	0.015289586
	<i>Tpm4</i>	1126.59605	1720.194	0.654923834	0.003016711
	<i>Tpm1</i>	3989.42775	6916.448333	0.576802942	0.002227663
	<i>Dmd</i>	29.0132125	59.90378667	0.484330192	0.014739867
	<i>Actn2</i>	28.7756675	139.40474	0.206418143	0.001313398
	<i>Acta2</i>	1333.0087	4338.853667	0.30722601	0.043526171
Mm_Primary_Focal_Segmental_Glomerulosclerosis_FSGS_WP2573_89874	<i>Vim</i>	839.006275	5155.641	0.162735589	0.00492182

	<i>Jag1</i>	163.870325	454.4074667	0.360624191	0.000939873
	<i>Tlr4</i>	46.4875025	82.52730667	0.563298433	0.02321352
	<i>Agrn</i>	116.2691825	223.1902333	0.520942072	0.020137847
	<i>Plaur</i>	46.1354675	134.2371867	0.343686192	0.004363717
	<i>Tgfb1</i>	172.230425	365.4635333	0.471265692	0.002123612
	<i>Cd151</i>	2039.922	4364.061	0.467436638	1.05E-05
	<i>Myo1e</i>	318.794375	551.6008	0.577944004	0.013217954
	<i>Lamb2</i>	180.7027	464.8498667	0.388733466	0.004751886
	<i>Vtn</i>	589.036225	2251.151667	0.261659947	0.000630694
	<i>Itgb4</i>	31.9832075	71.04363	0.450191066	0.002481815
	<i>Ctsl</i>	5221.62225	8314.422	0.628019873	0.014594389
	<i>Plce1</i>	117.1150625	278.8296	0.42002378	0.005062133
Mm_Matrix_Metalloproteinases_WP441_69114	<i>Mmp23</i>	38.3210925	85.85138667	0.446365446	0.005474584
	<i>Mmp2</i>	122.763455	1084.967567	0.113149424	0.000930202
	<i>Mmp15</i>	50.2912625	93.54439667	0.537619187	0.002008472
	<i>Mmp12</i>	92.7276125	317.8057667	0.291774481	0.025074631
	<i>Timp3</i>	949.175	1525.720333	0.62211598	0.015876356
	<i>Timp2</i>	1775.6685	3687.19	0.481577706	0.022914666
	<i>Mmp14</i>	33.121	145.59698	0.227484114	0.003437688
Mm_Inflammatory_Response_Pathway_WP458_78438	<i>Col3a1</i>	326.099725	3478.643667	0.093743354	0.000491964
	<i>Fn1</i>	35.0263875	607.7869933	0.05762938	0.030387613
	<i>Lamc1</i>	276.1241	467.9596	0.590059697	0.000317157
	<i>Colla2</i>	98.95484	964.4898333	0.102598116	0.001109313
	<i>Lamb2</i>	180.7027	464.8498667	0.388733466	0.004751886

	<i>Vtn</i>	589.036225	2251.151667	0.261659947	0.000630694
	<i>Colla1</i>	193.3673	1547.431667	0.124960154	0.000121359
Mm_Microglia_Pathogen_Phagocytosis_Pathway_WP3626_87399	<i>Vav3</i>	65.3230775	177.4979	0.368021692	0.001313054
	<i>Lyn</i>	427.572675	1068.103367	0.400310202	0.037134753
	<i>Clqb</i>	112.6643	180.2585667	0.625014955	0.028655717
	<i>Clqc</i>	41.6008625	93.15491667	0.446577207	0.01723451
	<i>Arpc1b</i>	471.65085	961.9741	0.490294749	0.009200175
	<i>Tyrobp</i>	27.26938	57.28381667	0.476039859	0.007274133
	<i>Itgam</i>	22.63767	42.04191	0.538454842	0.011538641
	<i>Plcg2</i>	40.5245975	61.07198333	0.663554633	0.033891134
	<i>Cyba</i>	83.6466425	137.6863	0.607516089	0.01177478
Mm_Factors_and_pathways_affecting_insulin-like_growth_factor_(IGF1)-Akt_signaling_WP3675_90178	<i>Igfbp5</i>	553.147425	2197.324333	0.251736813	0.000392009
	<i>Pdk1</i>	1323.19025	2059.256	0.642557433	0.001545921
	<i>Pld1</i>	135.126185	400.4532333	0.337433123	0.001321362
	<i>Ppargc1a</i>	164.4451	599.9447333	0.274100414	0.010033555
	<i>Smad3</i>	86.73054	149.1512333	0.581493951	0.004335903
	<i>Igfl</i>	185.5764	1552.777433	0.119512556	0.002938087
	<i>Igfbp4</i>	495.7088	1738.672	0.285107714	0.014088425
Mm_Irinotecan_Pathway_WP475_69144	<i>Bche</i>	18.856555	36.35101	0.51873538	0.00587686
	<i>Abcg2</i>	248.721675	661.3175	0.376100247	0.001721492
	<i>Ces1d</i>	47.91472	101.3924833	0.472566786	0.008830786
Mm_Statin_Pathway_WP1_73346	<i>Pltp</i>	402.6241	1533.294333	0.262587614	0.001958269
	<i>Abca1</i>	3880.021	6063.163	0.63993348	0.037501272
	<i>Scarb1</i>	578.510225	1043.131167	0.554590107	0.041360662

<i>ApoE</i>	12382.705	44541.50333	0.278003751	0.001195322
<i>Lrp1</i>	180.922825	596.3482667	0.303384507	0.000288625

Supplementary Table 4. The expression levels of genes involved in glycolysis or the tricarboxylic acid (TCA) cycle

Glycolysis

Gene Symbol	Average value (test: <i>Gck</i> ^{+/-} <i>db/db</i>)	Average value (control: <i>Gck</i> ^{+/+} <i>db/db</i>)	Ratio (test/control)	P-value
<i>Adh1</i>	20358.3225	15403.78	1.32164459	0.472674405
<i>Adh5</i>	58.379585	63.04105333	0.926056624	0.191007829
<i>Akr1a1</i>	7520.8275	8996.097	0.83601005	0.141958057
<i>Aldh2</i>	737.8592	721.3382667	1.022903171	0.805463794
<i>Aldh3a2</i>	4900.02975	4308.062	1.137409292	0.380166383
<i>Aldh7a1</i>	714.061025	759.608	0.940038842	0.136037097
<i>Aldh9a1</i>	1903.56425	1560.614333	1.219753151	0.279561892
<i>Aldn1b1</i>	19.0053275	17.99901667	1.055909212	0.977406775
<i>Aldoa</i>	23043.925	28168.70667	0.818068265	0.039625854
<i>Aldob</i>	82.3066675	673.8796	0.122138536	0.000108862
<i>Aldoc</i>	144.113975	226.7789667	0.635482105	0.080085587
<i>Dlat</i>	2080.175	2453.911333	0.847697703	0.031575591
<i>Dld</i>	4266.36275	4227.034	1.009304101	0.835698858
<i>Eno1</i>	7689.09575	16571.64	0.463991237	0.002324667
<i>Eno1b</i>	32.5652825	40.07652	0.812577602	0.002202492
<i>Eno2</i>	41.0012825	49.31694	0.831383344	0.160530945
<i>Eno3</i>	62.9921425	52.35201	1.203242101	0.092208151
<i>Fbp1</i>	37.3361025	35.21626667	1.060194792	0.593938791
<i>Fbp2</i>	65.22797	63.53738333	1.026607748	0.827713365
<i>G6pc2</i>	444359.4	321449.9	1.382359739	0.179610521
<i>Gapdh</i>	56832.3525	60973.58667	0.932081506	0.29585255
<i>Gapdhs</i>	8.9654375	7.994276667	1.121482014	0.386133689
<i>Gpi1</i>	7216.7365	11111.294	0.649495594	0.004126932
<i>Hk1</i>	84.9669275	289.7776667	0.293214203	0.002618936
<i>Ldha</i>	521.991225	732.2255667	0.712883091	0.000886298
<i>Pdha1</i>	1242.34675	1517.750333	0.81854487	0.142364434
<i>Pdhb</i>	21547.2475	20684.48333	1.041710695	0.838462558
<i>Pfkl</i>	200.911275	213.7794667	0.939806232	0.63991739
<i>Pfkm</i>	651.60205	574.7388	1.133735968	0.410052049

<i>Pfkp</i>	259.868625	408.0441333	0.636864015	0.002588289
<i>Pgam1</i>	2508.38125	2644.718	0.948449419	0.647881373
<i>Pgk1</i>	4532.0225	4375.321333	1.035814779	0.601640323
<i>Pgm1</i>	767.249925	644.4023	1.190638092	0.194919995
<i>Pgm2</i>	1260.05825	1241.859667	1.014654299	0.86227142
<i>Pkm</i>	38736.2925	49439.7	0.783505816	0.134577776
<i>Tpi1</i>	1489.9375	1613.567	0.923381242	0.544685407

TCA cycle

Gene Symbol	Average value (test: <i>Gck</i> ^{+/-} <i>db/db</i>)	Average value (control: <i>Gck</i> ^{+/+} <i>db/db</i>)	Ratio (test/control)	P-value
<i>Aco2</i>	9566.4945	7608.493333	1.257344139	0.050458868
<i>Cs</i>	2150.2025	2154.475333	0.998016764	0.915420695
<i>Fh1</i>	3476.364	2762.419667	1.258448903	0.187306047
<i>Idh2</i>	1524.70775	1235.638667	1.233943054	0.064801205
<i>Idh3a</i>	2476.54175	2595.194	0.954280008	0.554219508
<i>Idh3b</i>	3525.8995	3907.359333	0.902374007	0.179837722
<i>Idh3g</i>	16949.6	14107.44	1.201465326	0.01602424
<i>Mdh2</i>	6945.502	6638.983333	1.046169519	0.586226525
<i>Ogdh</i>	14328.25	13672.56	1.047956637	0.63161217
<i>Pdha1</i>	1242.34675	1517.750333	0.81854487	0.142364434
<i>Pdhb</i>	21547.2475	20684.48333	1.041710695	0.838462558
<i>Pdk1</i>	1323.19025	2059.256	0.642557433	0.001545921
<i>Pdk2</i>	1428.998	1155.464967	1.236729837	0.091458639
<i>Pdk3</i>	180.6734	188.3809	0.959085555	0.669163039
<i>Sdha</i>	353.49795	356.5083	0.991556017	0.998606274
<i>Sdhb</i>	2411.06525	2187.918	1.101990682	0.79117887
<i>Sdhc</i>	572.0353	516.4596333	1.107608926	0.155699615
<i>Sucla2</i>	16.6079225	16.52249667	1.005170274	0.987851187
<i>Suclg1</i>	2865.24925	3266.435	0.877179325	0.250446472
<i>Suclg2</i>	697.663225	889.4768333	0.784352328	0.04610927

Supplementary Table 5. The expression levels of genes involved in Ca²⁺-binding and signaling

Gene Symbol	Average value (test: <i>Gck</i> ^{+/-} <i>db/db</i>)	Average value (control: <i>Gck</i> ^{+/+} <i>db/db</i>)	Ratio (test/control)	P-value
<i>Cacng3</i>	51.5395275	48.10675	1.071357502	0.502758452
<i>Camk1d</i>	149.841125	174.9702333	0.856380666	0.529270752
<i>Camkk1</i>	14.73177	13.27643333	1.109618045	0.704966906
<i>Camkk2</i>	264.272325	338.4388333	0.780856979	0.25289089
<i>Mef2c</i>	1455.98875	3166.981	0.459740286	0.047085674
<i>Mef2d</i>	4337.2765	4113.387333	1.054429391	0.496301528
<i>Myo7a</i>	996.428675	1070.352033	0.930935472	0.408752668
<i>Nfatc1</i>	756.07745	714.9829667	1.057476171	0.993933252
<i>Pcp4</i>	1747.633725	705.7159667	2.476398165	0.090937905
<i>S100a1</i>	204.525575	302.3089	0.676545001	0.128835443
<i>S100a13</i>	122.213825	152.0565333	0.803739388	0.07854115
<i>S100a3</i>	12.4460725	11.29136333	1.102264814	0.326490352
<i>S100a4</i>	106.453875	142.8068333	0.745439644	0.050122917
<i>S100a6</i>	23.2272925	84.45539	0.275024395	0.004501011

Supplementary figure legends

Supplementary Fig. 1. Effects of glucokinase haploinsufficiency on changes in body weight and blood glucose levels.

A, B Area under the curve for the changes in **(A)** body weight and **(B)** fed blood glucose levels after 10 weeks of age in the $Gck^{+/+}db/+$, $Gck^{+/-}db/+$, $Gck^{+/+}db/db$, and $Gck^{+/-}db/db$ mice ($n = 14-18$). Values are means \pm SD. P values were determined using analysis of variance (ANOVA) followed by *post-hoc* Bonferroni's test. ** $P < 0.01$.

Supplementary Fig. 2. Effects of glucokinase haploinsufficiency on metabolic changes.

A Food intake in the $Gck^{+/+}db/db$ and $Gck^{+/-}db/db$ mice aged 23 weeks ($n = 4$). **B** Blood glucose levels during the intraperitoneal insulin tolerance test in the $Gck^{+/+}db/db$ and $Gck^{+/-}db/db$ mice aged 18 weeks ($n = 7-13$). **C** Fasting plasma triglyceride level in the $Gck^{+/+}db/db$ and $Gck^{+/-}db/db$ mice aged 23 weeks ($n = 6$). **D** Fasting plasma non-esterified fatty acid level in the $Gck^{+/+}db/db$ and $Gck^{+/-}db/db$ mice aged 23 weeks ($n = 6$). **E** Plasma alanine aminotransferase level in the $Gck^{+/+}db/db$ and $Gck^{+/-}db/db$ mice aged 23 weeks ($n = 6$). Values are means \pm SD. P values were determined using Student's t test.

Supplementary Fig. 3. Effects of glucokinase haploinsufficiency on alpha-cells.

The ratio of the number of alpha-cells to the total number of alpha- plus beta-cells in the

Gck^{+/+}*db/db* and *Gck*^{+/-}*db/db* mice aged 10 weeks (*n* = 4–6). Values are means ± SD. *P* values were determined using Student's *t* test.

Supplementary Fig. 4. Effects of glucokinase haploinsufficiency on glucose tolerance and beta-cell mass in *db/db* mice aged 10 weeks.

A Blood glucose levels during the OGTT in the *Gck*^{+/+}*db/db* and *Gck*^{+/-}*db/db* mice after a 16-h fast (*n* = 11–12). **B** Quantitation of beta cell mass in the *Gck*^{+/+}*db/db* and *Gck*^{+/-}*db/db* mice (*n* = 7). Values are means ± SD. *P* values were determined using Student's *t* test.

Supplementary Fig. 5. Effects of glucokinase haploinsufficiency on apoptosis and dedifferentiation in *db/db* mice aged 10 weeks.

A Apoptosis rate of beta-cells assessed using the TUNEL assay in the *Gck*^{+/+}*db/db* and *Gck*^{+/-}*db/db* mice (*n* = 4–6). **B** Gene expression levels of *Neurog3* and *Aldh1a* in the *Gck*^{+/+}*db/db* and *Gck*^{+/-}*db/db* mice (*n* = 5–6). Values are means ± SD. *P* values were determined using Student's *t* test.

Supplementary Fig. 6. Effects of glucokinase haploinsufficiency on apoptosis in *db/db* mice aged 24 weeks.

Apoptosis rate of beta-cells assessed using the TUNEL assay in the *Gck*^{+/+}*db/db* and

Gck^{+/-}*db/db* mice (*n* = 6). Values are means ± SD. *P* values were determined using Student's *t* test.

Supplementary Fig. 7. Effects of glucokinase haploinsufficiency on fibrosis.

Azan staining of pancreatic islets from the four groups; *Gck*^{+/+}*db/+*, *Gck*^{+/-}*db/+*, *Gck*^{+/+}*db/db*, and *Gck*^{+/-}*db/db* mice aged 24 weeks. Yellow scale bars represent 50 µm.

Supplementary Fig. 8. Effects of glucokinase haploinsufficiency on transcription factors by immunofluorescent staining.

A, B Quantitation of (A) MafA, (B) Nkx6.1 and insulin double-positive cells relative to insulin-positive cells (%) in the *Gck*^{+/+}*db/+*, *Gck*^{+/-}*db/+*, *Gck*^{+/+}*db/db*, and *Gck*^{+/-}*db/db* mice aged 10 weeks (*n* = 4–6). Values are means ± SD.

Supplementary Fig. 9. Effects of glucokinase haploinsufficiency on protein levels of transcription factors.

A, B Western blot for (A) MafA and (B) Nkx6.1 in the islets of the *Gck*^{+/+}*db/db* and *Gck*^{+/-}*db/db* mice aged 10 weeks.

Supplementary Fig. 10. Changes in body weight, blood glucose levels and beta-cell mass.

A–C (**A**) body weight, (**B**) blood glucose levels and (**C**) beta-cell mass in the $Gck^{+/+}db/+$, $Gck^{+/-}db/+$, $Gck^{+/+}db/db$, and $Gck^{+/-}db/db$ mice aged 5, 10, and 24 weeks. Values are means \pm SD.

Supplementary methods

Western blot analysis. The anti-MafA antibody was purchased from Bethyl Laboratories Inc. Montgomery, TX. The anti-Nkx6.1 antibody was purchased from Cell Signaling Technology Inc. Beverly, MA. Protein was prepared from more than 100 islets and 20 µg of protein samples were applied to the gel. Protein bands were visualized with ImmunoStar LD (FUJIFILM Wako Pure Chemical Corporation, Japan).