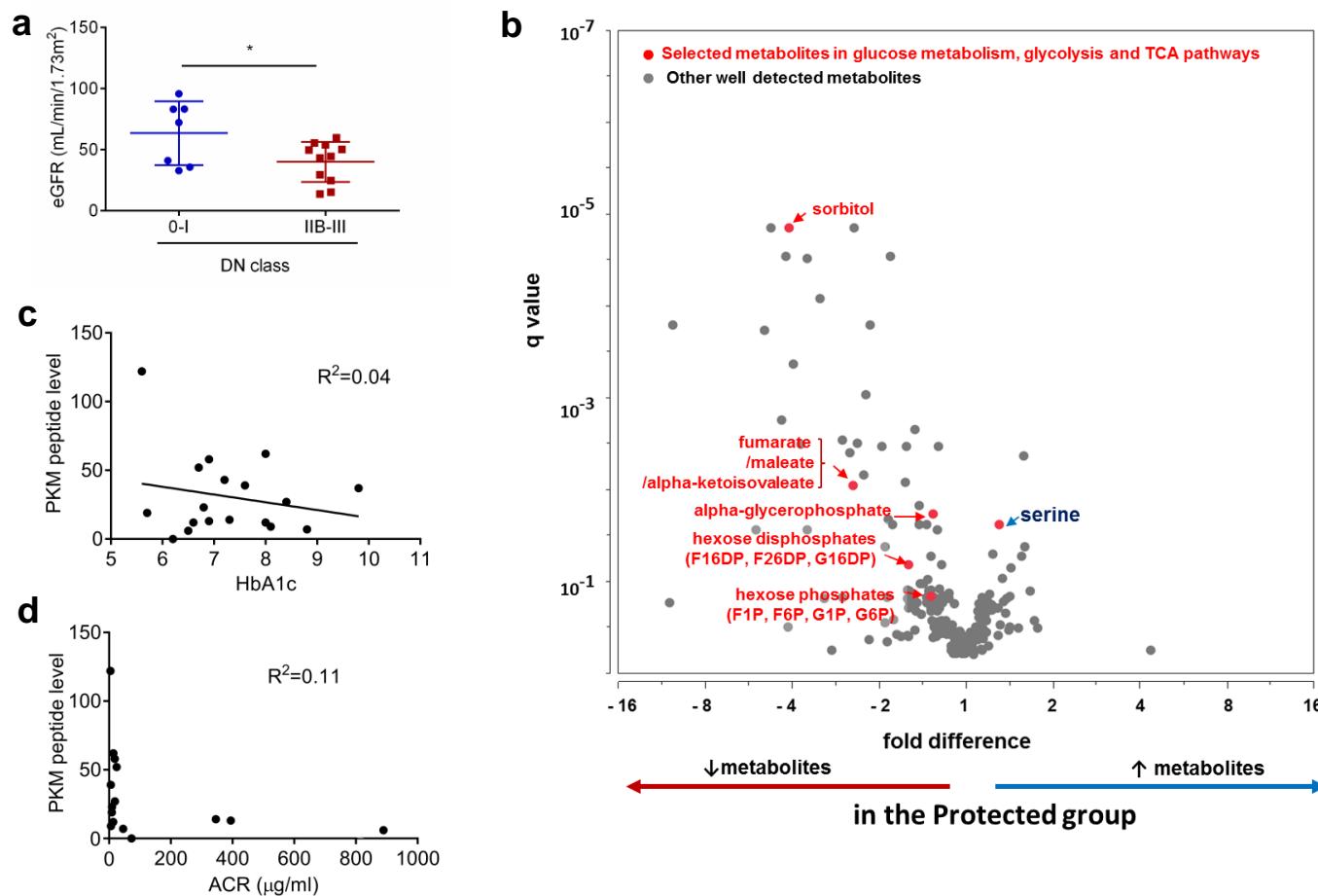
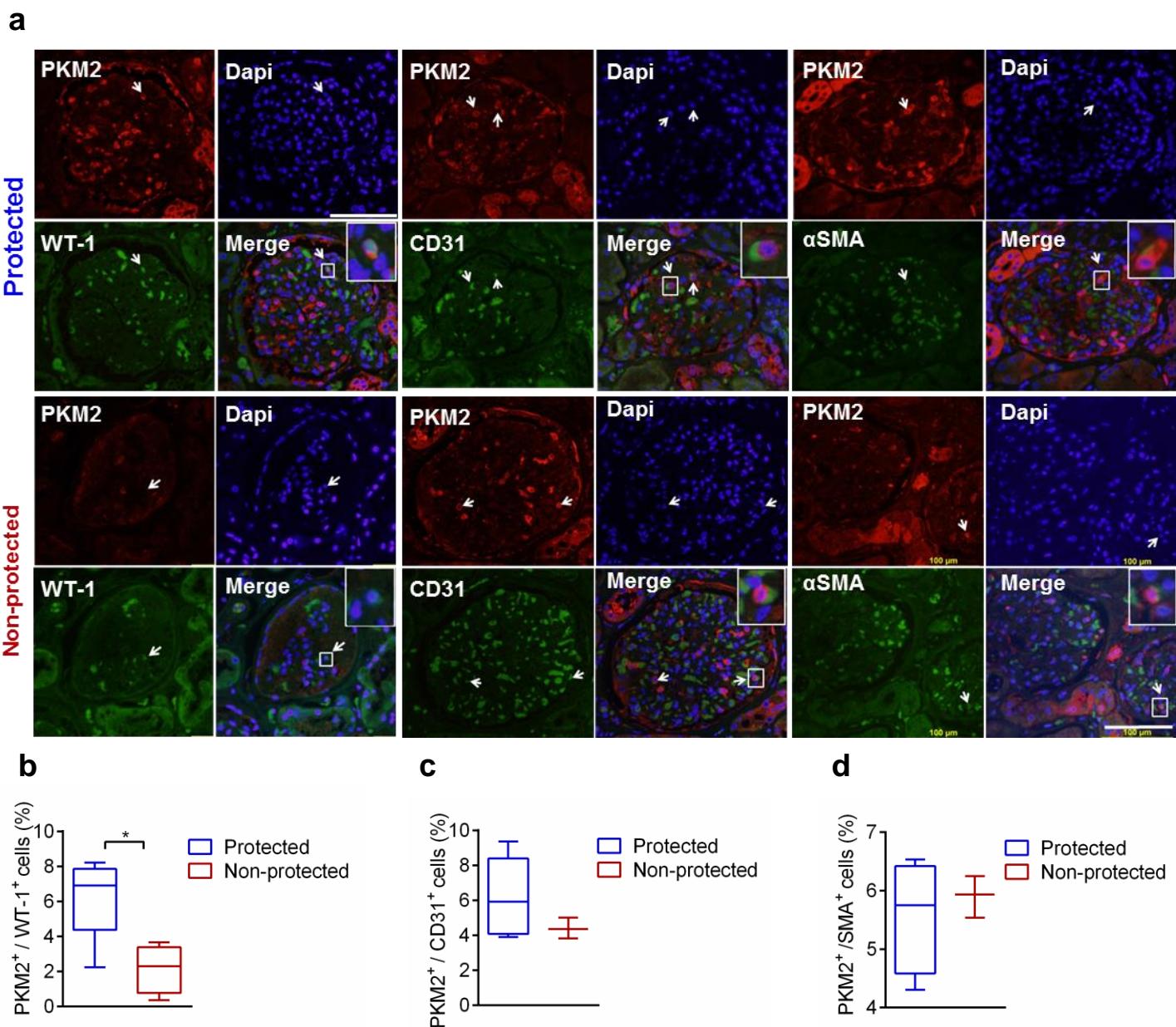


Supplementary Fig. 1



**Supplementary Fig. 1** Clinical parameters correlations with PKM and plasma metabolomics profiling in Joslin Medalists. **(a)** Association of eGFR and DN class. Protected (No or mild DN),  $n = 7$ ; Non-protected (DN),  $n = 11$ . All values are median and interquartile range and analyzed by unpaired student's t test. \* $P < 0.05$ . **(b)** Plasma metabolomics (volcano plot): fold differences between the protected ( $n = 16$ ) and non-protected ( $n = 13$ ) groups (x axis) are plotted against q value (significances of the associations adjusted for multiple testing). Metabolites of interest (glucose metabolism, glycolysis and TCA pathways) are presented as red circles. All other metabolites are presented as grey circles. Metabolomic profiling of plasma samples from 29 Medalists evaluated a total of 295 metabolites. 251 metabolites (85%) were detected in at least two thirds of the Medalists. Concentrations of 56 metabolites differed between the study groups by nominal  $P$  value ( $P < 0.05$ ) and associations remained significant for 38 metabolites in the analysis adjusted for multiple testing ( $q < 0.05$ ). There were 15 metabolites or biochemical groups present on the platform representing pathways of interest (glycolysis and TCA cycle). 5 metabolite/biochemical groups of the relevant pathways differed significantly between protected and non-protected. There were no significantly different metabolites in the semi-quantitative analysis of the non-well detectable metabolites (data not shown). Refer to Supplementary Table 7 for information on the selected metabolites. **(c)** Pearson correlation of glomerular PKM peptide number and HbA1c. Protected  $n = 7$ ; Non-protected  $n = 11$ . **(d)** Correlation of ACR and glomerular PKM peptide level. Protected  $n = 6$ ; Non-protected  $n = 9$ .

Supplementary Fig. 2



**Supplementary Fig. 2** PKM2 in glomerular cells from Joslin Medalists

(a) Representative images of co-immunofluorescent staining of PKM2 with

(b) Podocyte marker WT-1 (nuclear protein)

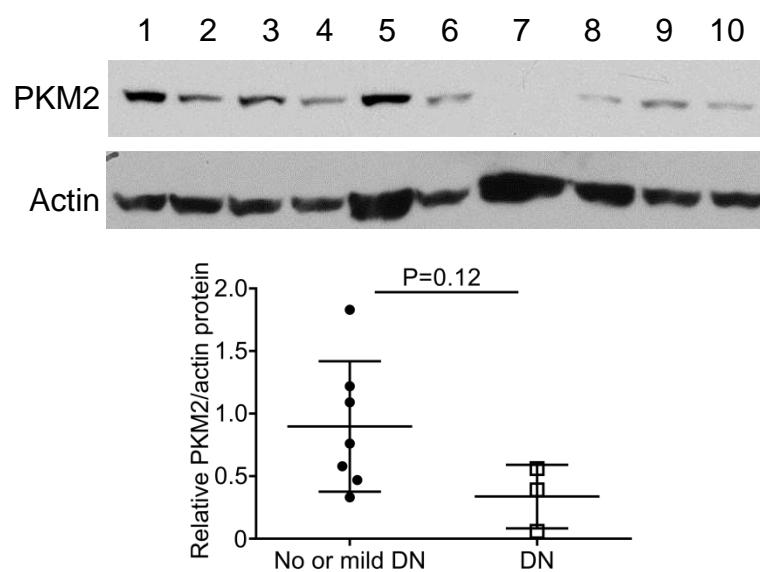
(c) Endothelial cell marker CD31 (cell surface protein)

(d) Mesangial cell marker  $\alpha$ SMA (cytosolic protein)

Scale bar, 100  $\mu\text{m}$ . Protected  $n = 5$ ; Non-protected  $n = 4$ .

For box plots, center lines represent the median; limits represent quartiles; whiskers represent minimum and maximum values. Data were analyzed by unpaired student's t test. \* $P < 0.05$ .

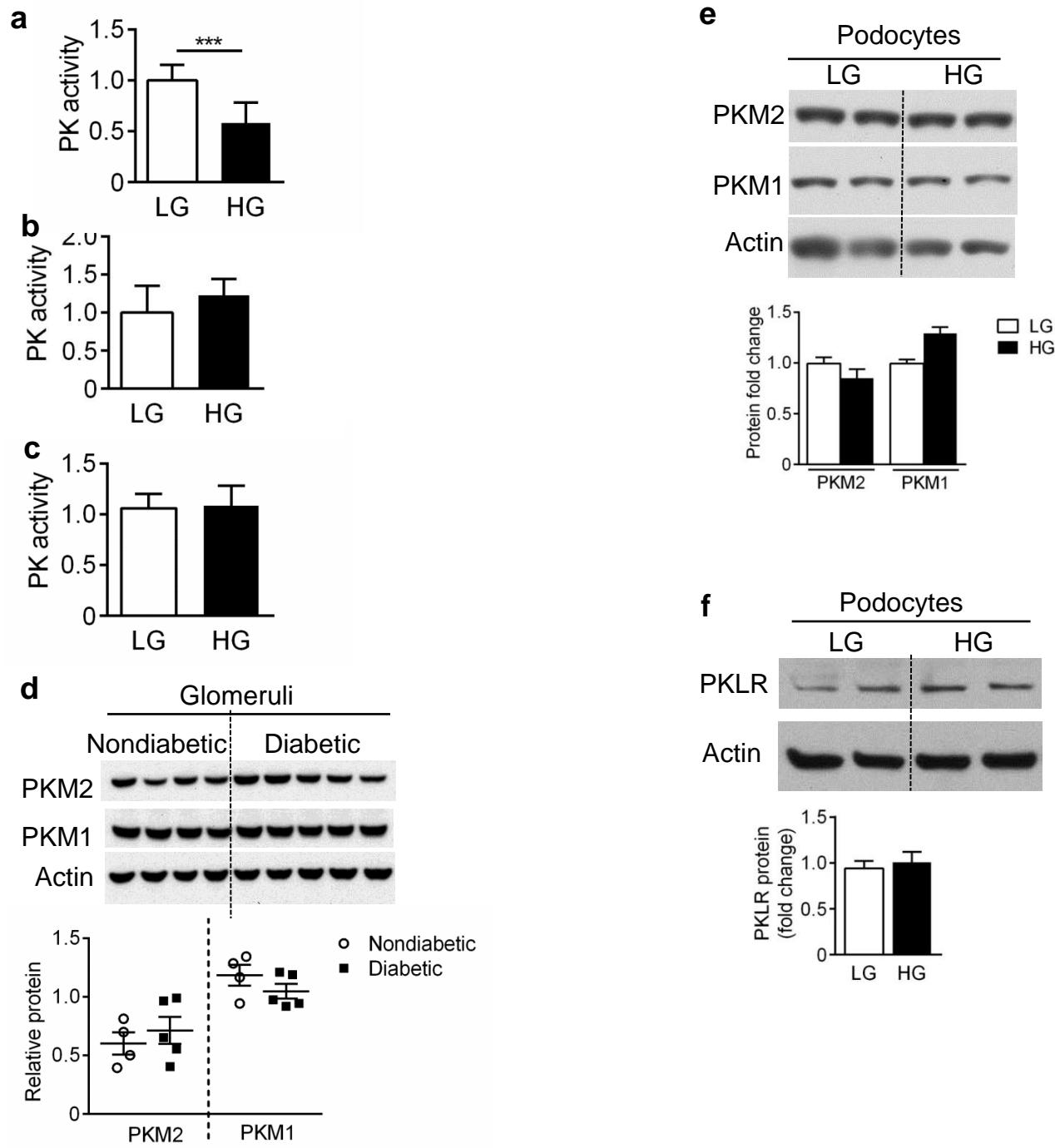
Supplementary Fig 3



**Supplementary Fig. 3** PKM2 protein levels in the glomeruli from non-Medalist cohort with diabetes

Representative blots were shown. No or mild DN (lane #1-6 and #8; DN class 0-IIA)  $n = 7$  subjects, DN (lane #7, 9-10; DN class IIB-IV)  $n = 3$  subjects. Samples were repeated in two independent Western blotting experiments. PKM2 protein was normalized to actin. The data shown in the graph is calculated with the average of the two independent Western blotting experiments for each subject. All values are mean  $\pm$  SEM and analyzed by unpaired student's t test.

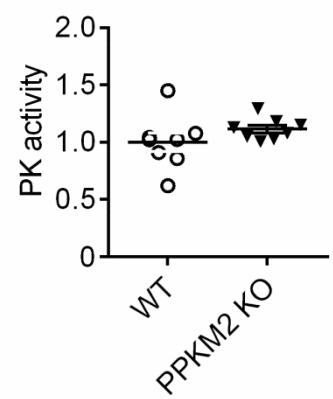
Supplementary Fig. 4



**Supplementary Fig. 4** Effects of high glucose and diabetes on PK activity and the expression of PKM isoforms and PKLR

PK activity in (a) human podocytes ( $n = 9$ ), (b) rat mesangial cells ( $n = 6$ ), (c) retinal endothelial cells ( $n = 6$ ) treated with high glucose (HG; 25mM D-glucose) for 24 hrs. All values are means  $\pm$  SD. (d) PKM2 and PKM1 in glomeruli from 2 months post-STZ DBA2/J mice. Non-diabetic  $n = 4$  mice, diabetic  $n = 5$  mice. (e,f) Representative blots of PKM1, PKM2 ( $n = 4$ ) and PKLR ( $n = 6$ ) in podocytes treated with LG and HG for 24hrs. All values are means  $\pm$  SEM. Data in this figure were analyzed by unpaired student's t test. \*\*\* $P < 0.001$ .

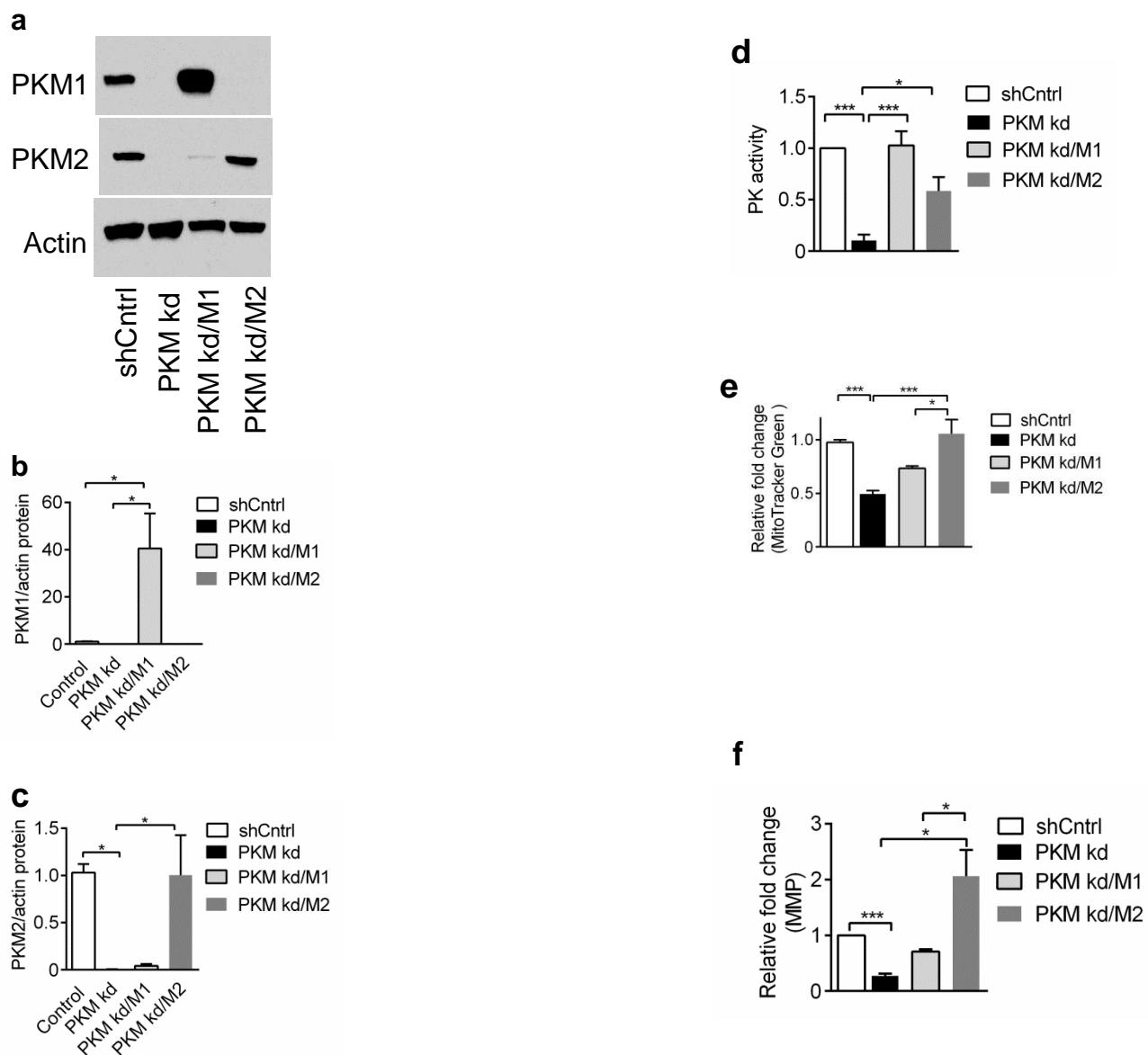
Supplementary Fig. 5



**Supplementary Fig. 5** PK activity in podocytes from PPKM2 KO mice

PK activity in podocytes isolated from WT and PPKM2 KO mice.  $n = 8$  mice. All values are means  $\pm$  SEM and analyzed using unpaired student's t test.

Supplementary Fig. 6

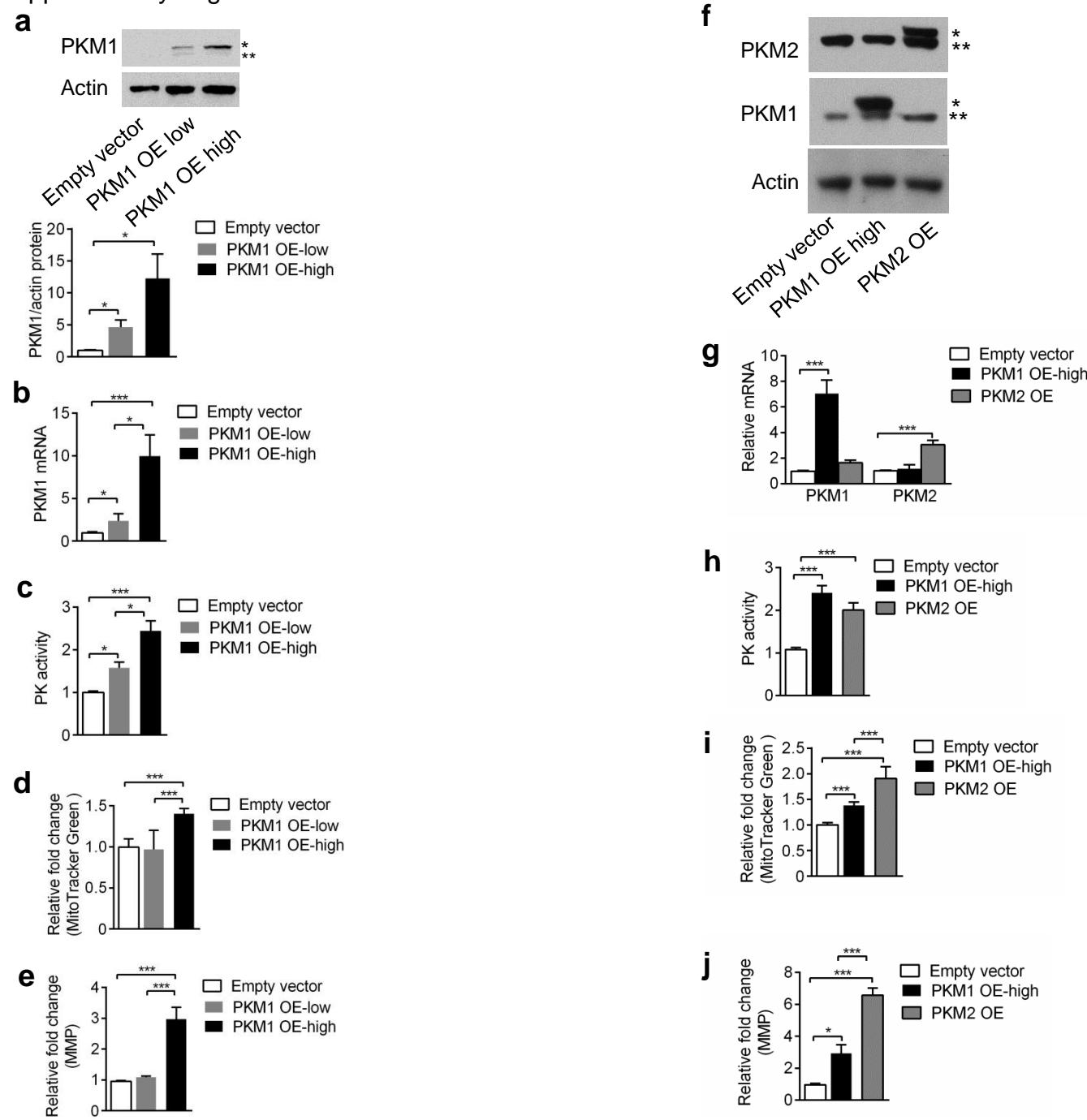


**Supplementary Fig. 6** The effects of re-expressing PKM1 or PKM2 in PKM knockdown podocytes on mitochondrial metabolism

Re-expressing of PKM1 or PKM2 in PKM knockdown podocytes stable cell lines. All representative blot images were shown.

(**a-c**) PKM1 and PKM2 protein levels ( $n = 3$ ); (**d**) PK activity ( $n = 4$ ), (**e**) mito Tracker Green ( $n = 6$ ) and (**f**) MMP ( $n = 5$ ). All values are means  $\pm$  SEM. Comparison of more than two groups was analyzed using ANOVA. When overall F-tests were significant ( $P < 0.05$ ), post hoc comparisons using Tukey's method of adjustment were conducted to determine the location of any significant pairwise differences. \*\*\* $P < 0.001$ , \*  $P < 0.05$ .

Supplementary Fig. 7

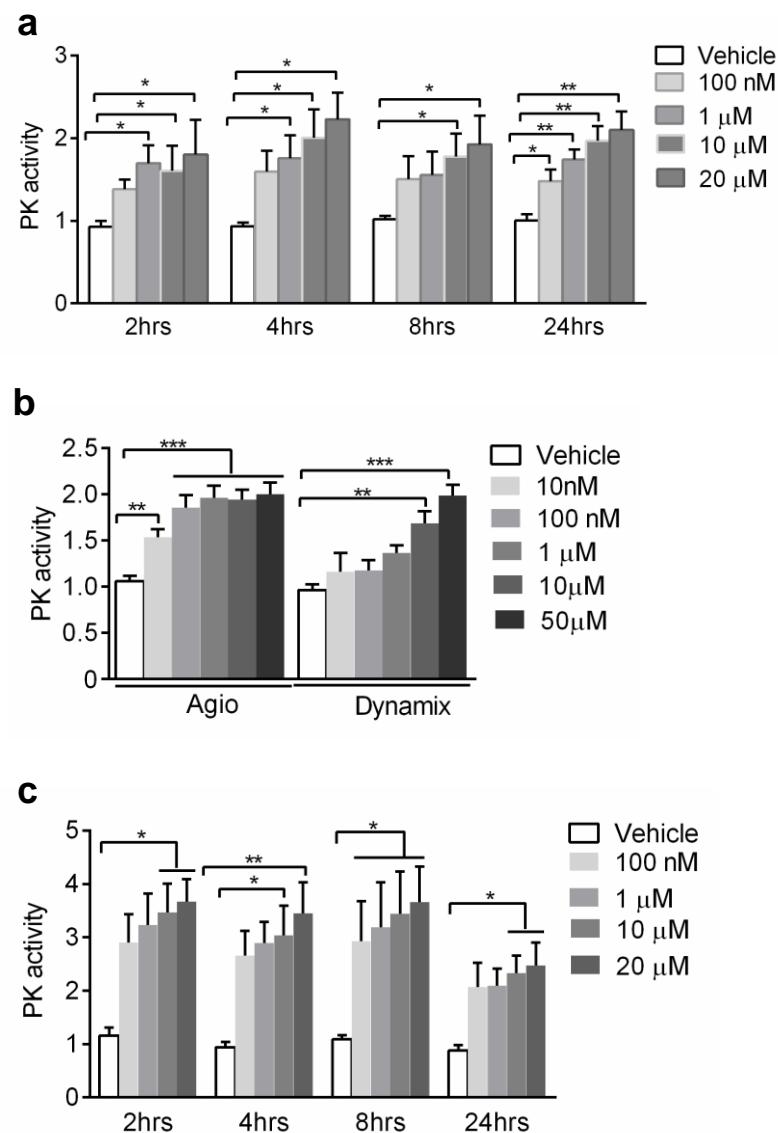


**Supplementary Fig. 7** Differential effects of PKM1 and PKM2 on mitochondrial metabolism

(a-e) Podocytes stable cell line overexpressing PKM1 at low (PKM1 OE-low) and high (PKM1 OE-high) levels. Western blotting  $n = 3$  (a); mRNA  $n = 4$  except  $n = 2$  for empty vector (b); PK activity  $n = 3$  (c); mitoTracker Green  $n = 6$  (d) and MMP  $n = 5$  (e) were performed in these cells.

(f-j) Podocytes stable cell line overexpressing PKM1 (high) and PKM2. Western blotting (f), mRNA  $n = 4$  (g), PK activity  $n = 8$  (h), mitoTracker Green  $n = 6$  (i) and MMP  $n = 5$  (j) were performed in these cells. Representative blot images were shown. \*, Flag-PKM; \*\* endogenous PKM. All values are means  $\pm$  SEM. Comparison of more than two groups was analyzed using ANOVA. When overall F-tests were significant ( $P < 0.05$ ), post hoc comparisons using Tukey's method of adjustment were conducted to determine the location of any significant pairwise differences. \*\*\* $P < 0.001$ , \*  $P < 0.05$ .

Supplementary Fig 8



**Supplementary Fig. 8** PK activity in mouse podocytes, proximal tubule cell line (HK-2 cells) and other small molecules of PKM2 activators

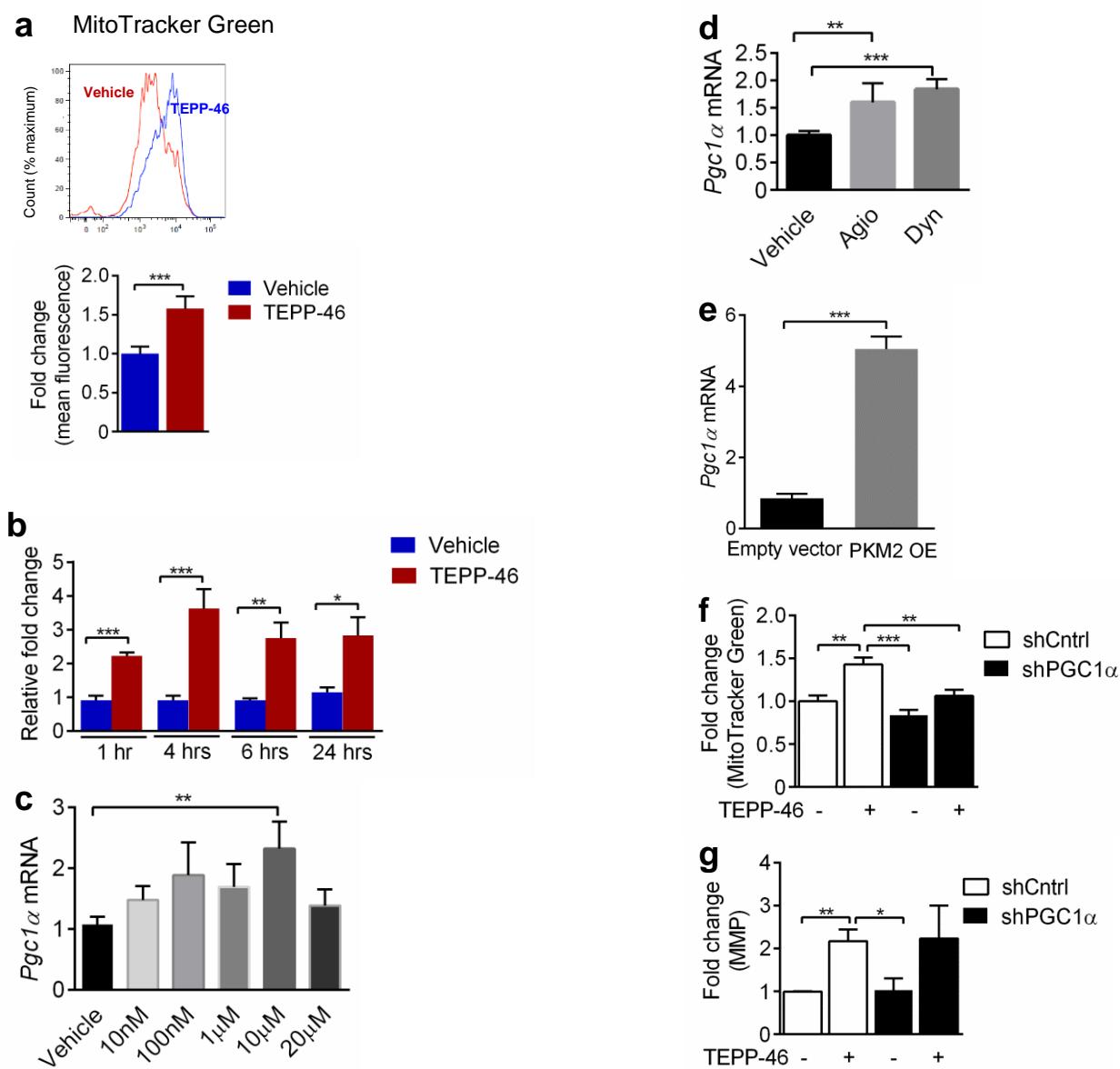
(a) PK activity in mouse podocytes treated with TEPP-46 at different concentrations and time points.  $n = 3$  independent experiments.

(b) PK activity in mouse podocytes treated with other PKM2 activators Agio (PKM2 Activator 1020) and Dynamix (SCHEMBL2694519) for 6 hrs with different concentrations.  $n = 5$  independent experiments.

(c) PK activity in HK-2 cells treated with TEPP-46 at different concentrations and time points.  $n = 4$  independent experiments.

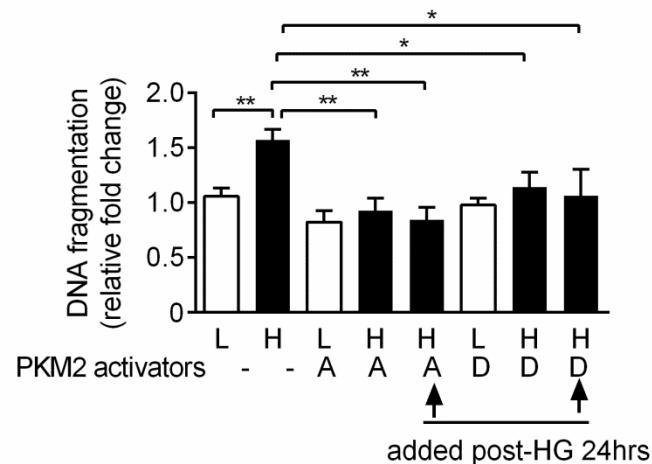
All values are means  $\pm$  SEM.. \*\*\* $P < 0.001$ , \*\* $P < 0.005$ , \* $P < 0.05$  vs. vehicle at the corresponding time point.

Supplementary Fig. 9



**Supplementary Fig. 9** PKM2 activation on PGC1 $\alpha$  expression and mitochondrial metabolism in podocytes. (a) Histogram of MitoTracker Green in podocytes treated with 10 $\mu$ M TEPP-46 for 24hrs. Quantification of MitoTracker Green mean fluorescence and the data were expressed as fold change;  $n = 7$  independent experiments. (b) MMP at different time points by TEPP-46;  $n = 4$  independent experiments. (c) Pgc1 $\alpha$  mRNA in mouse podocytes treated with TEPP-46 for 8hrs at different concentrations.  $n = 3$  independent experiments. (d) Pgc1 $\alpha$  mRNA in mouse podocytes treated with Vehicle ( $n = 7$ ), other PKM2 activators 10 $\mu$ M Agio ( $n = 4$ ) and Dynamix ( $n = 3$ ) for 6hrs. (e) Pgc1 $\alpha$  mRNA in mouse podocytes stable cell line with either Control (empty vector) or PKM2 overexpressing (PKM2 OE).  $n = 3$  independent experiments. (f) MitoTracker Green ( $n = 5$  independent experiments) and (g) MMP ( $n = 6$  independent experiments) in podocytes stable cell lines with either scramble shRNA Control or knockdown with shPGC1 $\alpha$  treated with +/- 10 $\mu$ M TEPP-46 for 24hrs. All values are means  $\pm$  SEM. For two group comparison, all values are analyzed using unpaired student's t test. Comparison of more than two groups was analyzed using ANOVA. When overall F-tests were significant ( $P < 0.05$ ), post hoc comparisons using Tukey's method of adjustment were conducted to determine the location of any significant pairwise differences. \*\*\* $P < 0.001$ , \*\* $P < 0.005$ , \* $P < 0.05$ .

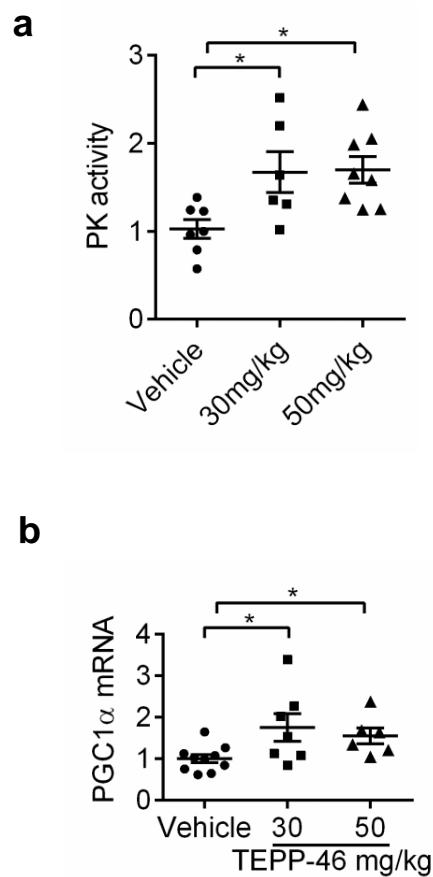
Supplementary Fig. 10



**Supplementary Fig. 10** Other small molecules of PKM2 activators prevented podocytes from apoptosis induced by high glucose

DNA fragmentation in podocytes treated with LG (L) or HG (H) with or without 10 $\mu$ M Agio (A) or Dynamix (D) for 72hrs. Treatment groups with arrows indicated the activators were added post-24hrs HG treatment. Replicates of experiments in each condition are in order  $n = 7, 7, 6, 5, 5, 4, 4$ , and 3. All values are means  $\pm$  SEM. Comparison of more than two groups was analyzed using ANOVA. When overall F-tests were significant ( $P < 0.05$ ), post hoc comparisons using Tukey's method of adjustment were conducted to determine the location of any significant pairwise differences. \*\* $P < 0.005$ ; \*  $P < 0.05$ .

Supplementary Fig.11



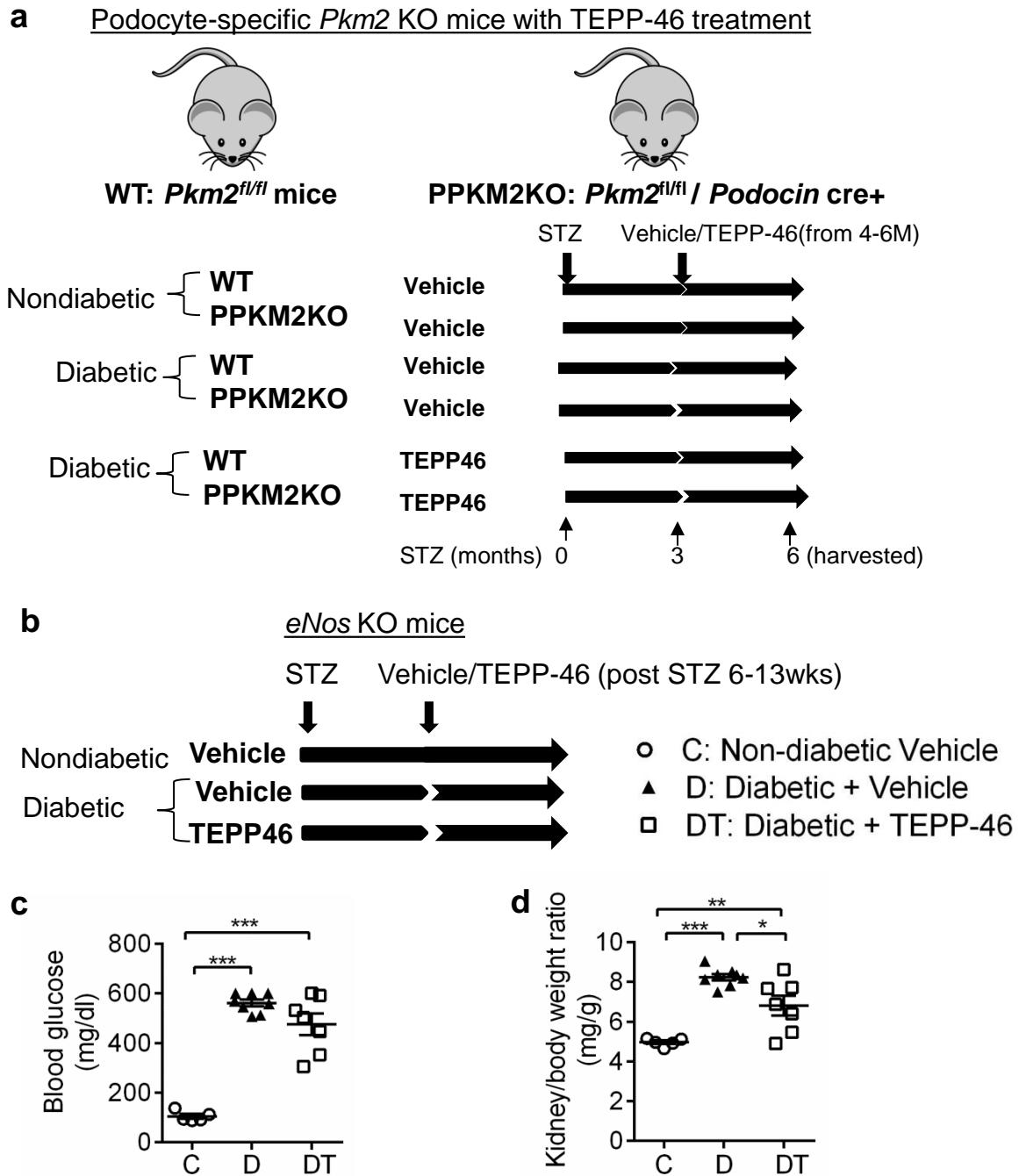
**Supplementary Fig. 11** TEPP-46 increases PK activity and PGC1 $\alpha$  expression in DBA2/J mice

(a) DBA/2J mice were orally gavaged vehicle ( $n = 7$  mice), 30 ( $n = 6$  mice) and 50mg/kg ( $n = 8$  mice) TEPP-46 and harvested post-24 hrs. Kidney cortex was collected for the measurement of PK activity.

(b) DBA/2J mice were orally gavaged vehicle, 30 and 50mg/kg TEPP-46 and harvested post-24 hrs. Kidney cortex was collected for Pgc1 $\alpha$  mRNA. Vehicle  $n = 10$ , 30mg/kg  $n = 7$ , 50mg/kg  $n = 6$ .

All values are means  $\pm$  SEM. Comparison of more than two groups was analyzed using ANOVA. When overall F-tests were significant ( $P < 0.05$ ), post hoc comparisons using Tukey's method of adjustment were conducted to determine the location of any significant pairwise differences. \*  $P < 0.05$ .

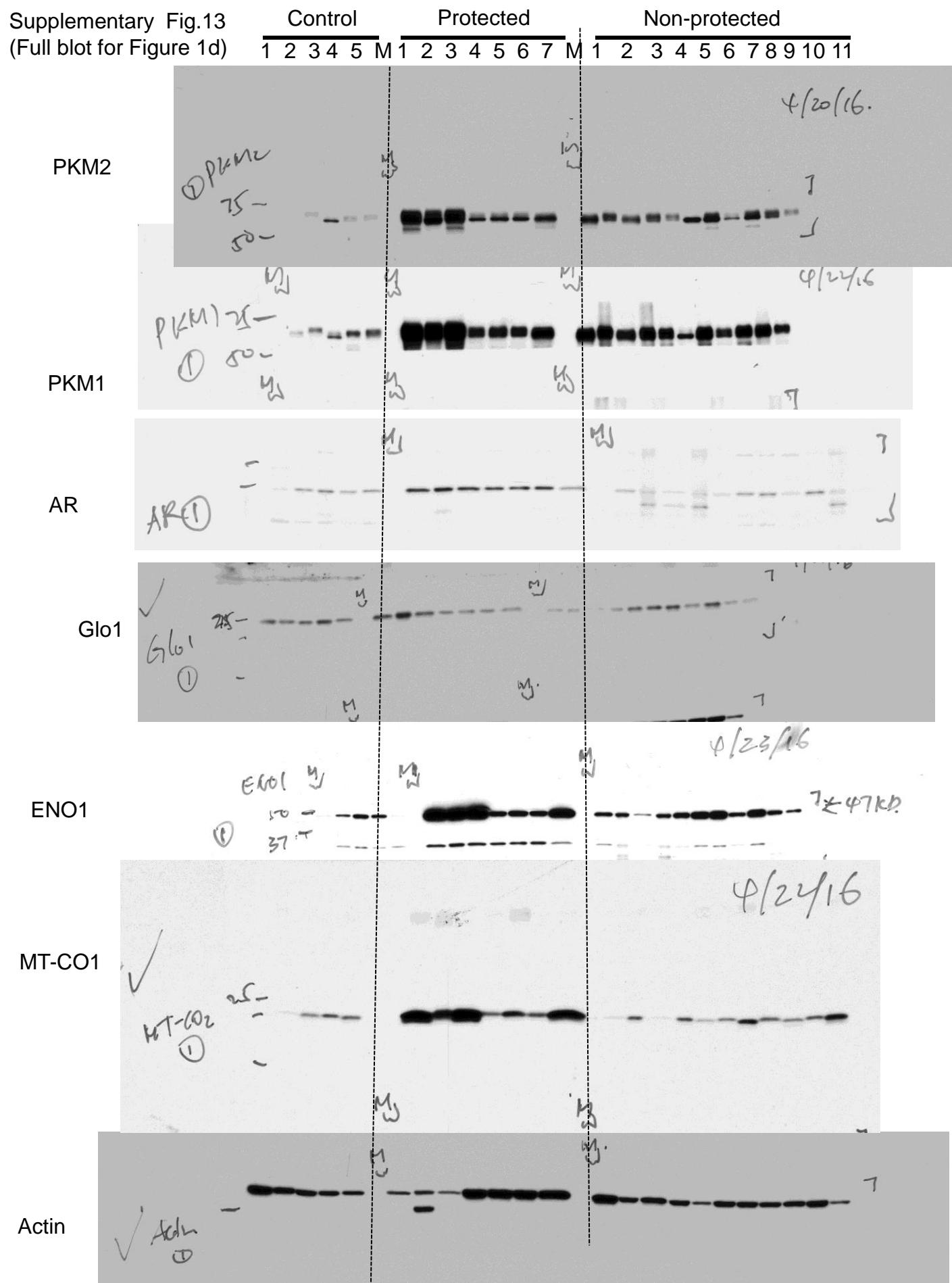
Supplementary Fig.12



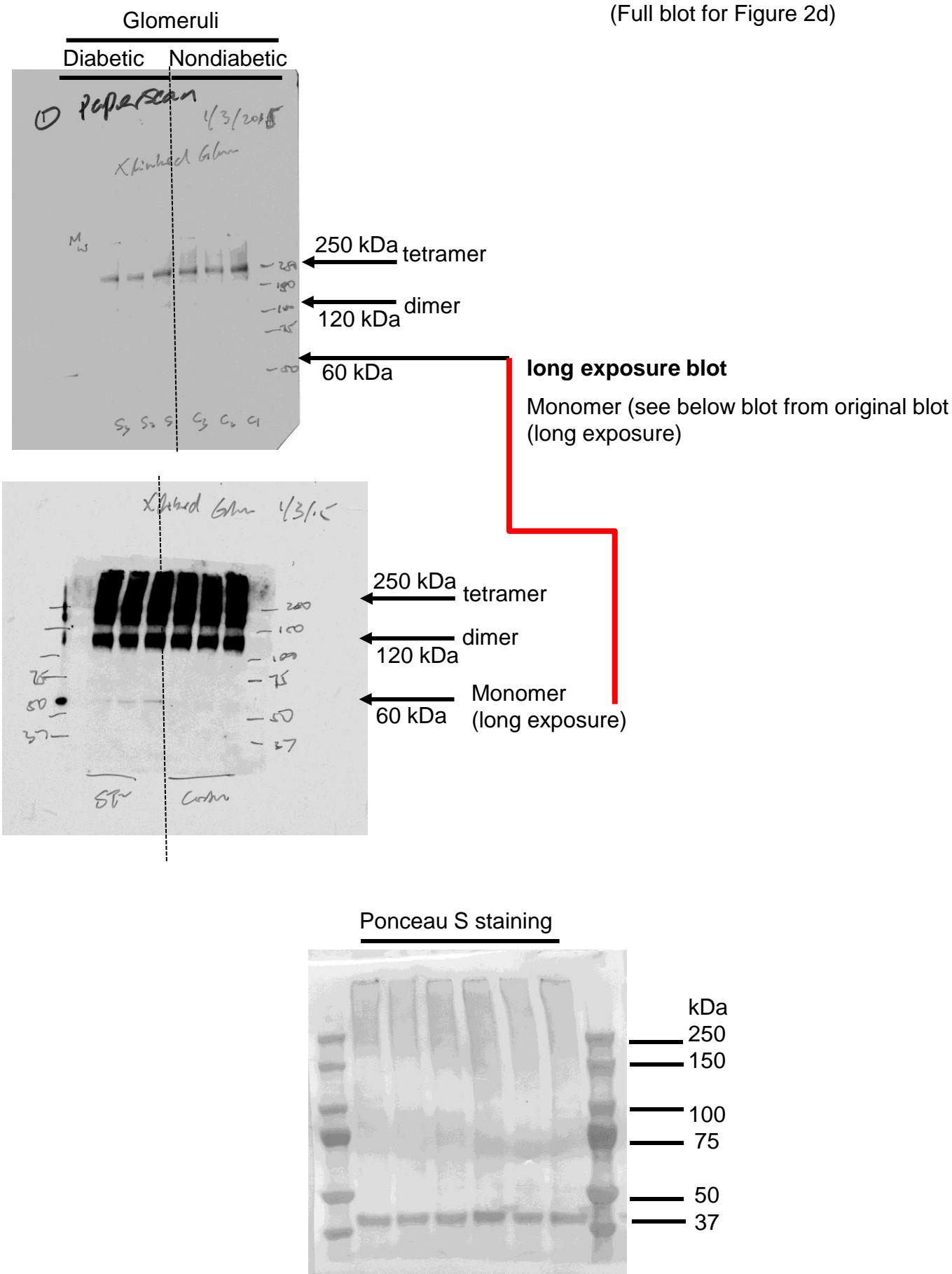
**Supplementary Fig. 12** The effect of TEPP-46 on diabetic PPKM2 KO and diabetic *eNos* KO mice

(a) Schema illustrating study design of TEPP-46 is acting through PKM2-specific manner using podocyte-specific *Pkm2* KO mice; (b) Schema illustrates STZ-induced diabetic eNOS mice treated with TEPP-46 post-STZ 6-13 weeks. eNOS KO mice were given vehicle or 50mg/kg TEPP-46 daily by oral gavaging for 7 weeks. Mice were harvested post-STZ 13 weeks. (c) Fasting blood glucose and (d) Kidney and body weight ratio. Non-diabetic vehicle,  $n = 5$  mice; diabetic vehicle,  $n = 8$  mice; diabetic TEPP-46,  $n = 7$  mice. All values are means  $\pm$  SEM. All data throughout this Figure were conducted using ANOVA. When overall F-tests were significant ( $P < 0.05$ ), post hoc comparisons using Tukey's method of adjustment were conducted to determine the location of any significant pairwise differences. \*\*\*  $P < 0.001$ , \*\*  $P < 0.005$ , \*  $P < 0.05$ .

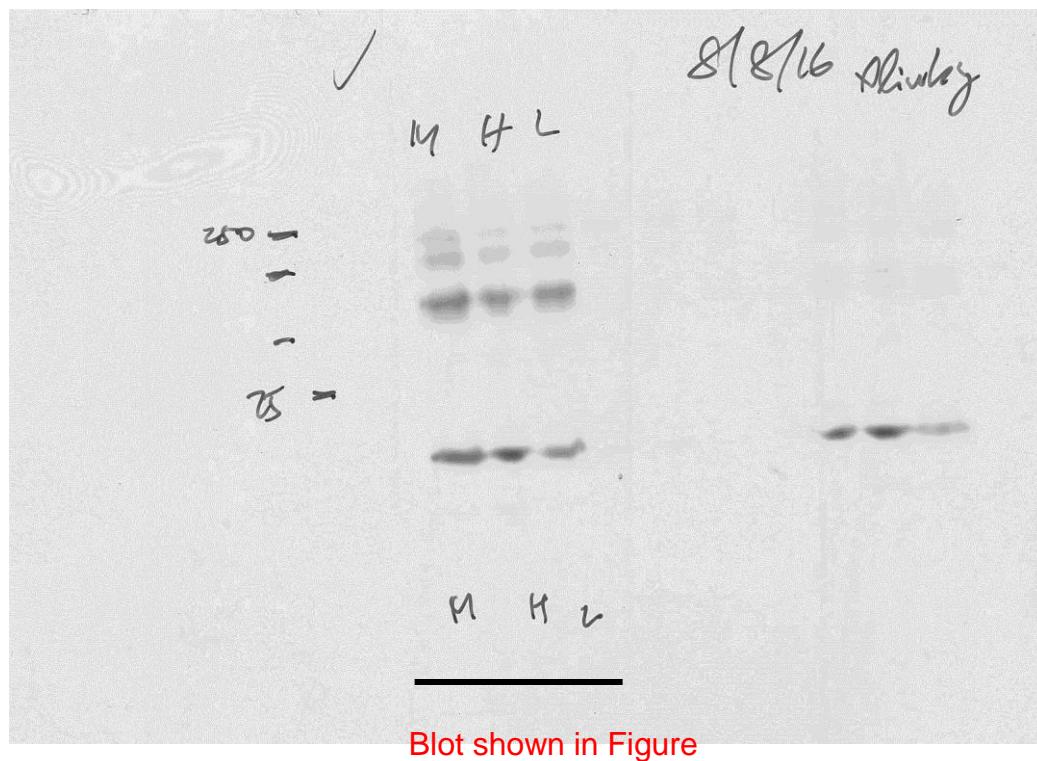
Supplementary Fig.13  
(Full blot for Figure 1d)



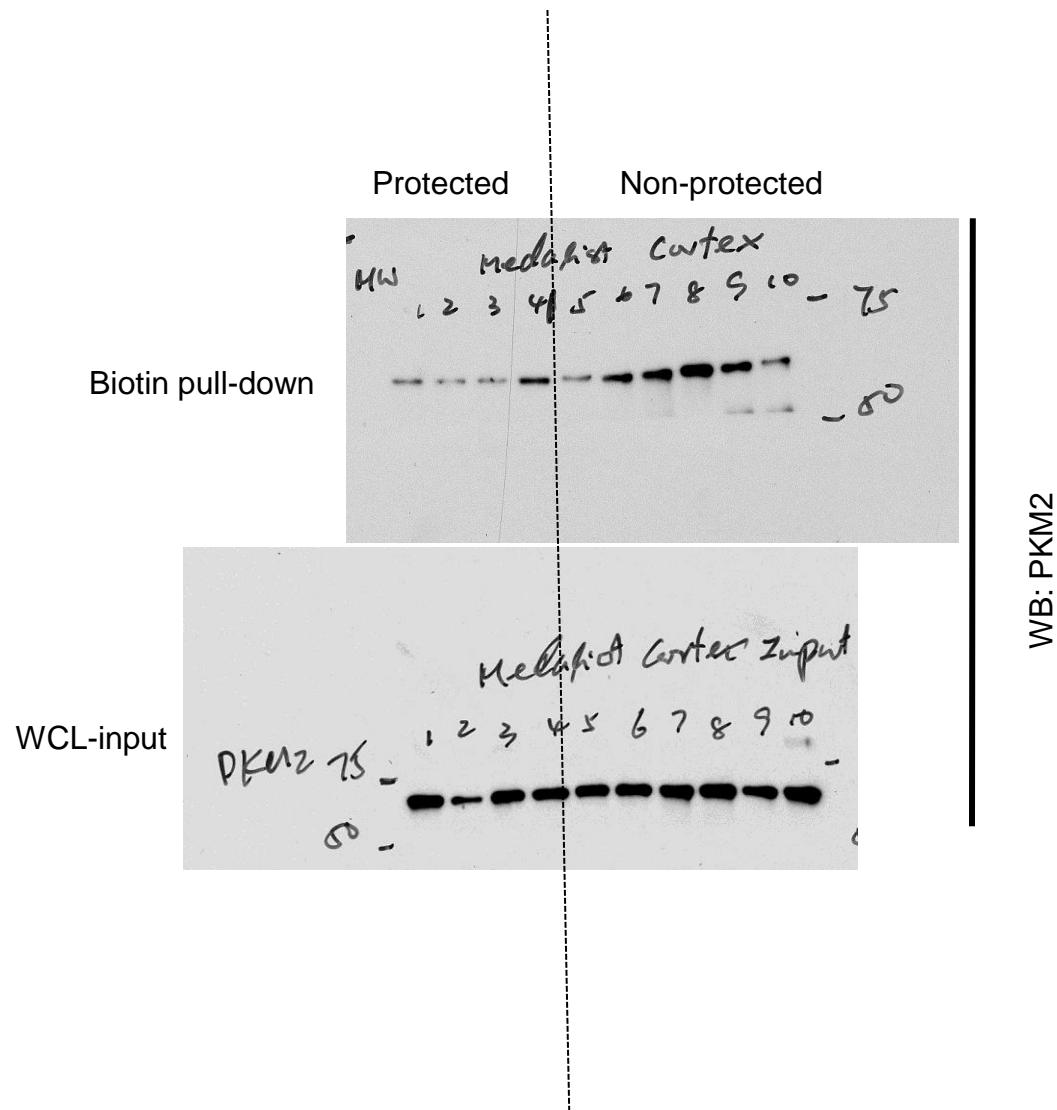
Supplementary Fig.14  
(Full blot for Figure 2d)



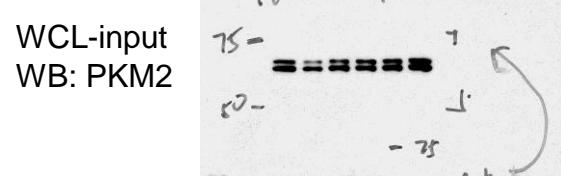
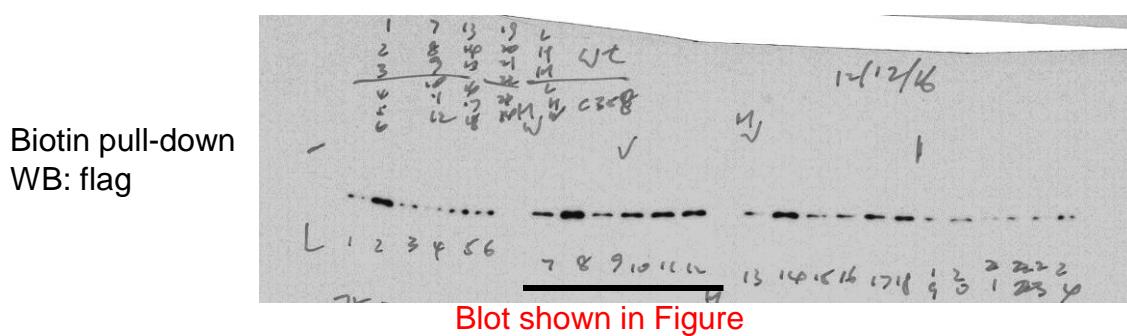
Supplementary Fig.15  
(Full blot for Figure 2e)



Supplementary Fig.16  
(Full blot for Figure 2f)

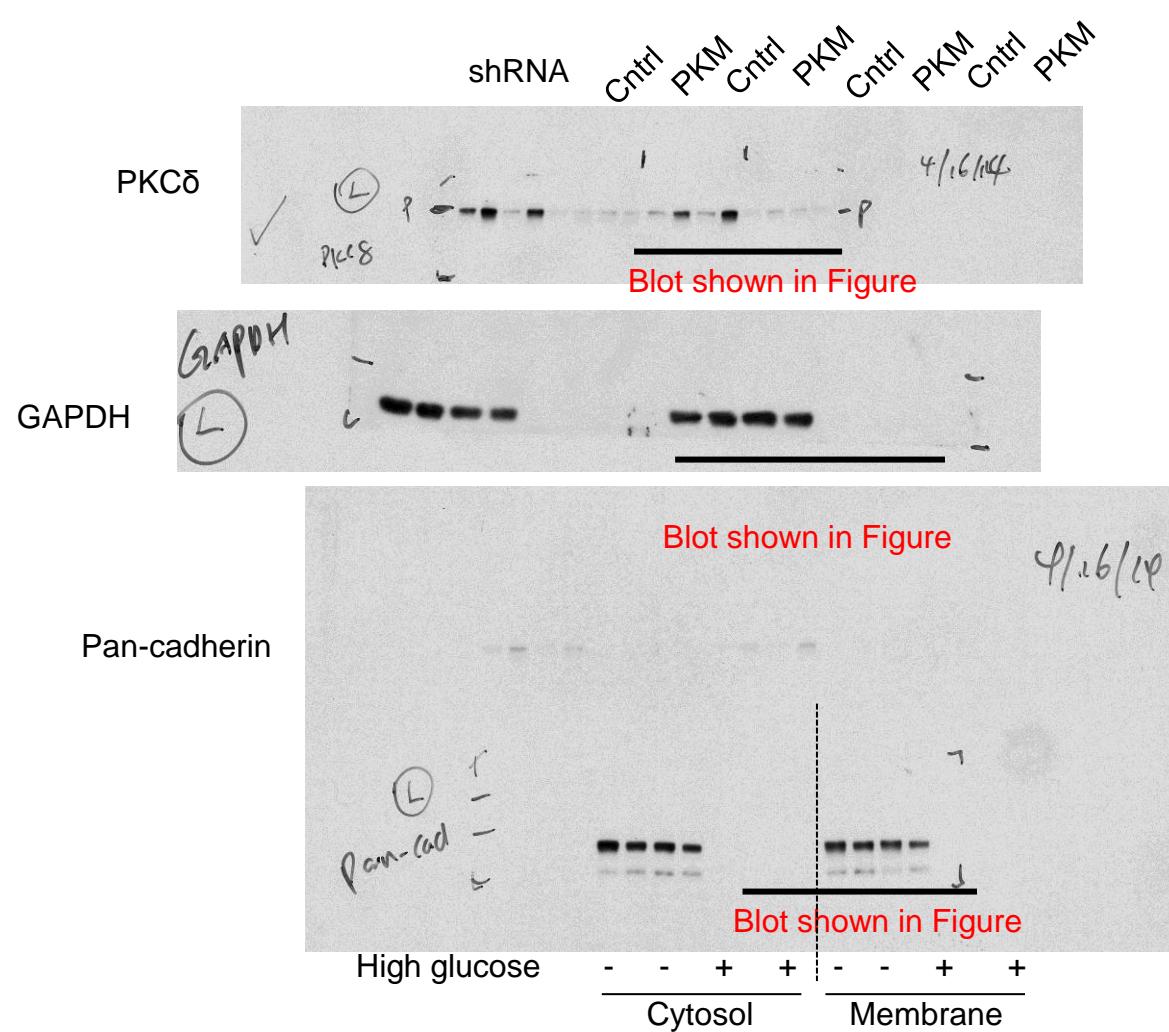


Supplementary Fig.17  
(Full blot for Figure 2g)

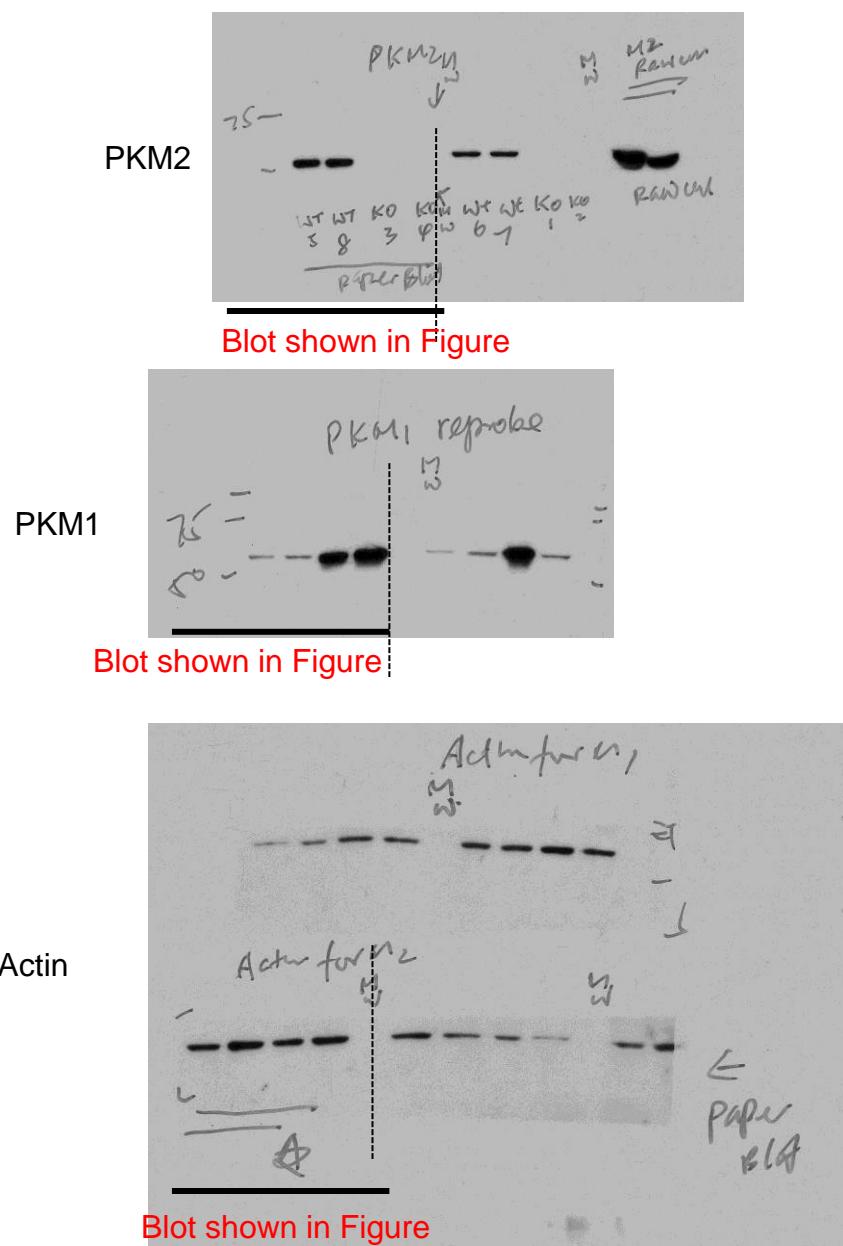


Blot shown in Figure

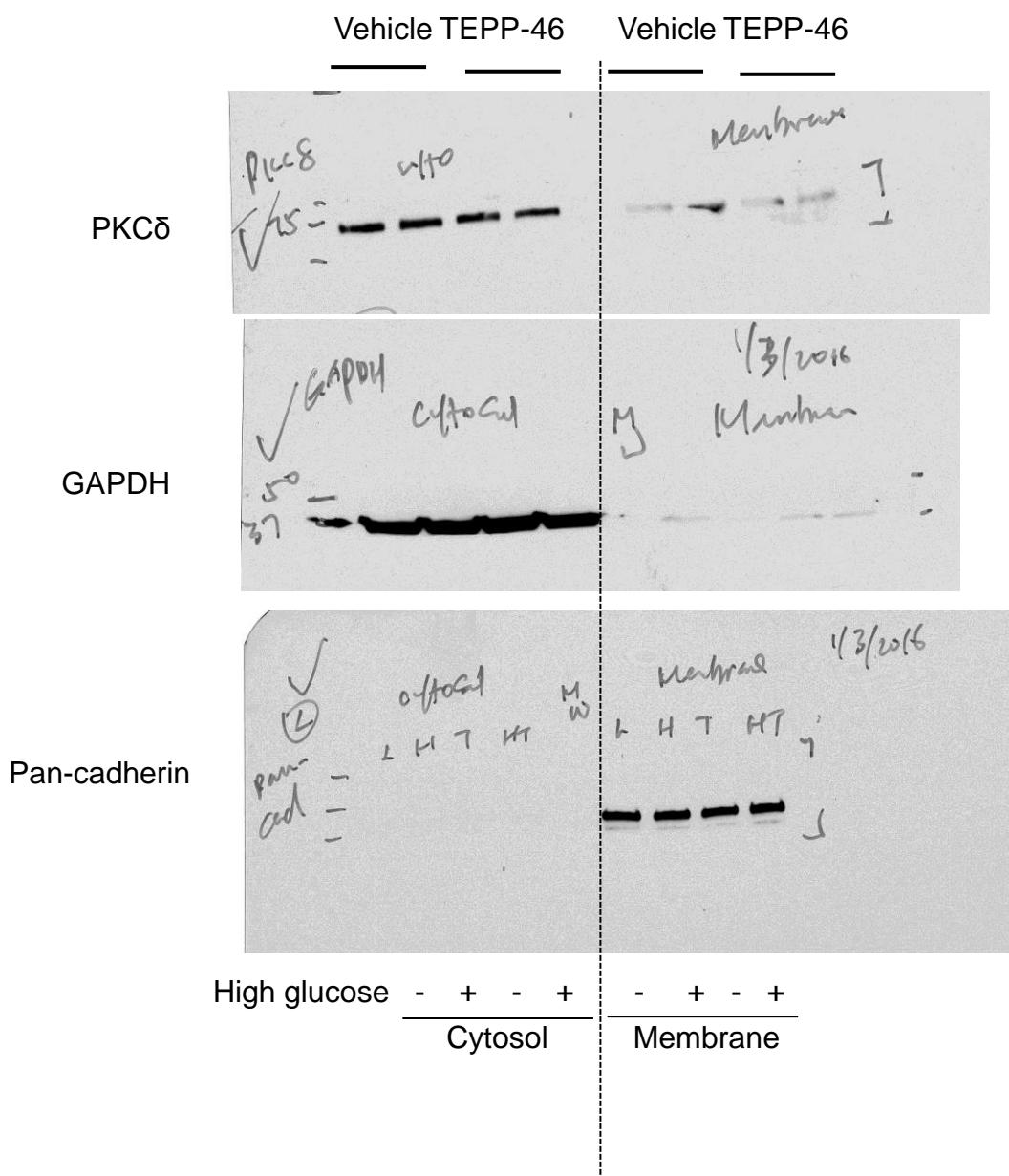
Supplementary Fig.18  
(Full blot for Figure 3b)



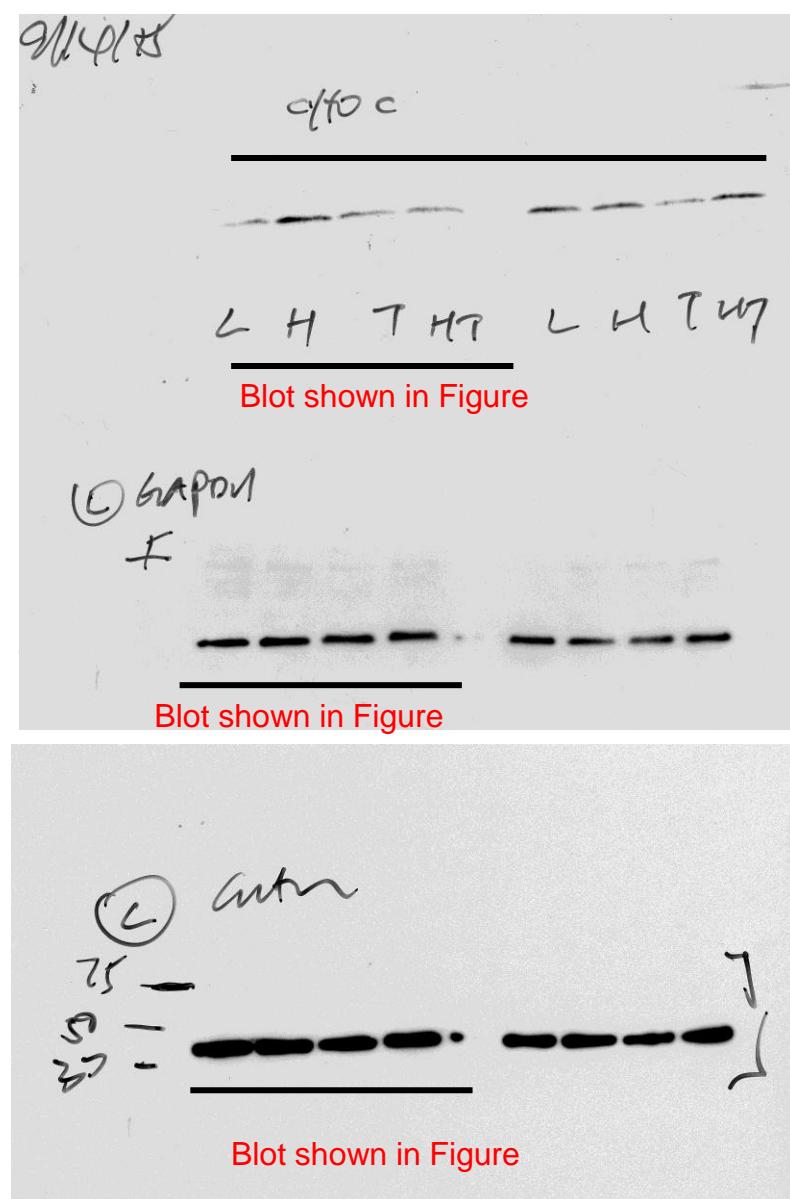
Supplementary Fig.19  
(Full blot for Figure 3f)



Supplementary Fig.20  
(Full blot for Figure 4b)



Supplementary Fig.21  
(Full blot for Figure 4m)



Supplemental Table 1: Clinical characteristics of Joslin Medalists and non-diabetic controls without nephropathy

Characteristics	DN class 0-I (N=7)	DN class IIB-III (N=11)	P value	Non-diabetic Controls (N=5)
Age (yr)	78 (59, 78)	80 (71, 85)	0.17	80 (78, 82)
Female	2 (28.6%)	5 (45.5%)	0.64	1 (20.0%)
Duration of Diseases (yr)	56 (53, 70)	64 (57, 74)	0.29	N/A
Age at Diagnosis (yr)	8 (3, 22)	10 (4, 23)	0.83	N/A
HbA1c (%)	6.9 (6.6, 8.0)	7.2 (6.5, 8.1)	0.61	N/A
Body Mass Index (kg/m <sup>2</sup> )	25.8 (23.8, 30.4)	27.5 (22.9, 29.0)	0.92	20.4 (19.1, 23.3)
ACR ( $\mu\text{g}/\text{mg}$ )	15.9 (5.4, 18.8)	45.5 (9.2, 346.0)	0.16	N/A
eGFR (mL/min/1.73m <sup>2</sup> )	72.3 (35.8, 83.3)	44.6 (24.8, 54.0)	0.03	N/A
Serum creatinine (mg/dl)	1.0 (0.9, 1.5)	1.3 (1.2, 2.1)	0.16	N/A
Systolic BP (mmHg)	122 (115, 130)	138 (118, 160)	0.11	N/A
Diastolic BP (mmHg)	60 (58, 66)	61 (58, 66)	0.94	N/A
Hypertension	3 (42.9%)	8 (72.7%)	0.11	2 (40.0%)
Antihypertensive Use	5 (71.4%)	9 (81.8%)	>0.99	N/A

Values are expressed as n (%) or median (quartile 1, quartile 3). HbA1c, hemoglobin A1c

ACR, albumin/creatinine ratio. P values were calculated using t-test or chi-squared test.

Supplemental Table 2: Clinical characteristics of Medalist from proteomics analysis

SID	Age (years)	Duration (years)	Sex	RPS DN Class	A1c	ACR ( $\mu\text{g}/\text{mg}$ )	eGFR ( $\text{mL}/\text{min}/1.73\text{m}^2$ )	IgA	IgG	Cystatin C (mg/L)	Creatinine (mg/dL)	BUN (mg/dL)
G15	71	56	F	0	6.7	23.90	35.8	neg	neg G but tissue ANA <sup>5</sup>	1.18	1.50	40
G3	79	57	F	I	7.6	5.40	32.9	neg	neg	1.76	1.50	36
G4	78	75	M	I	6.6	no report	41.2	neg	neg	1.74	1.60	31
G7	59	52	M	I	5.6	4.26	83.2	t-1 M <sup>1</sup>	neg	0.96	1.00	12
G19	56	53	M	I	8.0	13.40	95.8	neg	neg	0.75	0.90	16
G27	78	54	M	0	6.9	18.30	83.3	neg	neg	0.85	0.90	25
G13	78	70	M	I or IIA	8.4	18.80	72.3	1-2 M <sup>2</sup>	neg	1.07	1.00	25
G9	71	64	F	IIB	5.7	8.50	43.2	neg	neg	1.46	1.30	51
G12	87	77	M	IIB	7.3	346.03	49.8	neg	neg	1.37	1.30	32
G17	87	85	M	IIB	6.2	72.55	54.0	0-trace M <sup>3</sup>	neg	1.31	1.20	39
G26	85	57	M	IIB	6.8	9.15	55.6	0 - t M <sup>4</sup>	neg	1.71	1.20	44
G29	66	51	M	IIB	6.5	889.00	13.7	neg	neg	2.88	4.23	84
G24	78	65	F	IIB	8.1	5.99	44.6	neg	neg	1.84	1.20	36
G5	72	68	F	III	9.8	no report	24.8	neg	neg	3.03	2.00	80
G10	80	57	M	III	6.9	394.00	29.5	neg	neg	1.87	2.10	49
G18	63	61	F	IIB	8.8	45.50	59.7	neg	neg	1.05	1.00	30
G20	84	54	M	III	7.2	no report	15.2	neg	neg	6.24	3.48	101
G22	80	74	F	III	8.0	13.00	50.3	neg	neg	1.03	1.10	18

RPS DN class, Renal Pathology Society DN Classification; ACR, albumin creatinine ratio; eGFR, estimated glomerular filtration rate;

BUN, blood urea nitrogen; HTN, hypertension; BP, blood pressure; UNK, unknown.

<sup>1</sup>there is medium level deposition raising the possibility of IgA nephropathy; <sup>2</sup>this patient has IgA nephropathy;

<sup>3</sup>there is low level deposition that is insufficient for the diagnosis of IgA nephropathy

<sup>4</sup>there is low level deposition that is insufficient for the diagnosis of IgA nephropathy;

<sup>5</sup>the nuclei showed IgG staining that suggests that the patient was ANA; M= mesangial staining positive.

HTN	BP (mmHg)	Hypertension drugs
No	114/58	Yes
Yes	126/60	Yes
Yes	118/58	Yes
No	130/60	Yes
No	115/72	Yes
No	138/66	No
No	122/58	No
Yes	156/56	Yes
Yes	UNK	Yes
UNK	UNK	Yes
Yes	120/60	Yes
Yes	152/80	Yes
No	114/42	Yes
Yes	164/62	Yes
Yes	190/70	Yes
Yes	116/62	Yes
UNK	UNK	No
Yes	124/59	No

Supplemental Table 2

Nature Medicine: doi:10.1038/nm.4328

Supplementary Table 3: Up-regulated proteins in the glomeruli from Joslin Medalist Protected vs. Non-protected

Protein Name	Fold change	p value
HPRT1 Uncharacterized protein HPRT1	1.98	0.0001
PSMA3 Isoform 1 of Proteasome subunit alpha type-3	2.13	0.0010
LHPP Phospholysine phosphohistidine inorganic pyrophosphate phosphatase	1.51	0.0016
SOD1 Superoxide dismutase	2.59	0.0018
FGB Fibrinogen beta chain precursor	3.97	0.0020
TPI1 Isoform 1 of Triosephosphate isomerase	2.32	0.0024
SORD Sorbitol dehydrogenase	3.16	0.0029
NDUFB9 NADH-ubiquinone oxidoreductase B22 subunit	1.61	0.0031
SELENBP1 54 kDa protein	2.18	0.0032
GSTO1 Glutathione S-transferase omega 1	1.73	0.0036
ALDOA 45 kDa protein	2.45	0.0042
GAPDH Glyceraldehyde-3-phosphate dehydrogenase	2.51	0.0043
ESD 28 kDa protein	2.12	0.0053
PSMB4 Proteasome subunit beta type-4 precursor	1.77	0.0054
GOT1 Aspartate aminotransferase, cytoplasmic	2.41	0.0057
PEBP1 Phosphatidylethanolamine-binding protein 1	3.33	0.0057
AHCY Adenosylhomocysteinase	2.13	0.0061
ACY3 Aspartoacylase-2	1.71	0.0062
DPYS Dihydropyrimidinase	2.31	0.0062
UGDH UDP-glucose 6-dehydrogenase	2.11	0.0069
AKR1B1 Aldose reductase	1.79	0.0072
FGG 50 kDa protein	2.92	0.0075
GDI2 Rab GDP dissociation inhibitor beta	1.91	0.0075
MT-CO2 Cytochrome c oxidase subunit 2	2.06	0.0075
PKM2 Isoform M2 of Pyruvate kinase isozymes M1/M2	2.69	0.0086
VCP Transitional endoplasmic reticulum ATPase	1.77	0.0096
ENO1 Isoform alpha-enolase of Alpha-enolase	2.82	0.0098
PGM1 65 kDa protein	2.23	0.0102
MDH1 Malate dehydrogenase, cytoplasmic	2.46	0.0110
PSMA1 Isoform Short of Proteasome subunit alpha type-1	1.79	0.0119
NP Purine nucleoside phosphorylase	2.02	0.0126
CRYL1 Lambda-crystallin homolog	2.23	0.0132
A2M Alpha-2-macroglobulin precursor	3.51	0.0142
GLO1 Lactoylglutathione lyase	1.95	0.0148
DPYSL2 Dihydropyrimidinase-related protein 2	2.78	0.0150
TOMM40 Isoform 2 of Mitochondrial import receptor subunit TOM40 homolog	1.55	0.0153
NPEPPS Puromycin-sensitive aminopeptidase	2.49	0.0156
PSMB1 Proteasome subunit beta type-1 precursor	1.69	0.0160
BHMT Betaine--homocysteine S-methyltransferase 1	4.79	0.0161
LDHB L-lactate dehydrogenase B chain	2.45	0.0164
TXN Thioredoxin	1.72	0.0175
QPRT 34 kDa protein	2.44	0.0177
SPR Sepiapterin reductase	1.62	0.0181
CD9 CD9 antigen	1.64	0.0198

HP Haptoglobin precursor	3.65	0.0203
TALDO1 Transaldolase	1.72	0.0207
CA2 Carbonic anhydrase 2	1.85	0.0209
MSN Uncharacterized protein MSN (Fragment)	1.69	0.0209
Rheumatoid factor C6 light chain (Fragment)	1.83	0.0214
ADH5 Alcohol dehydrogenase class-3	1.57	0.0214
PSMB2 Proteasome subunit beta type-2	1.66	0.0218
APEH Acylamino-acid-releasing enzyme	1.78	0.0224
HEBP1 Heme-binding protein 1	1.56	0.0224
HAGH Hydroxyacylglutathione hydrolase	2.20	0.0226
APOA1BP Isoform 2 of Apolipoprotein A-I-binding protein precursor	1.51	0.0227
SERPING1 Plasma protease C1 inhibitor precursor	2.49	0.0252
LL22NC03-5H6.5 UPF0530 protein	1.65	0.0254
ALAD Delta-aminolevulinic acid dehydratase	1.64	0.0256
PGD 56 kDa protein	1.78	0.0257
PSME1 Proteasome activator complex subunit 1	1.64	0.0260
PRDX6 Peroxiredoxin-6	1.81	0.0261
ALDOB Fructose-bisphosphate aldolase B	3.40	0.0265
C22orf32 Similar to Cullin-associated NEDD8-dissociated protein 1	2.19	0.0267
GSTT1 Glutathione S-transferase theta 1	2.70	0.0268
FAH 33 kDa protein	2.02	0.0273
PGLS 6-phosphogluconolactonase	1.57	0.0292
NIT2 33 kDa protein	1.75	0.0303
CRYM Mu-crystallin homolog	1.65	0.0316
UGP2 Isoform 1 of UTP--glucose-1-phosphate uridylyltransferase	1.75	0.0321
FBP1 Fructose-1,6-bisphosphatase 1	1.91	0.0330
ACY1 Aminoacylase-1	2.60	0.0332
CP Ceruloplasmin precursor	3.16	0.0337
ORM1 orosomucoid 1 precursor	3.76	0.0340
GLRX Glutaredoxin-1	1.62	0.0340
SET Isoform 1 of Protein SET	1.59	0.0352
ACO1 Cytoplasmic aconitase hydratase	2.97	0.0352
GLOD4 Isoform 2 of Glyoxalase domain-containing protein 4	1.69	0.0353
LTB4DH NADP-dependent leukotriene B4 12-hydroxydehydrogenase	1.71	0.0365
GRHPR GRHPR protein (Fragment)	1.62	0.0368
TF Serotransferrin precursor	3.43	0.0370
GSTP1 Glutathione S-transferase P	1.82	0.0371
PEPD Uncharacterized protein PEPD (Fragment)	2.44	0.0393
GATM Isoform Cytoplasmic of Glycine amidinotransferase, mitochondrial	1.81	0.0416
FGA Isoform 2 of Fibrinogen alpha chain precursor	4.87	0.0447
NQO2 32 kDa protein	1.88	0.0449
CALB1 Calbindin	4.29	0.0472
PBLD Phenazine biosynthesis-like domain-containing protein	3.16	0.0473
C11orf54 Isoform 2 of Ester hydrolase C11orf54	2.50	0.0499

Joslin Medalist with no DN (n=7, Protected) vs. DN (n=11, Non-protected).

Values are expressed as fold change and p value was calculated using Mann–Whitney U test.

The data are sorted by P value using p<0.05 and fold change >=1.5 cut off

Supplementary Table 4: Up-regulated proteins in the glomeruli from Joslin

Medalist Protected vs. Non-protected

Joslin Medalist with no DN (n=7, Protected) vs. DN (n=11, Non-protected)

Values are expressed as fold change and P value was calculated using Mann–Whitney U test

The data are sorted by P value for all upregulated proteins.

Protein Name	Accession	Fold change	P value
HPRT1 Uncharacterized protein HPRT1	IPI00873466	1.98	0.0001
PSMA3 Isoform 1 of Proteasome subunit alpha type-3	IPI00419249	2.13	0.0010
LHPP Phospholysine phosphohistidine inorganic pyrophosphate phosphatase	IPI00005474	1.51	0.0016
SOD1 Superoxide dismutase	IPI00218733	2.59	0.0018
FGB Fibrinogen beta chain precursor	IPI00298497	3.97	0.0020
TPI1 Isoform 1 of Triosephosphate isomerase	IPI00465028	2.32	0.0024
SORD Sorbitol dehydrogenase	IPI00216057	3.16	0.0029
NDUFB9 NADH-ubiquinone oxidoreductase B22 subunit	IPI00790752	1.61	0.0031
SELENBP1 54 kDa protein	IPI00745729	2.18	0.0032
GSTO1 Glutathione S-transferase omega 1	IPI00642936	1.73	0.0036
ALDOA 45 kDa protein	IPI00796333	2.45	0.0042
GAPDH Glyceraldehyde-3-phosphate dehydrogenase	IPI00219018	2.51	0.0043
ESD 28 kDa protein	IPI00641040	2.12	0.0053
PSMB4 Proteasome subunit beta type-4 precursor	IPI00555956	1.77	0.0054
GOT1 Aspartate aminotransferase, cytoplasmic	IPI00219029	2.41	0.0057
PEBP1 Phosphatidylethanolamine-binding protein 1	IPI00219446	3.33	0.0057
AHCY Adenosylhomocysteinase	IPI00012007	2.13	0.0061
ACY3 Aspartoacylase-2	IPI00063025	1.71	0.0062
HAAO 3-hydroxyanthranilate 3,4-dioxygenase	IPI00009375	1.46	0.0062
ECE1 Isoform D of Endothelin-converting enzyme 1	IPI00216762	1.34	0.0062
HEBP2 HEBP2 protein (Fragment)	IPI00644697	1.31	0.0062
DPYS Dihydropyrimidinase	IPI00028910	2.31	0.0062
UGDH UDP-glucose 6-dehydrogenase	IPI00031420	2.11	0.0069
AKR1B1 Aldose reductase	IPI00413641	1.79	0.0072
FGG 50 kDa protein	IPI00877792	2.92	0.0075
GDI2 Rab GDP dissociation inhibitor beta	IPI00031461	1.91	0.0075
MT-CO2 Cytochrome c oxidase subunit 2	IPI00017510	2.06	0.0075
PKM2 Isoform M2 of Pyruvate kinase isozymes M1/M2	IPI00479186	2.69	0.0086
VCP Transitional endoplasmic reticulum ATPase	IPI00022774	1.77	0.0096
ENO1 Isoform alpha-enolase of Alpha-enolase	IPI00465248	2.82	0.0098
PGM1 65 kDa protein	IPI00844159	2.23	0.0102
MDH1 Malate dehydrogenase, cytoplasmic	IPI00291005	2.46	0.0110
PSMA1 Isoform Short of Proteasome subunit alpha type-1	IPI00016832	1.79	0.0119
NP Purine nucleoside phosphorylase	IPI00871140	2.02	0.0126
CRYL1 Lambda-crystallin homolog	IPI00006443	2.23	0.0132
A2M Alpha-2-macroglobulin precursor	IPI00478003	3.51	0.0142
GLO1 Lactoylglutathione lyase	IPI00220766	1.95	0.0148
DPYSL2 Dihydropyrimidinase-related protein 2	IPI00257508	2.78	0.0150
TOMM40 Isoform 2 of Mitochondrial import receptor subunit TOM40 homolog	IPI00376117	1.55	0.0153
NPEPPS Puromycin-sensitive aminopeptidase	IPI00026216	2.49	0.0156
PSMB1 Proteasome subunit beta type-1 precursor	IPI00025019	1.69	0.0160
BHMT Betaine--homocysteine S-methyltransferase 1	IPI00004101	4.79	0.0161
LDHB L-lactate dehydrogenase B chain	IPI00219217	2.45	0.0164
TXN Thioredoxin	IPI00552768	1.72	0.0175
QPRT 34 kDa protein	IPI00872692	2.44	0.0177
SPR Sepiapterin reductase	IPI00017469	1.62	0.0181

CAPZB cDNA FLJ60094, highly similar to F-actin capping protein subunit beta	IPI00218782	1.51	0.0194
CD9 CD9 antigen	IPI00215997	1.64	0.0198
HP Haptoglobin precursor	IPI00641737	3.65	0.0203
TALDO1 Transaldolase	IPI00744692	1.72	0.0207
XYLT1 Xylosyltransferase 1	IPI00183487	1.17	0.0208
LYPLA1 Isoform 2 of Acyl-protein thioesterase 1	IPI00398727	1.17	0.0208
CA2 Carbonic anhydrase 2	IPI00218414	1.85	0.0209
MSN Uncharacterized protein MSN (Fragment)	IPI00872814	1.69	0.0209
ALDH16A1 Isoform 1 of Aldehyde dehydrogenase family 16 member A1	IPI00217920	1.40	0.0213
BPNT1 Isoform 1 of 3(2),5-bisphosphate nucleotidase 1	IPI00410214	1.37	0.0213
ACMSD Isoform 1 of 2-amino-3-carboxymuconate-6-semialdehyde decarboxylase	IPI00152656	1.23	0.0213
GLTP Glycolipid transfer protein	IPI00184363	1.23	0.0213
- Rheumatoid factor C6 light chain (Fragment)	IPI00829956	1.83	0.0214
ADH5 Alcohol dehydrogenase class-3	IPI00746777	1.57	0.0214
FDPS Putative uncharacterized protein	IPI00101405	1.26	0.0214
PSMB2 Proteasome subunit beta type-2	IPI00028006	1.66	0.0218
APEH Acylamino-acid-releasing enzyme	IPI00337741	1.78	0.0224
HEBP1 Heme-binding protein 1	IPI00148063	1.56	0.0224
HAGH Hydroxyacylglutathione hydrolase	IPI00745553	2.20	0.0226
APOA1BP Isoform 2 of Apolipoprotein A-I-binding protein precursor	IPI00848298	1.51	0.0227
DIABLO Isoform 2 of Diablo homolog, mitochondrial precursor	IPI00219865	1.46	0.0233
SERPING1 Plasma protease C1 inhibitor precursor	IPI00291866	2.49	0.0252
EIF6 Eukaryotic translation initiation factor 6	IPI00010105	1.38	0.0253
LL22NC03-5H6.5 UPF0530 protein	IPI00550644	1.65	0.0254
ALAD Delta-aminolevulinic acid dehydratase	IPI00790373	1.64	0.0256
PGD 56 kDa protein	IPI00747533	1.78	0.0257
PSME1 Proteasome activator complex subunit 1	IPI00479722	1.64	0.0260
PRDX6 Peroxiredoxin-6	IPI00220301	1.81	0.0261
ALDOB Fructose-bisphosphate aldolase B	IPI00218407	3.40	0.0265
C22orf32 Similar to Cullin-associated NEDD8-dissociated protein 1	IPI00746694	2.19	0.0267
GSTT1 Glutathione S-transferase theta 1	IPI00893316	2.70	0.0268
FAH 33 kDa protein	IPI00793664	2.02	0.0273
PGLS 6-phosphogluconolactonase	IPI00029997	1.57	0.0292
S100A9 Protein S100-A9	IPI00027462	1.38	0.0292
GPI Glucose-6-phosphate isomerase	IPI00027497	1.34	0.0295
NIT2 33 kDa protein	IPI00872668	1.75	0.0303
CRYM Mu-crystallin homolog	IPI00000949	1.65	0.0316
HSPA4 Heat shock 70 kDa protein 4	IPI00002966	1.48	0.0320
UGP2 Isoform 1 of UTP--glucose-1-phosphate uridylyltransferase	IPI00329331	1.75	0.0321
FBP1 Fructose-1,6-bisphosphatase 1	IPI00073772	1.91	0.0330
ACY1 Aminoacylase-1	IPI00009268	2.60	0.0332
- Rheumatoid factor D5 light chain (Fragment)	IPI00816799	1.39	0.0334
CP Ceruloplasmin precursor	IPI00017601	3.16	0.0337
ORM1 orosomucoid 1 precursor	IPI00884926	3.76	0.0340
GLRX Glutaredoxin-1	IPI00219025	1.62	0.0340
SET Isoform 1 of Protein SET	IPI00072377	1.59	0.0352
ACO1 Cytoplasmic aconitate hydratase	IPI00008485	2.97	0.0352
GLOD4 Isoform 2 of Glyoxalase domain-containing protein 4	IPI00745272	1.69	0.0353
LTB4DH NADP-dependent leukotriene B4 12-hydroxydehydrogenase	IPI00292657	1.71	0.0365
GRHPR GRHPR protein (Fragment)	IPI00550682	1.62	0.0368
TF Serotransferrin precursor	IPI00022463	3.43	0.0370
GSTP1 Glutathione S-transferase P	IPI00219757	1.82	0.0371

Supplementary Table 4

PEPD Uncharacterized protein PEPD (Fragment)	IPI00872063	2.44	0.0393
DCI Isoform 2 of 3,2-trans-enoyl-CoA isomerase, mitochondrial precursor	IPI00398758	1.44	0.0400
GATM Isoform Cytoplasmic of Glycine amidinotransferase, mitochondrial	IPI00216279	1.81	0.0416
RPSA 16 kDa protein	IPI00790580	1.45	0.0426
PPP1R7 Isoform 1 of Protein phosphatase 1 regulatory subunit 7	IPI00033600	1.28	0.0440
FGA Isoform 2 of Fibrinogen alpha chain precursor	IPI00029717	4.87	0.0447
NQO2 32 kDa protein	IPI00871850	1.88	0.0449
PNPO 19 kDa protein	IPI00793232	1.47	0.0449
ALDH9A1 4-trimethylaminobutyraldehyde dehydrogenase	IPI00873817	1.44	0.0459
CALB1 Calbindin	IPI00220361	4.29	0.0472
PBLD Phenazine biosynthesis-like domain-containing protein	IPI00024896	3.16	0.0473
C11orf54 Isoform 2 of Ester hydrolase C11orf54	IPI00761072	2.50	0.0499
ALDH7A1 aldehyde dehydrogenase 7 family, member A1	IPI00221234	1.73	0.0513
PGK1 Phosphoglycerate kinase 1	IPI00169383	1.68	0.0514
PSMB5 Proteasome subunit beta type-5 precursor	IPI00479306	1.43	0.0516
ALDH1L2 Isoform 3 of Probable 10-formyltetrahydrofolate dehydrogenase ALDH1L2	IPI00878818	1.38	0.0518
DDAH1 N(G),N(G)-dimethylarginine dimethylaminohydrolase 1	IPI00220342	1.84	0.0522
HIBCH 46 kDa protein	IPI00874185	1.70	0.0565
NME2 Nucleoside diphosphate kinase	IPI00604590	1.41	0.0569
CNDP2 Cytosolic non-specific dipeptidase	IPI00177728	2.33	0.0571
SOD2 manganese superoxide dismutase isoform A precursor	IPI00847322	1.58	0.0571
PSMA5 Proteasome subunit alpha type-5	IPI00291922	1.52	0.0571
GPX1 glutathione peroxidase 1 isoform 1	IPI00293975	1.81	0.0578
LDHD Isoform 1 of Probable D-lactate dehydrogenase, mitochondrial precursor	IPI00329133	1.25	0.0586
SLC9A3R1 Ezrin-radixin-moesin-binding phosphoprotein 50	IPI00003527	1.96	0.0628
FH Isoform Cytoplasmic of Fumarate hydratase, mitochondrial precursor	IPI00759715	1.62	0.0631
ACO2 Aconitase 2, mitochondrial	IPI00790739	1.80	0.0634
DPP3;BBS1 Isoform 1 of Dipeptidyl-peptidase 3	IPI00020672	1.42	0.0635
PLS3 plastin 3	IPI00216694	1.84	0.0648
GDA Guanine deaminase	IPI00465184	2.04	0.0657
GLDC 115 kDa protein	IPI00295388	1.72	0.0657
RPL13 60S ribosomal protein L13	IPI00465361	1.47	0.0665
HDDC3 Isoform 1 of HD domain-containing protein 3	IPI00789618	1.23	0.0676
ME3 NADP-dependent malic enzyme, mitochondrial	IPI00003970	1.17	0.0676
NARS Asparaginyl-tRNA synthetase, cytoplasmic	IPI00306960	1.11	0.0676
COQ7 20 kDa protein	IPI00645720	1.11	0.0676
ASXL2 154 kDa protein	IPI00873208	1.11	0.0676
ESAM Endothelial cell-selective adhesion molecule	IPI00303161	2.06	0.0681
- Similar to V1-17 protein	IPI00887169	1.54	0.0681
- Extracellular signal-regulated kinase-2 splice variant	IPI00874012	1.46	0.0681
RPL26 Uncharacterized protein RPL26	IPI00433834	1.43	0.0681
- cDNA FLJ55703, highly similar to Solute carrier family 2, facilitated glucose transporter membe	IPI00909237	1.40	0.0681
GK Isoform 3 of Glycerol kinase	IPI00216067	1.37	0.0681
- Ig kappa chain V-III region NG9 (Fragment)	IPI00387116	1.34	0.0681
TSN Translin	IPI00018768	1.31	0.0681
FABP4 Fatty acid-binding protein, adipocyte	IPI00215746	1.31	0.0681
RPL23 Similar to ribosomal protein L23	IPI00795408	1.31	0.0681
- Cryocrytalglobulin CC2 lambda light chain variable region (Fragment)	IPI00890733	1.31	0.0681
- Uncharacterized protein USMG5P1	IPI00640630	1.26	0.0681
- Complement factor B	IPI00893864	1.26	0.0681
PITPNA Phosphatidylinositol transfer protein alpha isoform	IPI00216048	1.23	0.0681
ITIH2 Inter-alpha (Globulin) inhibitor H2	IPI00645038	1.23	0.0681

Supplementary Table 4

PRPS1 Ribose-phosphate pyrophosphokinase (Fragment)	IPI00816572	1.23	0.0681
SLC36A2 Isoform 1 of Proton-coupled amino acid transporter 2	IPI00376258	1.20	0.0681
GMPR2 GMPR2 protein	IPI00449197	1.20	0.0681
KNG1 Kininogen 1	IPI00797833	1.20	0.0681
PA2G4 PA2G4 protein (Fragment)	IPI00807557	1.20	0.0681
RPL4 60S ribosomal protein L4	IPI00003918	1.17	0.0681
TFG Protein TFG	IPI00294619	1.17	0.0681
MLYCD Isoform Cytoplasmic+peroxisomal of Malonyl-CoA decarboxylase, mitochondrial	IPI00759655	1.17	0.0681
NCKAP1 NCK-associated protein 1 isoform 2	IPI00409684	1.14	0.0681
NIF3L1 Isoform 2 of NIF3-like protein 1	IPI00873590	1.14	0.0681
GPD1 Glycerol-3-phosphate dehydrogenase [NAD+], cytoplasmic	IPI00295777	2.97	0.0684
GOT2 Aspartate aminotransferase, mitochondrial precursor	IPI00018206	1.45	0.0692
TKT Transketolase variant (Fragment)	IPI00788802	1.45	0.0695
C7orf24 Uncharacterized protein C7orf24	IPI00031564	1.44	0.0711
TP53I3 Isoform 1 of Putative quinone oxidoreductase	IPI00384643	1.35	0.0711
ACP1 Acid phosphatase 1, soluble	IPI00893203	1.68	0.0714
NAPRT1 Isoform 3 of Nicotinate phosphoribosyltransferase	IPI00880164	1.29	0.0730
QDPR Dihydropteridine reductase	IPI00014439	2.10	0.0734
BDH2 Isoform 1 of 3-hydroxybutyrate dehydrogenase type 2	IPI00607799	2.86	0.0740
TMED4 Transmembrane emp24 domain-containing protein 4	IPI00296259	1.45	0.0747
STIP1 Stress-induced-phosphoprotein 1	IPI00013894	1.39	0.0749
ATP6V1E1 Vacuolar proton pump subunit E 1	IPI00003856	1.75	0.0769
ALDH1L1 Formyltetrahydrofolate dehydrogenase isoform a variant	IPI00793673	1.56	0.0769
CS 48 kDa protein	IPI00793839	1.48	0.0769
PSMA7 Isoform 1 of Proteasome subunit alpha type-7	IPI00024175	1.44	0.0782
GSR Isoform Cytoplasmic of Glutathione reductase, mitochondrial precursor	IPI00759575	1.38	0.0785
NDRG1 Protein NDRG1	IPI00022078	2.05	0.0791
KRAS Isoform 2B of GTPase KRas precursor	IPI00423570	1.43	0.0821
CMBL Carboxymethylenebutenolidase homolog	IPI00383046	1.94	0.0874
SRI sorcin isoform b	IPI00414264	1.50	0.0879
DLAT Dihydrolipoyllysine-residue acetyltransferase component of pyruvate dehydrogenase complex	IPI00021338	1.36	0.0887
HPD 40 kDa protein	IPI00795913	2.29	0.0902
PFN1 Profilin-1	IPI00216691	1.43	0.0911
FAHD2A Fumarylacetate hydrolase domain-containing protein 2A	IPI00329742	1.21	0.0919
TPP2 Tripeptidyl peptidase II	IPI00640197	1.21	0.0919
FAHD1 Fumarylacetate hydrolase domain containing 1	IPI00604759	1.56	0.0925
SLC23A1 Isoform 1 of Solute carrier family 23 member 1	IPI00303368	1.47	0.0932
RENBP N-acylglucosamine 2-epimerase	IPI00796170	1.38	0.0932
ITGA5 Integrin alpha-5	IPI00306604	1.31	0.0932
NDUFB10 NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 10	IPI00479905	1.47	0.0935
DCXR 26 kDa protein	IPI00797917	1.91	0.0937
ACAT1 Acetyl-CoA acetyltransferase, mitochondrial precursor	IPI00030363	1.66	0.0937
MME Neprilysin	IPI00247063	1.43	0.0937
PRDX3 peroxiredoxin 3 isoform b	IPI00374151	1.39	0.0937
ALB Isoform 1 of Serum albumin precursor	IPI00745872	1.75	0.0938
PTER Phosphotriesterase-related protein	IPI00100933	1.48	0.0989
EPHX1 Epoxide hydrolase 1	IPI00009896	1.32	0.1022
ETFB Isoform 1 of Electron transfer flavoprotein subunit beta	IPI00004902	1.46	0.1025
ABAT 4-aminobutyrate aminotransferase, mitochondrial precursor	IPI00009532	1.61	0.1027
TAGLN2 21 kDa protein	IPI00644531	1.56	0.1027
C10orf65 Isoform 1 of Dihydrodipicolinate synthase-like, mitochondrial precursor	IPI00642544	1.28	0.1042
SLC44A2 cDNA FLJ14613 fis, clone NT2RP1001113, highly similar to Choline transporter-like protein 2	IPI00645589	1.46	0.1051

Supplementary Table 4

FABP1 FABP1 protein (Fragment)	IPI00010290	3.38	0.1061
RPL35 60S ribosomal protein L35	IPI00412607	1.49	0.1093
PSMA6 Proteasome subunit alpha type-6	IPI00029623	1.34	0.1104
HSPE1 10 kDa heat shock protein, mitochondrial	IPI00220362	1.67	0.1105
FTH1 Ferritin heavy chain	IPI00554521	1.34	0.1108
PSMA2 Proteasome subunit alpha type-2	IPI00219622	1.49	0.1117
HRSP12 Ribonuclease UK114	IPI00005038	1.72	0.1119
HIBADH 3-hydroxyisobutyrate dehydrogenase, mitochondrial precursor	IPI00013860	1.36	0.1126
MTAP S-methyl-5-thioadenosine phosphorylase	IPI00011876	1.30	0.1197
ASL 58 kDa protein	IPI00872756	1.39	0.1201
CPNE2 Copine II	IPI00645310	1.37	0.1201
GNPDA1 Glucosamine-6-phosphate isomerase	IPI00009305	1.33	0.1203
GC vitamin D-binding protein precursor	IPI00742696	1.85	0.1218
ITIH4 Isoform 1 of Inter-alpha-trypsin inhibitor heavy chain H4 precursor	IPI00294193	2.38	0.1221
SLC6A19 Sodium-dependent neutral amino acid transporter B	IPI00456145	1.69	0.1221
DECRL 2,4-dienoyl-CoA reductase, mitochondrial precursor	IPI00003482	1.38	0.1231
ETFA Electron transfer flavoprotein subunit alpha, mitochondrial precursor	IPI00010810	1.41	0.1233
ATP5H Isoform 1 of ATP synthase subunit d, mitochondrial	IPI00220487	1.33	0.1235
FECH Ferrochelatase	IPI00645429	1.45	0.1266
NACA nascent polypeptide-associated complex alpha subunit isoform a	IPI00797126	1.30	0.1299
PSMB3 Proteasome subunit beta type-3	IPI00028004	1.45	0.1323
HPX Hemopexin precursor	IPI0022488	2.33	0.1350
ATP1B1 Isoform 2 of Sodium/potassium-transporting ATPase subunit beta-1	IPI00871221	1.38	0.1450
FTL Ferritin light chain	IPI00738499	1.21	0.1465
LAP3 Isoform 2 of Cytosol aminopeptidase	IPI00789806	1.86	0.1467
TAGLN Transgelin	IPI00216138	2.20	0.1469
DMGDH Dimethylglycine dehydrogenase, mitochondrial precursor	IPI00296196	1.76	0.1469
CAT Catalase	IPI00465436	1.32	0.1469
CAPN2 Uncharacterized protein CAPN2	IPI00872686	1.55	0.1470
GALM Aldose 1-epimerase	IPI00060200	1.60	0.1472
SERPINB1 Leukocyte elastase inhibitor	IPI00027444	1.86	0.1491
DDAH2 N(G),N(G)-dimethylarginine dimethylaminohydrolase 2	IPI00000760	1.35	0.1516
- Proteasome (Prosome, macropain) subunit, beta type, 9	IPI00894395	1.41	0.1519
MYH11 smooth muscle myosin heavy chain 11 isoform SM1B	IPI00743857	1.25	0.1523
PAFAH1B2 Platelet-activating factor acetylhydrolase IB subunit beta	IPI00026546	1.16	0.1523
HDGF Hepatoma-derived growth factor	IPI00020956	1.18	0.1527
PEF1 Peflin	IPI00018235	1.15	0.1527
GARS Glycyl-tRNA synthetase	IPI00783097	1.15	0.1527
CEACAM1 Biliary glycoprotein	IPI00385428	1.15	0.1527
EPHX2 Epoxide hydrolase 2	IPI00104341	1.76	0.1576
SDHALP1 28 kDa protein	IPI00789678	1.43	0.1593
DLST Dihydrolipoylysine-residue succinyltransferase component of 2-oxoglutarate dehydrogenase complex	IPI00420108	1.43	0.1600
ECH1 Delta(3,5)-Delta(2,4)-dienoyl-CoA isomerase, mitochondrial precursor	IPI00011416	1.26	0.1600
TPM4 Isoform 1 of Tropomyosin alpha-4 chain	IPI00010779	1.53	0.1604
LCP1 Plastin-2	IPI00010471	1.24	0.1605
C6orf108 c-Myc-responsive protein Rcl	IPI00007926	2.21	0.1606
LCN2 Uncharacterized protein LCN2	IPI00743064	1.51	0.1626
ACOX2 Peroxisomal acyl-coenzyme A oxidase 2	IPI00293125	1.44	0.1639
ATP6V0D1 Vacuolar proton pump subunit d 1	IPI00034159	1.36	0.1651
RPS24 Isoform 2 of 40S ribosomal protein S24	IPI00847986	1.42	0.1687
PARK7 Protein DJ-1	IPI00298547	1.28	0.1712
CAPN1 Calpain-1 catalytic subunit	IPI00011285	1.41	0.1725
AGMAT Agmatinase, mitochondrial precursor	IPI00305360	1.44	0.1736
SDHB Succinate dehydrogenase [ubiquinone] iron-sulfur subunit, mitochondrial precursor	IPI00294911	1.55	0.1741

Supplementary Table 4

MGLL Monoglyceride lipase	IPI00455206	1.41	0.1790
CPNE3 Copine-3	IPI0024403	1.29	0.1799
UBE2V2 Ubiquitin-conjugating enzyme E2 variant 2	IPI0019600	1.36	0.1824
AKR7A2 Aflatoxin B1 aldehyde reductase member 2	IPI00305978	1.19	0.1873
DPP4 Dipeptidyl peptidase 4	IPI0018953	1.37	0.1882
MCCC2 Isoform 1 of Methylcrotonoyl-CoA carboxylase beta chain, mitochondrial	IPI00784044	1.63	0.1891
COL14A1 Isoform 2 of Collagen alpha-1(XIV) chain precursor	IPI00550918	1.29	0.1951
LOC641293 Similar to 60S ribosomal protein L21	IPI00845507	1.45	0.1977
ST13 Suppression of tumorigenicity 13	IPI00892883	1.36	0.1992
ECHDC2 Isoform 1 of Enoyl-CoA hydratase domain-containing protein 2, mitochondrial precursor	IPI00384676	1.28	0.2000
ACE Isoform Somatic-1 of Angiotensin-converting enzyme, somatic isoform precursor	IPI00437751	1.99	0.2039
HK1 Isoform 2 of Hexokinase-1	IPI00220663	1.45	0.2041
UQCRC1 Cytochrome b-c1 complex subunit 1, mitochondrial precursor	IPI00013847	1.50	0.2046
CRYZ Quinone oxidoreductase	IPI00000792	1.42	0.2046
GLUD1 Glutamate dehydrogenase 1, mitochondrial precursor	IPI00016801	1.28	0.2046
TMEM65 Transmembrane protein 65	IPI00375577	1.37	0.2070
FSCN1 FSCN1 protein (Fragment)	IPI00747810	1.33	0.2070
AQP1 Aquaporin 1 splice variant 2	IPI00428490	3.03	0.2100
TNXB 456 kDa protein	IPI00644296	1.86	0.2100
- A30	IPI00830122	1.80	0.2100
ADH1B;ADH1C Uncharacterized protein ADH1C (Fragment)	IPI00872991	1.43	0.2100
AGT Angiotensinogen precursor	IPI00032220	1.40	0.2100
- Myosin-reactive immunoglobulin kappa chain variable region (Fragment)	IPI00384401	1.40	0.2100
WASF2 Wiskott-Aldrich syndrome protein family member 2	IPI00472164	1.34	0.2100
EML1 Isoform 3 of Echinoderm microtubule-associated protein-like 1	IPI00550611	1.34	0.2100
DCN Isoform A of Decorin precursor	IPI00012119	1.31	0.2100
EFNB1 Ephrin-B1	IPI00024307	1.31	0.2100
XPNPEP1 Xaa-Pro aminopeptidase 1	IPI00793375	1.31	0.2100
MARCKSL1 MARCKS-related protein	IPI00641181	1.29	0.2100
- Uncharacterized protein ENSP00000375034	IPI00854743	1.29	0.2100
FLJ22662 hypothetical protein LOC79887	IPI00016255	1.26	0.2100
- Rheumatoid factor G9 heavy chain (Fragment)	IPI00815662	1.26	0.2100
- V2-6 protein	IPI00829740	1.26	0.2100
DDT 14 kDa protein	IPI00878984	1.26	0.2100
LOC100129243 similar to hCG1994130	IPI00888774	1.26	0.2100
PFAS Phosphoribosylformylglycinamide synthase	IPI00004534	1.23	0.2100
SNAP23 Isoform SNAP-23a of Synaptosomal-associated protein 23	IPI00010438	1.23	0.2100
CTSL1 Cathepsin L1 precursor	IPI00012887	1.23	0.2100
IGLV1-40 V1-13 protein (Fragment)	IPI00789259	1.23	0.2100
- 13 kDa protein	IPI00829803	1.23	0.2100
DPYSL3 Dihydropyrimidinase-related protein 3	IPI00872788	1.23	0.2100
FLJ10769 Isoform 1 of Uncharacterized protein FLJ10769 precursor	IPI00873027	1.23	0.2100
PVALB Parvalbumin (Fragment)	IPI00877795	1.23	0.2100
RCN1 Reticulocalbin-1	IPI00015842	1.20	0.2100
AHSG Alpha-2-HS-glycoprotein precursor	IPI00022431	1.20	0.2100
FOLH1 Isoform PSMA of Glutamate carboxypeptidase 2	IPI00216910	1.20	0.2100
GCK Isoform 1 of Glucokinase	IPI00244083	1.20	0.2100
KIRREL Isoform 2 of Kin of IRRE-like protein 1	IPI00470361	1.20	0.2100
CORO1A 40 kDa protein	IPI00642725	1.20	0.2100
PEA15 Phosphoprotein enriched in astrocytes 15	IPI00643342	1.20	0.2100
- cDNA FLJ51351, highly similar to GTPase, IMAP family member 4	IPI00908338	1.20	0.2100
NPTN Isoform 2 of Neuroplastin	IPI00018311	1.17	0.2100
S100A6 Protein S100-A6	IPI00027463	1.17	0.2100
GPD1L Glycerol-3-phosphate dehydrogenase 1-like protein	IPI00032959	1.17	0.2100
RDH14;NT5C1B Retinol dehydrogenase 14	IPI00177940	1.17	0.2100
PSMD9 Isoform p27-S of 26S proteasome non-ATPase regulatory subunit 9	IPI00216220	1.17	0.2100
OPRS1 Isoform 1 of Sigma 1-type opioid receptor	IPI00218268	1.17	0.2100
SUMO2 Small ubiquitin-related modifier 2	IPI00299149	1.17	0.2100
CARHSP1 Calcium-regulated heat stable protein 1	IPI00304409	1.17	0.2100

Supplementary Table 4

HSP90AB4P Putative heat shock protein HSP 90-beta 4	IPI00555565	1.17	0.2100
IPI00746278	IPI00746278	1.17	0.2100
PICALM Uncharacterized protein PICALM	IPI00871890	1.17	0.2100
OSBPL8 Oxysterol-binding protein	IPI00873898	1.17	0.2100
SERPINA5 Plasma serine protease inhibitor precursor	IPI00007221	1.14	0.2100
PSMD8 proteasome 26S non-ATPase subunit 8	IPI00010201	1.14	0.2100
CDC37 Hsp90 co-chaperone Cdc37	IPI00013122	1.14	0.2100
RPL36 60S ribosomal protein L36	IPI00216237	1.14	0.2100
PRX Isoform 3 of Periaxin	IPI00221069	1.14	0.2100
NAPG Gamma-soluble NSF attachment protein	IPI00293817	1.14	0.2100
TARS Threonyl-tRNA synthetase, cytoplasmic	IPI00329633	1.14	0.2100
HNRNPAB Isoform 3 of Heterogeneous nuclear ribonucleoprotein A/B	IPI00334713	1.14	0.2100
- Tryptophanyl-tRNA synthetase (Fragment)	IPI00383754	1.14	0.2100
- Amyloid lambda 6 light chain variable region SAR (Fragment)	IPI00386839	1.14	0.2100
FLJ11151 Isoform 2 of Uncharacterized metallophosphoesterase CSTP1	IPI00426077	1.14	0.2100
REN Isoform 2 of Renin	IPI00552207	1.14	0.2100
NCALD Neurocalcin delta variant (Fragment)	IPI00555920	1.14	0.2100
CES1 carboxylesterase 1 isoform c precursor	IPI00607693	1.14	0.2100
NUDT5 Uncharacterized protein NUDT5	IPI00646762	1.14	0.2100
ASPA 30 kDa protein	IPI00790886	1.14	0.2100
SNRPD3 19 kDa protein	IPI00879750	1.14	0.2100
HLA-DRB5;hCG_1998957;LOC100133811;RNASE2;ZNF749;HLA-DRB3;HLA-DRB1;HLA-DRB	IPI00887556	1.14	0.2100
FAM62B 98 kDa protein	IPI00893476	1.14	0.2100
- cDNA FLJ59206, highly similar to Eukaryotic translation initiation factor 4B	IPI00908588	1.14	0.2100
TIMM13 Mitochondrial import inner membrane translocase subunit Tim13	IPI00001589	1.11	0.2100
PRPSAP2 Phosphoribosyl pyrophosphate synthetase-associated protein 2	IPI00003168	1.11	0.2100
BCS1L Mitochondrial chaperone BCS1	IPI00003985	1.11	0.2100
RAD23A UV excision repair protein RAD23 homolog A	IPI00008219	1.11	0.2100
ATP6V0A4 Vacuolar proton translocating ATPase 116 kDa subunit a isoform 4	IPI00009852	1.11	0.2100
SLC5A2 Sodium/glucose cotransporter 2	IPI00012449	1.11	0.2100
C1QA Complement C1q subcomponent subunit A	IPI00022392	1.11	0.2100
SH3GLB1 Isoform 2 of Endophilin-B1	IPI00022824	1.11	0.2100
FKBP3 FK506-binding protein 3	IPI00024157	1.11	0.2100
M6PR Cation-dependent mannose-6-phosphate receptor	IPI00025049	1.11	0.2100
YBX1 Nuclease-sensitive element-binding protein 1	IPI00031812	1.11	0.2100
HNRPDL Isoform 3 of Heterogeneous nuclear ribonucleoprotein D-like	IPI00045498	1.11	0.2100
NANS Sialic acid synthase	IPI00147874	1.11	0.2100
TOLLIP cDNA FLJ39374 fis, clone PEBLM2008576, highly similar to Homo sapiens TOLLIP pro	IPI00167490	1.11	0.2100
ARL1 ADP-ribosylation factor-like protein 1	IPI00219518	1.11	0.2100
DPP6 Isoform DPPX-L of Dipeptidyl aminopeptidase-like protein 6	IPI00301512	1.11	0.2100
- Ig lambda chain V-III region SH	IPI00382436	1.11	0.2100
RPL32 60S ribosomal protein L32	IPI00395998	1.11	0.2100
PEX19 Peroxisomal biogenesis factor 19	IPI00642757	1.11	0.2100
LPHN2 Uncharacterized protein LPHN2	IPI00746327	1.11	0.2100
MYH10 Isoform 3 of Myosin-10	IPI00790503	1.11	0.2100
RPL23A Protein	IPI00794894	1.11	0.2100
STRAP 12 kDa protein	IPI00796172	1.11	0.2100
CFI cDNA FLJ58124, highly similar to Complement factor I	IPI00796990	1.11	0.2100
COPS7A 18 kDa protein	IPI00798179	1.11	0.2100
COMM8 Uncharacterized protein COMM8	IPI00871891	1.11	0.2100
ADPRH [Protein ADP-ribosylarginine] hydrolase	IPI00009258	1.09	0.2100
NMNAT1 Nicotinamide mononucleotide adenyllyltransferase 1	IPI00009726	1.09	0.2100
EIF3E Eukaryotic translation initiation factor 3 subunit E	IPI00013068	1.09	0.2100
SLC1A1 Excitatory amino acid transporter 3	IPI00015475	1.09	0.2100
SNRPG Small nuclear ribonucleoprotein G	IPI00016572	1.09	0.2100
ENPP3 Ectonucleotide pyrophosphatase/phosphodiesterase family member 3	IPI00020999	1.09	0.2100
APOA2 Apolipoprotein A-II precursor	IPI00021854	1.09	0.2100
PSMC5 26S protease regulatory subunit 8	IPI00023919	1.09	0.2100
MMP8 Neutrophil collagenase	IPI00027846	1.09	0.2100

Supplementary Table 4

GMPPB Isoform 1 of Mannose-1-phosphate guanyltransferase beta	IPI00030920	1.09	0.2100
GPNAT1 Glucosamine 6-phosphate N-acetyltransferase	IPI00061525	1.09	0.2100
GBA2 Isoform 1 of Non-lysosomal glucosylceramidase	IPI00100668	1.09	0.2100
DARS Aspartyl-tRNA synthetase, cytoplasmic	IPI00216951	1.09	0.2100
PAFAH1B1 Isoform 1 of Platelet-activating factor acetylhydrolase IB subunit alpha	IPI00218728	1.09	0.2100
ITIH1 Inter-alpha-trypsin inhibitor heavy chain H1	IPI00292530	1.09	0.2100
F9 Coagulation factor IX precursor	IPI00296176	1.09	0.2100
FAM49B Protein FAM49B	IPI00303318	1.09	0.2100
DOLPP1 Dolichyldiphosphatase 1	IPI00329410	1.09	0.2100
NUP93 Nuclear pore complex protein Nup93	IPI00397904	1.09	0.2100
ALPL Alkaline phosphatase, tissue-nonspecific isozyme precursor	IPI00419916	1.09	0.2100
CROCC Isoform 1 of Rootletin	IPI00456492	1.09	0.2100
COPS5 COP9 signalosome subunit 5 variant (Fragment)	IPI00556139	1.09	0.2100
CARS cysteinyl-tRNA synthetase isoform d	IPI00556541	1.09	0.2100
TIMP3 TIMP metallopeptidase inhibitor 3	IPI00640293	1.09	0.2100
FHL1 Isoform 1 of Four and a half LIM domains protein 1	IPI00647207	1.09	0.2100
NUDT16 Nucleoside diphosphate-linked moiety X motif 16	IPI00783497	1.09	0.2100
NT5C 20 kDa protein	IPI00790117	1.09	0.2100
TRAM1 TRAM1 protein (Fragment)	IPI00790653	1.09	0.2100
- VH87-2 protein (Fragment)	IPI00827892	1.09	0.2100
UNC84A Unc-84 homolog A	IPI00844303	1.09	0.2100
MIOX Myo-inositol oxygenase	IPI00852977	1.09	0.2100
- Ribonuclease T2	IPI00855775	1.09	0.2100
SEPT9 22 kDa protein	IPI00871679	1.09	0.2100
TBCA 16 kDa protein	IPI00872214	1.09	0.2100
MOBKL1B Uncharacterized protein MOBKL1B (Fragment)	IPI00879358	1.09	0.2100
LOC650788 similar to 40S ribosomal protein S28	IPI00887241	1.09	0.2100
- Cryocrystalglobulin CC1 heavy chain variable region (Fragment)	IPI00890754	1.09	0.2100
C2orf30 chromosome 2 open reading frame 30 isoform 2	IPI00894202	1.09	0.2100
IPIr00045565	IPIr00045565	1.09	0.2100
IPIr00305305	IPIr00305305	1.09	0.2100
MAT2A S-adenosylmethionine synthetase isoform type-2	IPI00010157	1.06	0.2100
DNAJB1 DnaJ homolog subfamily B member 1	IPI00015947	1.06	0.2100
CSPG4 Chondroitin sulfate proteoglycan 4	IPI00019157	1.06	0.2100
ZYX Zyxin	IPI00020513	1.06	0.2100
IMPA1 Inositol monophosphatase	IPI00020906	1.06	0.2100
MRPL15 39S ribosomal protein L15, mitochondrial	IPI00023086	1.06	0.2100
GSX1 GS homeobox 1	IPI00028199	1.06	0.2100
C9orf142 Isoform 1 of Uncharacterized protein C9orf142	IPI00030968	1.06	0.2100
BAT2 Isoform 2 of Large proline-rich protein BAT2	IPI00084746	1.06	0.2100
GPSN2 Isoform 1 of Synaptic glycoprotein SC2	IPI00100656	1.06	0.2100
COMMD1 COMM domain-containing protein 1	IPI00171117	1.06	0.2100
ALMS1 ALMS1	IPI00178743	1.06	0.2100
MTPN Myotrophin	IPI00179589	1.06	0.2100
GPHN Isoform 2 of Gephyrin	IPI00184477	1.06	0.2100
IL18 Interleukin-18 precursor	IPI00290198	1.06	0.2100
C18orf19 Uncharacterized protein C18orf19	IPI00290799	1.06	0.2100
SLC25A40 Solute carrier family 25 member 40	IPI00290827	1.06	0.2100
TSNAX Translin-associated protein X	IPI00293350	1.06	0.2100
STT3A Dolichyl-diphosphooligosaccharide--protein glycosyltransferase subunit STT3A	IPI00297492	1.06	0.2100
PDHX Pyruvate dehydrogenase protein X component, mitochondrial	IPI00298423	1.06	0.2100
ELAVL1 cDNA FLJ60076, highly similar to ELAV-like protein 1	IPI00301936	1.06	0.2100
CRK v-crk sarcoma virus CT10 oncogene homolog isoform b	IPI00305469	1.06	0.2100
MCFD2 Multiple coagulation factor deficiency protein 2	IPI00328680	1.06	0.2100
MDP-1 Isoform 2 of Magnesium-dependent phosphatase 1	IPI00385758	1.06	0.2100
LPHN2 Isoform 1 of Latrophilin-2	IPI00410232	1.06	0.2100
C2orf55 Uncharacterized protein C2orf55	IPI00410436	1.06	0.2100
INPP5A Inositol polyphosphate-5-phosphatase, 40kDa	IPI00413212	1.06	0.2100
SLC22A11 Isoform 2 of Solute carrier family 22 member 11	IPI00418660	1.06	0.2100

Supplementary Table 4

UBE2I Ubiquitin carrier protein	IPI00450472	1.06	0.2100
CUL4B Isoform 2 of Cullin-4B	IPI00480142	1.06	0.2100
SARS Seryl-tRNA synthetase	IPI00514587	1.06	0.2100
PREX1 Isoform 3 of Phosphatidylinositol 3,4,5-trisphosphate-dependent Rac exchanger 1 protein	IPI00552692	1.06	0.2100
HM13 Isoform 5 of Minor histocompatibility antigen H13	IPI00552772	1.06	0.2100
ALDH3B1 Aldehyde dehydrogenase 3B1 variant (Fragment)	IPI00555728	1.06	0.2100
DBP D site of albumin promoter (Albumin D-box) binding protein variant (Fragment)	IPI00556150	1.06	0.2100
TM9SF3 SM-11044 binding protein	IPI00644458	1.06	0.2100
USP7 Ubiquitin carboxyl-terminal hydrolase	IPI00646721	1.06	0.2100
CPNE1 Copine I	IPI00647692	1.06	0.2100
SAT2 SAT2 protein	IPI00744810	1.06	0.2100
- cDNA FLJ38090 fis, clone CTONG2026513	IPI00746933	1.06	0.2100
FAM98B family with sequence similarity 98, member B isoform 1	IPI00760837	1.06	0.2100
PYGL Glycogen phosphorylase, liver form	IPI00783313	1.06	0.2100
GCHFR 8 kDa protein	IPI00793097	1.06	0.2100
PTDSS1 PTDSS1 protein	IPI00794618	1.06	0.2100
VPS28 23 kDa protein	IPI00794724	1.06	0.2100
TYMP cDNA, FLJ95575, highly similar to Homo sapiens endothelial cell growth factor 1 (platelet)	IPI00852987	1.06	0.2100
FUS Uncharacterized protein FUS	IPI00854677	1.06	0.2100
CUL5 Uncharacterized protein CUL5 (Fragment)	IPI00871370	1.06	0.2100
COL1A2 130 kDa protein	IPI00873137	1.06	0.2100
CGNL1 Isoform 2 of Cingulin-like protein 1	IPI00877055	1.06	0.2100
IARS Isoleucyl-tRNA synthetase	IPI00877938	1.06	0.2100
TCFL5 Isoform 3 of Transcription factor-like 5 protein	IPI00880158	1.06	0.2100
FUSSEL18 functional smad suppressing element 18	IPI00886861	1.06	0.2100
LOC651709 similar to facioscapulohumeral muscular dystrophy	IPI00888492	1.06	0.2100
- Uncharacterized protein ENSP00000343301 (Fragment)	IPI00890757	1.06	0.2100
TSSC1 15 kDa protein	IPI00894442	1.06	0.2100
IPI00894504	IPI00894504	1.06	0.2100
LCE3D Late cornified envelope 3D	IPI00902813	1.06	0.2100
- cDNA FLJ52861, moderately similar to Homo sapiens hydroxysteroid dehydrogenase like 1 (HS	IPI00909286	1.06	0.2100
- cDNA FLJ59387, highly similar to Protein D11Lgp1 homolog	IPI00909449	1.06	0.2100
- cDNA FLJ60588, highly similar to Protein arginine N-methyltransferase 1	IPI00909470	1.06	0.2100
- NADH dehydrogenase subunit 4	IPI00910137	1.06	0.2100
- cDNA FLJ56904, highly similar to RNA-binding protein Musashi homolog 2	IPI00910884	1.06	0.2100
IPIr00008531	IPIr00008531	1.06	0.2100
IPIr00022200	IPIr00022200	1.06	0.2100
IPIr00028031	IPIr00028031	1.06	0.2100
IPIr00103552	IPIr00103552	1.06	0.2100
IPIr00167941	IPIr00167941	1.06	0.2100
IPIr00293895	IPIr00293895	1.06	0.2100
IPIr00375415	IPIr00375415	1.06	0.2100
IPIr00383951	IPIr00383951	1.06	0.2100
IPIr00384789	IPIr00384789	1.06	0.2100
IPIr00413568	IPIr00413568	1.06	0.2100
IPIr00654875	IPIr00654875	1.06	0.2100
IPIr00744706	IPIr00744706	1.06	0.2100
IPIr00749276	IPIr00749276	1.06	0.2100
IPIr00794549	IPIr00794549	1.06	0.2100
AKR7A3 Aflatoxin B1 aldehyde reductase member 3	IPI00293721	1.72	0.2120
HSD17B8 Estradiol 17-beta-dehydrogenase 8	IPI00021890	1.26	0.2152
TMEM126A Transmembrane protein 126A	IPI00031064	1.39	0.2161
NDUFB6 NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 6	IPI00219385	1.19	0.2183
UQCRC2 Cytochrome b-c1 complex subunit 2, mitochondrial precursor	IPI00305383	1.46	0.2207
HADH Isoform 2 of Hydroxyacyl-coenzyme A dehydrogenase, mitochondrial precursor	IPI00298406	1.42	0.2210
ECHS1 Enoyl-CoA hydratase, mitochondrial precursor	IPI00024993	1.18	0.2210
PHB2 Prohibitin-2	IPI00027252	1.33	0.2212
ANPEP Aminopeptidase N	IPI00221224	2.08	0.2215
- Putative uncharacterized protein DKFZp686M24218	IPI00784998	1.89	0.2288

Supplementary Table 4

ATP5L ATP synthase subunit g, mitochondrial	IPI00027448	1.90	0.2317
SLC3A1 Neutral and basic amino acid transport protein rBAT	IPI00029268	2.08	0.2320
RPL24 20 kDa protein	IPI00873403	1.26	0.2355
C14orf124 Isoform 2 of UPF0105 protein C14orf124	IPI00643286	1.19	0.2355
PFDN2 Prefoldin subunit 2	IPI00006052	1.13	0.2355
ALDOC Fructose-bisphosphate aldolase	IPI00792375	1.35	0.2361
PRTN3 Myeloblastin	IPI00027409	1.33	0.2361
CDH2 Uncharacterized protein CDH2	IPI00658202	1.33	0.2361
SERPINF1 Pigment epithelium-derived factor precursor	IPI00006114	1.30	0.2361
ATP6V1G1 Vacuolar proton pump subunit G 1	IPI00025285	1.29	0.2361
TMEM33 Transmembrane protein 33	IPI00299084	1.28	0.2361
F2 Prothrombin precursor (Fragment)	IPI00019568	1.21	0.2361
NQO1 NAD(P)H menadione oxidoreductase 1, dioxin-inducible isoform b	IPI00619966	1.21	0.2362
NIPSNAP1 Protein NipSnap homolog 1	IPI00304435	1.24	0.2383
PSMB8 Isoform 1 of Proteasome subunit beta type-8	IPI00000783	1.29	0.2496
CAPNS1 Calpain small subunit 1	IPI00025084	1.41	0.2499
PLS1 PLS1 protein	IPI00789401	1.17	0.2509
AGXT2 Alanine-glyoxylate aminotransferase 2, mitochondrial precursor	IPI00011075	1.44	0.2514
GPX4 Isoform Mitochondrial of Phospholipid hydroperoxide glutathione peroxidase, mitochondrial	IPI00304814	1.26	0.2549
HGD;LOC100132552 homogentisate 1,2-dioxygenase	IPI00887960	1.14	0.2556
IDH1 Isocitrate dehydrogenase [NADP] cytoplasmic	IPI00027223	1.48	0.2561
C8orf55 Uncharacterized protein C8orf55 precursor	IPI00171421	1.21	0.2565
hCG_39912 hypothetical protein LOC642250	IPI00887088	1.55	0.2573
ATP5F1 ATP synthase subunit b, mitochondrial precursor	IPI00029133	1.27	0.2574
PCCB Propionyl-CoA carboxylase beta chain, mitochondrial precursor	IPI00007247	1.27	0.2574
HSPD1 60 kDa heat shock protein, mitochondrial precursor	IPI00784154	1.35	0.2576
ALDH2 Mitochondrial aldehyde dehydrogenase 2 variant (Fragment)	IPI00792207	1.33	0.2576
WARS Tryptophanyl-tRNA synthetase, cytoplasmic	IPI00295400	1.27	0.2613
PPA1 Inorganic pyrophosphatase	IPI00015018	1.20	0.2613
FABP3 Fatty acid-binding protein, heart	IPI00219684	1.41	0.2642
PCBD1 Pterin-4-alpha-carbinolamine dehydratase	IPI00218568	1.35	0.2642
RAB33B Ras-related protein Rab-33B	IPI00021475	1.30	0.2642
RPL10 ribosomal protein L10	IPI00853161	1.27	0.2642
ATP5I ATP synthase, H+ transporting, mitochondrial F0 complex, subunit E	IPI00218848	1.21	0.2642
EIF2S1 Eukaryotic translation initiation factor 2 subunit 1	IPI00219678	1.19	0.2642
SH3BGRL 13 kDa protein	IPI00872670	1.19	0.2642
HNMT Histamine N-methyltransferase	IPI00030023	1.17	0.2642
MCEE Methylmalonyl-CoA epimerase, mitochondrial precursor	IPI00107722	1.16	0.2642
- cDNA FLJ53377, highly similar to Procollagen-lysine, 2-oxoglutarate 5-dioxygenase 1	IPI00910343	1.16	0.2642
TCP1 T-complex protein 1 isoform b	IPI00550591	1.31	0.2656
SHOX2 Isoform 2 of Short stature homeobox protein 2	IPI00218369	1.13	0.2746
ATP6V1H Isoform 2 of Vacuolar proton pump subunit H	IPI00414079	1.54	0.2747
PGAM1 Phosphoglycerate mutase 1	IPI00549725	1.43	0.2751
DCTN1 Isoform p135 of Dynactin subunit 1	IPI00219114	1.17	0.2754
MAT2B Isoform 1 of Methionine adenosyltransferase 2 subunit beta	IPI00002324	1.15	0.2758
ATP6V1A Vacuolar ATP synthase catalytic subunit A	IPI00007682	1.77	0.2769
RPL14 RPL14 protein	IPI00555744	1.36	0.2788
SLC5A12 Isoform 1 of Sodium-coupled monocarboxylate transporter 2	IPI00760881	1.34	0.2788
sp CASB_BOVIN	sp CASB_BOVIN	1.56	0.2794
CD34 Isoform CD34-T of Hematopoietic progenitor cell antigen CD34	IPI00299994	1.50	0.2803
RPL11 Isoform 2 of 60S ribosomal protein L11	IPI00746438	1.11	0.2931
MCTS1 cDNA FLJ59683, highly similar to Homo sapiens malignant T cell amplified sequence 1	IPI00645446	1.11	0.2934
API5 Isoform 1 of Apoptosis inhibitor 5	IPI00555572	1.08	0.2934
ISYNA1 52 kDa protein	IPI00645069	1.08	0.2934
AZU1 Azurocidin	IPI00022246	1.83	0.2958
DBI Isoform a 1 of Acyl-CoA-binding protein	IPI00010182	1.57	0.2958
- cDNA FLJ54049, highly similar to Multimerin-2	IPI00908953	1.35	0.2958
LRG1 Leucine-rich alpha-2-glycoprotein precursor	IPI00022417	1.30	0.2958
LOC554235 Putative L-aspartate dehydrogenase	IPI00419903	1.30	0.2958

Supplementary Table 4

SLC13A3 Isoform 3 of Solute carrier family 13 member 3	IPI00747380	1.24	0.2958
ME2 NAD-dependent malic enzyme, mitochondrial precursor	IPI00011201	1.22	0.2958
CA12 Isoform 2 of Carbonic anhydrase 12 precursor	IPI00221392	1.32	0.2958
GPX3 Glutathione peroxidase 3 precursor	IPI00026199	1.10	0.2964
SNCA Isoform 2-4 of Alpha-synuclein	IPI00218467	1.17	0.2967
- Immunglobulin heavy chain variable region (Fragment)	IPI00783287	1.30	0.2971
MAOB Amine oxidase [flavin-containing] B	IPI00328156	1.33	0.2974
ATP5O ATP synthase subunit O, mitochondrial precursor	IPI00007611	1.30	0.2974
ENPEP Glutamyl aminopeptidase	IPI00014375	1.26	0.2974
CA1 Carbonic anhydrase 1	IPI00215983	1.15	0.2976
CALML3 Calmodulin-like protein 3	IPI00216984	1.09	0.3019
RPL19 60S ribosomal protein L19	IPI00025329	1.20	0.3020
CSRP1 Cysteine and glycine-rich protein 1	IPI00442073	1.21	0.3097
VAPA Vesicle-associated membrane protein-associated protein A	IPI00170692	1.21	0.3131
IVD Isovaleryl-CoA dehydrogenase, mitochondrial precursor	IPI00789848	1.35	0.3179
HBB Hemoglobin subunit beta	IPI00654755	1.20	0.3189
IDH3B Isoform A of Isocitrate dehydrogenase [NAD] subunit beta, mitochondrial	IPI00304419	1.09	0.3286
USP14 cDNA, FLJ96494, highly similar to Homo sapiens ubiquitin specific peptidase 14 (tRNA-g	IPI00871297	1.09	0.3286
S100A10 Protein S100-A10	IPI00183695	1.17	0.3295
- 19 kDa protein	IPI00872915	1.53	0.3384
ATP1A1 ATPase, Na+/K+ transporting, alpha 1 polypeptide	IPI00646182	1.52	0.3416
sp TRYP_PIG	sp TRYP_PIG	1.23	0.3416
ALDH4A1 Aldehyde dehydrogenase 4 family, member A1	IPI00647328	1.18	0.3416
HBA1;HBA2 Alpha 2 globin variant (Fragment)	IPI00853068	1.17	0.3416
CYCS Cytochrome c	IPI00465315	1.30	0.3503
CDC42 Isoform 2 of Cell division control protein 42 homolog precursor	IPI00016786	1.24	0.3631
EEF2 Elongation factor 2	IPI00186290	1.13	0.3644
CLDN3 Claudin-3	IPI00007364	1.10	0.3649
SCRN2 Secernin-2	IPI00062266	1.10	0.3649
PABPC1 70 kDa protein	IPI00796945	1.07	0.3649
SRP68 Isoform 1 of Signal recognition particle 68 kDa protein	IPI00168388	1.07	0.3649
SAA1;SAA2 serum amyloid A2 isoform a	IPI00006146	1.02	0.3649
ECHDC1 enoyl Coenzyme A hydratase domain containing 1 isoform 3	IPI00645630	1.02	0.3649
AZGP1 alpha-2-glycoprotein 1, zinc	IPI00166729	1.20	0.3697
APOB Apolipoprotein B-100 precursor	IPI00022229	2.44	0.3836
NDUFS8 NADH dehydrogenase [ubiquinone] iron-sulfur protein 8, mitochondrial precursor	IPI00010845	1.16	0.3861
ICAM1 Intercellular adhesion molecule 1 precursor	IPI00008494	1.41	0.3864
ARPC1A Actin-related protein 2/3 complex subunit 1A	IPI00333068	1.19	0.3864
DERA Putative deoxyribose-phosphate aldolase	IPI00219677	1.20	0.3874
BRP44 Brain protein 44	IPI00640179	1.20	0.3878
PTRF cDNA FLJ53495, highly similar to Polymerase I and transcript release factor	IPI00514023	1.12	0.3880
HMGCL Hydroxymethylglutaryl-CoA lyase, mitochondrial precursor	IPI00293564	1.21	0.3881
ACADS Short/branched chain specific acyl-CoA dehydrogenase, mitochondrial precursor	IPI00024623	1.21	0.3884
LOC654188 similar to peptidylprolyl isomerase A-like	IPI00887678	1.09	0.3891
PCCA propionyl-Coenzyme A carboxylase, alpha polypeptide isoform b	IPI00895869	1.27	0.3896
ATP5A1 ATP synthase subunit alpha, mitochondrial precursor	IPI00440493	1.17	0.3896
sp CAS2_BOVIN	sp CAS2_BOVIN	1.36	0.3934
AUH Isoform 1 of Methylglutaconyl-CoA hydratase, mitochondrial precursor	IPI00017802	1.20	0.4049
TMEM109 Transmembrane protein 109 precursor	IPI00031697	1.30	0.4057
OXCT1 Succinyl-CoA:3-ketoacid-coenzyme A transferase 1, mitochondrial precursor	IPI00026516	1.23	0.4093
ABHD10 Abhydrolase domain-containing protein 10, mitochondrial precursor	IPI00020075	1.21	0.4119
CFL1 Cofilin-1	IPI00012011	1.33	0.4143
PHB Prohibitin	IPI00017334	1.23	0.4145
ATP5C1 Isoform Liver of ATP synthase subunit gamma, mitochondrial precursor	IPI00478410	1.05	0.4145
DAK Dihydroxyacetone kinase	IPI00551024	1.21	0.4257
AOX1 aldehyde oxidase 1	IPI00872655	1.71	0.4258
ABHD14B Uncharacterized protein ABHD14B	IPI00747859	1.19	0.4277
ALDH5A1 aldehyde dehydrogenase 5A1 precursor, isoform 1	IPI00336008	1.37	0.4378
GBAS Protein NipSnap homolog 2	IPI00016077	1.16	0.4395

Supplementary Table 4

HLA-DRA HLA class II histocompatibility antigen, DR alpha chain	IPI00005171	1.54	0.4400
LTF Truncated lactoferrin	IPI00789477	1.28	0.4407
- cDNA FLJ76502, highly similar to Homo sapiens ubiquinol-cytochrome c reductase, Rieske iron-sulfur protein	IPI00883602	1.24	0.4409
MDH2 Malate dehydrogenase, mitochondrial precursor	IPI00291006	1.35	0.4412
KRT18P33 similar to hCG21219	IPI00888063	1.19	0.4412
VPS26A Vacuolar protein sorting-associated protein 26A	IPI00411426	1.16	0.4485
PGM2 Phosphoglucomutase-2	IPI00550364	1.12	0.4485
COX7A2 Uncharacterized protein COX7A2	IPI00872879	1.23	0.4495
BLVRA Biliverdin reductase A precursor	IPI00294158	1.03	0.4544
GSS Glutathione synthetase	IPI00010706	1.34	0.4552
RPL15 22 kDa protein	IPI00790569	1.16	0.4552
DAG1 Dystroglycan precursor	IPI00028911	1.13	0.4552
ATP2B4 ATP2B4 protein	IPI00856079	1.31	0.4556
CAPS;LOC643635;ABHD6 calcyphosine isoform b	IPI00103067	1.19	0.4556
C1QC Complement C1q subcomponent subunit C	IPI00022394	1.04	0.4559
ZNF503 Isoform 2 of Zinc finger protein 503	IPI00843984	1.15	0.4651
LOC642103 similar to hCG1811191	IPI00741768	1.40	0.4678
ACADS Short-chain specific acyl-CoA dehydrogenase, mitochondrial precursor	IPI00027701	1.21	0.4678
PSME2 proteasome activator subunit 2	IPI00746205	1.14	0.4678
GSTA1 Glutathione S-transferase A1	IPI00657682	1.42	0.4683
MVP Major vault protein	IPI00000105	1.30	0.4683
PRDX1 19 kDa protein	IPI00640741	1.40	0.4685
ASS1 Argininosuccinate synthase	IPI00020632	1.35	0.4685
BCAT2 cDNA FLJ36308 fis, clone THYMU2004916, highly similar to Branched-chain-amino-acid aminotransferase	IPI00181135	1.17	0.4767
BBOX1 Gamma-butyrobetaine dioxygenase	IPI00027416	1.10	0.4807
ATP6V1F Vacuolar proton pump subunit F	IPI00004488	1.13	0.4819
TPT1 Translationally-controlled tumor protein	IPI00550900	1.08	0.4819
NDUFA6 NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 6, 14kDa	IPI00419266	1.14	0.4825
PDCD6IP Dopamine receptor interacting protein 4	IPI00871576	1.37	0.4829
MT-ND5 NADH dehydrogenase subunit 5	IPI00221391	1.15	0.4829
ATP6V0A1 97 kDa protein	IPI00892784	1.33	0.4832
COX5B Cytochrome c oxidase subunit 5B, mitochondrial precursor	IPI00021785	1.22	0.4864
APOD Apolipoprotein D precursor	IPI00006662	1.32	0.4879
PSMB6 20 kDa protein	IPI00789119	1.13	0.4883
DNAJA1 DnaJ homolog subfamily A member 1	IPI00012535	1.18	0.4936
TMEM111 18 kDa protein	IPI00789434	1.14	0.4936
LSS Lanosterol synthase	IPI00009747	1.10	0.4936
CCT2 T-complex protein 1 subunit beta	IPI00297779	1.19	0.4941
ARPC2 Actin-related protein 2/3 complex subunit 2	IPI00005161	1.26	0.4963
THEM2 Thioesterase superfamily member 2	IPI00020530	1.20	0.4970
AK2 Isoform 2 of Adenylate kinase isoenzyme 2, mitochondrial	IPI00218988	1.04	0.4970
RAB21 Ras-related protein Rab-21	IPI00007755	1.21	0.5023
- PC1/MRPS28 fusion protein	IPI00854568	1.33	0.5061
- cDNA FLJ58737, highly similar to Splicing factor 3A subunit 3	IPI00908449	1.16	0.5172
CDH16 Isoform 1 of Cadherin-16 precursor	IPI00025240	1.16	0.5178
RPS16 40S ribosomal protein S16	IPI00221092	1.17	0.5196
SPCS3 Signal peptidase complex subunit 3	IPI00300299	1.11	0.5207
RPS18;LOC100130553 40S ribosomal protein S18	IPI00013296	1.20	0.5216
C20orf3 Adipocyte plasma membrane-associated protein	IPI00031131	1.11	0.5252
sp CAS1_BOVIN	sp CAS1_BOVIN	1.45	0.5257
ACOX1 Isoform 2 of Peroxisomal acyl-coenzyme A oxidase 1	IPI00477729	1.07	0.5257
CLIC2 Uncharacterized protein CLIC2	IPI00514835	1.18	0.5325
NLN cDNA FLJ14696 fis, clone NT2RP2005775, highly similar to NEUROLYSIN	IPI00872224	1.08	0.5325
ACOX3 Isoform 1 of Peroxisomal acyl-coenzyme A oxidase 3	IPI00020226	1.07	0.5325
MUC1 Isoform 1 of Mucin-1	IPI00013955	1.41	0.5341
PPP2R4 Protein phosphatase 2A activator, regulatory subunit 4	IPI00893197	1.18	0.5341
RPL28 Ribosomal protein L28 variant (Fragment)	IPI00816097	1.15	0.5341
TMEM14C Transmembrane protein 14C	IPI00009346	1.14	0.5341
CRP Isoform 1 of C-reactive protein precursor	IPI00022389	1.14	0.5341

Supplementary Table 4

BAX Isoform Alpha of Apoptosis regulator BAX	IPI00443773	1.15	0.5356
RPL5 60S ribosomal protein L5	IPI00000494	1.40	0.5363
F13A1 coagulation factor XIII A1 subunit precursor	IPI00884176	1.72	0.5367
LBP Lipopolysaccharide-binding protein precursor	IPI00032311	1.08	0.5420
UQCRB Cytochrome b-c1 complex subunit 7	IPI00220416	1.02	0.5438
DDC Aromatic-L-amino-acid decarboxylase	IPI00025394	1.25	0.5440
LYZ Lysozyme C precursor	IPI00019038	1.01	0.5473
DHODH Dihydroorotate dehydrogenase, mitochondrial	IPI00024462	1.05	0.5500
ATP5D ATP synthase subunit delta, mitochondrial precursor	IPI00024920	1.09	0.5507
ATP6V1C1 Uncharacterized protein ATP6V1C1	IPI00873237	1.24	0.5509
GNB2L1 Guanine nucleotide-binding protein subunit beta-2-like 1	IPI00848226	1.16	0.5536
GNB1 Guanine nucleotide binding protein (G protein), beta polypeptide 1	IPI00639998	1.25	0.5544
BSG Isoform 1 of Basigin precursor	IPI00218019	1.13	0.5544
DPEP1 Dipeptidase 1 precursor	IPI00059476	1.58	0.5559
HADHA Trifunctional enzyme subunit alpha, mitochondrial precursor	IPI00031522	1.26	0.5561
GCDH Isoform Long of Glutaryl-CoA dehydrogenase, mitochondrial precursor	IPI00024317	1.07	0.5611
DCTN3 Isoform 3 of Dynactin subunit 3	IPI00514971	1.10	0.5697
RPL3 60S ribosomal protein L3	IPI00550021	1.14	0.5754
PSMA4 Proteasome subunit beta type	IPI00789638	1.14	0.5754
THBS1 Thrombospondin-1 precursor	IPI00296099	1.10	0.5754
SRPRB 11 kDa protein	IPI00797747	1.10	0.5754
FTCD Isoform D of Formimidoyltransferase-cyclodeaminase	IPI00218977	1.05	0.5793
CTSA cathepsin A isoform a precursor	IPI00640525	1.26	0.5825
- 48 kDa protein	IPI00005800	1.20	0.5843
GGT1 Isoform 1 of Gamma-glutamyltranspeptidase 1 precursor	IPI00018901	1.23	0.5851
MPST 3-mercaptopyruvate sulfurtransferase	IPI00165360	1.25	0.5857
ATP6V1B2 Vacuolar ATP synthase subunit B, brain isoform	IPI00007812	1.25	0.5867
COX4I1 Cytochrome c oxidase subunit 4 isoform 1, mitochondrial precursor	IPI00006579	1.09	0.5867
BPGM Bisphosphoglycerate mutase	IPI00215979	1.01	0.6041
COMM3 COMM domain-containing protein 3	IPI00015773	1.07	0.6051
- Uncharacterized protein ENSP00000260968	IPI00479058	1.22	0.6053
TOMM70A Mitochondrial precursor proteins import receptor	IPI00015602	1.30	0.6063
TSPAN9 Tetraspanin-9	IPI00027437	1.29	0.6063
SLC25A10 Isoform 1 of Mitochondrial dicarboxylate carrier	IPI00015920	1.33	0.6070
C21orf33 Isoform Long of ES1 protein homolog, mitochondrial precursor	IPI00024913	1.09	0.6169
TPP1 Isoform 2 of Tripeptidyl-peptidase 1 precursor	IPI00554617	1.10	0.6179
IPI00216024	IPI00216024	1.39	0.6180
NDUFA9 NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 9, mitochondrial prec	IPI00003968	1.18	0.6180
CBX3;LOC653972 Chromobox protein homolog 3	IPI00297579	1.09	0.6186
COPS8 COP9 signalosome subunit 8 isoform 2	IPI00377080	1.09	0.6186
DNAJC11 Isoform 2 of DnaJ homolog subfamily C member 11	IPI00607744	1.06	0.6186
SUSD2 Sushi domain-containing protein 2	IPI00021302	1.36	0.6189
IFITM1 Interferon-induced transmembrane protein 1	IPI00300620	1.35	0.6189
PDLIM5 PDZ and LIM domain 5 isoform e	IPI00103146	1.17	0.6189
KHK 31 kDa protein	IPI00893008	1.29	0.6271
UBE2L3 Ubiquitin-conjugating enzyme E2 L3	IPI00021347	1.07	0.6271
PYGB Glycogen phosphorylase, brain form	IPI00004358	1.40	0.6274
TMED7;TICAM2 Toll-like receptor adapter molecule 2	IPI00428967	1.18	0.6274
ERAP1 Isoform 1 of Endoplasmic reticulum aminopeptidase 1	IPI00477831	1.17	0.6274
CTSC Dipeptidyl-peptidase 1 precursor	IPI00022810	1.05	0.6386
SCPEP1 Isoform 1 of Retinoid-inducible serine carboxypeptidase precursor	IPI00012426	1.31	0.6427
PPAP2B Lipid phosphate phosphohydrolase 3	IPI00021453	1.77	0.6430
ACE2 Isoform 1 of Angiotensin-converting enzyme 2 precursor	IPI00465187	1.54	0.6443
RPS4X 40S ribosomal protein S4, X isoform	IPI00217030	1.17	0.6483
PTGES2 Prostaglandin E synthase 2	IPI00303568	1.09	0.6483
CAPZA1 Uncharacterized protein CAPZA1 (Fragment)	IPI00873484	1.08	0.6483
TFRC Transferrin receptor protein 1	IPI00022462	1.03	0.6631
STX12 Syntaxin 12	IPI00513853	1.08	0.6631
PTGDS Prostaglandin D2 synthase 21kDa	IPI00513767	1.29	0.6634

Supplementary Table 4

PARVA Isoform 1 of Alpha-parvin	IPI00018963	1.21	0.6634
NPHS1;PRODH2 Isoform 1 of Nephrin	IPI00747010	1.09	0.6634
RPL31 ribosomal protein L31 isoform 3	IPI00856058	1.05	0.6634
ZMPSTE24 CAAAX prenyl protease 1 homolog	IPI00027180	1.03	0.6634
ATP5J ATP synthase, H+ transporting, mitochondrial F0 complex, subunit F6 isoform b precursor	IPI00456008	1.08	0.6659
HMGCS2 Hydroxymethylglutaryl-CoA synthase, mitochondrial precursor	IPI00008934	1.13	0.6694
- Ig kappa chain V-IV region Len	IPI00387120	1.52	0.6784
MYL1 Myosin light chain 1, skeletal muscle isoform	IPI00216070	1.44	0.6784
M6PRBP1 Isoform B of Mannose-6-phosphate receptor-binding protein 1	IPI00303882	1.35	0.6784
CNN3 46 kDa protein	IPI00873410	1.27	0.6784
SYPL1 Isoform 2 of Synaptophysin-like protein 1	IPI00335277	1.24	0.6784
PURB Transcriptional activator protein Pur-beta	IPI00045051	1.24	0.6784
RPS6 Ribosomal protein S6	IPI00643522	1.21	0.6784
EBP 3-beta-hydroxysteroid-Delta(8),Delta(7)-isomerase	IPI00008599	1.20	0.6784
- cDNA FLJ59582, highly similar to Ras-related protein Rab-3A	IPI00910170	1.20	0.6784
MACF1 620 kDa protein	IPI00902728	1.19	0.6784
EPB41 Isoform 4 of Protein 4.1	IPI00218699	1.19	0.6784
HNRNPU Isoform Long of Heterogeneous nuclear ribonucleoprotein U	IPI00883857	1.18	0.6784
PCMT1 Isoform 2 of Protein-L-isoaspartate(D-aspartate) O-methyltransferase	IPI00828189	1.15	0.6784
PARP4 Poly [ADP-ribose] polymerase 4	IPI00296909	1.14	0.6784
PPIH Peptidyl-prolyl cis-trans isomerase H	IPI00007346	1.13	0.6784
COPS4 COP9 signalosome complex subunit 4	IPI00171844	1.13	0.6784
LOC643287 similar to prothymosin alpha	IPI00737372	1.13	0.6784
EPB42 Isoform Short of Erythrocyte membrane protein band 4.2	IPI00827872	1.13	0.6784
SNX12 Isoform 2 of Sorting nexin-12	IPI00844112	1.13	0.6784
MTP18 16 kDa protein	IPI00879813	1.13	0.6784
ACAT2 Acetyl-CoA acetyltransferase, cytosolic	IPI00291419	1.13	0.6784
EPRS Bifunctional aminoacyl-tRNA synthetase	IPI00013452	1.11	0.6784
LOC285053 similar to ribosomal protein L18a isoform 1	IPI00472864	1.11	0.6784
ERAP2 Isoform 1 of Endoplasmic reticulum aminopeptidase 2	IPI00465261	1.10	0.6784
CCDC47 Isoform 2 of Coiled-coil domain-containing protein 47	IPI00743775	1.10	0.6784
RAB39 Ras-related protein Rab-39A	IPI00001618	1.10	0.6784
PLTP Isoform 1 of Phospholipid transfer protein precursor	IPI00643034	1.09	0.6784
PDCD10 15 kDa protein	IPI00790953	1.09	0.6784
SURF4 Surfeit 4	IPI00399142	1.08	0.6784
ASPN ASPN protein	IPI00418431	1.08	0.6784
HNRNPM Isoform 1 of Heterogeneous nuclear ribonucleoprotein M	IPI00171903	1.08	0.6784
SEC31A Isoform 4 of Protein transport protein Sec31A	IPI00515103	1.08	0.6784
HDHD2 Isoform 1 of Haloacid dehalogenase-like hydrolase domain-containing protein 2	IPI00783874	1.08	0.6784
REXO2 Isoform 2 of Oligoribonuclease, mitochondrial precursor (Fragment)	IPI00217330	1.07	0.6784
UNC84B cDNA FLJ55508, highly similar to Sad1/unc-84-like protein 2	IPI00295940	1.07	0.6784
RNPEP Uncharacterized protein RNPEP	IPI00647400	1.07	0.6784
GDPD3 Isoform 1 of Glycerophosphodiester phosphodiesterase domain-containing protein 3	IPI00549640	1.07	0.6784
CORO1C Coronin-1C_i3 protein	IPI00867509	1.07	0.6784
LOC653658 similar to 40S ribosomal protein S23	IPI00888094	1.07	0.6784
CRB2 Isoform 3 of Crumbs homolog 2	IPI00607804	1.06	0.6784
ACP2 Lysosomal acid phosphatase	IPI00003807	1.05	0.6784
S100A8 Protein S100-A8	IPI00007047	1.05	0.6784
ALDH1A3 Aldehyde dehydrogenase 1A3	IPI00026663	1.05	0.6784
FHIT Bis(5'-adenosyl)-triphosphatase	IPI00028095	1.05	0.6784
VBP1 Von Hippel-Lindau binding protein 1	IPI00334159	1.05	0.6784
GMFB 18 kDa protein	IPI00549557	1.05	0.6784
CD163 Isoform 2 of Scavenger receptor cysteine-rich type 1 protein M130	IPI00759642	1.05	0.6784
ARHGDIA 26 kDa protein	IPI00796541	1.14	0.6785
XPNPEP2 Xaa-Pro aminopeptidase 2 precursor	IPI00439344	1.38	0.6795
GLG1 79 kDa protein	IPI00647145	1.08	0.6799
NIPSNAP3A 32 kDa protein	IPI00871176	1.12	0.6800
ARMET Protein ARMET	IPI00328748	1.07	0.6801
ALDH1A1 Retinal dehydrogenase 1	IPI00218914	1.54	0.6803

Supplementary Table 4

CCT6A T-complex protein 1 subunit zeta	IPI00027626	1.01	0.6809
NDUFB7 NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 7	IPI00219772	1.05	0.6828
MGST3 Microsomal glutathione S-transferase 3	IPI00024266	1.11	0.6830
GPD2 Isoform 1 of Glycerol-3-phosphate dehydrogenase, mitochondrial precursor	IPI00017895	1.07	0.6830
SLC25A12 Calcium-binding mitochondrial carrier protein Aralar1	IPI00386271	1.29	0.6833
ENPP6 Ectonucleotide pyrophosphatase/phosphodiesterase family member 6 precursor	IPI00157414	1.31	0.6873
RPS20 16 kDa protein	IPI00794659	1.23	0.6873
MTCH1 Isoform 2 of Mitochondrial carrier homolog 1	IPI00479697	1.13	0.6873
VWF cDNA FLJ59036, highly similar to von Willebrand factor	IPI00788786	1.18	0.6881
MUPCDH Isoform 1 of Mucin and cadherin-like protein	IPI00336112	1.32	0.6883
RPS14 40S ribosomal protein S14	IPI00026271	1.17	0.6883
SLC9A3R2 solute carrier family 9 isoform 3 regulator 2 isoform b	IPI00645815	1.84	0.6905
CMPK1 cytidine monophosphate (UMP-CMP) kinase 1, cytosolic	IPI00219953	1.09	0.6908
LTA4H Isoform 2 of Leukotriene A-4 hydrolase	IPI00514090	1.05	0.7080
ASPH Aspartyl/asparaginyl beta-hydroxylase	IPI00294834	1.02	0.7080
FAM151A Isoform 1 of Protein FAM151A	IPI00300865	1.50	0.7146
CTSZ Cathepsin Z precursor	IPI00002745	1.11	0.7147
NDUFB8 NADH dehydrogenase	IPI00642807	1.12	0.7150
DLD Dihydrolipoyl dehydrogenase, mitochondrial precursor	IPI00015911	1.07	0.7163
SQRDL Sulfide:quinone oxidoreductase, mitochondrial precursor	IPI00009634	1.10	0.7170
CTSD Cathepsin D precursor	IPI00011229	1.03	0.7170
HAO2 Hydroxyacid oxidase 2	IPI00641158	1.13	0.7177
- cDNA FLJ57678, highly similar to Transmembrane protein 16F	IPI00910110	1.33	0.7270
DNAJB11 DnaJ homolog subfamily B member 11	IPI00008454	1.16	0.7305
UBE2N Ubiquitin carrier protein (Fragment)	IPI00874051	1.20	0.7307
FCGRT IgG receptor FcRn large subunit p51 (Fragment)	IPI00026646	1.20	0.7307
ITGB2 Integrin beta chain, beta 2 variant (Fragment)	IPI00746851	1.04	0.7397
RBBP4 cDNA FLJ53908, highly similar to Histone-binding protein RBBP4	IPI00877934	1.04	0.7397
C20orf116 Isoform 1 of Uncharacterized protein C20orf116	IPI00028387	1.03	0.7397
BAT5 HLA-B associated transcript 5	IPI00791049	1.03	0.7397
ADAM10 Uncharacterized protein ADAM10	IPI00794448	1.03	0.7397
PDLIM1 PDZ and LIM domain protein 1	IPI00010414	1.02	0.7397
C19orf10 UPF0556 protein C19orf10	IPI00056357	1.02	0.7397
QPCTL 33 kDa protein	IPI00061796	1.02	0.7397
BRI3BP BRI3-binding protein	IPI00103599	1.02	0.7397
RTN2 Isoform RTN2-C of Reticulon-2	IPI00410134	1.02	0.7397
COPZ1 13 kDa protein	IPI00792696	1.02	0.7456
PECI Peroxisomal 3,2-trans-enoyl-CoA isomerase	IPI00639841	1.11	0.7467
COL6A2 Isoform 2C2 of Collagen alpha-2(VI) chain precursor	IPI00304840	1.05	0.7467
CHCHD3 Coiled-coil-helix-coiled-coil-helix domain-containing protein 3, mitochondrial precursor	IPI00015833	1.07	0.7478
ANXA3 Uncharacterized protein ANXA3 (Fragment)	IPI00745868	1.06	0.7491
CYP4A11 Cytochrome P450 4A11 precursor	IPI00872799	1.10	0.7501
ISOC2 Isoform 1 of Isochorismatase domain-containing protein 2, mitochondrial precursor	IPI00551022	1.03	0.7509
CTNNA1 Isoform 2 of Catenin alpha-1	IPI00473136	1.03	0.7510
VCL Isoform 2 of Vinculin	IPI00307162	1.02	0.7510
SERPINA1 Isoform 1 of Alpha-1-antitrypsin precursor	IPI00553177	1.52	0.7513
SLC25A5 ADP/ATP translocase 2	IPI00007188	1.18	0.7513
HSPA9 Stress-70 protein, mitochondrial precursor	IPI00007765	1.10	0.7513
AIFM1 Isoform 3 of Apoptosis-inducing factor 1, mitochondrial precursor	IPI00157908	1.06	0.7513
ARPC1B Actin-related protein 2/3 complex subunit 1B	IPI00005160	1.36	0.7648
IGJ immunoglobulin J chain	IPI00178926	1.74	0.7745
- cDNA FLJ78321	IPI00877095	1.03	0.7832
CCT4 T-complex protein 1, delta subunit	IPI00873222	1.06	0.7843
SEPT7 Isoform 2 of Septin-7	IPI00816201	1.20	0.7845
TPD52L2 Isoform 1 of Tumor protein D54	IPI00306825	1.18	0.7848
IPI00873444	IPI00873444	1.04	0.7856
NNT NAD(P) transhydrogenase, mitochondrial	IPI00337541	1.04	0.7856
SLC4A1 Band 3 anion transport protein	IPI00791534	1.11	0.7857
SFXN1 Sideroflexin-1	IPI00009368	1.04	0.7857

Supplementary Table 4

AADACL1 arylacetamide deacetylase-like 1	IPI00002230	1.04	0.7965
UMOD Isoform 3 of Uromodulin	IPI00744076	1.07	0.7968
JUP Junction plakoglobin	IPI00554711	1.05	0.8035
LYPLA2 Acyl-protein thioesterase 2	IPI00027032	1.02	0.8035
GOSR2 17 kDa protein	IPI00795521	1.01	0.8035
RBP4 Retinol-binding protein 4	IPI00022420	1.60	0.8088
- RPS9 protein (Fragment)	IPI00847192	1.02	0.8154
ANXA7 annexin VII isoform 2	IPI00514510	1.06	0.8183
- Uncharacterized protein ENSP0000381447 (Fragment)	IPI00872387	1.06	0.8195
ATP6V1D Vacuolar proton pump subunit D	IPI00001568	1.08	0.8197
PDCD6 Programmed cell death protein 6	IPI00025277	1.07	0.8201
ITGA3 Isoform Alpha-3B of Integrin alpha-3 precursor	IPI00290043	1.13	0.8206
IGHA1;IGHV3OR16-13 IGHA1 protein	IPI00430842	2.13	0.8207
RAP1B Ras-related protein Rap-1b precursor	IPI00015148	1.24	0.8208
TXNDC12 Thioredoxin domain-containing protein 12 precursor	IPI00026328	1.05	0.8421
PCDH24 Protocadherin-24 precursor	IPI00307446	1.09	0.8494
SEPT2 cDNA FLJ55467, highly similar to Septin-2	IPI00871851	1.36	0.8545
SERPINB6 Serpin B6	IPI00749398	1.59	0.8557
ACTR3 Actin-related protein 3	IPI00028091	1.06	0.8560
HADHB Trifunctional enzyme subunit beta, mitochondrial precursor	IPI00022793	1.10	0.8561
ANXA1 Annexin A1	IPI00218918	1.06	0.8561
CRYAA 17 kDa protein	IPI00796777	1.18	0.8630
ATP1B3 15 kDa protein	IPI00789521	1.27	0.8634
DSTN destin isoform b	IPI00845388	1.04	0.8634
RPS8 40S ribosomal protein S8	IPI00216587	1.12	0.8635
PTBP1 Isoform 2 of Polypyrimidine tract-binding protein 1	IPI00334175	1.11	0.8635
PROM1 Prominin-1 precursor	IPI00012540	1.08	0.8635
TXNDC13 Thioredoxin domain-containing protein 13	IPI00100247	1.06	0.8705
TMPO Lamina-associated polypeptide 2, isoforms beta/gamma variant (Fragment)	IPI00873716	1.14	0.8714
THSD7A Thrombospondin type-1 domain-containing protein 7A	IPI00741524	1.06	0.8769
RPS5 40S ribosomal protein S5	IPI00008433	1.07	0.8770
TXNRD1 Isoform 5 of Thioredoxin reductase 1, cytoplasmic	IPI00554786	1.01	0.8890
BLVRB Flavin reductase	IPI00783862	1.10	0.8917
RTN4 Isoform 2 of Reticulon-4	IPI00298289	1.08	0.8917
CCT7 T-complex protein 1 subunit eta	IPI00018465	1.11	0.8917
KRT8 Keratin, type II cytoskeletal 8	IPI00554648	1.03	0.8919
RAB7A Ras-related protein Rab-7a	IPI00016342	1.03	0.8919
GYPA Glycophorin-A	IPI00298800	1.02	0.9086
CYFIP1 Isoform 2 of Cytoplasmic FMR1-interacting protein 1	IPI00550212	1.12	0.9087
LDHAL3 hypothetical protein	IPI00888324	1.08	0.9087
BCKDHA cDNA FLJ45695 fis, clone FEBRA2013570, highly similar to 2-oxoisovalerate dehydrogenase	IPI00444329	1.02	0.9087
RPL27 60S ribosomal protein L27	IPI00382885	1.03	0.9176
MRC1 Macrophage mannose receptor 1	IPI00027848	1.16	0.9178
NME3 Nucleoside diphosphate kinase 3	IPI00012315	1.05	0.9206
DNPEP 52 kDa protein	IPI00658215	1.03	0.9206
LOC100130562 hypothetical protein isoform 2	IPI00888909	1.05	0.9244
GLYATL1 Isoform 2 of Glycine N-acyltransferase-like protein 1	IPI00168156	1.04	0.9263
IQGAP1 Ras GTPase-activating-like protein IQGAP1	IPI00009342	1.03	0.9276
RAB11B Ras-related protein Rab-11B	IPI00020436	1.04	0.9278
HSP90B1 Endoplasmic reticulum protein	IPI00027230	1.03	0.9278
PURA Transcriptional activator protein Pur-alpha	IPI00023591	1.44	0.9444
GSTZ1 Uncharacterized protein GSTZ1 (Fragment)	IPI00874143	1.12	0.9444
ASNA1 Arsenical pump-driving ATPase	IPI00013466	1.07	0.9444
LXN Latexin	IPI00106687	1.07	0.9444
CPNE8 CDNA FLJ25727 fis, clone TST05479	IPI00334276	1.02	0.9444
CBR4 Isoform 1 of Carbonyl reductase 4	IPI00384297	1.02	0.9444
EIF3I Eukaryotic translation initiation factor 3 subunit I	IPI00012795	1.01	0.9444
CTSG Cathepsin G	IPI00028064	1.29	0.9444
BPI Bactericidal permeability-increasing protein	IPI00827847	1.16	0.9444

Supplementary Table 4

RPL31 60S ribosomal protein L31	IPI00026302	1.15	0.9444
RPL31 ribosomal protein L31 isoform 2	IPI00848331	1.15	0.9444
HNRNPD Isoform 4 of Heterogeneous nuclear ribonucleoprotein D0	IPI00220685	1.13	0.9444
- cDNA FLJ53069, highly similar to AP-2 complex subunit mu-1	IPI00909772	1.11	0.9444
CR1 Complement receptor type 1	IPI00412546	1.08	0.9444
PDIA5 Protein disulfide-isomerase A5	IPI00031479	1.08	0.9444
ANK1 Isoform Er16 of Ankyrin-1	IPI00646300	1.07	0.9444
PSMC6 proteasome 26S ATPase subunit 6	IPI00021926	1.07	0.9444
FAAH Fatty-acid amide hydrolase 1	IPI00012107	1.03	0.9444
- cDNA FLJ52895, highly similar to Carbonic anhydrase 3	IPI00909152	1.03	0.9444
CSTB Cystatin-B	IPI00021828	1.02	0.9444
CTNND1 Isoform 3AB of Catenin delta-1	IPI00219734	1.02	0.9444
ITGAM Integrin, alpha M	IPI00645887	1.01	0.9444
- cDNA FLJ51212, moderately similar to Brain acid soluble protein 1	IPI00908521	1.09	0.9543
DUSP3 23 kDa protein	IPI00790757	1.06	0.9543
CHMP4B Charged multivesicular body protein 4b	IPI00025974	1.01	0.9543
SNRPA1 U2 small nuclear ribonucleoprotein A	IPI00297477	1.05	0.9569
IKIP Isoform 4 of Inhibitor of nuclear factor kappa-B kinase-interacting protein	IPI00043598	1.03	0.9570
EEF1G 50 kDa protein	IPI00747497	1.11	0.9622
ADD1 Isoform 1 of Alpha-adducin	IPI00019901	1.03	0.9628
ENG Isoform Long of Endoglin	IPI00017567	1.12	0.9633
CDH13 Cadherin-13 precursor	IPI00024046	1.05	0.9633
CLIC1 Chloride intracellular channel protein 1	IPI00010896	1.02	0.9635
CAP1 Adenylyl cyclase-associated protein 1	IPI00008274	1.03	0.9636
SFXN2 Sideroflexin-2	IPI00043564	1.06	0.9637
PDHB Isoform 1 of Pyruvate dehydrogenase E1 component subunit beta, mitochondrial	IPI00003925	1.04	0.9639
ATP6V0C Vacuolar ATP synthase 16 kDa proteolipid subunit	IPI00018855	1.27	1.0000
TMED9 transmembrane emp24 protein transport domain containing 9	IPI00023542	1.17	1.0000
CCT8 T-complex protein 1 subunit theta	IPI00784090	1.13	1.0000
- Transthyretin	IPI00855916	1.09	1.0000
SDCBP Syntenin isoform 3	IPI00479018	1.08	1.0000
RAB8B 6 kDa protein	IPI00789827	1.05	1.0000
COX5A Cytochrome c oxidase subunit 5A, mitochondrial precursor	IPI00025086	1.05	1.0000
RPS13 40S ribosomal protein S13	IPI00221089	1.04	1.0000

Supplementary Table 5: Proteins listed in the 12 top-ranked enrichment pathways

Gene Ontology Term (biological process)	Proteins	Count	p value
glucose metabolic process	ALDOA, LDHB, SORD, TALDO1, PGD, ALDOB, UGDH, FBP1, TPI1, PGLS, PKM2, PGM1, GAPDH, UGP2, MDH1, ENO1	16	2.13E-15
glucose catabolic process	ALDOA, LDHB, TPI1, PGLS, TALDO1, PKM2, ALDOB, PGM1, PGD, GAPDH, MDH1, ENO1	12	8.14E-15
alcohol catabolic process	ALDOA, LDHB, TPI1, PGLS, TALDO1, SORD, PKM2, ALDOB, PGM1, PGD, GAPDH, MDH1, ENO1	13	1.05E-14
cellular carbohydrate catabolic process	ALDOA, LDHB, TPI1, PGLS, TALDO1, SORD, PKM2, ALDOB, PGM1, PGD, GAPDH, MDH1, ENO1	13	1.91E-14
hexose catabolic process	ALDOA, LDHB, TPI1, PGLS, TALDO1, PKM2, ALDOB, PGM1, PGD, GAPDH, MDH1, ENO1	12	6.25E-14
hexose metabolic process	ALDOA, LDHB, SORD, TALDO1, PGD, ALDOB, UGDH, FBP1, TPI1, PGLS, PKM2, PGM1, GAPDH, UGP2, MDH1, ENO1	16	6.27E-14
monosaccharide catabolic process	ALDOA, LDHB, TPI1, PGLS, TALDO1, PKM2, ALDOB, PGM1, PGD, GAPDH, MDH1, ENO1	12	8.71E-14
carbohydrate catabolic process	ALDOA, LDHB, TPI1, PGLS, TALDO1, SORD, PKM2, ALDOB, PGM1, PGD, GAPDH, MDH1, ENO1	13	4.14E-13
monosaccharide metabolic process	ALDOA, LDHB, SORD, TALDO1, PGD, ALDOB, UGDH, FBP1, TPI1, PGLS, PKM2, PGM1, GAPDH, UGP2, MDH1, ENO1	16	5.31E-13
coenzyme metabolic process	LDHB, TALDO1, ACO1, ALDOB, PGD, GSTT1, SOD1, HAGH, TPI1, PGLS, QPRT, GLO1, MDH1	13	2.43E-11
cofactor metabolic process	LDHB, ALAD, TALDO1, ACO1, ALDOB, PGD, GSTT1, SOD1, HAGH, TPI1, PGLS, QPRT, GLO1, MDH1	14	2.62E-11
glycolysis	ALDOA, LDHB, TPI1, PKM2, ALDOB, PGM1, GAPDH, MDH1, ENO1	9	1.15E-10

Supplementary Table 6: Clinical characteristics of Joslin Medalist for metabolomics analysis

Characteristics	Protected group (N=16)	Risk group (N=13)	P value
Age (yr)	63(57, 70)	73(66, 77)	0.02
Female	50.00%	38.00%	0.71
Duration of Disease (yr)	53(51, 59)	54(52, 62)	0.31
Age at Diagnosis (yr)	6(4, 11)	14(10, 19)	0.01
HbA1c (%)	8.8(8.0, 9.1)	6.5(6.0, 6.9)	<0.0001
ACR ( $\mu\text{g}/\text{mg}$ )	16(8, 23)	187(96, 590)	<0.0001
eGFR ( $\text{mL}/\text{min}/1.73\text{m}^2$ )	93(63, 97)	28(16, 31)	<0.0001
Serum creatinine (mg/dl)	0.9(0.7, 1.1)	2.2(1.7, 3.5)	<0.0001
Hypertension	50%	56%	0.11

Values are expressed as n (%) or median (quartile 1, quartile 3). HbA1c, hemoglobin A1c;

ACR, albumin/creatinine ratio, eGFR, estimated glomerular filtration rate.

P values were calculated using Fisher's or Wilcoxon Exact.

Supplementary Table 7: Plasma metabolomic profiling from Joslin Medalist between the Protected and Non-protected group

## (A) Plasma metabolites in glycolysis, glucose metabolism and TCA pathways

Metabolites	HMDB ID	detectability [%]	Ratio (Protected vs. Non-Protected)	Nominal significance (p)	Significance adjusted for the multiple testing (q)
sorbitol	HMDB00247	100	0.24	1.93E-07	1.0 x 10 <sup>-5</sup>
aconitate	HMDB00072	100	0.28	1.18E-06	3.0 x 10 <sup>-5</sup>
isocitrate	HMDB00193	100	0.66	2.01E-04	2.2 x 10 <sup>-3</sup>
fumarate/maleate/alpha-ketoisovalerate	HMDB00134	100	0.41	1.45E-03	9.0 x 10 <sup>-3</sup>
alpha-ketoglutarate	HMDB00208	100	0.77	3.19E-03	0.018
serine	HMDB00187	100	1.30	4.45E-03	0.024
F16DP/F26DP/G16DP	HMDB01058	100	0.63	1.77E-02	0.065
F1P/F6P/G1P/G6P	HMDB01401	100	0.76	5.53E-02	0.145
lactate	HMDB00190	100	0.78	9.49E-02	0.176
DHAP/glyceraldehyde 3P	HMDB01473	100	1.11	2.53E-01	0.323
PEP	HMDB00263	100	1.15	2.67E-01	0.325
succinate	HMDB00254	100	1.06	3.39E-01	0.361
citrate	HMDB00094	100	0.96	6.86E-01	0.515
ribose-5-P/ribulose5-P	HMDB01548	100	1.01	7.22E-01	0.537
3-phosphoglycerate	HMDB00807	100	1.05	7.66E-01	0.554
fructose/glucose/galactose	HMDB00122	100	0.99	9.60E-01	0.605

## (B) Other plasma metabolites

Metabolites	HMDB ID	detectability [%]	Ratio (Protected vs. Non-Protected)	Nominal significance (p)	Significance adjusted for the multiple testing (q)
allantoin	HMDB00462	100	0.21	2.23E-07	1.0 x 10 <sup>-5</sup>
adipate	HMDB00448	100	0.41	2.72E-07	1.0 x 10 <sup>-5</sup>
creatinine	HMDB00562	100	0.55	8.55E-07	3.0 x 10 <sup>-5</sup>
glucuronate	HMDB00127	100	0.24	9.28E-07	3.0 x 10 <sup>-5</sup>
cytosine	HMDB00630	100	0.31	3.71E-06	8.0 x 10 <sup>-5</sup>
SDMA	HMDB03334	100	0.46	8.32E-06	1.6 x 10 <sup>-4</sup>
cystathionine	HMDB00099	100	0.10	9.38E-06	1.6 x 10 <sup>-4</sup>
kynurenic acid	HMDB00715	100	0.20	1.17E-05	1.8 x 10 <sup>-4</sup>
5-methyl-THF	HMDB01396	100	0.25	3.07E-05	4.3 x 10 <sup>-4</sup>
trimethylamine-N-oxide	HMDB00925	100	0.45	7.05E-05	9.1 x 10 <sup>-4</sup>
quinolinate	HMDB00232	100	0.23	1.44E-04	1.7 x 10 <sup>-3</sup>
lactose	HMDB00186	100	0.42	3.23E-04	3.1 x 10 <sup>-3</sup>
aminoisobutyric acid	HMDB02166	100	0.27	3.47E-04	3.1 x 10 <sup>-3</sup>
xanthosine	HMDB00299	100	0.51	4.14E-04	3.4 x 10 <sup>-3</sup>
urate	HMDB00289	100	0.80	4.15E-04	3.4 x 10 <sup>-3</sup>
oxalate	HMDB02329	100	0.62	4.37E-04	3.4 x 10 <sup>-3</sup>
butyrylcarnitine/isobutyrylcarnitine	HMDB02013/	100	0.40	5.41E-04	4.0 x 10 <sup>-3</sup>
tryptophan	HMDB00929	100	1.58	5.99E-04	4.2 x 10 <sup>-3</sup>
acetylglycine	HMDB00532	100	0.44	1.03E-03	6.9 x 10 <sup>-3</sup>
acetylcarnitine	HMDB00201	100	0.61	1.28E-03	8.3 x 10 <sup>-3</sup>
adenine	HMDB00034	100	0.69	2.46E-03	0.015
orotate	HMDB00226	100	0.54	3.78E-03	0.021
valerylcarnitine/ isovalerylcarnitine/ 2-methylbutyroylcarnitine	HMDB13128/	100	0.56	4.65E-03	0.024
butyrobetaine	HMDB01161	100	0.69	4.77E-03	0.024
kynurenine	HMDB00684	100	0.73	4.92E-03	0.024
malonylcarnitine	HMDB02095	100	0.28	5.74E-03	0.027
hippurate	HMDB00714	100	0.19	6.08E-03	0.027
choline	HMDB00097	100	0.79	6.13E-03	0.027
sucrose	HMDB00258	100	0.53	9.57E-03	0.041
ADP	HMDB01341	100	1.60	1.00E-02	0.042

lysine	HMDB00182	100	1.24	1.22E-02	0.050
GDP	HMDB01201	100	1.56	1.33E-02	0.053
thymine	HMDB00262	100	0.76	1.36E-02	0.053
2-deoxycytidine	HMDB00014	100	0.82	1.72E-02	0.065
guanosine	HMDB00133	100	1.43	1.98E-02	0.071
arginine	HMDB00517	100	1.34	2.62E-02	0.092
anthranilic acid	HMDB01123	100	0.74	2.74E-02	0.095
propionylcarnitine	HMDB00824	100	0.69	3.14E-02	0.105
C56:7 TAG	HMDB05462	100	0.71	3.17E-02	0.105
C54:5 TAG	HMDB05385	100	0.81	3.76E-02	0.122
C36:3 PC	n/a	100	0.63	3.87E-02	0.122
C54:6 TAG	HMDB05391	100	0.76	3.94E-02	0.122
NAD	HMDB00902	100	0.64	4.14E-02	0.126
cAMP	HMDB00058	100	0.75	4.22E-02	0.126
C20:5 CE	HMDB06731	100	1.67	4.31E-02	0.127
C24:1 SM	HMDB12107	100	0.88	4.69E-02	0.135
C52:5 TAG	HMDB05380	100	0.87	4.90E-02	0.138
valine	HMDB00883	100	1.21	4.99E-02	0.138
C54:7 TAG	HMDB05447	100	0.66	5.39E-02	0.145
C56:9 TAG	HMDB05448	100	0.84	5.51E-02	0.145
ADMA	HMDB01539	100	0.83	5.59E-02	0.145
GMP	HMDB01397	100	1.41	5.69E-02	0.145
heptanoylcarnitine	HMDB13238	100	0.53	6.22E-02	0.150
citrulline	HMDB00904	100	0.73	6.26E-02	0.150
glutamine	HMDB00641	100	1.14	6.29E-02	0.150
dimethylglycine	HMDB00092	100	0.78	6.31E-02	0.150
NMMA	n/a	100	0.83	6.41E-02	0.150
hypoxanthine	HMDB00157	100	0.37	6.47E-02	0.150
C36:1 DAG	HMDB07216	100	0.87	6.60E-02	0.151
C54:1 TAG	HMDB05395	100	0.81	6.75E-02	0.152
inosine	HMDB00195	100	0.32	6.98E-02	0.155
UMP	HMDB00288	100	1.38	7.08E-02	0.155
histidine	HMDB00177	100	1.14	7.26E-02	0.155
C18:1 CE	HMDB00918	100	1.35	7.87E-02	0.165
pantothenate	HMDB00210	100	0.64	8.14E-02	0.169
thyroxine	HMDB00248	100	1.19	8.31E-02	0.170
C34:1 PC	HMDB07972	100	0.68	8.54E-02	0.170
pyroglutamic acid	HMDB00267	100	0.73	8.54E-02	0.170
C56:2 TAG	HMDB05404	100	0.83	8.71E-02	0.171
spermidine	HMDB01257	100	1.20	8.90E-02	0.172
thiamine	HMDB00235	100	0.09	8.96E-02	0.172
C18:0 LPC	HMDB10384	100	1.11	9.16E-02	0.174
C58:11 TAG	HMDB10531	100	1.14	9.28E-02	0.174
C18:0 SM	HMDB01348	100	0.91	9.63E-02	0.176
uridine	HMDB00296	100	1.23	9.82E-02	0.177
hydroxyphenylpyruvate	HMDB06915	100	0.76	1.08E-01	0.191
oleylcarnitine	HMDB05065	100	0.63	1.08E-01	0.191
malate	HMDB00156	100	0.81	1.10E-01	0.192
uracil	HMDB00300	100	0.66	1.13E-01	0.193
C22:1 SM	HMDB12104	100	1.24	1.13E-01	0.193
C18:0 LPE	HMDB11130	100	1.16	1.14E-01	0.193
C14:0 CE	HMDB06725	100	1.29	1.16E-01	0.194
UDP	HMDB00295	100	1.27	1.19E-01	0.196
UDP-glucuronate	HMDB00935	100	1.23	1.24E-01	0.203
C24:0 SM	HMDB11697	100	1.10	1.30E-01	0.211
C54:10 TAG	n/a	100	0.76	1.33E-01	0.212
linoleyl_carnitine	HMDB06469	100	0.67	1.33E-01	0.212
C52:2 TAG	HMDB05369	100	0.79	1.35E-01	0.212

histamine	HMDB00870	100	1.37	1.41E-01	0.219
C34:1 DAG	HMDB07102	100	0.70	1.46E-01	0.224
C32:0 PC	HMDB07871	100	1.16	1.48E-01	0.226
threonine	HMDB00167	100	1.11	1.64E-01	0.247
glutamate	HMDB00148	100	0.56	1.74E-01	0.261
C56:1 TAG	HMDB05396	100	0.82	1.81E-01	0.265
niacinamide	HMDB01406	100	1.17	1.84E-01	0.265
C52:3 TAG	HMDB05384	100	0.76	1.84E-01	0.265
C56:3 TAG	HMDB05410	100	0.85	1.85E-01	0.265
serotonin	HMDB00259	100	1.73	1.86E-01	0.265
C18:0 CE	HMDB10368	100	1.13	1.91E-01	0.271
propionate	HMDB00237	100	0.80	1.95E-01	0.273
salicylurate	HMDB00840	100	0.52	2.00E-01	0.278
phenylalanine	HMDB00159	100	0.90	2.13E-01	0.292
C48:0 TAG	HMDB05356	100	1.32	2.17E-01	0.296
palmitoylcarnitine	HMDB00222	100	0.77	2.28E-01	0.309
4-pyridoxate	HMDB00017	100	0.24	2.35E-01	0.310
methionine	HMDB00696	100	1.08	2.35E-01	0.310
C36:1 PC	HMDB08038	100	1.15	2.53E-01	0.323
glycocholate	HMDB00138	100	1.77	2.55E-01	0.323
C56:4 TAG	HMDB05398	100	0.87	2.56E-01	0.323
methionine sulfoxide	HMDB02005	100	0.83	2.61E-01	0.323
tyrosine	HMDB00158	100	1.10	2.61E-01	0.323
C38:3 PC	n/a	100	0.86	2.62E-01	0.323
C52:1 TAG	HMDB05367	100	0.89	2.66E-01	0.325
C34:2 DAG	HMDB07103	100	1.11	2.72E-01	0.328
3-hydroxykynurenate	HMDB00732	100	1.13	2.75E-01	0.329
lauroylcarnitine	HMDB02250	100	0.66	2.85E-01	0.335
C50:1 TAG	HMDB05360	100	0.79	2.89E-01	0.338
C22:0 SM	HMDB12103	100	0.95	2.96E-01	0.343
C50:0 TAG	HMDB05357	100	1.03	3.09E-01	0.355
leucine	HMDB00687	100	1.11	3.10E-01	0.355
aspartate	HMDB00191	100	0.83	3.13E-01	0.355
C38:2 PC	HMDB08270	100	0.95	3.17E-01	0.357
C38:4 PC	HMDB08048	100	0.95	3.20E-01	0.358
alpha-glycerophosphocholine	HMDB00086	100	0.92	3.29E-01	0.360
C58:10 TAG	HMDB05476	100	0.88	3.31E-01	0.360
C58:12 TAG	HMDB10514	100	0.83	3.32E-01	0.360
C48:1 TAG	HMDB05359	100	1.06	3.34E-01	0.360
C20:3 CE	HMDB06736	100	1.07	3.39E-01	0.361
glycodeoxycholate/glycochenodeoxycholate	HMDB00631	100	0.96	3.50E-01	0.369
C40:6 PC	HMDB08057	100	0.88	3.53E-01	0.369
C54:4 TAG	HMDB05370	100	0.83	3.54E-01	0.369
carnitine	HMDB00062	100	0.91	3.59E-01	0.372
C20:3 LPC	HMDB10388	100	0.86	3.62E-01	0.372
C18:2 LPE	HMDB11507	100	1.07	3.64E-01	0.372
isoleucine	HMDB00172	100	1.08	3.71E-01	0.374
C50:3 TAG	HMDB05433	100	0.88	3.72E-01	0.374
taurodeoxycholate/taurochenodeoxycholate	HMDB00896	100	0.58	3.73E-01	0.374
C20:4 LPC	HMDB10395	100	1.06	3.80E-01	0.379
pipecolic acid	HMDB00070	100	1.29	3.89E-01	0.383
C18:2 CE	HMDB00610	100	1.05	3.91E-01	0.383
C18:2 LPC	HMDB10386	100	1.06	3.91E-01	0.383
NADP	HMDB00217	100	1.12	3.95E-01	0.384
nonanoylcarnitine	HMDB13288	100	0.79	3.98E-01	0.385
C16:1 SM	n/a	100	0.97	4.02E-01	0.386
C34:2 PC	HMDB07973	100	0.97	4.05E-01	0.386
C16:1 LPC	HMDB10383	100	1.09	4.09E-01	0.386

C18:1 LPC	HMDB02815	100	1.06	4.10E-01	0.386
C16:0 LPC	HMDB10382	100	1.04	4.15E-01	0.388
C22:6 LPE	HMDB11526	100	1.06	4.18E-01	0.388
hexanoylcarnitine	HMDB00705	100	0.62	4.19E-01	0.388
myristoylcarnitine	HMDB05066	100	0.78	4.24E-01	0.390
decanoylcarnitine	HMDB00651	100	0.59	4.39E-01	0.398
C50:4 TAG	HMDB05435	100	0.79	4.41E-01	0.398
C20:5 LPC	HMDB10397	100	1.05	4.43E-01	0.398
C54:8 TAG	HMDB10518	100	0.77	4.50E-01	0.402
creatine	HMDB00064	100	0.91	4.53E-01	0.403
C16:1 CE	HMDB00658	100	1.13	4.58E-01	0.405
C46:1 TAG	HMDB10412	100	1.06	4.63E-01	0.407
C18:3 CE	HMDB10370	100	0.98	4.66E-01	0.407
C16:0 CE	HMDB00885	100	1.05	4.77E-01	0.415
chenodeoxycholate/deoxycholate	HMDB00518	100	1.05	4.82E-01	0.416
phosphoethanolamine	HMDB00224	100	1.07	4.92E-01	0.419
betaine	HMDB00043	100	1.03	4.93E-01	0.419
1-methylhistamine	HMDB00898	100	1.14	4.94E-01	0.419
C20:4 CE	HMDB06726	100	1.05	5.05E-01	0.427
phosphocholine	HMDB01565	100	1.10	5.10E-01	0.427
C56:8 TAG	HMDB05392	100	1.07	5.18E-01	0.431
asparagine	HMDB00168	100	1.04	5.32E-01	0.440
C58:9 TAG	HMDB05463	100	0.92	5.44E-01	0.448
C52:6 TAG	HMDB05436	100	0.92	5.48E-01	0.449
C34:4 PC	HMDB07883	100	1.02	5.52E-01	0.449
octanoylcarnitine	HMDB00791	100	0.53	5.55E-01	0.449
C58:8 TAG	HMDB05413	100	1.05	5.74E-01	0.460
alanine	HMDB00161	100	1.04	5.76E-01	0.460
C58:6 TAG	HMDB05458	100	0.91	5.77E-01	0.460
ornithine	HMDB00214	100	0.96	5.85E-01	0.464
alpha-glycerophosphate	HMDB00126	100	1.04	5.94E-01	0.466
AMP	HMDB00045	100	1.02	6.03E-01	0.466
C18:2 SM	HMDB12101	100	1.05	6.04E-01	0.466
C14:0 SM	HMDB12097	100	1.04	6.04E-01	0.466
xanthine	HMDB00292	100	1.03	6.05E-01	0.466
C36:2 PC	HMDB08039	100	0.98	6.05E-01	0.466
C22:6 LPC	HMDB10404	100	1.00	6.59E-01	0.502
C36:2 DAG	HMDB07218	100	0.89	6.68E-01	0.507
C16:0 LPE	HMDB11503	100	0.97	6.80E-01	0.514
C16:0 SM	HMDB10169	100	0.99	7.14E-01	0.533
C36:4 PC-A	HMDB07983	100	0.99	7.40E-01	0.543
C38:5 PC	HMDB08114	100	0.97	7.41E-01	0.543
1-methylnicotinamide	HMDB00699	100	1.07	7.69E-01	0.554
cotinine	HMDB01046	100	4.36	7.70E-01	0.554
adenosine	HMDB00050	100	0.34	7.75E-01	0.555
C18:1 SM	HMDB12101	100	0.98	7.78E-01	0.555
C32:2 PC	HMDB07874	100	1.00	7.82E-01	0.555
C48:3 TAG	HMDB05432	100	0.95	7.93E-01	0.560
cis/trans-hydroxyproline	HMDB00725	100	1.14	7.99E-01	0.560
C22:6 CE	HMDB06733	100	0.99	8.00E-01	0.560
C20:4 LPE	HMDB11517	100	0.98	8.12E-01	0.564
C48:4 TAG	n/a	100	0.95	8.13E-01	0.564
C48:2 TAG	HMDB05376	100	0.95	8.22E-01	0.568
C56:6 TAG	HMDB05456	100	0.95	8.48E-01	0.583
C32:1 PC	HMDB07873	100	0.97	8.59E-01	0.586
beta-alanine	HMDB00056	100	0.96	8.66E-01	0.586
homovanillate	HMDB00118	100	1.00	8.68E-01	0.586
C50:2 TAG	HMDB05377	100	0.94	8.86E-01	0.586

sarcosine	HMDB00271	100	1.00	8.90E-01	0.586
glycine	HMDB00123	100	1.00	8.90E-01	0.586
taurine	HMDB00251	100	0.96	8.91E-01	0.586
C38:6 PC	HMDB07991	100	1.00	8.91E-01	0.586
glucose	HMDB03345	100	0.97	8.96E-01	0.586
C36:4 PC-B	HMDB08138	100	1.00	8.98E-01	0.586
C50:5 TAG	HMDB10471	100	0.91	9.04E-01	0.587
hexacosanoyl_carnitine	HMDB06347	100	1.00	9.06E-01	0.587
C34:3 PC	HMDB08006	100	1.00	9.12E-01	0.588
stearoylcarnitine	HMDB00848	100	0.91	9.21E-01	0.592
C54:2 TAG	HMDB05403	100	0.93	9.51E-01	0.605
C18:1 LPE	HMDB11506	100	0.98	9.52E-01	0.605
C58:7 TAG	n/a	100	0.97	9.61E-01	0.605
proline	HMDB00162	100	0.99	9.65E-01	0.605
C46:2 TAG	HMDB10419	100	0.90	9.70E-01	0.605
C52:4 TAG	HMDB05363	100	0.90	9.84E-01	0.612
putrescine	HMDB01414	100	1.06	9.91E-01	0.614
cytidine	HMDB00089	97	0.37	2.78E-04	0.003
IMP	HMDB00175	97	1.41	2.82E-01	0.334
C14:0 LPC	HMDB10379	97	1.17	3.28E-01	0.360
C44:1 TAG	n/a	93	0.63	4.32E-01	0.395
5-HIAA	HMDB00763	90	1.52	2.52E-01	0.323
taurocholate	HMDB00036	86	0.46	5.09E-01	0.427
glycerol	HMDB00131	86	1.19	6.56E-01	0.502
C56:5 TAG	HMDB05406	83	0.96	8.95E-01	0.586
C60:12 TAG	HMDB05478	83	0.97	9.61E-01	0.605
glutathione oxidized	HMDB03337	76	1.41	2.35E-01	0.310
cholate	HMDB00619	76	1.06	8.94E-01	0.586
UDP-galactose/UDP-glucose	HMDB00286	72	1.13	7.29E-01	0.539
xanthureneate	HMDB00881	69	0.63	7.18E-02	0.155
C44:0 TAG	n/a	69	0.89	7.60E-01	0.554
C42:0 TAG	n/a	66	NA	NA	NA
acetylcholine	HMDB00895	62	NA	NA	NA
carnitine C20:4	n/a	62	NA	NA	NA
C46:0 TAG	HMDB10411	55	NA	NA	NA
CDP	HMDB01546	48	NA	NA	NA
homocystine	HMDB00676	48	NA	NA	NA
anserine	HMDB00194	45	NA	NA	NA
guanine	HMDB00132	45	NA	NA	NA
N-carbamoyl-beta-alanine	HMDB00026	45	NA	NA	NA
cAMP	HMDB00058	41	NA	NA	NA
arachidonyl carnitine	HMDB06455	24	NA	NA	NA
2-deoxyadenosine	HMDB00101	14	NA	NA	NA
carnosine	HMDB00033	14	NA	NA	NA
erythrose-4-phosphate	HMDB01321	14	NA	NA	NA
5'-adenosylhomocysteine	HMDB00939	10	NA	NA	NA
GABA	HMDB00112	10	NA	NA	NA
2-amino adipate	HMDB00510	3	NA	NA	NA
adenylosuccinate	HMDB00536	3	NA	NA	NA
C54:3 TAG	HMDB05405	3	NA	NA	NA
3-hydroxyanthranilic acid	HMDB01476	0	NA	NA	NA
5-aminolevulinic acid	HMDB01149	0	NA	NA	NA
5-hydroxytryptophan	HMDB00472	0	NA	NA	NA
argininosuccinate	HMDB00052	0	NA	NA	NA
bilirubin	HMDB00054	0	NA	NA	NA
CMP	HMDB00095	0	NA	NA	NA
cobalamin	HMDB02174	0	NA	NA	NA
dCMP	HMDB01202	0	NA	NA	NA

dTMP	HMDB01227	0	NA	NA	NA
dUMP	HMDB01409	0	NA	NA	NA
folate	HMDB00121	0	NA	NA	NA
glutathione reduced	HMDB00125	0	NA	NA	NA
homocysteine	HMDB00742	0	NA	NA	NA
homogentistate	HMDB00130	0	NA	NA	NA
methyl-hydroxyisobutyric acid	n/a	0	NA	NA	NA
methylmalonate	HMDB00202	0	NA	NA	NA
mevalonic acid	HMDB00227	0	NA	NA	NA
nicotinate	HMDB01488	0	NA	NA	NA
nicotinic acid mononucleotide	HMDB01132	0	NA	NA	NA
phosphotyrosine	HMDB06049	0	NA	NA	NA
pyridoxal 5-phosphate	HMDB01491	0	NA	NA	NA
pyruvate	HMDB00243	0	NA	NA	NA
thymidine	HMDB00273	0	NA	NA	NA
triiodothyronine	HMDB00265	0	NA	NA	NA
XMP	HMDB01554	0	NA	NA	NA

HMDB ID - Human Metabolome Database identifier; TCA - tricarboxylic acid cycle;

q, positive false discovery rate adjusted significance for multiple testing.

Supplemental Table 8: Joslin Medalist kidney pathology assessment

SID	RPS DN Class	Global GS (%)	GBM thickness (microns±SD)	Glomerular Tuft Mean Area ( $\mu\text{m}^2$ )	IFTA (0-3)
G15	0	0.19	303±31	17083	1
G3	I	0.23	452±68	24125	1
G4	I	0.19	493±80	23589	1
G7	I	0.03	443±115	24728	1
G19	I	0.07	480±115	23239	1
G27	0	0.05	379±39	21907	1
G13	I or IIA	0.11	535±80	22894	2
G9	IIB	0.11	421±75	17219	1
G12	IIB	0.13	479±98	15566	1
G17	IIB	0.04	509±126	18350	1
G26	IIB	0.25	493±157	17099	2
G29	IIB	0.49	1008±226	35946	3
G24	IIB	0.65	527±89	13822	2
G5	III	0.39	696±245	30554	2
G10	III	0.16	691±198	24972	2
G18	IIB	0.06	514±94	22695	2
G20	III	0.35	711±132	29082	2
G22	III	0.09	625±165	20007	1

RPS, Renal Pathology Society; GS, glomerulosclerosis; GBM, glomerular basement membrane;  
 IFTA, interstitial fibrosis and tubular atrophy; IAH, index of arteriolar hyalinosis; SD, standard deviation.

Mesangial expansion	Interstitial Inflammation	Arteriosclerosis	Arteriolar Hyalinosis	IAH
no-mild	1	2	2	1.63
no	0	2	0	1.25
no	1	1	1	1.36
no	0	0	0	1.07
no-mild	1	2	2	1.69
no	1	2	1	1.10
mild-moderate	1	2	2	2.02
moderate	1	1	1	1.45
mild-moderate	1	2	2	1.88
moderate	1	2	2	1.78
moderate	1	2	2	2.07
moderate	1	2	2	2.32
moderate	1	2	1	1.52
severe	1	2	2	2.34
severe with focal nodules	1	2	2	2.73
moderate with focal nodules	1	2	2	2.34
moderate with focal small nodules	1	2	2	2.81
moderate with focal small nodules	1	2	2	2.35

Supplemental Table 8

Nature Medicine: doi:10.1038/nm.4328

Supplemental Table 9: Clinical characteristics of non-Medalist individual with diabetes

<b>SID</b>	<b>Diabetes</b>	<b>Duration (years)</b>	<b>Age (years)</b>	<b>Sex</b>	<b>BMI (kg/m^2)</b>	<b>RPS DN Class</b>	<b>Glucose (mg/dL)</b>	<b>Creatinine (mg/dL)</b>	<b>HTN (yrs)</b>
T1DK1	T1DM	21	32	M	20.6	IIB	159	1.8	Yes
T1DK2	T1DM	26	49	F	41.5	IIB	281	4.3	Yes
T2DK1	T2DM	3	50	M	29.2	IV	202	7.5	Yes
T2DK2	T2DM	10	43	M	29.6	IIA	295	4.5	Yes
T2DK3	T2DM	15	62	F	40.2	IIA	214	1.5	Yes
T2DK4	T2DM	10	70	F	25.7	0	334	1.4	UNK
T2DK5	T2DM	15	61	M	20	I	138	2.4	Yes
T2DK6	T2DM	4	64	M	28.2	IIA	358	1.5	Yes
T2DK7	T2DM	1 month	62	M	23.2	0	146	1.3	Yes
T2DK8	T2DM	18	63	F	28	IIA	137	0.6	Yes

RPS DN class, Renal Pathology Society DN Classification; HTN, hypertension; UNK, unknown.

Supplementary Table 10: Metabolic characteristics of nondiabetic and diabetic WT and PPKM2KO mice

Characteristics	Nondiabetic		Diabetic	
	WT	PPKM2KO	WT	PPKM2KO
Body weight (g)	37.3±6.6 (n=14)	40.9±5.1 (n=11)	26.0±2.5*** (n=13)	26.8±2.4###, NS (n=21)
Fasting blood glucose (mg/dl)	144±35 (n=14)	153±27 (n=11)	521±87*** (n=10)	519±51###, NS (n=16)
SBP (mmHg)	99±4 (n=8)	115±24 (n=4)	109±13 (n=6)	106±15NS (n=6)
Kidney weight (mg)	155.7±15.7 (n=9)	169.2±20.8 (n=11)	229.5±24.3*** (n=8)	236.3±48.3###, NS (n=5)

Data were collected post-STZ 6 months and are presented as mean±SD. SBP, systolic blood pressure.

\*\*\* P<0.001 vs. Nondiabetic WT; ### P<0.001 vs. Nondiabetic PPKM2KO; NS, not significant vs. Diabetic WT.

Number of mice in each group is shown.

Supplementary Table 11: Metabolic characteristics of nondiabetic and diabetic DBA2/J mice treated with TEPP-46

	Nondiabetic Vehicle	Diabetic Vehicle	Diabetic TEPP-46
Body weight (g)	36.1±5.2 (n=9)	22.9±0.7 *** (n=8)	23.6±1.3**** (n=11)
Fasting blood glucose (mg/dl)	120±20 (n=9)	520±80 *** (n=8)	497±137*** (n=11)
SBP (mmHg)	105±9 (n=12)	110±17 (n=7)	105±9 (n=7)
Kidney weight (mg)	263.1±27.9 (n=6)	297.3±31.2 (n=8)	282.1±28.0 (n=11)
KW/BW (mg/g)	7.1±0.9 (n=6)	13.0±1.6 *** (n=8)	11.9±0.98*** (n=11)
HW/BW (mg/g)	4.97±0.57 (n=6)	5.61±0.50 (n=12)	5.18±0.27 (n=4)

Mice were treated with either vehicle or TEPP-46 for further 3 months after 3 months of diabetes.

Data were collected post-STZ 6 months and are presented as mean±SD.

SBP, systolic blood pressure; KW/BW, kidney weight/body weight ratio; HW/BW, heart weight/body weight ratio;

\*\*\* P<0.001 vs. Nondiabetic Vehicle; Number of mice in each group is shown.

Supplementary Table 12: Blood counts and plasma chemistries of DBA2/J mice treated with TEPP-46 for further 3 months after 3 months of diabetes

Treatment group	WBC ( $\times 10^3$ )	HEMATOCRIT (% PCV)	PLATELETS ( $\times 10^3$ )	Aspartate Aminotransferase (IU/L)	Alanine Aminotransferase (IU/L)	Gamma-Glutamyl Transferase (IU/L)	TOTAL BILIRUBIN (mg/dL)	BUN (mg/dL)	Creatinine (mg/dL)	Total cholesterol (mg/dl)	Triglyceride (mg/dl)
Nondiabetic Vehicle	13.9 $\pm$ 5.2 (n=10)	42.0 $\pm$ 3.4 (n=10)	712.6 $\pm$ 62.0 (n=10)	117 $\pm$ 49 (n=6)	23 $\pm$ 19 (n=6)	4 $\pm$ 1 (n=6)	0.3 $\pm$ 0.1 (n=6)	20 $\pm$ 6 (n=10)	0.11 $\pm$ 0.05 (n=6)	106.6 $\pm$ 10.5 (n=6)	183.4 $\pm$ 27.5 (n=6)
Diabetic Vehicle	17.9 $\pm$ 5.6 (n=16)	46.6 $\pm$ 6.0* (n=16)	960.8 $\pm$ 212.2*** (n=16)	364 $\pm$ 175* (n=5)	232 $\pm$ 78** (n=5)	6 $\pm$ 5 (n=5)	2.1 $\pm$ 0.2* (n=5)	23 $\pm$ 14 (n=9)	0.10 $\pm$ 0.06 (n=7)	155.4 $\pm$ 45.1* (n=7)	312.8 $\pm$ 203.0 (n=7)
Diabetic TEPP-46	13.6 $\pm$ 2.0# (n=9)	45.4 $\pm$ 4.0 (n=9)	897.1 $\pm$ 219.9* (n=9)	269 $\pm$ 84* (n=5)	179 $\pm$ 89* (n=5)	6 $\pm$ 2 (n=5)	1.0 $\pm$ 0.1*** (n=5)	25 $\pm$ 8 (n=9)	0.10 $\pm$ 0.03 (n=6)	154.6 $\pm$ 29.9*** (n=9)	242.1 $\pm$ 59.2 (n=9)

Data are presented as mean $\pm$ SD. WBC: White Blood Cells; PCV: Packed Cell Volume.

\*\*\* P<0.001, \*\*P<0.005, \* P<0.05 vs. Nondiabetic Vehicle; # P<0.05 vs. Diabetic Vehicle. Number of mice in each group is shown.

Supplementary Table 13: Metabolic characteristics of nondiabetic and diabetic *eNos* KO mice treated with TEPP-46

	Nondiabetic Vehicle	Diabetic Vehicle	Diabetic TEPP-46
Body weight (g)	27.3±2 (n=5)	21.6±0.7** (n=8)	21.7±1.6*** (n=7)
Fasting blood glucose (mg/dl)	105±21 (n=5)	539±28*** (n=8)	455±109 *** (n=7)
SBP (mmHg)	133±6.6 (n=10)	128±9* (n=9)	123±6 (n=9)
Plasma creatinine (mg/dL)	0.17±0.03 (n=5)	0.15±0.04 (n=7)	0.11±0.03 (n=5)
BUN (mg/dL)	30±6(n=5)	39±10 (n=7)	31±11(n=6)
Kidney weight (mg)	135.7±13.8 (n=5)	178.2±10.5**(n=8)	146.5±23.5 ## (n=7)

*eNos* KO mice were treated with either vehicle or TEPP-46 for 6 wks after 7 wks of diabetes.

Data were collected post-STZ 13 weeks. SBP, systolic blood pressure.

Data are presented as mean±SD. \*\*\*P<0.001, \*\*P<0.005, \*P<0.05 vs. Nondiabetic Vehicle;  
##P<0.005 vs. Diabetic Vehicle. Number of mice in each group is shown.

Supplementary Table 14: SYBR green RT-qPCR primer sequences

Gene symbol	Forward primer (5'-3')	Reverse primer (5'-3')
<i>mFn</i>	CGAGGTGACAGAGACCACAA	CTGGAGTCAAGCCAGACACA
<i>mCol1</i>	GTCCAACCCCCAAAGAC	CATCTCTGAGTTGGTGTACGT
<i>mCol3a</i>	ACAGCTGGTGAACCTGGAAG	ACCAGGAGATCCATCTCGAC
<i>mCol4a</i>	GACAGCCAGGTTGACAGGT	GGCAGCTCTCTCCTTCTGA
<i>mTgfβ1</i>	CCTGAGTGGCTGTCTTTGA	CGTGGAGTTGTTATCTTGCTG
<i>36b4</i>	GCTCCAAGCAGATGCAGCA	CCGGATGTGAGGCAGCAG
<i>mPpargc1a</i>	GTCAACAGCAAAAGCCACAA	TCTGGGGTCAGAGGAAGAGA
<i>mOpa1</i>	GTGTGCTGGAAATGATTGCTC	TGGTGAGATCAAATTCCCGAG
<i>mPkm1</i>	GCTGTTGAAGAGCTTGTGC	TTATAAGAGGCCTCCACGCT
<i>mPkm2</i>	TGTCTGGAGAACAGCCAAG	TCCTCGAATAGCTGCAAGTG