

## Supplementary material

Supplementary table 1:

(A)		(B)					
Group	Creatinine (nmol/mg protein)	Age	Group	BUN (mg/dl)	Age	Group	BUN (mg/dl)
WT	0,080	10 weeks	WT	30,650	23 weeks	WT	48,411
WT	0,081		WT	34,390		WT	46,542
WT	0,076		WT	32,520		WT	30,654
WT	0,052		WT	40,000		WT	34,393
<i>Pcca</i> <sup>-/-</sup>	0,135		<i>Pcca</i> <sup>-/-</sup>	48,410		<i>Pcca</i> <sup>-/-</sup>	72,710
<i>Pcca</i> <sup>-/-</sup>	0,200		<i>Pcca</i> <sup>-/-</sup>	72,710		<i>Pcca</i> <sup>-/-</sup>	64,299
<i>Pcca</i> <sup>-/-</sup>	0,502		<i>Pcca</i> <sup>-/-</sup>	46,540		<i>Pcca</i> <sup>-/-</sup>	58,692
<i>Pcca</i> <sup>-/-</sup>	0,372		<i>Pcca</i> <sup>-/-</sup>	50,280		<i>Pcca</i> <sup>-/-</sup>	54,019

Supplementary table 1: (A) Absolute concentrations of creatinine measured in crude kidney lysates of 23 week old WT and *Pcca*<sup>-/-</sup>(A138T) mice. Values expressed as nmol/mg protein. N=4. (B) Absolute concentrations of blood urea nitrogen (BUN) measured in the serum of 10 and 23 week old WT and *Pcca*<sup>-/-</sup>(A138T) mice. Values expressed as mg/dl.

Supplementary table 2:

Aminothiols (nmol/mg protein)				
Group	Free Cysteine	CSSC	Free Glutathione	GSSG
WT	16,348	4,666	0,073	0,004
WT	10,335	3,735	0,037	0,003
WT	13,695	4,897	0,056	0,006
WT	16,254	6,758	0,047	0,005
<i>Pcca</i> <sup>-/-</sup>	10,134	5,195	0,064	0,008
<i>Pcca</i> <sup>-/-</sup>	7,528	3,142	0,030	0,004
<i>Pcca</i> <sup>-/-</sup>	10,176	4,358	0,050	0,005
<i>Pcca</i> <sup>-/-</sup>	13,369	5,912	0,003	0,002

Supplementary table 2: Absolute concentrations of reduced (cysteine) and oxidized cysteine (CSSC) and reduced (glutathione) and oxidized (GSSG) glutathione measured in crude kidney lysates of 23 week old WT and *Pcca*<sup>-/-</sup>(A138T) mice. Values expressed as nmol/mg protein.

**Supplementary table 3:**

Amino acids in nmol/mg protein										
Group	Alanine	Arginine	Asparagine	Aspartic Acid	GABA	Glutamine	Glutamic Acid	Glycine	Isoleucine/Leucine	
WT	1,695	1,623	288,783	1,301	0,240	1,396	9,785	429,594	2,220	
WT	1,156	0,954	156,434	1,029	0,156	1,024	7,328	283,741	1,372	
WT	1,262	1,107	181,536	1,095	0,254	1,250	8,201	390,541	1,696	
WT	1,798	1,550	192,138	1,559	0,366	1,555	10,336	472,615	2,288	
<i>Pcca</i> <sup>-/-</sup>	1,184	1,064	149,025	2,861	0,150	0,801	10,645	312,527	1,524	
<i>Pcca</i> <sup>-/-</sup>	1,402	1,198	133,272	1,893	0,165	1,310	7,182	311,480	1,844	
<i>Pcca</i> <sup>-/-</sup>	1,376	1,357	135,680	3,066	0,129	1,267	8,448	420,480	1,690	
<i>Pcca</i> <sup>-/-</sup>	1,299	1,284	173,946	2,697	0,140	1,246	8,887	336,498	1,588	

  

Amino acids in nmol/mg protein										
Group	Histidine	Lysine	Methionine	Phenylalanine	Proline	Serine	Threonine	Tryptophane	Tyrosine	Valine
WT	0,476	1,820	1,527	1,796	1,331	431,384	1,331	6,921	0,503	2,339
WT	0,275	1,019	0,545	1,174	0,775	396,956	0,794	6,624	0,300	1,433
WT	0,336	1,318	1,027	1,477	1,119	265,934	0,932	4,618	0,364	1,736
WT	0,451	1,612	1,290	1,966	1,590	274,293	1,409	6,670	0,504	2,301
<i>Pcca</i> <sup>-/-</sup>	0,376	1,431	1,022	1,294	0,886	676,148	0,886	11,581	0,380	1,541
<i>Pcca</i> <sup>-/-</sup>	0,362	1,559	1,133	1,648	1,018	642,601	0,991	5,031	0,419	1,859
<i>Pcca</i> <sup>-/-</sup>	0,365	1,638	1,178	1,491	0,973	495,360	0,960	8,384	0,403	1,709
<i>Pcca</i> <sup>-/-</sup>	0,362	1,686	1,056	1,474	0,912	493,733	0,912	7,596	0,388	1,664

**Supplementary table 3:** Absolute concentrations of amino acids measured in crude kidney lysates of 23 week old WT and *Pcca*<sup>-/-</sup>(A138T) mice. N=4. Values expressed as nmol/mg protein.

**Supplementary table 4:**

**(A)**

TCA metabolites in nmol/mg protein							
Group	alpha-ketoglutarate	Citrate	Ethylmalonate	Itaconate	Malate	Malonate	Succinate
WT	1,998	0,132	0,047	0,097	4,140	1,338	0,324
WT	2,321	0,038	0,059	0,039	4,648	1,718	0,529
WT	2,231	0,047	0,027	0,042	3,368	1,461	0,413
WT	1,877	0,059	0,023	0,087	3,344	1,281	0,439
<i>Pcca</i> <sup>-/-</sup>	3,916	0,091	0,048	0,114	7,611	2,575	0,761
<i>Pcca</i> <sup>-/-</sup>	3,021	0,074	0,140	0,084	4,666	1,984	0,749
<i>Pcca</i> <sup>-/-</sup>	4,002	0,130	0,039	0,170	9,963	2,657	1,005
<i>Pcca</i> <sup>-/-</sup>	3,752	0,108	0,100	0,120	7,444	2,438	0,745

**(B)**

Disease specific metabolites in nmol/mg protein				
Group	Lactate	MMA	Methylcitrate	Propionate
WT	60,114	0,016	0,010	0,032
WT	71,599	0,019	0,012	0,034
WT	54,963	0,014	0,007	0,031
WT	60,071	0,009	0,004	0,058
<i>Pcca</i> <sup>-/-</sup>	45,704	0,027	0,176	0,035
<i>Pcca</i> <sup>-/-</sup>	64,640	0,017	0,267	0,037
<i>Pcca</i> <sup>-/-</sup>	80,303	0,021	0,403	0,073
<i>Pcca</i> <sup>-/-</sup>	75,959	0,030	0,251	0,039

**Supplementary table 4: (A)** Absolute concentrations of tricarboxylic citric acid cycle metabolites in crude kidney lysates of 23 week old WT and *Pcca*<sup>-/-</sup>(A138T) mice. **(B)** Absolute concentrations of disease specific metabolites in crude kidney lysates of 23 week old WT and *Pcca*<sup>-/-</sup>(A138T) mice. N=4. Values expressed as nmol/mg protein.

Supplementary table 5:

Metabolite	Acylcarnitines in nmol/mg protein							
	WT	WT	WT	WT	<i>Pcca</i> <sup>-/-</sup>	<i>Pcca</i> <sup>-/-</sup>	<i>Pcca</i> <sup>-/-</sup>	<i>Pcca</i> <sup>-/-</sup>
C0	3,491	2,042	4,422	3,314	3,279	2,972	3,514	3,677
C2	1,262	0,938	1,396	1,308	1,018	0,899	1,024	0,975
C3	0,014	0,010	0,014	0,011	0,052	0,083	0,079	0,203
C4	0,011	0,007	0,007	0,007	0,004	0,006	0,005	0,007
C4OH	0,019	0,016	0,027	0,019	0,012	0,013	0,016	0,017
C4DC	0,017	0,017	0,020	0,012	0,007	0,012	0,013	0,011
C5 + C4:1OH	0,005	0,005	0,006	0,006	0,007	0,010	0,008	0,011
C5:1	0,016	0,025	0,026	0,030	0,004	0,030	0,027	0,021
C5OH	0,026	0,021	0,023	0,023	0,023	0,029	0,023	0,026
C6	0,012	0,026	0,024	0,017	0,004	0,029	0,032	0,017
C6:1	0,011	0,006	0,007	0,006	0,004	0,008	0,006	0,006
C6OH	0,018	0,015	0,019	0,021	0,008	0,017	0,024	0,017
C6DC	0,025	0,019	0,023	0,021	0,008	0,031	0,020	0,019
C8	0,012	0,019	0,019	0,014	0,007	0,021	0,029	0,011
C10	0,037	0,032	0,040	0,031	0,048	0,055	0,031	0,057
C10:1	0,024	0,019	0,026	0,027	0,004	0,014	0,023	0,017
C10:2	0,014	0,020	0,018	0,016	0,003	0,017	0,021	0,011
C12	0,014	0,014	0,014	0,018	0,003	0,012	0,020	0,010
C12OH	0,024	0,026	0,033	0,036	0,005	0,034	0,036	0,024
C14	0,008	0,007	0,005	0,007	0,004	0,008	0,007	0,011
C14:1	0,007	0,006	0,009	0,007	0,003	0,007	0,008	0,007
C14:2	0,007	0,007	0,009	0,008	0,004	0,008	0,011	0,013
C14OH	0,014	0,017	0,021	0,022	0,003	0,026	0,019	0,020
C16	0,015	0,011	0,014	0,015	0,008	0,010	0,016	0,009
C16OH	0,010	0,008	0,016	0,017	0,012	0,039	0,014	0,013
C18	0,011	0,013	0,014	0,014	0,005	0,015	0,010	0,009
C18:1	0,010	0,012	0,017	0,015	0,006	0,010	0,022	0,007
C18:2	0,011	0,012	0,013	0,012	0,005	0,009	0,016	0,007
C18OH	0,009	0,008	0,013	0,013	0,003	0,012	0,013	0,011
C18:1OH	0,011	0,008	0,012	0,014	0,003	0,013	0,013	0,011
C18:2OH	0,013	0,012	0,014	0,011	0,005	0,017	0,018	0,012

Supplementary table 5: Absolute concentrations of acylcarnitines in crude kidney lysates of 23 week old WT and *Pcca*<sup>-/-</sup>(A138T) mice. Values expressed as nmol/mg protein.

Supplementary figure 6:

(A)

Gene	Genotype	Ct value		
		4 weeks	23 weeks	40 weeks
<i>Gapdh</i>	WT	15,56	15,99	18,74
<i>Gapdh</i>	WT	15,14	15,99	18,92
<i>Fgf21</i>	WT	28,63	34,54	32,47
<i>Fgf21</i>	WT	28,91	30,35	32,33
<i>Len2</i>	WT	25,95	24,81	28,23
<i>Len2</i>	WT	25,64	25,00	28,31
<i>Havcr1</i>	WT	27,94	28,78	29,86
<i>Havcr1</i>	WT	28,00	28,14	29,71
<i>Sdh</i>	WT	22,35	22,04	21,32
<i>Sdh</i>	WT	22,34	22,21	21,35
<i>Cyts</i>	WT	17,66	18,58	18,21
<i>Cyts</i>	WT	17,80	18,84	18,17
<i>Pdha1</i>	WT	23,41	23,37	23,02
<i>Pdha1</i>	WT	23,04	23,32	22,66
<i>Gapdh</i>	WT	16,52	14,98	17,49
<i>Gapdh</i>	WT	15,84	14,73	17,16
<i>Fgf21</i>	WT	28,63	29,43	28,46
<i>Fgf21</i>	WT	29,31	28,53	28,36
<i>Len2</i>	WT	26,02	23,87	26
<i>Len2</i>	WT	26,36	24,12	26,18
<i>Havcr1</i>	WT	27,47	26,24	27,62
<i>Havcr1</i>	WT	27,64	26,37	27,36
<i>Sdh</i>	WT	23,51	21,90	20,51
<i>Sdh</i>	WT	23,06	22,18	20,74
<i>Cyts</i>	WT	18,33	17,67	17,75
<i>Cyts</i>	WT	18,55	17,85	17,83
<i>Pdha1</i>	WT	23,82	22,92	22,15
<i>Pdha1</i>	WT	24	22,87	21,93
<i>Gapdh</i>	WT	15,32	15,29	-
<i>Gapdh</i>	WT	14,93	15,37	-
<i>Fgf21</i>	WT	33,33	29,37	-
<i>Fgf21</i>	WT	33,35	29,16	-
<i>Len2</i>	WT	26,88	25,26	-
<i>Len2</i>	WT	27,04	25,35	-
<i>Havcr1</i>	WT	29,82	27,88	-
<i>Havcr1</i>	WT	29,91	27,58	-
<i>Sdh</i>	WT	19,64	20,96	-
<i>Sdh</i>	WT	19,66	20,91	-
<i>Cyts</i>	WT	17,03	17,13	-
<i>Cyts</i>	WT	17,10	17,31	-
<i>Pdha1</i>	WT	21,12	22,34	-
<i>Pdha1</i>	WT	21,42	22,38	-

(B)

Gene	Genotype	Ct value		
		4 weeks	23 weeks	40 weeks
<i>Gapdh</i>	<i>Pccar<sup>-/-</sup></i>	16,03	16,09	16,96
<i>Gapdh</i>	<i>Pccar<sup>-/-</sup></i>	15,92	16,07	16,69
<i>Fgf21</i>	<i>Pccar<sup>-/-</sup></i>	29,45	29,21	27,34
<i>Fgf21</i>	<i>Pccar<sup>-/-</sup></i>	29,41	29,31	27,12
<i>Len2</i>	<i>Pccar<sup>-/-</sup></i>	26,38	25,34	25,95
<i>Len2</i>	<i>Pccar<sup>-/-</sup></i>	26,26	25,06	25,71
<i>Havcr1</i>	<i>Pccar<sup>-/-</sup></i>	28,32	27,07	26,54
<i>Havcr1</i>	<i>Pccar<sup>-/-</sup></i>	28,09	27,02	26,71
<i>Sdh</i>	<i>Pccar<sup>-/-</sup></i>	21,79	23,12	23,12
<i>Sdh</i>	<i>Pccar<sup>-/-</sup></i>	21,67	22,94	23,93
<i>Cyts</i>	<i>Pccar<sup>-/-</sup></i>	18,02	18,48	20,28
<i>Cyts</i>	<i>Pccar<sup>-/-</sup></i>	18,00	18,50	20,45
<i>Pdha1</i>	<i>Pccar<sup>-/-</sup></i>	23,23	24,11	24,61
<i>Pdha1</i>	<i>Pccar<sup>-/-</sup></i>	23,03	23,92	24,38
<i>Gapdh</i>	<i>Pccar<sup>-/-</sup></i>	15,44	16,11	18,95
<i>Gapdh</i>	<i>Pccar<sup>-/-</sup></i>	15,37	16,07	18,68
<i>Fgf21</i>	<i>Pccar<sup>-/-</sup></i>	27,09	29,97	29,07
<i>Fgf21</i>	<i>Pccar<sup>-/-</sup></i>	25,54	29,17	29,14
<i>Len2</i>	<i>Pccar<sup>-/-</sup></i>	24,34	25,74	27,86
<i>Len2</i>	<i>Pccar<sup>-/-</sup></i>	24,39	25,65	27,95
<i>Havcr1</i>	<i>Pccar<sup>-/-</sup></i>	26,02	27,40	28,29
<i>Havcr1</i>	<i>Pccar<sup>-/-</sup></i>	26,05	27,54	28,39
<i>Sdh</i>	<i>Pccar<sup>-/-</sup></i>	22,29	21,56	23,71
<i>Sdh</i>	<i>Pccar<sup>-/-</sup></i>	22,17	21,45	23,74
<i>Cyts</i>	<i>Pccar<sup>-/-</sup></i>	18,85	17,91	20,46
<i>Cyts</i>	<i>Pccar<sup>-/-</sup></i>	18,40	17,98	20,73
<i>Pdha1</i>	<i>Pccar<sup>-/-</sup></i>	23,36	22,73	25,14
<i>Pdha1</i>	<i>Pccar<sup>-/-</sup></i>	23,09	22,74	25,27
<i>Gapdh</i>	<i>Pccar<sup>-/-</sup></i>	16,01	18,30	17,03
<i>Gapdh</i>	<i>Pccar<sup>-/-</sup></i>	15,74	18,22	16,92
<i>Fgf21</i>	<i>Pccar<sup>-/-</sup></i>	30,04	30,51	26,15
<i>Fgf21</i>	<i>Pccar<sup>-/-</sup></i>	31,03	30,06	27,02
<i>Len2</i>	<i>Pccar<sup>-/-</sup></i>	25,80	27,48	25,29
<i>Len2</i>	<i>Pccar<sup>-/-</sup></i>	25,67	27,39	25,13
<i>Havcr1</i>	<i>Pccar<sup>-/-</sup></i>	28,72	28,69	26,39
<i>Havcr1</i>	<i>Pccar<sup>-/-</sup></i>	28,85	28,58	26,65
<i>Sdh</i>	<i>Pccar<sup>-/-</sup></i>	20,59	23,09	25,68
<i>Sdh</i>	<i>Pccar<sup>-/-</sup></i>	20,81	23,08	25,56
<i>Cyts</i>	<i>Pccar<sup>-/-</sup></i>	17,07	20,11	20,77
<i>Cyts</i>	<i>Pccar<sup>-/-</sup></i>	17,09	20,34	20,7
<i>Pdha1</i>	<i>Pccar<sup>-/-</sup></i>	21,92	24,62	25,13
<i>Pdha1</i>	<i>Pccar<sup>-/-</sup></i>	22,22	24,59	25,11

Supplementary figure 6: Ct values of the investigated genes in 4, 23 and 40 week old WT (A) and *Pccar<sup>-/-</sup>*(A138T, (B)) mice. Glyceraldehyde-3-phosphate dehydrogenase (*Gapdh*), Fibroblast growth factor 21 (*Fgf21*), Lipocalin2 (*Lcn2*), Kidney injury molecule 1 (*Havcr1*), Succinate dehydrogenase (*Sdh*), Cytochrome c (*Cyts*), Pyruvate dehydrogenase (*Pdha1*).