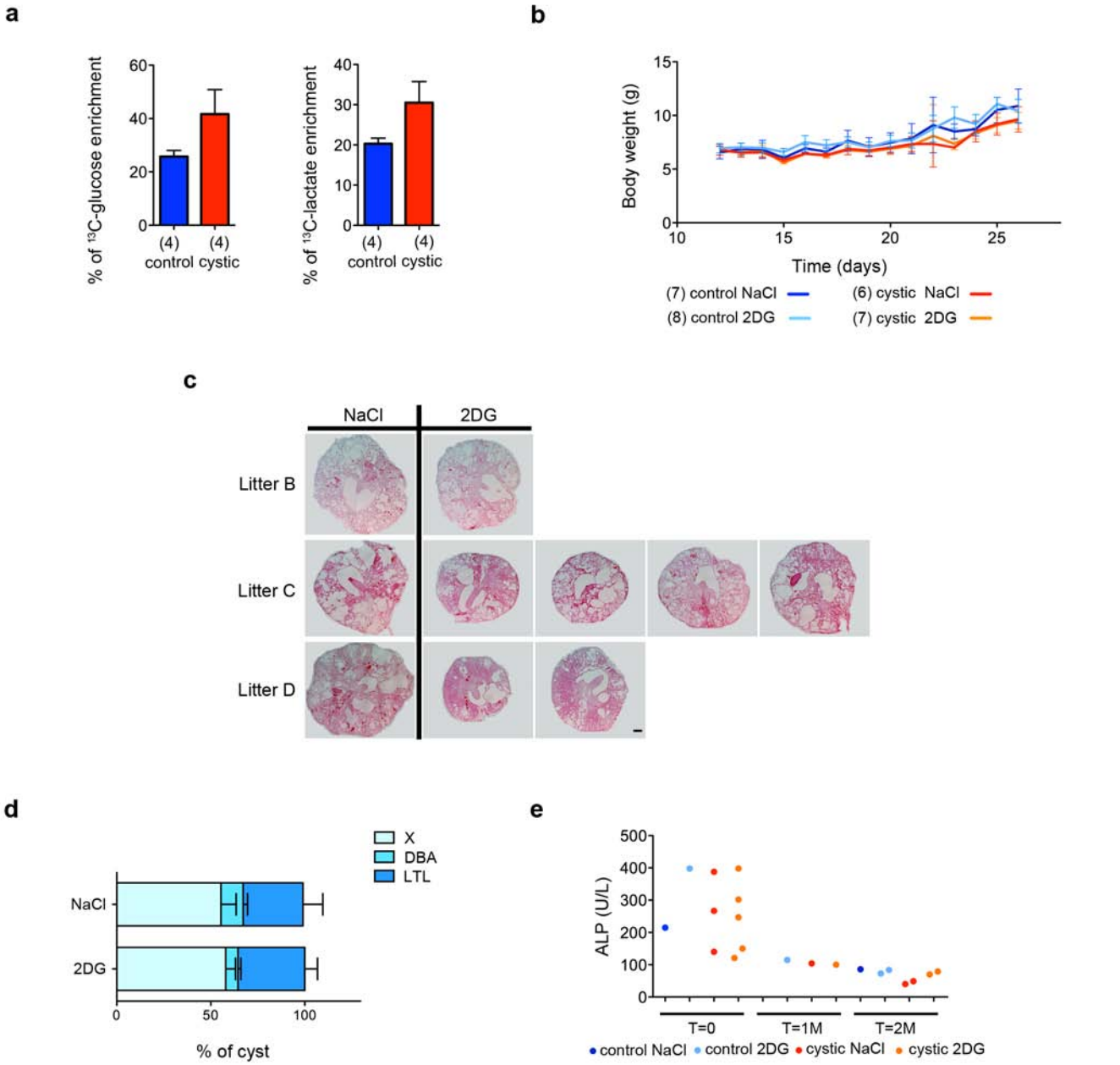
[a]Litter	[b]genotype	[c]phenotype	[d]treatment	[e]T=0 MRI TKV (cm^3)	[e]T=1M MRI TKV (cm^3)	[e]T=2M MRI TKV (cm^3)
A	*Pkd1*$^{\Delta C/flox}$	control	2DG	/	0.42	0.39
	Pkd1$^{\Delta C/flox}$: TmCre	cystic	NaCl	/	1.56	3.80
	Pkd1$^{\Delta C/flox}$: TmCre	cystic	2DG	/	1.32	2.58
B	*Pkd1*$^{flox/+}$: TmCre	control	NaCl	0.38	0.49	0.56
	Pkd1$^{\Delta C/flox}$	control	2DG	0.28	0.34	0.35
	Pkd1$^{\Delta C/flox}$: TmCre	cystic	NaCl	0.79	1.72	3.91
	Pkd1$^{\Delta C/flox}$: TmCre	cystic	2DG	0.61	1.21	3.23
C	*Pkd1*$^{flox/+}$	control	2DG	0.36	0.36	0.41
	Pkd1$^{\Delta C/flox}$: TmCre	cystic	NaCl	1.19	2.48	3.71
	Pkd1$^{\Delta C/flox}$: TmCre	cystic	NaCl	0.83	2.65	3.61
	Pkd1$^{\Delta C/flox}$: TmCre	cystic	2DG	1.19	2.24	3.70
	Pkd1$^{\Delta C/flox}$: TmCre	cystic	2DG	1.19	2.31	3.37
	Pkd1$^{\Delta C/flox}$: TmCre	cystic	2DG	0.60	1.10	2.27
	Pkd1$^{\Delta C/flox}$: TmCre	cystic	2DG	0.59	1.30	3.01
D	*Pkd1*$^{\Delta C/flox}$	control	NaCl	0.43	0.46	0.49
	Pkd1$^{\Delta C/flox}$	control	2DG	0.60	0.67	0.70
	Pkd1$^{flox/+}$	control	2DG	0.32	0.32	0.33
	Pkd1$^{\Delta C/flox}$: TmCre	cystic	NaCl	1.18	2.26	4.14
	Pkd1$^{\Delta C/flox}$: TmCre	cystic	NaCl	1.31	2.79	5.32
	Pkd1$^{\Delta C/flox}$: TmCre	cystic	2DG	1.02	1.46	2.24
	Pkd1$^{\Delta C/flox}$: TmCre	cystic	2DG	0.71	1.00	1.41
E	*Pkd1*$^{HA/+}$: TmCre	control	NaCl	0.42	0.47	0.48
	Pkd1$^{flox/+}$	control	2DG	0.37	0.38	0.42
	Pkd1$^{\Delta C/flox}$: TmCre	cystic	NaCl	0.91	1.92	3.78
	Pkd1$^{\Delta C/flox}$: TmCre	cystic	2DG	1.01	2.22	3.49

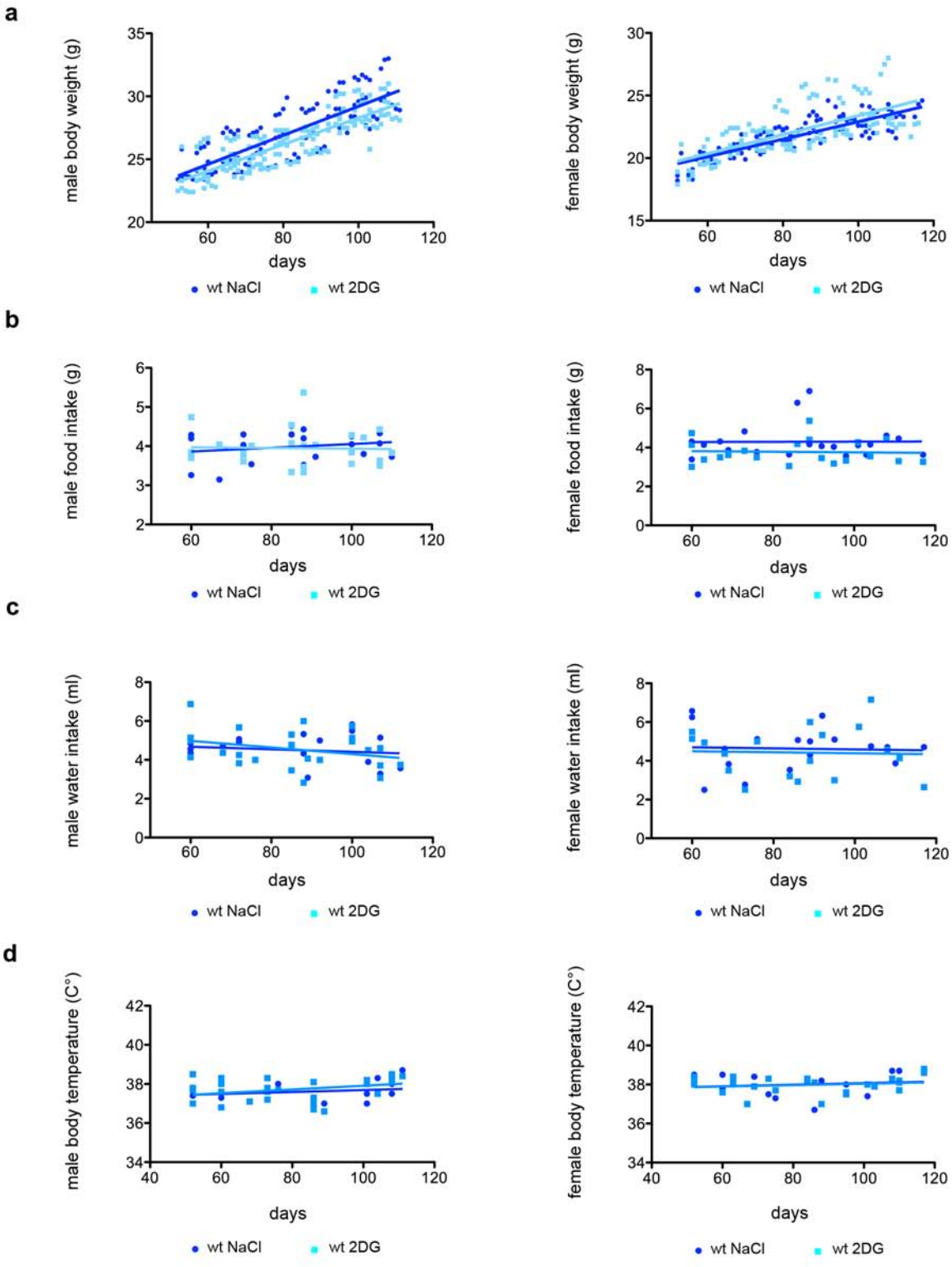
Supplementary Table 1. Measurements of kidney volume by MRI of each long-term animal model employed in the study. a. Animals are shown within the individual litters. 5 independent litters were employed for the studies divided in A to E; **b.** the precise genotype of each animal employed in the study is shown; **c.** the phenotype classified as control (non cystic) or cystic kidneys are indicated; **d.** the type of treatement 2-deoxy-D-glucose (2DG) or vehicle only (NaCl) is indicated; e. total kidney volumes were calculated in cm^3 at the different timepoints: T=0, prior to treatment T=1M and T=2M one and two months after treatment respectively are indicated for each animal.

Biochemical parameter	Wt NaCl mean ± SEM			Wt 2DG mean ± SEM		
	T=0 MRI P55	T=1M MRI P85	P130	T=0 MRI P55	T=1M MRI P85	P130
BUN	40.00 ± 5.72	42.57 ± 2.67	39.33 ± 3.09	34.90 ± 5.01	43.70 ± 2.72	42.86 ± 3.13
ALT	39.86 ± 6.50	41.86 ± 2.33	50.00 ± 15.13	42.70 ± 6.53	60.75 ± 8.53	81.25 ± 22.47
AST	92.43 ± 16.32	81.86 ± 13.12	126.50 ± 34.70	109.10 ± 13.96	105.60 ± 13.84	121.4 ± 8.05
LDH-P	768.30 ± 85.29	720.40 ± 113.60	726.20 ± 104.00	814.80 ± 78.37	753 ± 65.53	701.90 ± 79.24
ALB	2.93 ± 0.13	3.14 ± 0.092	3.27 ± 0.099	2.83 ± 0.094	2.93 ± 0.075	3.17 ± 0.100
CK	661.1 ± 241.3	401.3 ± 125.6	1036 ± 350.3	741.6 ± 177.1	323.3 ± 57.2	585.9 ± 143.0

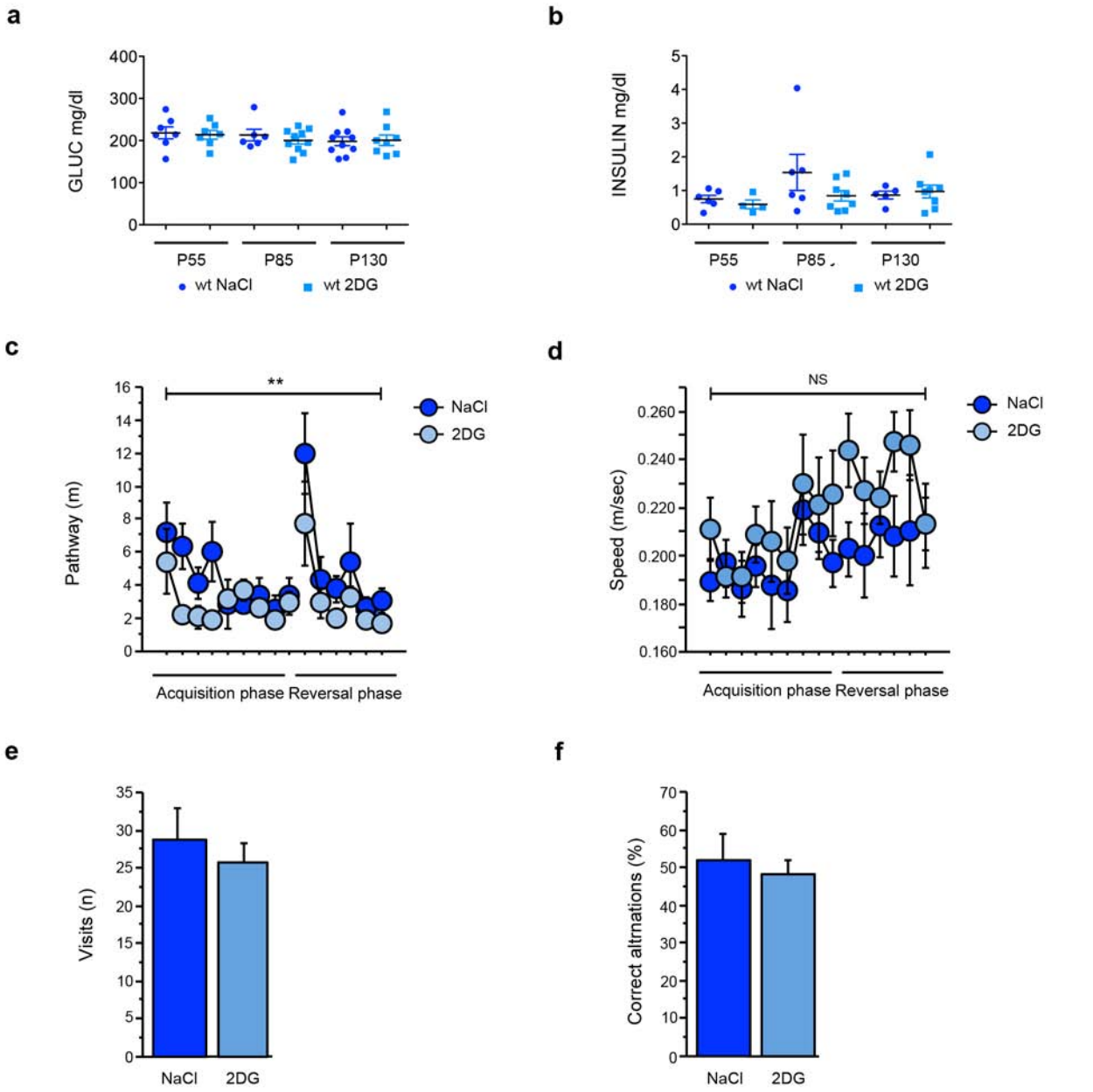
Supplementary Table 2: Biochemical parameters at various timepoints after long-term 2DG treatment as compared to NaCl treatment. Blood Urea Nitrogen (BUN), alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate deshydrogenase-P (LDH-P), albumin (ALB) and creatine kinase (CK) were measured in the sera collected at P55, P85 and P130 from mice treated with vehicle or 2DG at 100 mg per Kg. Data are presented as Mean +/- SEM



Chiaravalli et al, 2DG in PKD. Supplementary figure 1



Chiaravalli et al, 2DG in PKD. Supplementary figure 2



Chiaravalli et al, 2DG in PKD. Supplementary Figure 3

Supplementary Figure 1

a. The percentage of ^{13}C-glucose and ^{13}C-lactate enrichment (calculated as described in Materials and Methods) was higher in the kidneys from the cystic mice from the medium-term model as described in **Figure 1a**. **b**. Growth curve from mice treated with 2DG or vehicle during the medium-term-experiment. **c**. Histology of kidney sections from four litters collected from long term model treated with 2DG or vehicle. **d**. Percentage of cyst that stain positive for DBA, LTL or negative for both (X) in the long-term PKD model treated with NaCl or 2DG. No significant differences in the origin of cyst distribution could be observed, suggesting that 2DG acts equally on all cysts. **e**. Alkaline Phosphatase (ALP) concentration of the serum collected at the same time point of the first (T=0), second (T=1M) and third (T=2M) MRI (one, two and three months after tamoxifen induction) of the long term experiment.

Supplementary Figure 2: 2DG treatment has no systemic effects. Body weight (**a**), food intake (**b**), water intake (**c)** and body temperature (**d**) were not altered in males (left) and females (right) after treatment with 100 mg per kg 2DG 5 days a week for 2.5 months.

Supplementary Figure 3: 2DG treated mice show no differences in glucose and insulin levels and normal motor ability and working memory. a-b. Analysis of glucose (**a**) or insulin (**b**) levels at the different time points in mice treated with 2DG or NaCl show no differences in circulating insulin or glucose levels. **c.** Improved pathway to reach the platform in the 2DG treated versus NaCl treated animals in the Morris water maze test was observed (ANOVA repeated measures for pathway $F[1, 12]=9.7$, $p=0.0009$ with no interaction between treatment*days $F[1, 14]=0.9$, $p=0.5$). **d.** No differences were observed between groups during the water maze test in the speed ($F[1,12]=1.15$, $p=0.3$). **e-f.** Spontaneous alternation test was performed to assess short-term working memory. No differences between 2DG and vehicle treated mice were observed for the number of visits ($F[1,12]=0.4$, $p=0.53$) (**e**) and for the percentage of correct alternations ($F[1,12]=0.23$, $p=0.63$) (**f**). Data points and bars represent the mean +/- SEM in from **a** to **d**. Histograms represent the mean ± SEM in **e** and **f**.