Supplemental Information

Parameter	Estimate	Standard Error	*t* Value	*Pr* > |*t*|
Intercept	-51.07	26.10	-1.96	0.05
Baseline serum glucose	0.54	0.27	2.05	0.04
Baseline htTKV	0.10	0.01	11.85	<.0001
***PKD1* mutation**	-6.12	10.67	-0.57	0.57
***PKD2* mutation**	-13.14	12.42	-1.06	0.29
***n* =232**				
Intercept	-60.10	23.64	-2.54	0.01
Baseline serum glucose	0.56	0.26	2.14	0.03
Baseline htTKV	0.10	0.01	12.50	<.0001
***n* =234**				
Intercept	-91.00	45.34	-2.01	0.05
Baseline serum glucose	0.95	0.46	2.06	0.04
Baseline TKV	0.10	0.01	12.62	<.0001
***PKD1* mutation**	-13.09	18.51	-0.71	0.48
***PKD2* mutation**	-22.60	21.58	-1.05	0.30
***n* =232**				
Intercept	-108.29	40.97	-2.64	0.01
Baseline serum glucose	0.99	0.46	2.16	0.03
Baseline TKV	0.10	0.01	13.26	<.0001
***n* =234**				

Supplemental Table 1. Linear regression models, Related to Figure 1. Relationship between baseline serum glucose levels (after overnight fasting) and average annual change in height-adjusted total kidney volume (htTKV) and TKV among ADPKD patients from the CRISP cohort was explored in linear regression models adjusted for baseline htTKV or TKV with or without adjustment for *PKD1* and *PKD2* mutations (no mutation was used as a reference group for *PKD1* and *PKD2* mutation groups).

Nutritional Information of Rodent Diets

	Pico Lab Rodent Diet 20	**Envigo TD.110408**	**Bio Serv F3666**
Macronutrients *% weight*			
Protein	21.00	8.90	8.60
Carbohydrates	53.40	2.40	3.20
Fat	6.30	79.00	75.10
Fiber	4.60	4.90	4.80
Ash	5.90	3.00	3.00
Supplements *g/kg*			
Choline Bitartrate	N/A	5.00	N/A
DL-Methionine	N/A	1.50	N/A
Calories *% total kcal*			
Protein	24.52	4.70	4.65
Carbohydrates	62.35	1.30	1.73
Fat	13.13	94.00	91.28
Calories *kcal/g*			
Protein	0.92	0.36	0.34
Carbohydrates	2.33	0.10	0.13
Fat	0.49	7.14	6.76
Total	3.74	7.60	7.23
Amino Acids *g/kg*			
Alanine	11.90	2.80	2.30
Arginine	12.90	3.40	3.10
Aspartic Acid	21.90	6.30	5.50
Cystine	3.60	0.30	0.30
Glutamic Acid	41.80	20.50	17.30
Glycine	9.70	1.60	2.10
Histidine	5.30	2.60	2.30
Isoleucine	8.60	5.20	4.70
Leucine	15.70	8.20	7.10
Lysine	11.80	7.20	6.30
Methionine	6.20	3.90	2.20
Phenylalanine	9.10	4.50	3.80
Proline	13.10	9.50	8.70
Serine	9.80	5.00	4.80

Threonine	7.80	3.90	3.70
Tryptophan	2.40	1.10	1.00
Tyrosine	6.00	4.70	4.80
Valine	9.70	6.00	5.50
Carbohydrates *g/kg*			
Monosaccharides	2.29	0.00	7.00
-Glucose	1.01	0.00	7.00
-Fructose	1.28	0.00	0.00
Disaccharides	24.52	24.34	24.90
-Sucrose	17.36	24.34	24.90
-Lactose	7.16	0.00	0.00
Polysaccharides	150.90	0.00	0.00
-Starch	150.59	0.00	0.00
Fatty Acids *g/kg*			
C18:2 Linoleic	21.20	114.44	115.00
C18:3 Linolenic	2.70	7.52	6.70
Total Saturated	7.80	333.31	303.00
Total Monosaturated	9.60	286.09	288.00
Total Polyunsaturated	23.90	118.16	122.00
Minerals			
Calcium *g/kg*	8.10	5.80	5.70
Chloride *g/kg*	5.20	1.78	1.70
Copper *mg/kg*	14.00	8.74	6.60
Chromium *mg/kg*	10.00	2.29	2.20
Fluoride *mg/kg*	9.30	0.00	0.00
Iodine *mg/kg*	0.97	0.25	0.20
Iron *mg/kg*	185.00	51.92	38.70
Magnesium *g/kg*	2.20	0.58	0.56
Manganese *mg/kg*	84.00	61.60	63.60
Phosphorus *g/kg*	6.40	6.40	4.90
Potassium *g/kg*	11.00	3.45	3.90
Selenium *mg/kg*	0.37	0.12	0.19
Sodium *mg/kg*	3000.00	1180.00	1128.00
Sulfur *mg/kg*	3300.00	686.00	366.00
Zinc *mg/kg*	89.00	32.00	36.00
Vitamins			
Ascorbic Acid *mg/kg*	0.00	0.00	0.00
Biotin *mg/kg*	0.30	0.40	0.42
Choline *mg/kg*	2000.00	2295.34	274.00

Folic Acid *mg/kg*	3.00	4.00	4.20
Niacin *mg/kg*	85.00	60.00	62.80
Pantothenic Acid *mg/kg*	17.00	29.31	30.90
Pyridoxine *mg/kg*	9.60	14.00	12.10
Riboflavin *mg/kg*	8.00	12.00	12.60
Thiamin *mg/kg*	17.00	9.72	11.20
Vitamin A *IU/kg*	15000.00	8000.00	15500.00
Vitamin B12 *mcg/kg*	51.00	20.00	21.00
Vitamin D3 *IU/kg*	2300.00	2000.00	2090.00
Vitamin E *IU/kg*	99.00	100.00	244.00
Vitamin K3 *mg/kg*	3.30	3.00	2.20

Supplemental Table 2. Nutritional contents of experimental diets, Related to Figures 1-7. Description of nutritional content in each diet provided to experimental animals.

Animal ID	Sex	Age at Trial (months)	Pre-fast Weight (kg)	Post-fast Weight (kg)	Initial TKV (ml)	Pre-fast TKV (ml)	Disease Progression (TKV increase, ml/month)	Post-fast TKV (ml)	Fasting-induced TKV change (%)
Cat 1	M	64.5	4.4	4.1	64.3 (-17 months)	91.9	1.6	64.8	-29.5
Cat 2	F	34.2	3.4	2.95	56.7 (-15 months)	99.1	2.8	88.7	-10.5
Cat 3	F/de-sexed	51.4	3.4	3.4	23.0 (-17 months)	29.8	0.4	24.9	-16.3
Cat 4	M/de-sexed	64.0	5.7	5.45	72.6 (-21 months)	70.9	-0.1	68.4	-3.5

Supplemental Table 3. Animal data from acute fasting experiment in feline ADPKD model, Related to Figure 6. Age, sex, mass, total kidney volume, and changes pre and post-fast measures of total kidney volume.

Supplemental Figure 1. Related to Figures 1 and 2. *Tissue weights of rats in TRF experiments.* Tissue weights of time-restricted animals. Error bars represent SD. Statistical significance was determined using Mann-Whitney analysis.

Supplemental Figure 2. Related to Figure 1. *Weekly blood glucose values of TRF experimental animals.* Blood glucose values collected weekly at the end of the 16 hour fast prior to feeding. At 8 weeks, blood glucose was measured prior to the fasting period and again 10 hours later prior to sacrifice and after animals had been fed (Post-prandial=PP). Error bars represent SD. Statistical significance was determined using Mann-Whitney analysis. *n* =8 male and 12 female Cy/+ rats; *n* =13 male and 8 female wild-type rats for Time-Restricted Feeding experiments.

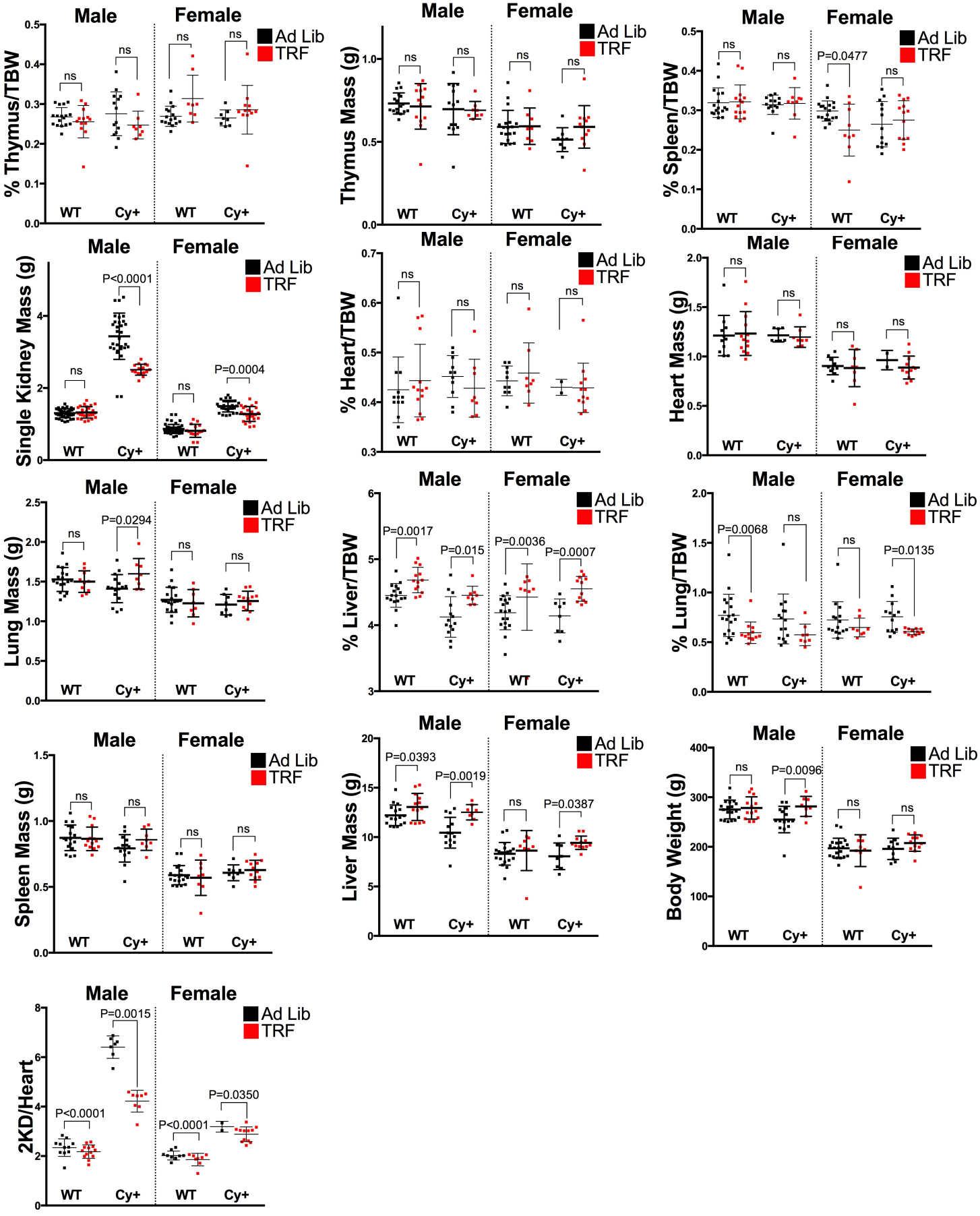
Supplemental Figure 3. Related to Figure 3. *Tissue weights of juvenile rats in ketogenic diet experiments.* Tissue weights of juvenile ketogenic animals. Error bars represent SD. Statistical significance was determined using Mann-Whitney analysis. *n* =8 male and 7 female Cy+ rats; *n* =13 male and 6 female wild-type rats for ketogenic diet experiments

Supplemental Figure 4. Related to Figure 5. *Tissue weights of adult rats in ketogenic diet experiments.* Tissue weights of adult ketogenic animals. Error bars represent SD. Statistical significance was determined using Mann-Whitney analysis. *n* =12 male and 10 female cystic rats; *n* =10 male and 14 female wild-type rats for adult ketogenic diet experiments.

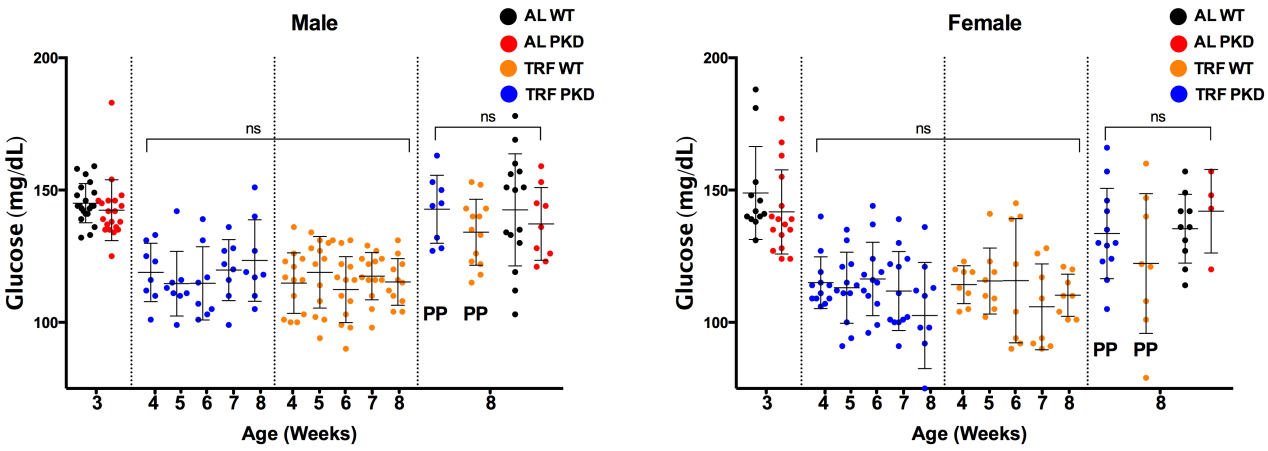
Supplemental Figure 5. Related to Figure 6 *Tissue weights of rats in acute fasting experiments.* Tissue weights of fasted rats. Error bars represent SD. Statistical significance was determined using Mann-Whitney analysis. *n* =8 male and 5 female cystic rats; *n* =7 male and 5 female wild-type rats.

Supplemental Figure 6. Related to Figure 6. *CT scans of ADPKD cats.* CT scans of PKD cats prior to fasting treatment.

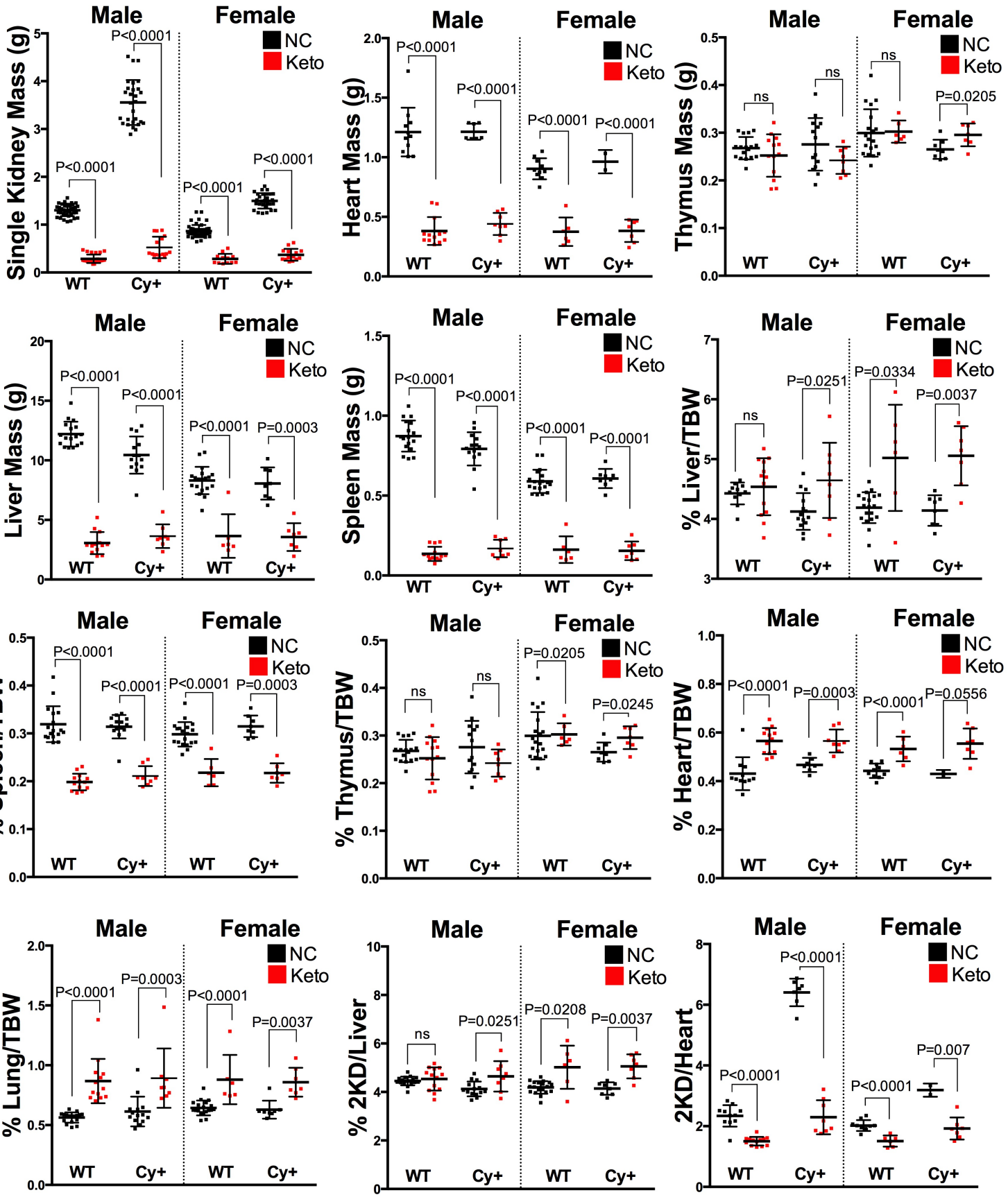
Supplemental Figure 7. Related to Figure 7*. Tissue weights, food intake and blood values of BHB treated rats.* A.) Water consumed between salt and BHB treated male and female rats. **B.)** Food intake of water, salt and BHB treated male and female rats. **C.)** BHB consumed for male and female rats. **D.)** Blood glucose of water, salt and BHB treated male and female rats. **E.)** Blood BHB levels of water, salt and BHB treated male and female rats. **F.)** Tissue weights of water, salt and BHB treated male and female rats. Each data point (Male *n* =5 water, *n* =2 Salt, *n* =4 BHB; Female *n* =6 water, *n* =3 salt, *n* =5 BHB) for food and water intake represents a single cage of group housed rats. Error bars represent SD. Statistical significance was determined using Mann-Whitney analysis.



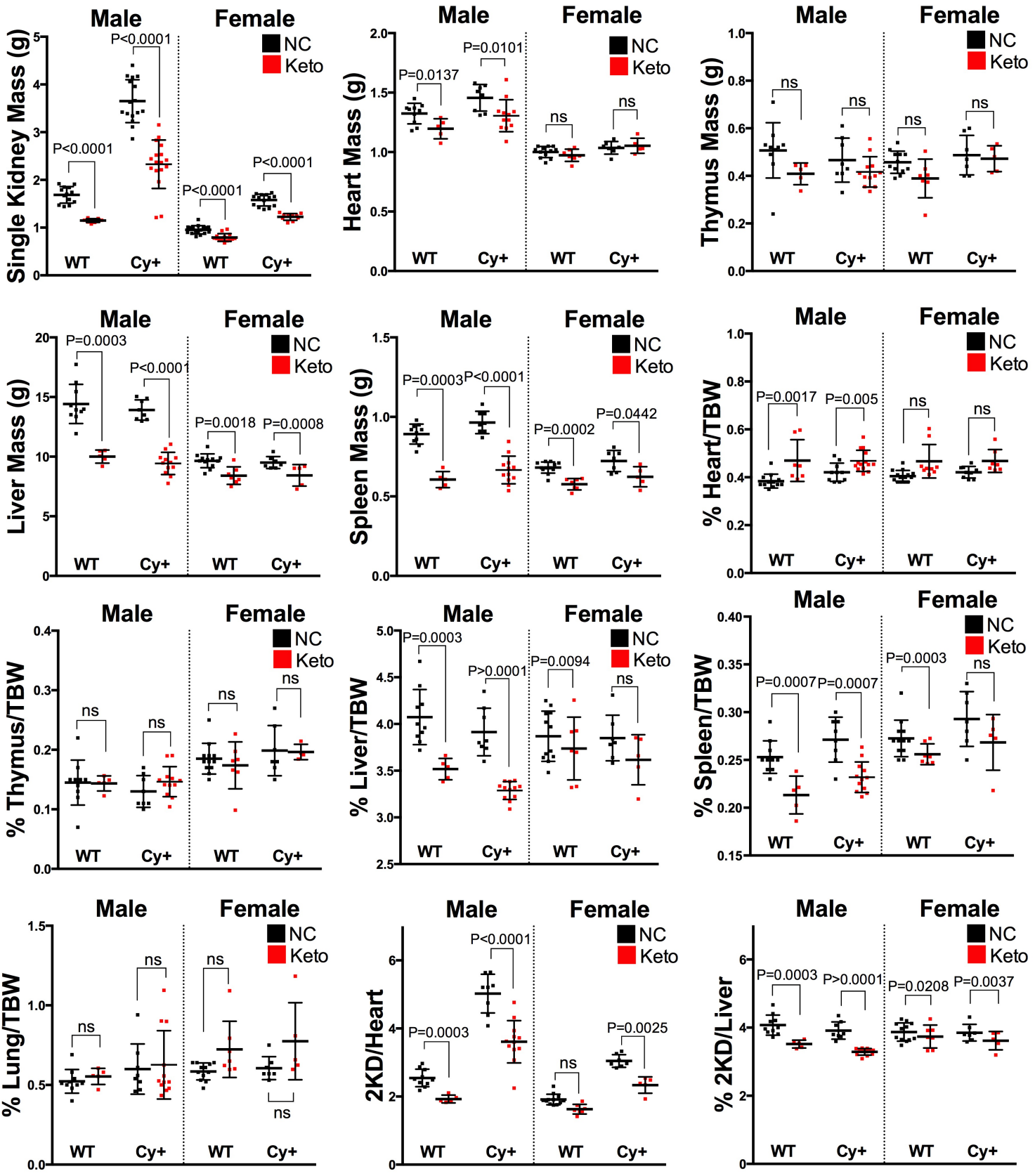
Supplemental Figure 1



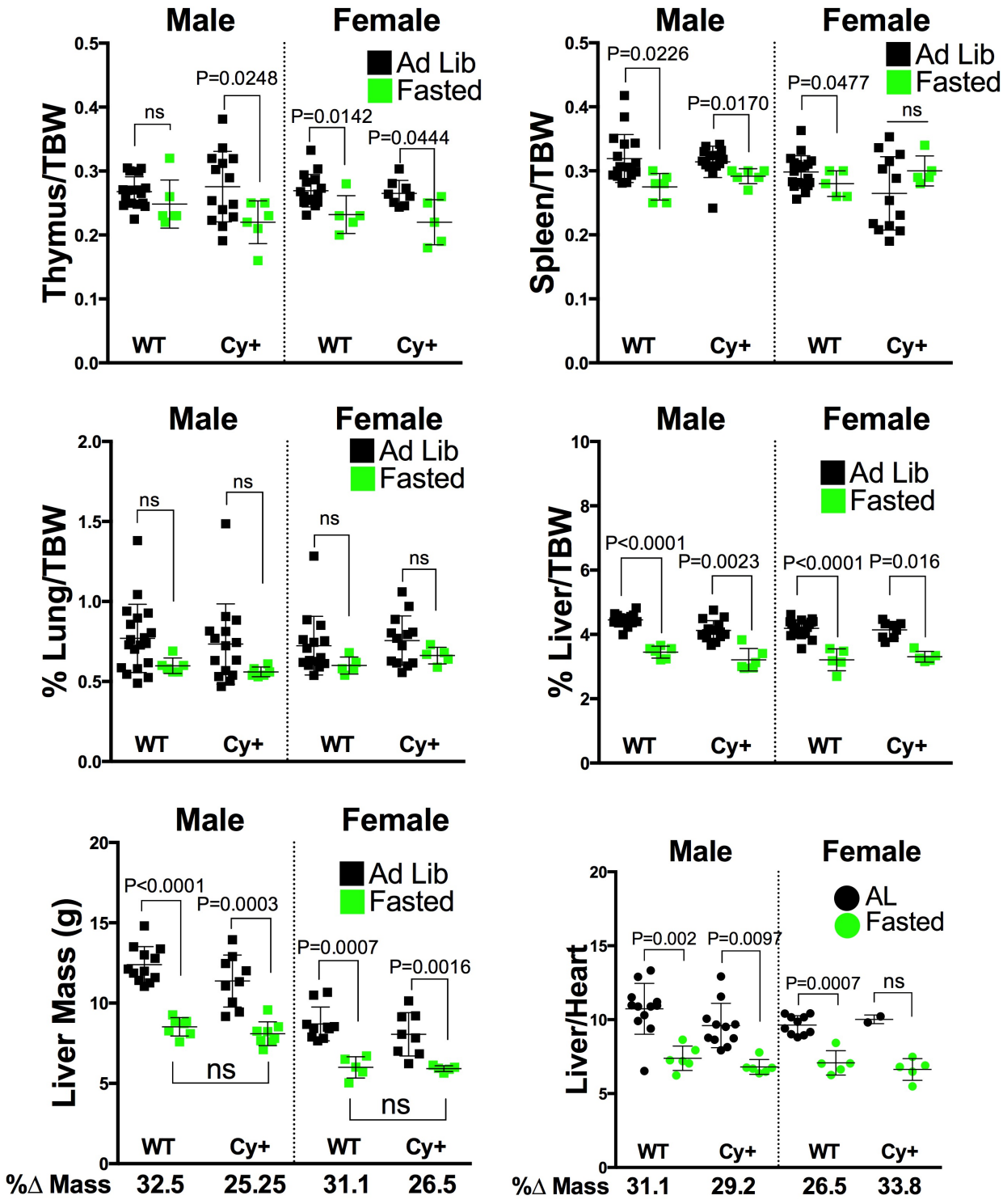
Supplemental Figure 2



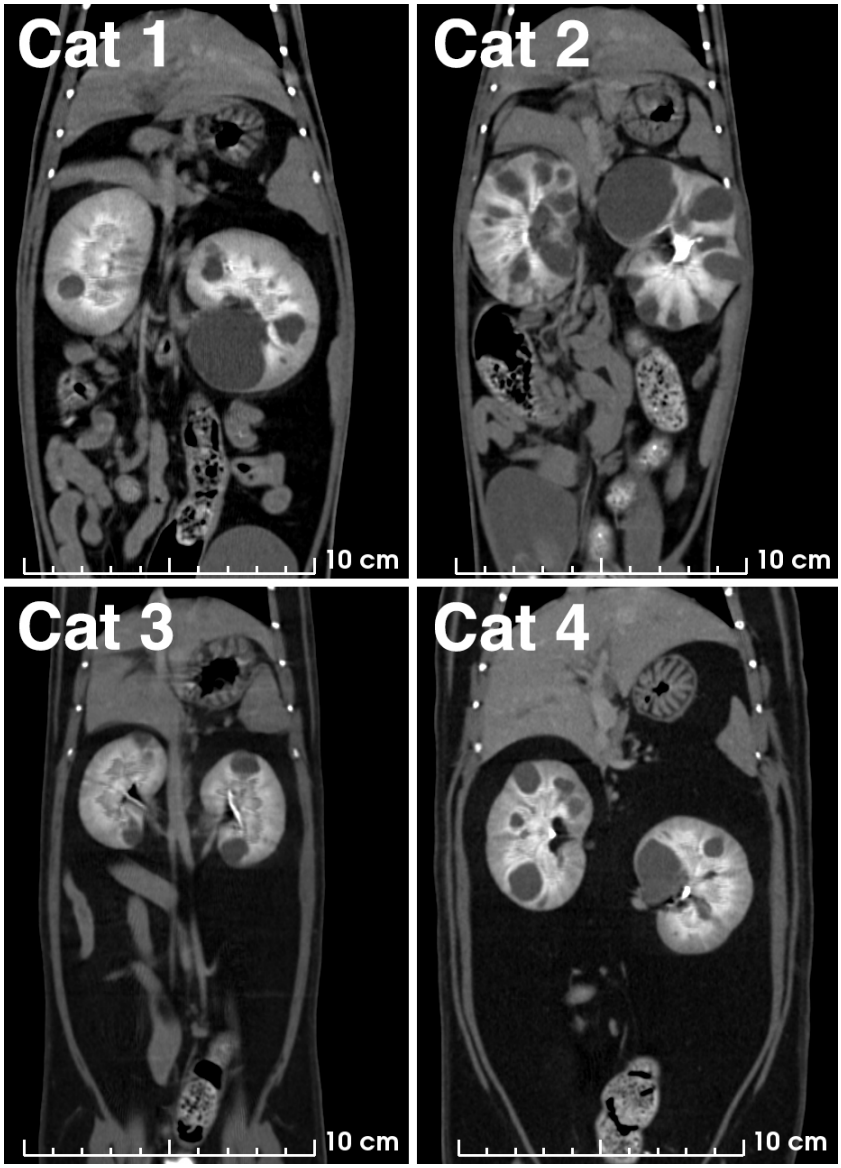
Supplemental Figure 3



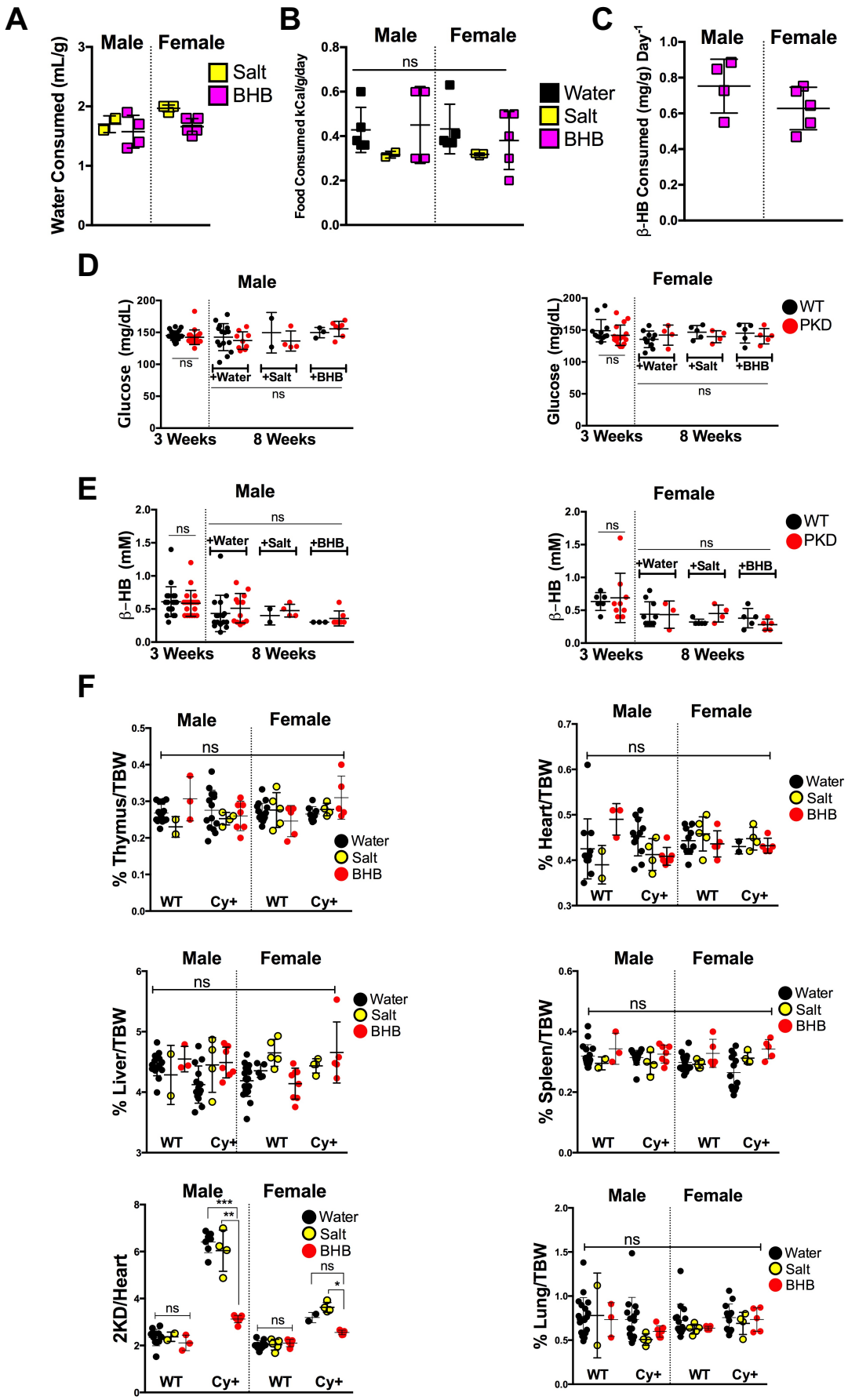
Supplemental Figure 4



Supplemental Figure 5



Supplemental Figure 6



Supplemental Figure 7