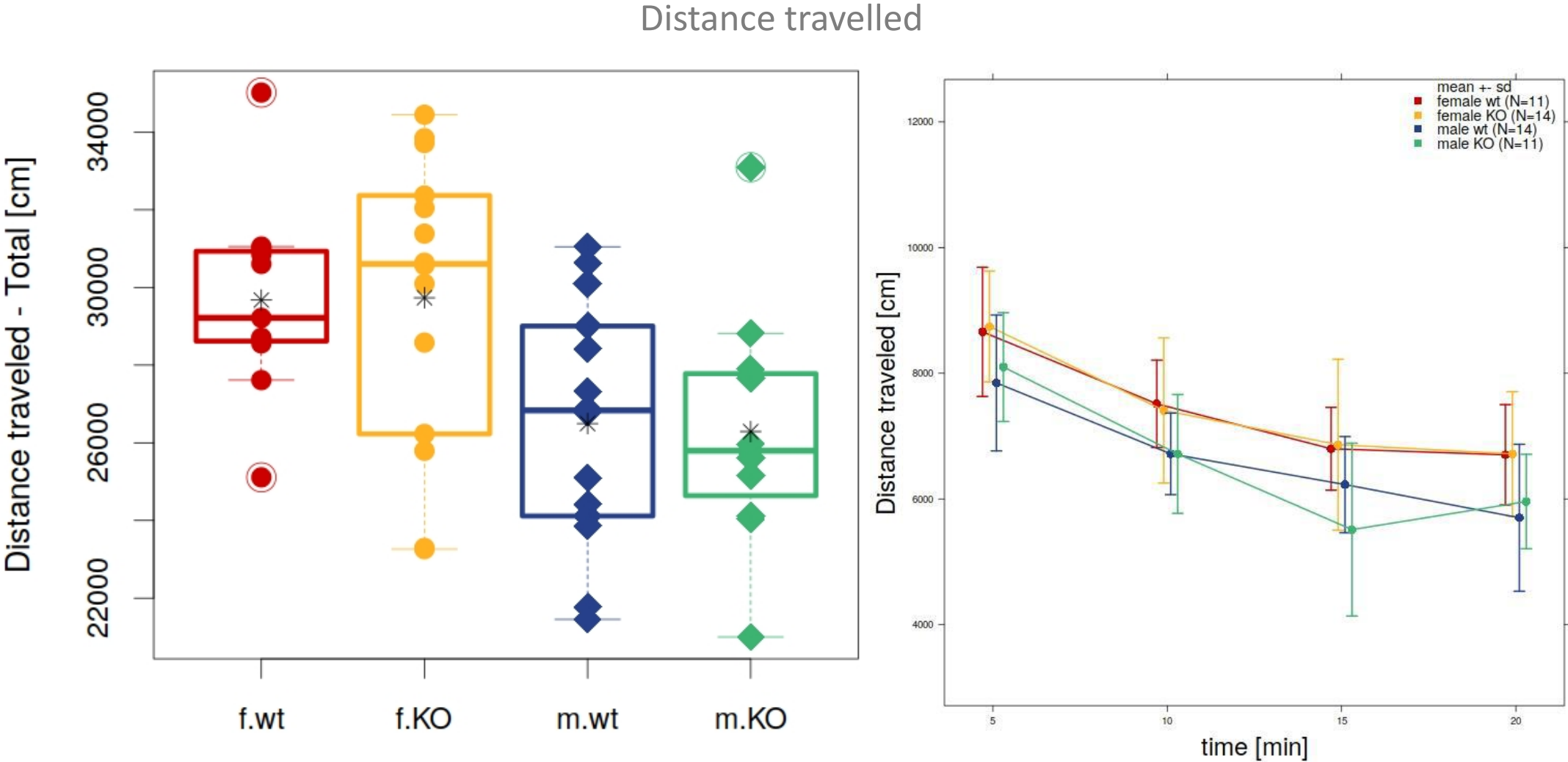




Supplemental phenotyping data: Mouse line U90926 (cDNA sequence U90926)

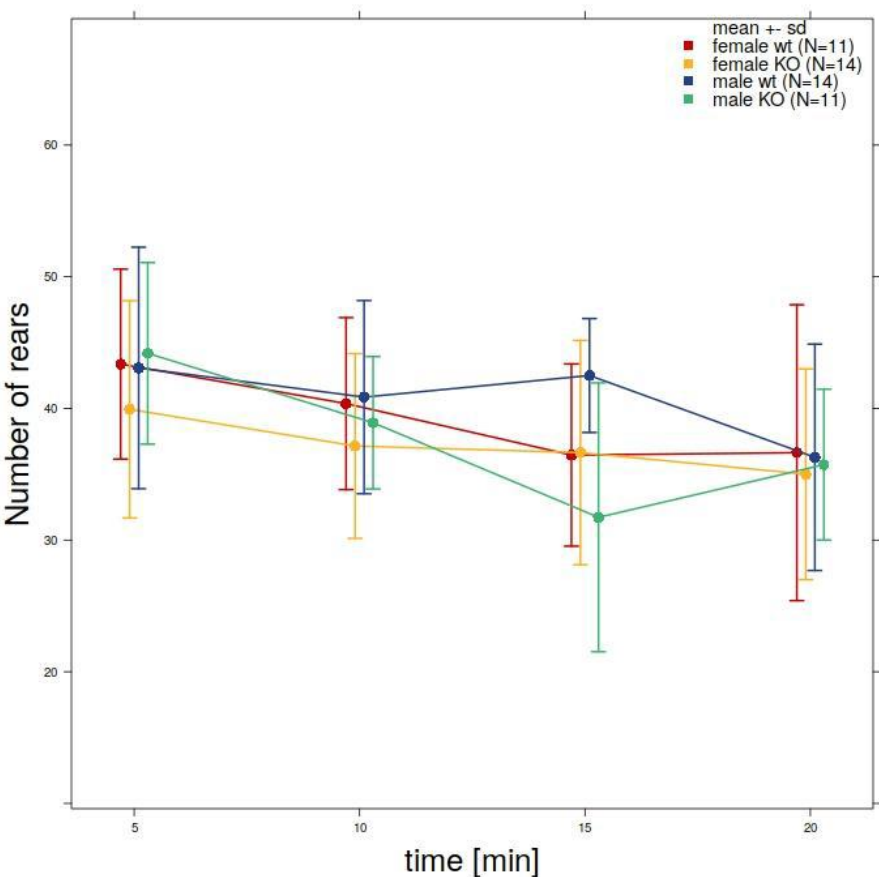
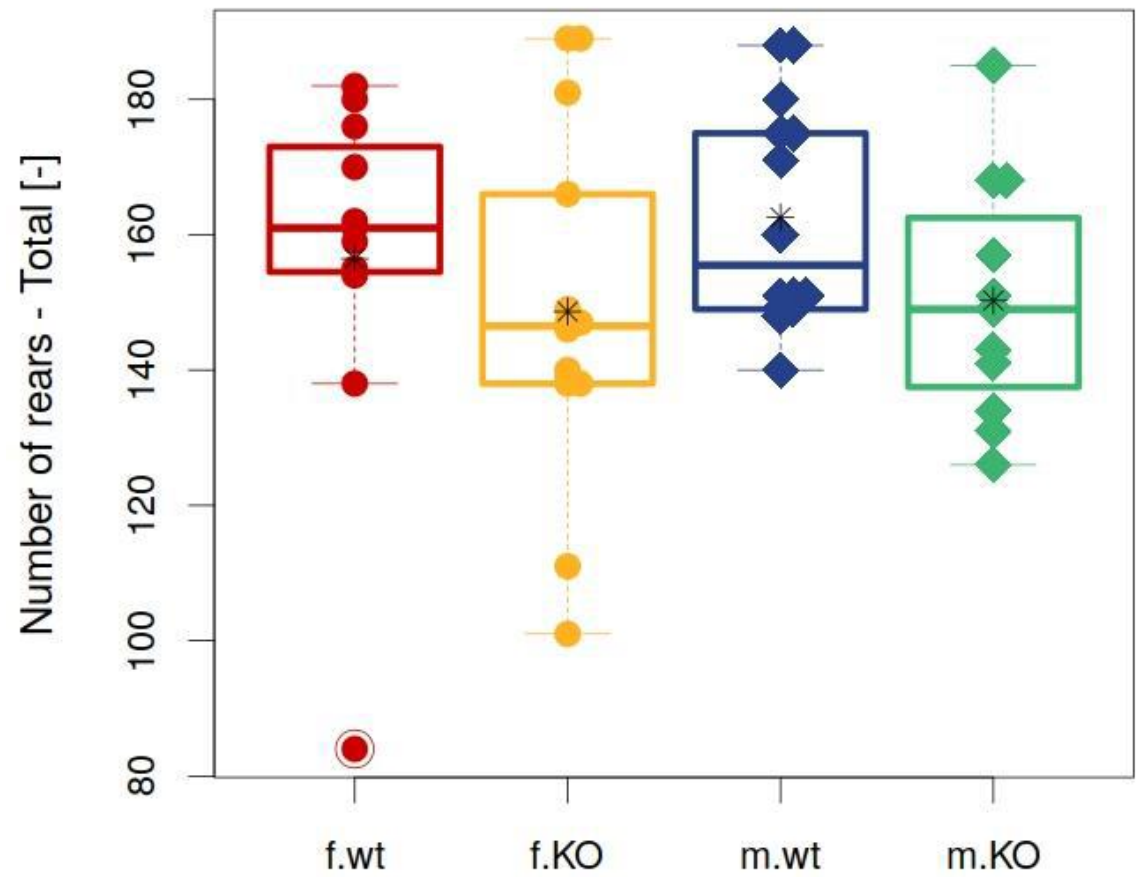
In this screening approach more than 500 parameters were measured and no correction for multiple testing was performed. Data is analyzed using automated R-scripts. Statistical analysis was dependent on the data (ANOVA, Linear Model, Wilcoxon rank-sum test as appropriate).

<https://www.mouseclinic.de/about-gmc/the-arrive-essential-10/index.html>



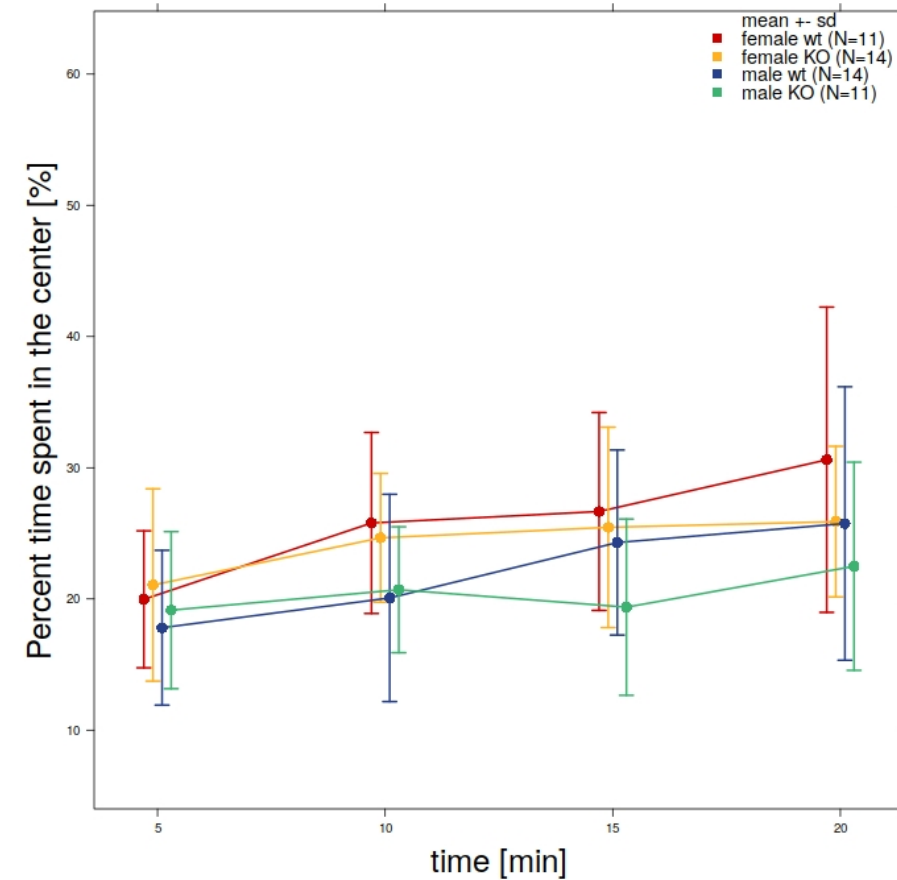
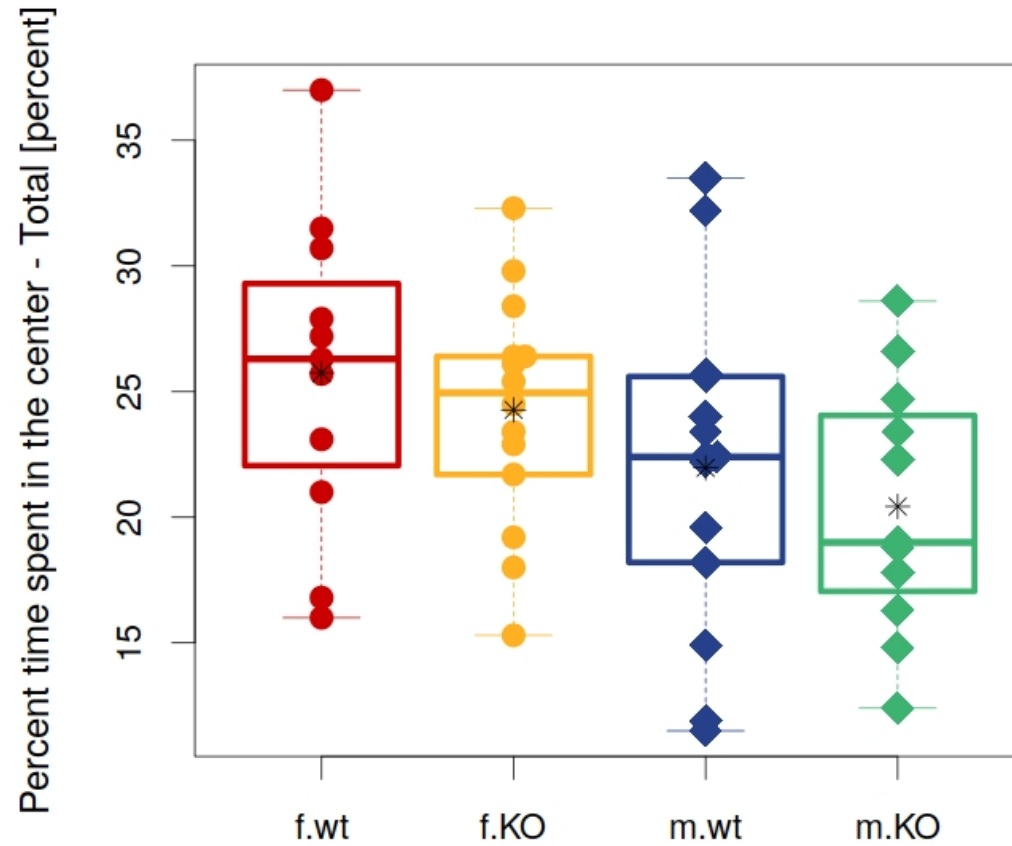
No genotype effect on distance travelled

Rearing activity

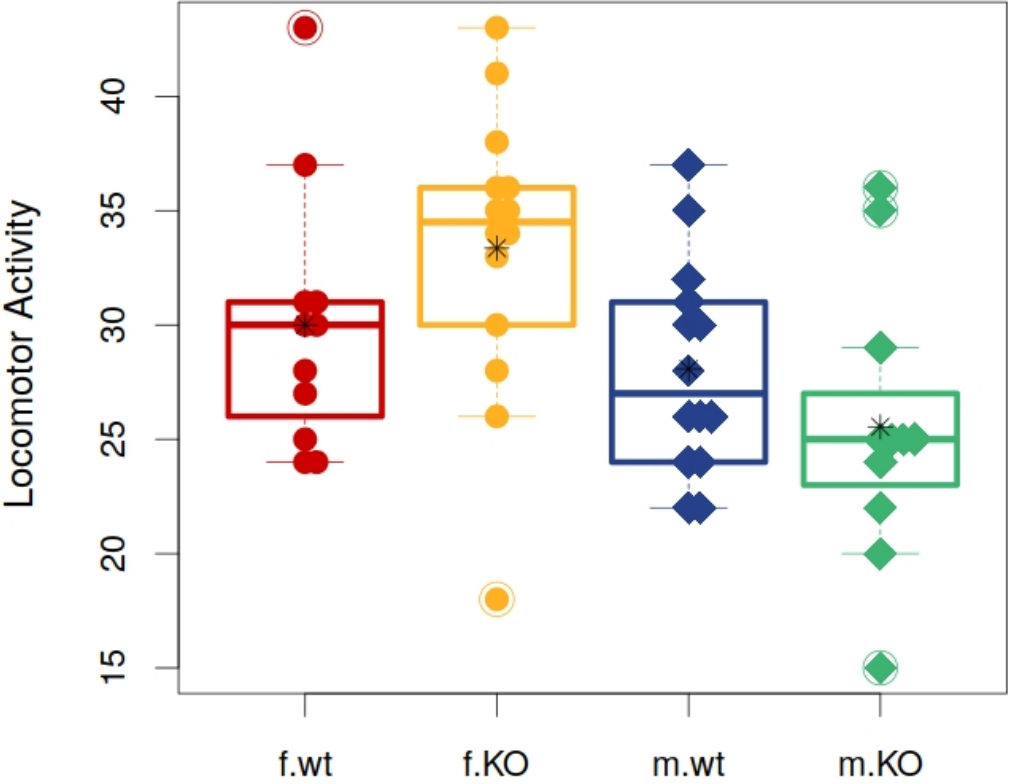


No genotype effect on rearing activity

Time spent and distance in centre

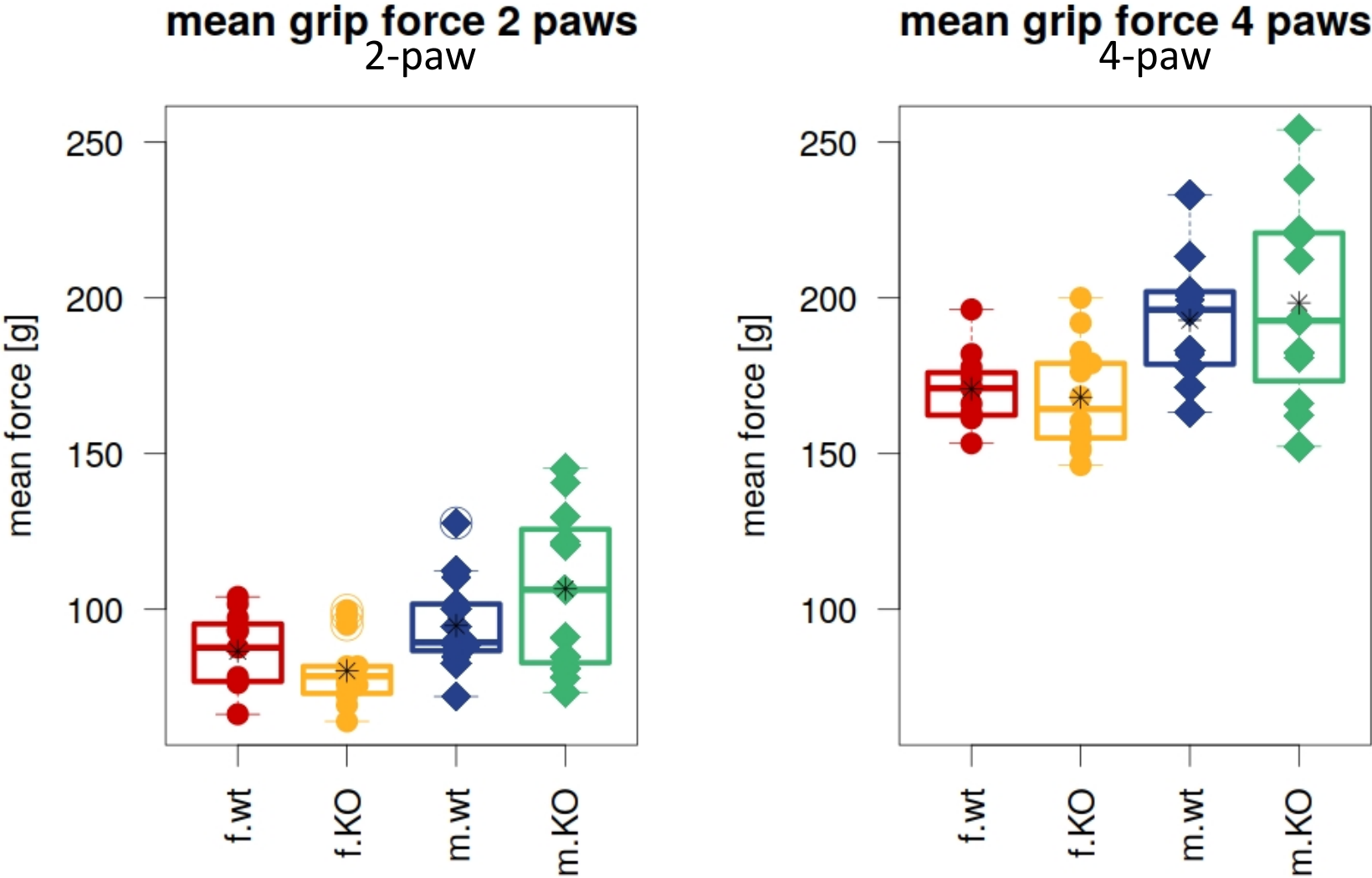


No genotype effect on centre time



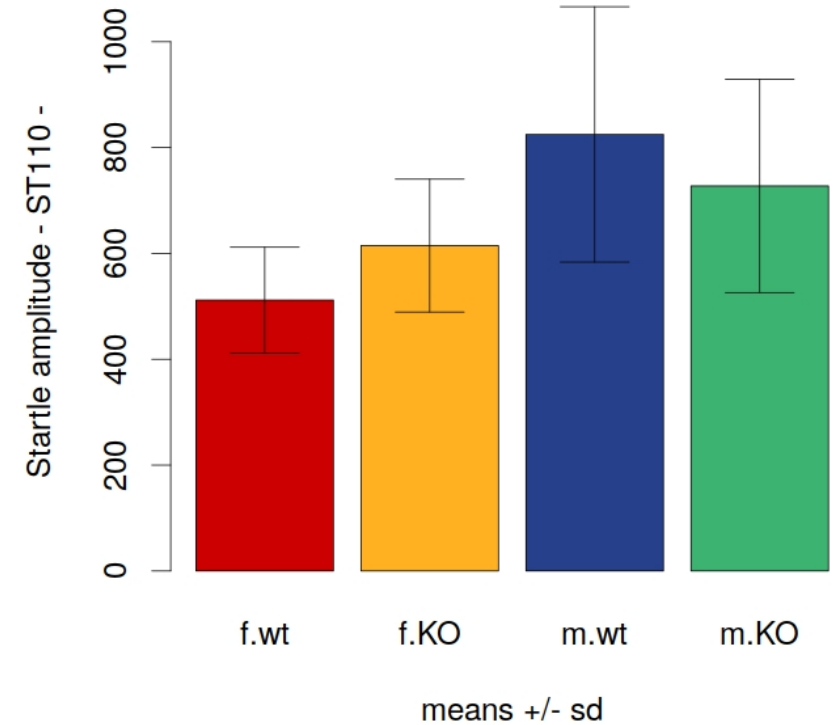
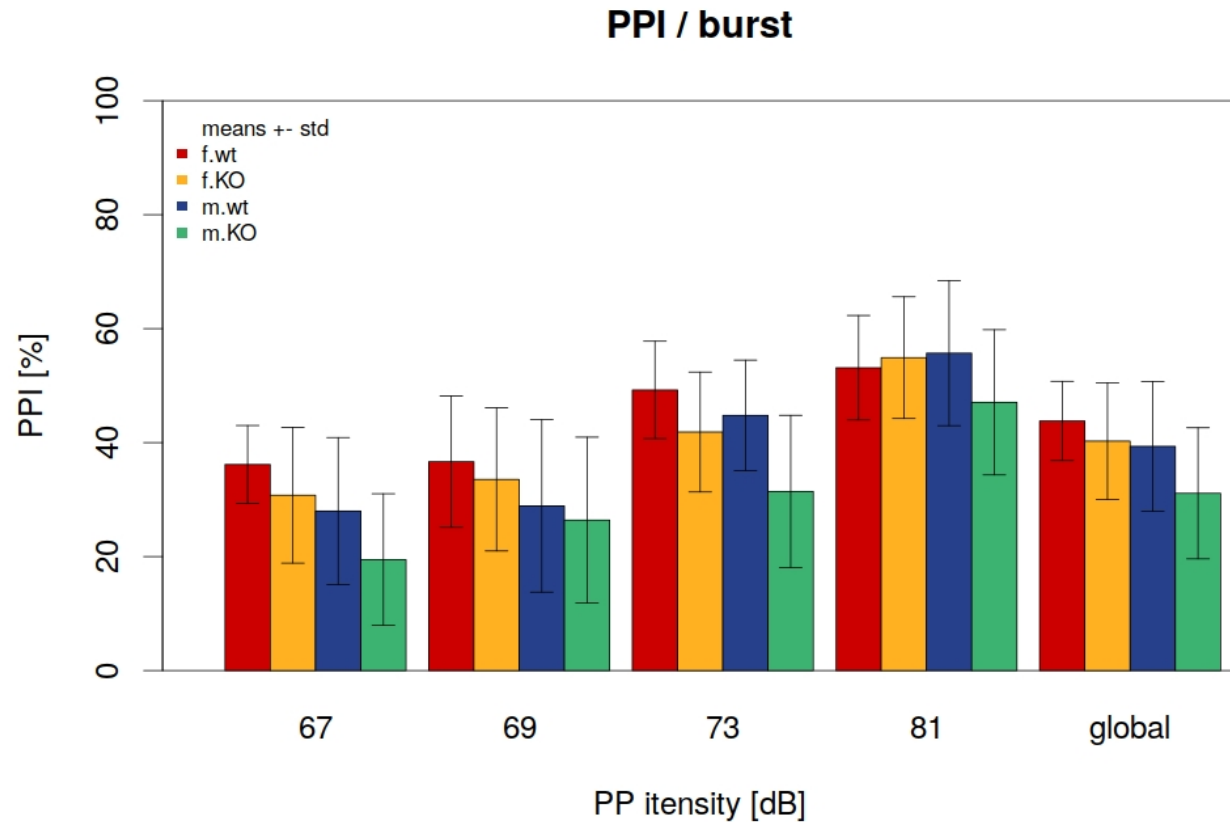
No difference for any SHIRPA parameter

Results grip strength (9 weeks):



No genotype-related differences at grip strength

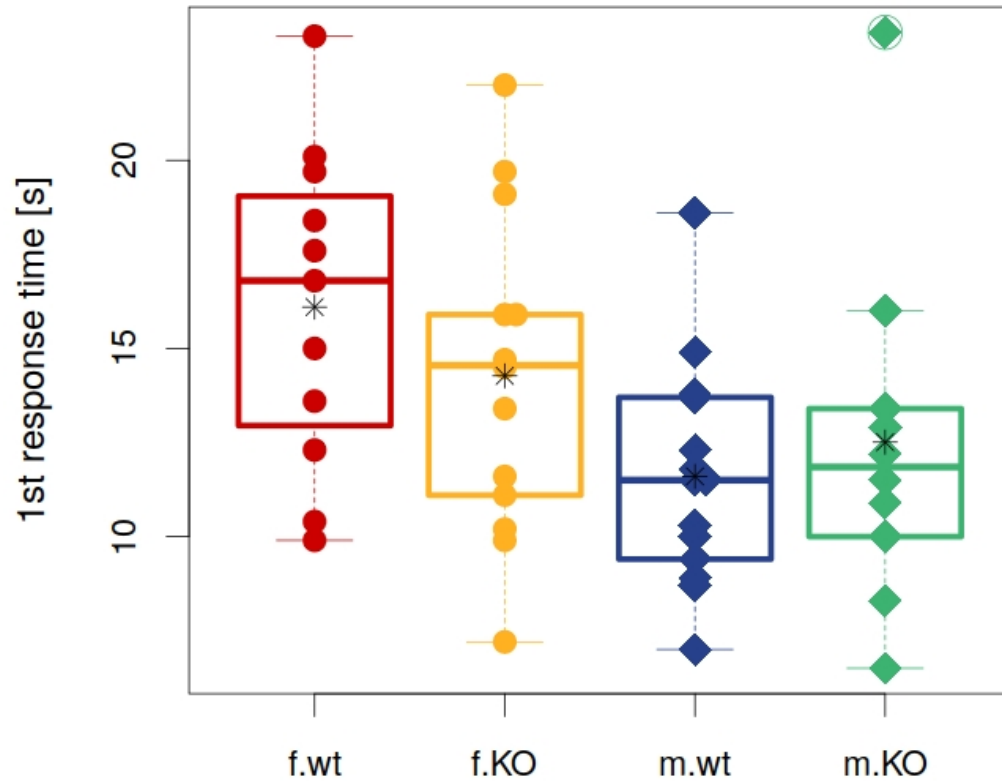
Results acoustic startle reactivity/prepulse inhibition (10 weeks)



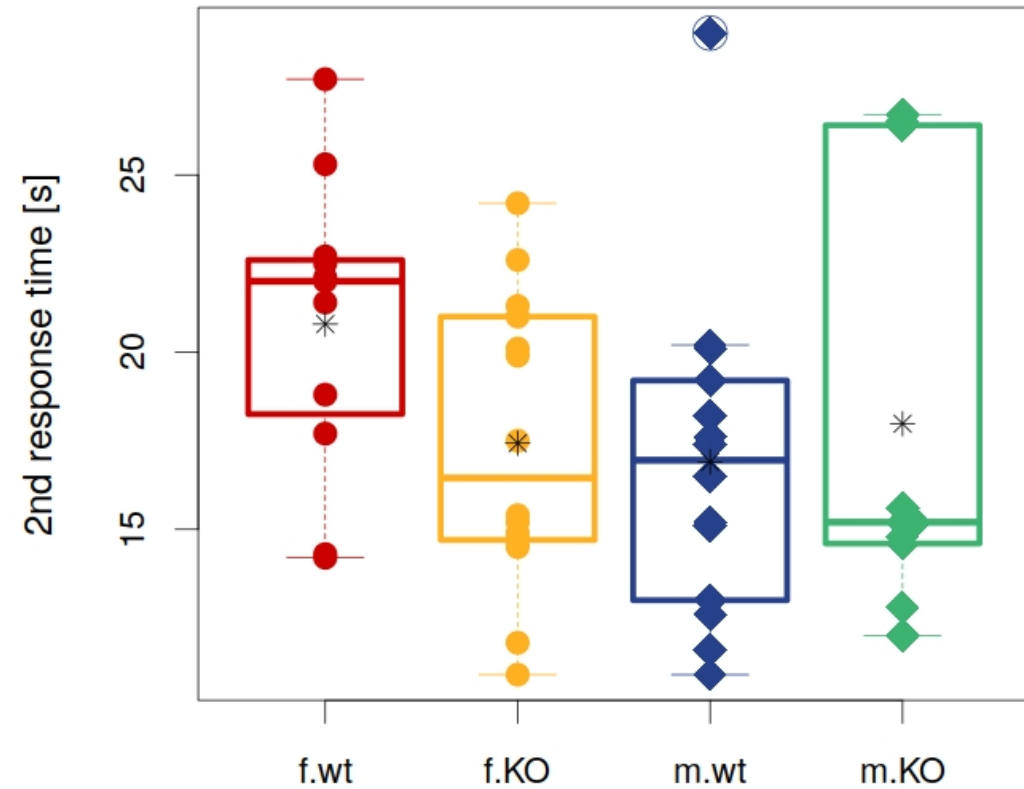
Slightly decreased prepulse inhibition
(67 dB $p = 0.035$, 73 dB $p = 0.001$) and
No significant effects on acoustic startle

Results Hot plate results (12 weeks)

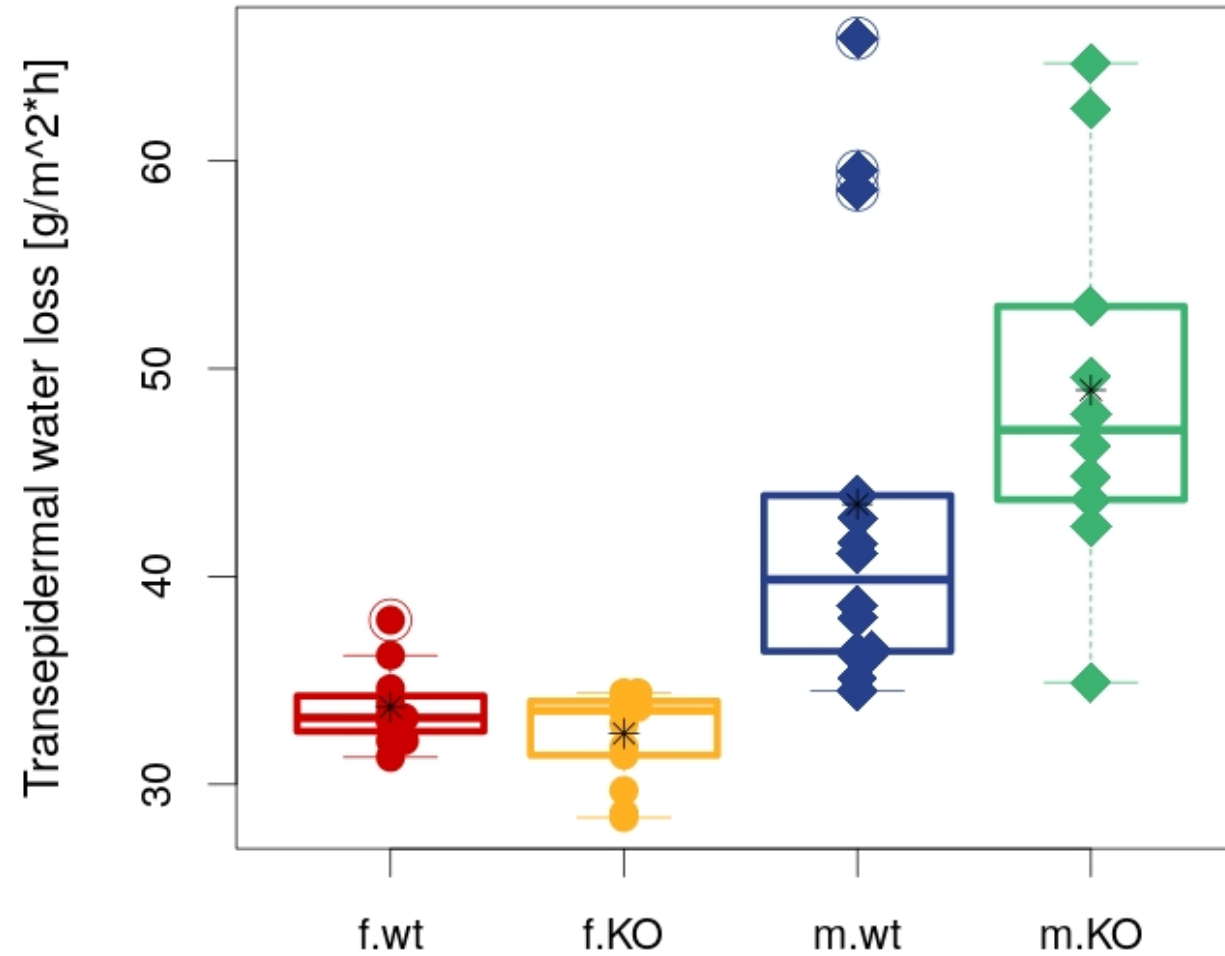
First reaction latencies



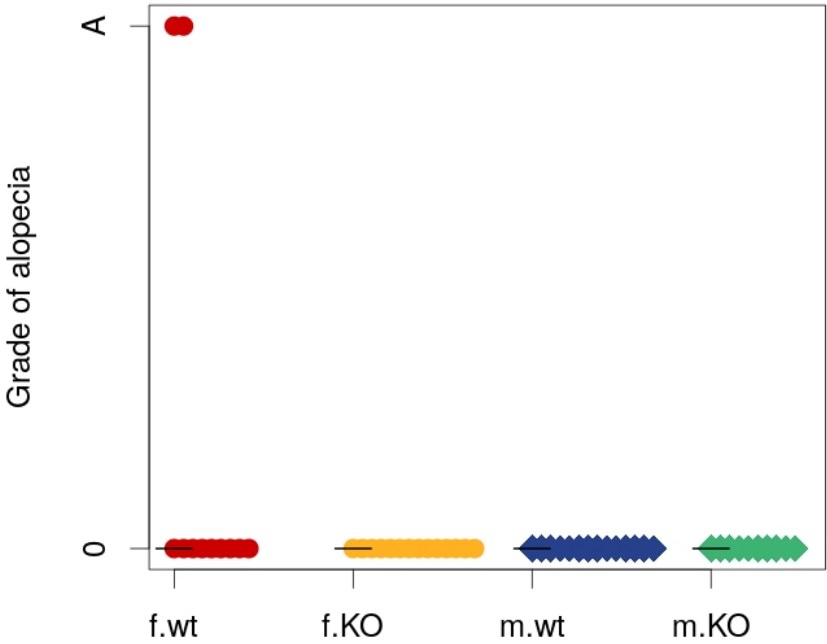
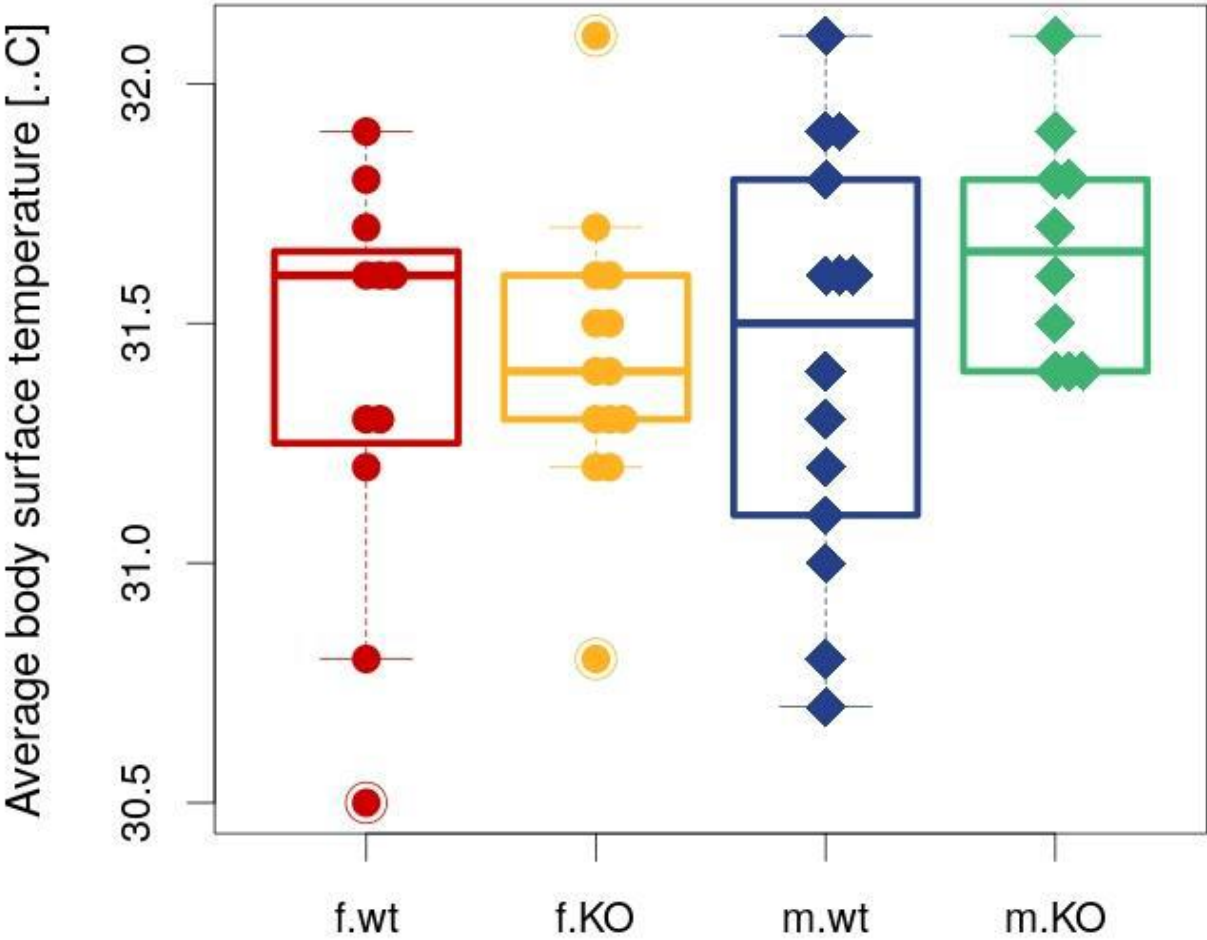
Second reaction latencies



No genotype effect on hotplate latencies or types or reactions (not shown)



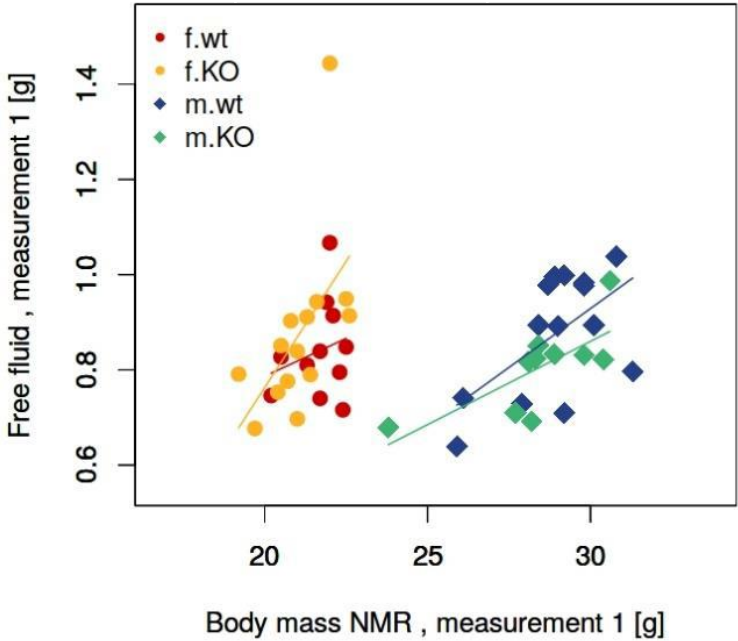
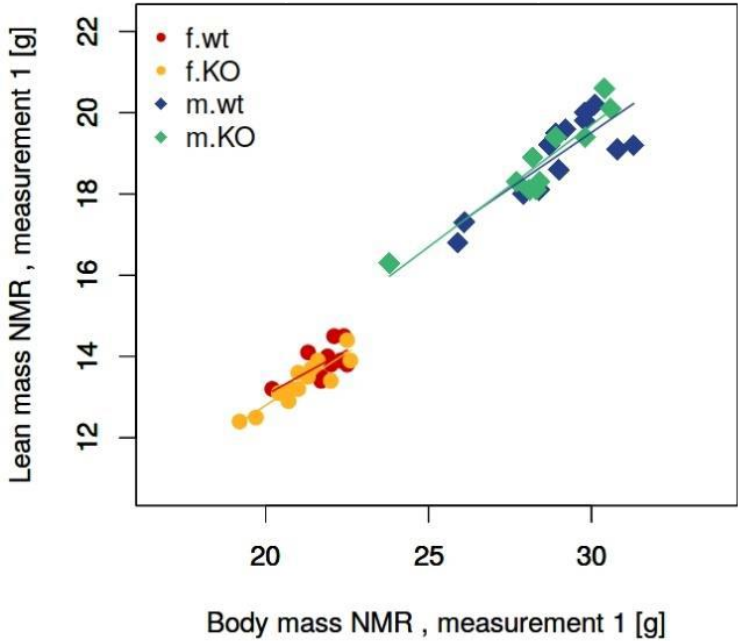
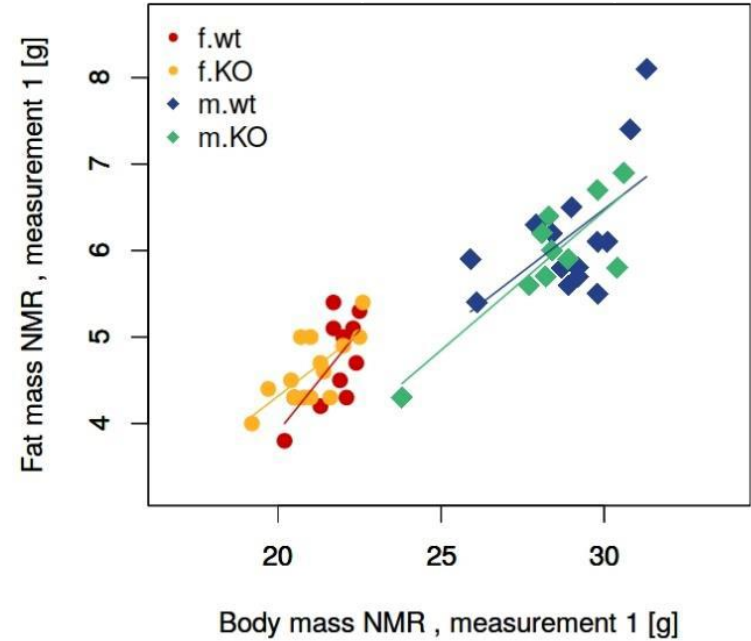
No significant differences in the TEWL, values are in the normal range of WT mice



No differences in the body surface temperature or alopecia degree

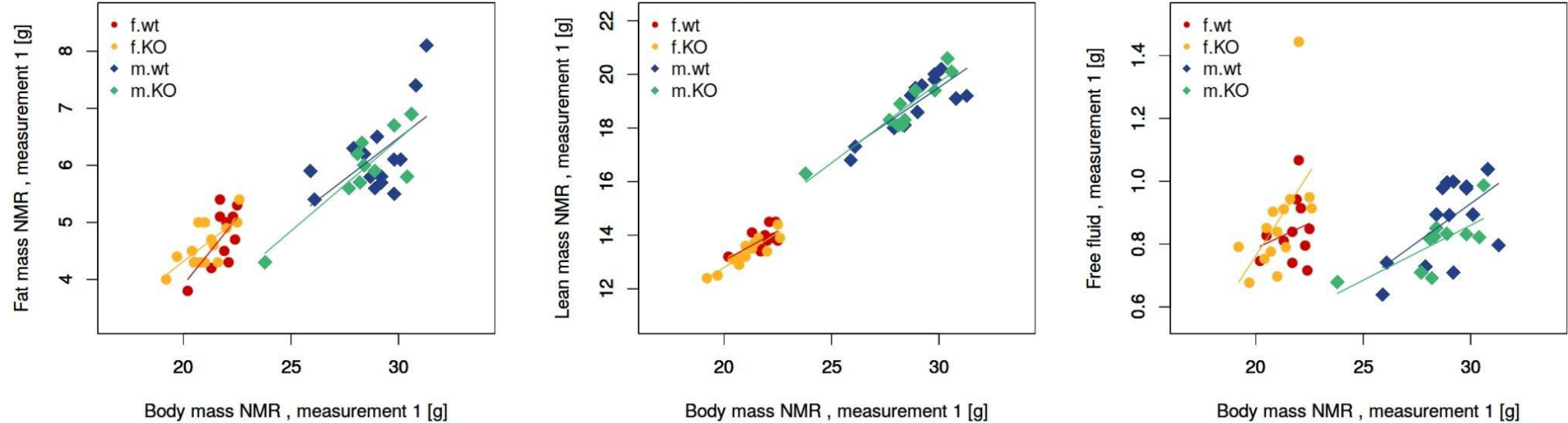
Body composition analysis I (13 weeks old)

	female		male		linear model	linear model	linear model	linear model
	wt	KO	wt	KO	sex	genotype	Bodymass	sex:genotype
	n=11	n=14	n=14	n=10				
	mean ± sd	mean ± sd	mean ± sd	mean ± sd	p-value	p-value	p-value	p-value
Body mass NMR	21.7 ± 0.8	21.1 ± 1	28.9 ± 1.5	28.4 ± 1.9	< 0.001	0.143	NA	0.873
Fat mass NMR	4.7 ± 0.5	4.6 ± 0.4	6.2 ± 0.7	6 ± 0.7	0.022	0.805	< 0.001	0.478
Lean mass NMR	13.8 ± 0.5	13.3 ± 0.5	18.9 ± 1	18.8 ± 1.2	0.002	0.969	< 0.001	0.4
Free fluid	0.8 ± 0.1	0.9 ± 0.2	0.9 ± 0.1	0.8 ± 0.1	0.001	0.769	< 0.001	0.116
Adiposity Index	0.3 ± 0	0.3 ± 0	0.3 ± 0	0.3 ± 0	0.004	0.764	0.022	0.321



Body composition analysis I (13 weeks old)

	female		male		linear model	linear model	linear model	linear model
	wt	KO	wt	KO	sex	genotype	Bodymass	sex:genotype
	n=11	n=14	n=14	n=10				
	mean ± sd	mean ± sd	mean ± sd	mean ± sd	p-value	p-value	p-value	p-value
Body mass NMR	21.7 ± 0.8	21.1 ± 1	28.9 ± 1.5	28.4 ± 1.9	< 0.001	0.143	NA	0.873
Fat mass NMR	4.7 ± 0.5	4.6 ± 0.4	6.2 ± 0.7	6 ± 0.7	0.022	0.805	< 0.001	0.478
Lean mass NMR	13.8 ± 0.5	13.3 ± 0.5	18.9 ± 1	18.8 ± 1.2	0.002	0.969	< 0.001	0.4
Free fluid	0.8 ± 0.1	0.9 ± 0.2	0.9 ± 0.1	0.8 ± 0.1	0.001	0.769	< 0.001	0.116
Adiposity Index	0.3 ± 0	0.3 ± 0	0.3 ± 0	0.3 ± 0	0.004	0.764	0.022	0.321



No differences concerning body composition parameters

Indirect Calorimetry (13 weeks old) – Results Overview

	female		male		Linear model	Linear model	Linear model	Linear model
	wt	KO	wt	KO	sex	genotype	body mass	sex:genotype
	n=11	n=14	n=14	n=10				
	mean ± sd	mean ± sd	mean ± sd	mean ± sd	p-value	p-value	p-value	p-value
Avg. body weight [g]	21.3 ± 0.8	20.5 ± 0.7	27.9 ± 1.6	27.6 ± 1.8	< 0.001	0.12	NA	0.503
Body weight loss [Δ g]	0.13 ± 0.48	0.3 ± 0.51	0.44 ± 0.43	0.41 ± 0.39	0.12	0.581	NA	0.457
Food intake [g]	2.7 ± 0.4	2.6 ± 0.5	2.8 ± 0.6	2.8 ± 0.4	0.156	0.851	0.074	0.647
Avg. VO2 [ml/(h animal)]	83.504 ± 3.986	84.734 ± 4.8	98.605 ± 5.223	97.446 ± 4.061	0.254	0.493	0.006	0.218
Min. VO2 [ml/(h animal)]	62.273 ± 3.663	62.429 ± 4.751	71.929 ± 5.313	72.6 ± 4.427	0.122	0.594	0.309	0.93
Max. VO2 [ml/(h animal)]	110.364 ± 3.88	115.714 ± 9.73	132.357 ± 8.205	129.1 ± 5.744	0.978	0.213	0.002	0.017
Avg. RER VCO2/VO2	0.877 ± 0.014	0.88 ± 0.023	0.867 ± 0.02	0.868 ± 0.019	0.052	0.739	NA	0.854
Avg. heat [kJ/(h animal)]	1.718 ± 0.081	1.744 ± 0.1	2.024 ± 0.113	2 ± 0.083	< 0.001	0.964	NA	0.376
Avg. distance [cm]	2945 ± 653	3792 ± 2446	2976 ± 579	2981 ± 830	0.352	0.309	NA	0.315
Avg. rearing [counts]	135 ± 82	142 ± 58	123 ± 60	88 ± 33	0.064	0.414	NA	0.23

Indirect Calorimetry (13 weeks old) – Results Overview

	female		male		Linear model	Linear model	Linear model	Linear model
	wt	KO	wt	KO	sex	genotype	body mass	sex:genotype
	n=11	n=14	n=14	n=10				
	mean ± sd	mean ± sd	mean ± sd	mean ± sd	p-value	p-value	p-value	p-value
Avg. body weight [g]	21.3 ± 0.8	20.5 ± 0.7	27.9 ± 1.6	27.6 ± 1.8	< 0.001	0.12	NA	0.503
Body weight loss [Δ g]	0.13 ± 0.48	0.3 ± 0.51	0.44 ± 0.43	0.41 ± 0.39	0.12	0.581	NA	0.457
Food intake [g]	2.7 ± 0.4	2.6 ± 0.5	2.8 ± 0.6	2.8 ± 0.4	0.156	0.851	0.074	0.647
Avg. VO2 [ml/(h animal)]	83.504 ± 3.986	84.734 ± 4.8	98.605 ± 5.223	97.446 ± 4.061	0.254	0.493	0.006	0.218
Min. VO2 [ml/(h animal)]	62.273 ± 3.663	62.429 ± 4.751	71.929 ± 5.313	72.6 ± 4.427	0.122	0.594	0.309	0.93
Max. VO2 [ml/(h animal)]	110.364 ± 3.88	115.714 ± 9.73	132.357 ± 8.205	129.1 ± 5.744	0.978	0.213	0.002	0.017
Avg. RER VCO2/VO2	0.877 ± 0.014	0.88 ± 0.023	0.867 ± 0.02	0.868 ± 0.019	0.052	0.739	NA	0.854
Avg. heat [kJ/(h animal)]	1.718 ± 0.081	1.744 ± 0.1	2.024 ± 0.113	2 ± 0.083	< 0.001	0.964	NA	0.376
Avg. distance [cm]	2945 ± 653	3792 ± 2446	2976 ± 579	2981 ± 830	0.352	0.309	NA	0.315
Avg. rearing [counts]	135 ± 82	142 ± 58	123 ± 60	88 ± 33	0.064	0.414	NA	0.23

No differences concerning energy metabolism

Results electrocardiography in U90926 wt versus KO mice (15 weeks)

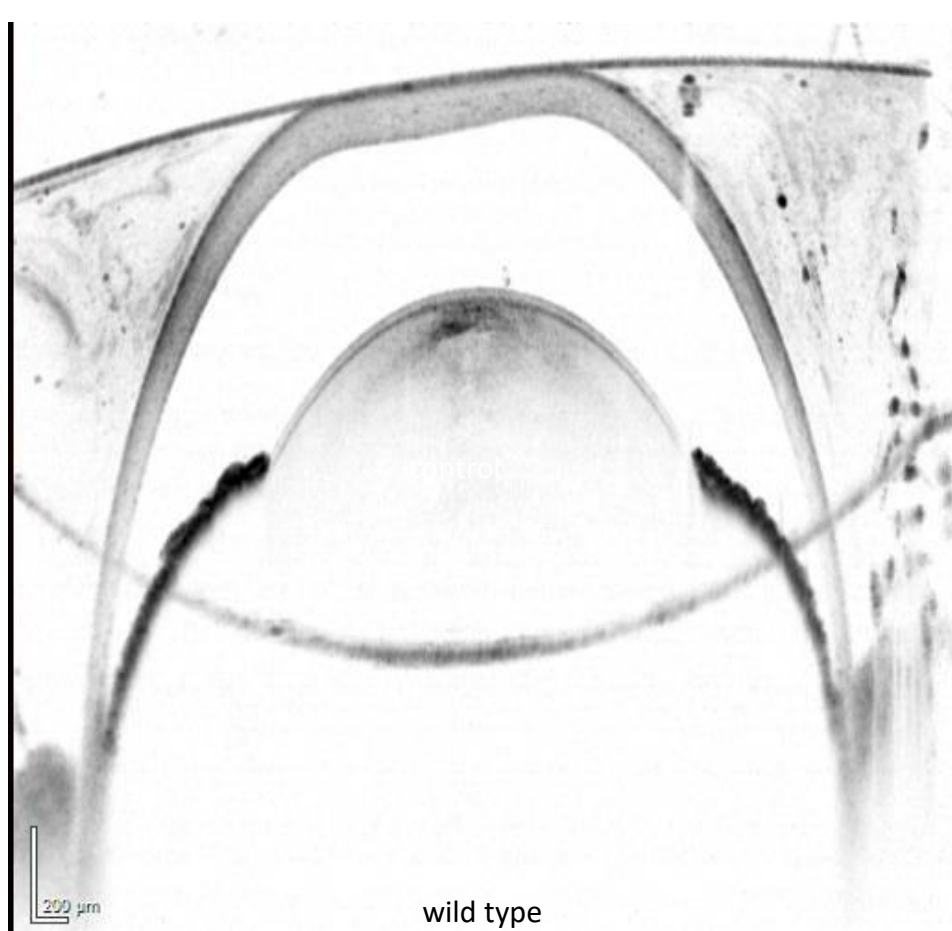
	female		male		female	male	overall
	wt	KO	wt	KO			
	n=11	n=13	n=14	n=10			
	median [25%, 75%]	median [25%, 75%]	median [25%, 75%]	median [25%, 75%]	p-value	p-value	p-value
Heart Rate [bpm]	762.4 [749.5 , 773.9]	752.5 [745 , 759.3]	756.5 [752.7 , 768.5]	755.4 [748.9 , 768.2]	0.186	0.875	0.208
RR [ms]	78.7 [77.5 , 80]	79.8 [79 , 80.5]	79.3 [78 , 79.8]	79.5 [78.1 , 80.2]	0.163	0.852	0.183
PR [ms]	30.2 [28.9 , 30.6]	30.1 [29.3 , 30.7]	29.9 [28.5 , 32.9]	31 [29.6 , 32.1]	0.876	0.784	0.577
QRS [ms]	13.7 [12.3 , 14.5]	12.7 [12.2 , 13.2]	12.7 [11.7 , 13.7]	12.8 [12.2 , 13.3]	0.171	0.655	0.223
QT [ms]	22.9 [22.1 , 23.9]	21.6 [20.8 , 22.3]	21.4 [19.6 , 23.4]	21.9 [20 , 22.6]	0.079	0.989	0.303
QTc [ms]	81.9 [79.4 , 84.5]	76.2 [72.9 , 79.3]	75.8 [69.5 , 83.7]	77.7 [70.5 , 81]	0.029	1	0.205
QT dispersion [ms]	1.9 [1.2 , 2.6]	0.9 [0.4 , 1.3]	1.1 [0.7 , 3.5]	1.2 [0.7 , 2.2]	0.09	0.516	0.086
QTc dispersion [ms]	6.6 [4 , 9.8]	3.2 [1.2 , 4.8]	4 [2.7 , 12.6]	4.5 [2.6 , 7.8]	0.13	0.463	0.094
P [ms]	10.2 [9.6 , 12.4]	10.1 [8.9 , 11.9]	11.2 [9.9 , 13.4]	11.3 [10.7 , 12.2]	0.433	0.886	0.477

Data presented in medians and confidence intervals. Statistics: Wilcoxon Rank Sum Test

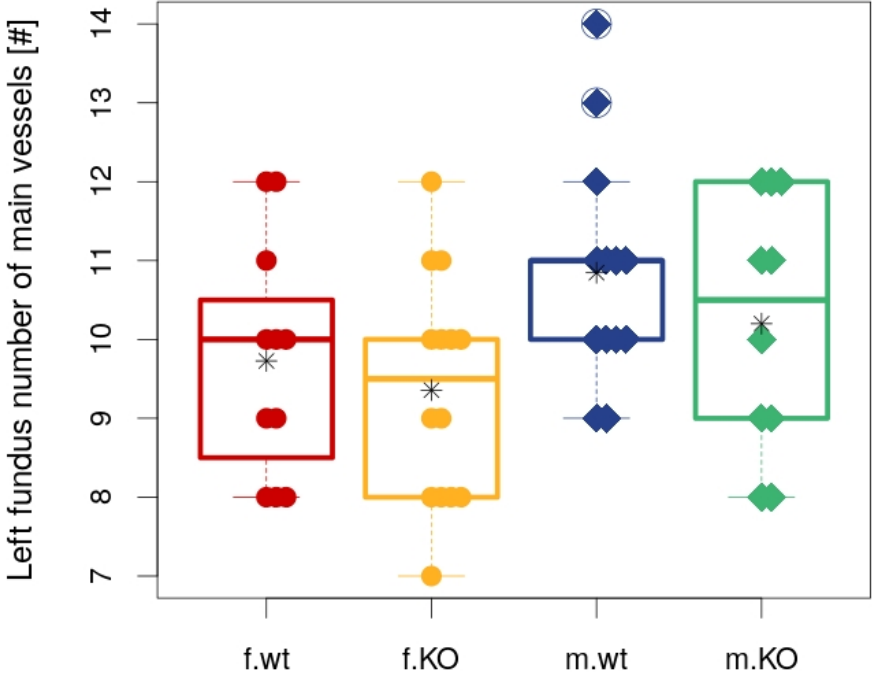
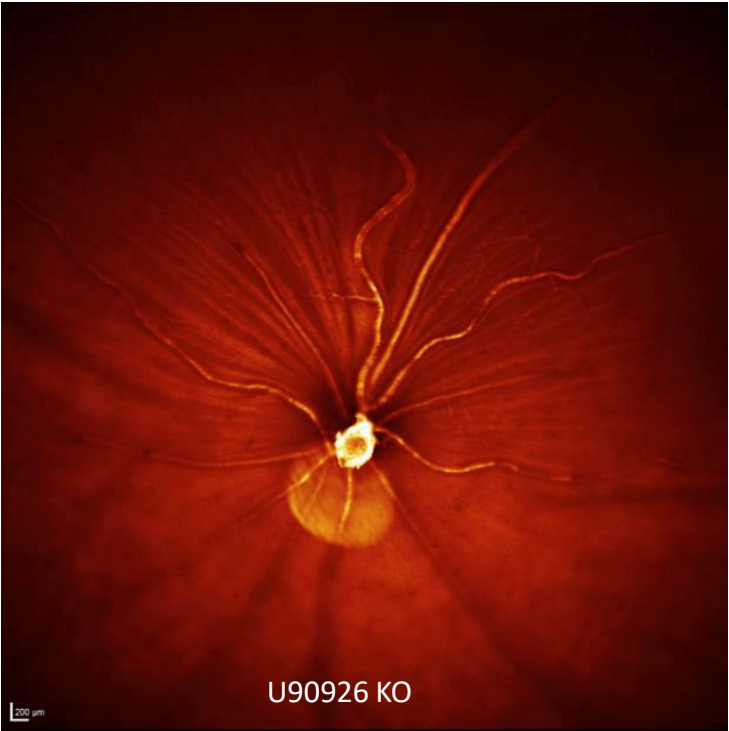
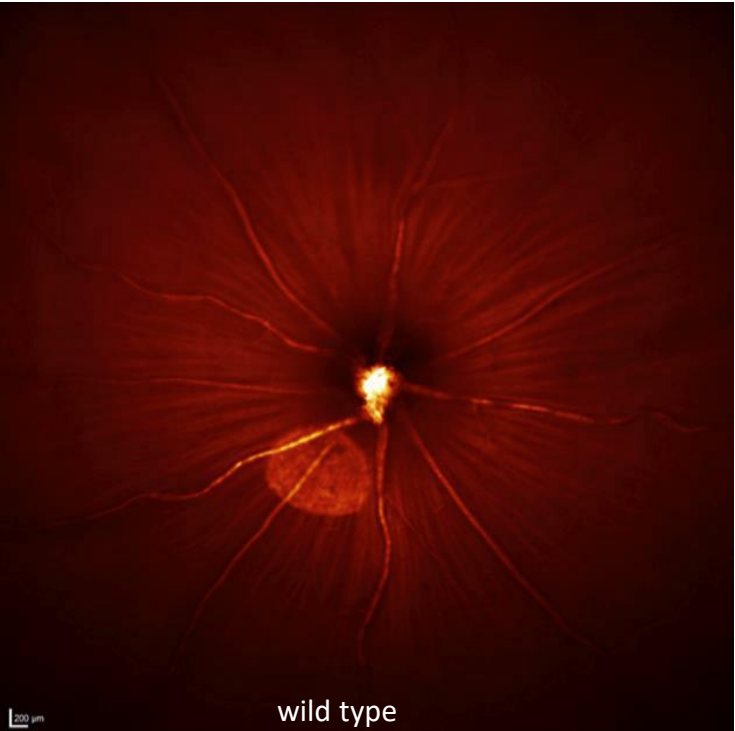
Results echocardiography in U90926 wt versus KO mice

	female		male		female	male	overall
	wt	KO	wt	KO			
	n=11	n=14	n=14	n=10			
	Median [25%, 75%]	Median [25%, 75%]	Median [25%, 75%]	Median [25%, 75%]	p-value	p-value	p-value
IVSs [mm]	0.55 [0.55, 0.56]	0.55 [0.55, 0.55]	0.55 [0.53, 0.58]	0.54 [0.52, 0.56]	0.909	0.33	0.474
IVSd [mm]	0.54 [0.53, 0.56]	0.54 [0.53, 0.55]	0.55 [0.53, 0.56]	0.53 [0.53, 0.54]	0.841	0.199	0.314
LVPWs [mm]	0.56 [0.54, 0.57]	0.55 [0.52, 0.56]	0.55 [0.55, 0.58]	0.55 [0.53, 0.56]	0.36	0.376	0.178
LVPWd [mm]	0.55 [0.55, 0.56]	0.55 [0.54, 0.56]	0.57 [0.54, 0.58]	0.54 [0.53, 0.55]	0.729	0.146	0.121
LVIDs [mm]	1.22 [1, 1.7]	1.62 [1.42, 1.96]	1.87 [1.2, 2.31]	1.58 [1.29, 1.87]	0.217	0.785	0.666
LVIDd [mm]	2.74 [2.5, 3.08]	3.12 [2.96, 3.35]	3.31 [2.79, 3.78]	3.27 [2.95, 3.54]	0.066	0.698	0.418
Weight [g]	23.1 [22.1, 23.4]	22.3 [21.4, 22.9]	30 [29.3, 30.9]	29.1 [28.4, 29.6]	0.298	0.149	0.081
Heart rate Echo [bpm]	486.01 [397.31, 588.1]	380.13 [303.35, 445.37]	416.04 [308.13, 568.89]	467.09 [418.45, 644.54]	0.12	0.285	0.684
Respiration Rate Echo [1/min]	200 [183.22, 217.31]	193.56 [178.16, 200.85]	231.89 [199.18, 241.22]	237.62 [220.78, 250.7]	0.366	0.24	0.725
Fractional shortening [percent]	53.1 [47.84, 61.62]	49.4 [42.34, 57.45]	45.94 [41.03, 57.66]	50.34 [42.7, 57.37]	0.344	0.977	0.656
Ejection fraction [percent]	85.89 [80.38, 91.6]	81.73 [74.6, 89.15]	78.06 [72.65, 88.97]	82.93 [75.21, 88.18]	0.344	0.931	0.641
Left ventricular mass corrected [mg]	33.06 [25.95, 37.35]	41.94 [35.91, 46.22]	46.41 [33.88, 53.45]	42.66 [34.51, 46.51]	0.044	0.395	0.555
Stroke Volume [μl]	24.01 [19.11, 28.61]	32.51 [27.43, 34.6]	37.17 [26, 41.05]	33.9 [29.9, 41.72]	0.051	0.666	0.572
Cardiac output [ml/min]	10.599 [9.832, 13.82]	10.574 [8.804, 12.595]	15.072 [10.261, 17.81]	14.857 [12.578, 16.595]	0.647	0.666	0.913
Left ventricular mass [mg]	39.71 [32.45, 44.72]	47.09 [42.08, 51.69]	53.9 [40.93, 61.06]	51.48 [41.61, 56.92]	0.075	0.508	0.529

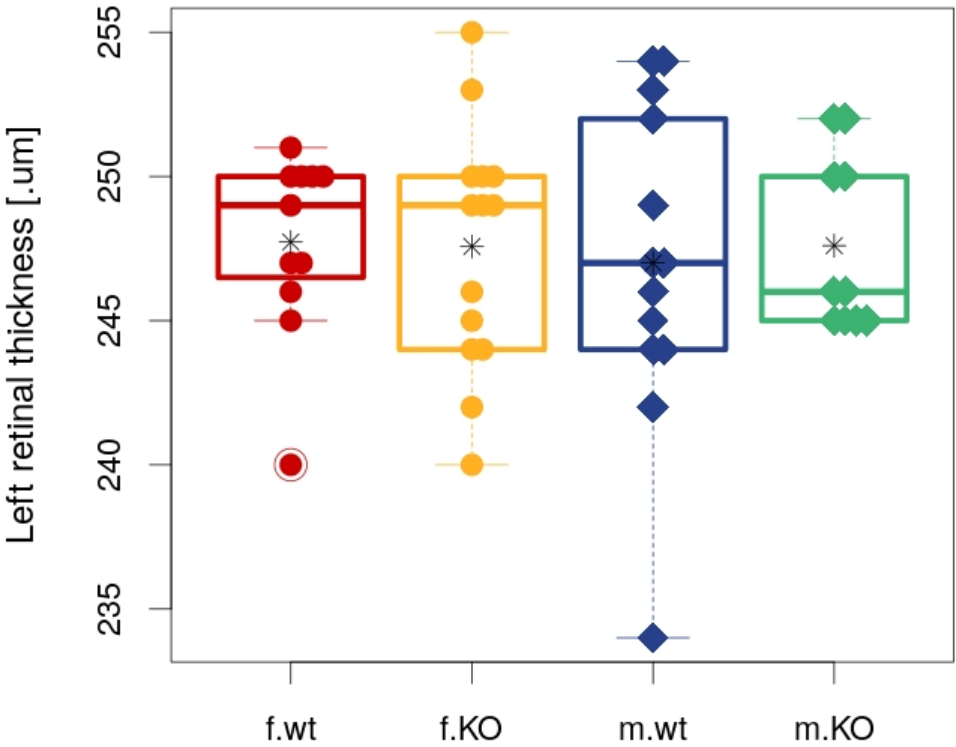
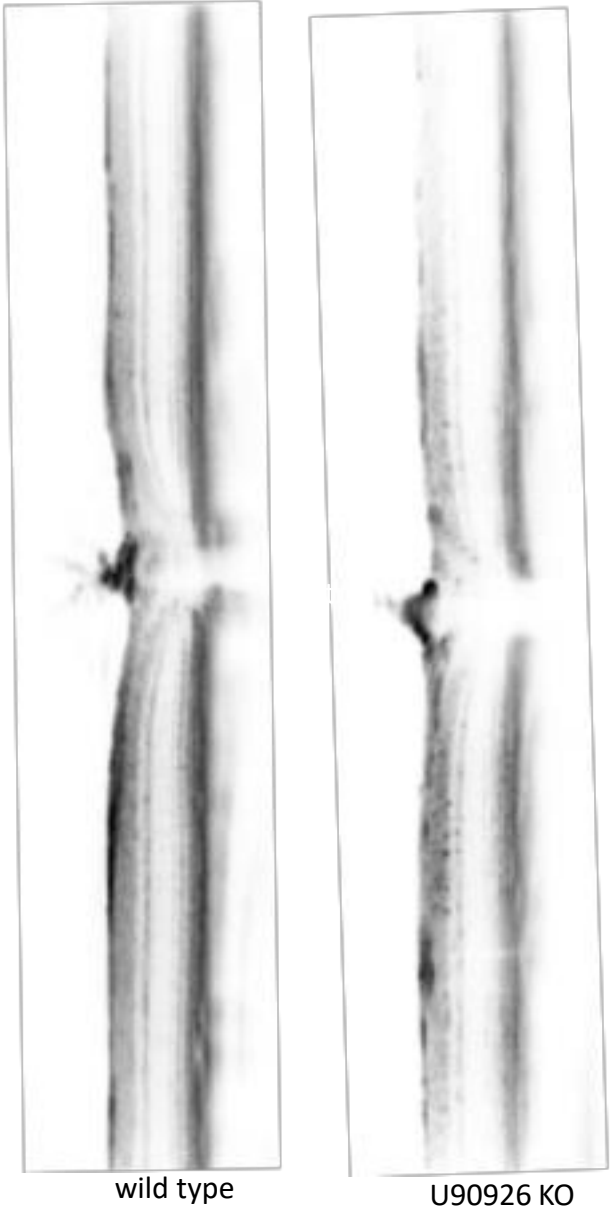
Results eye morphology – anterior segment (16 weeks)



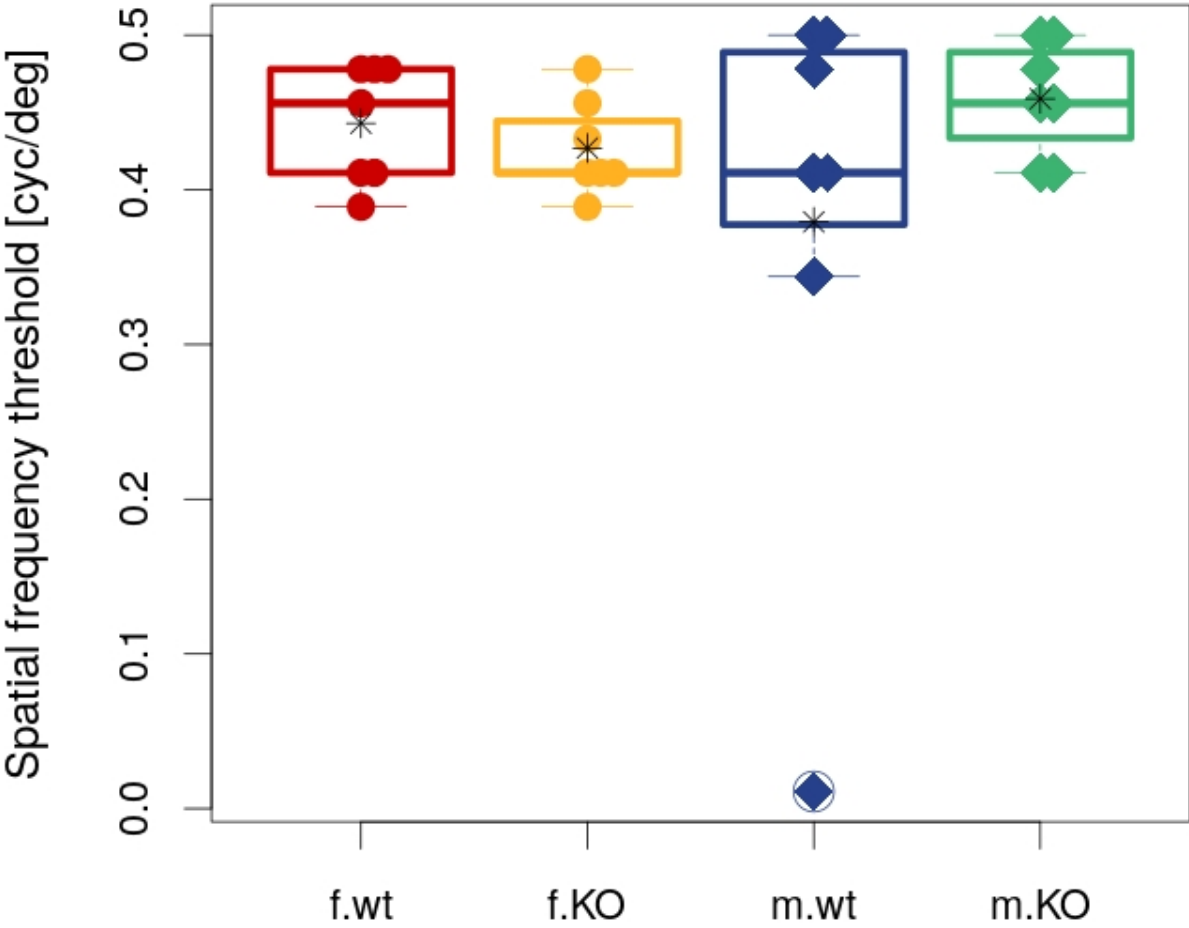
Lens and cornea are developed properly.



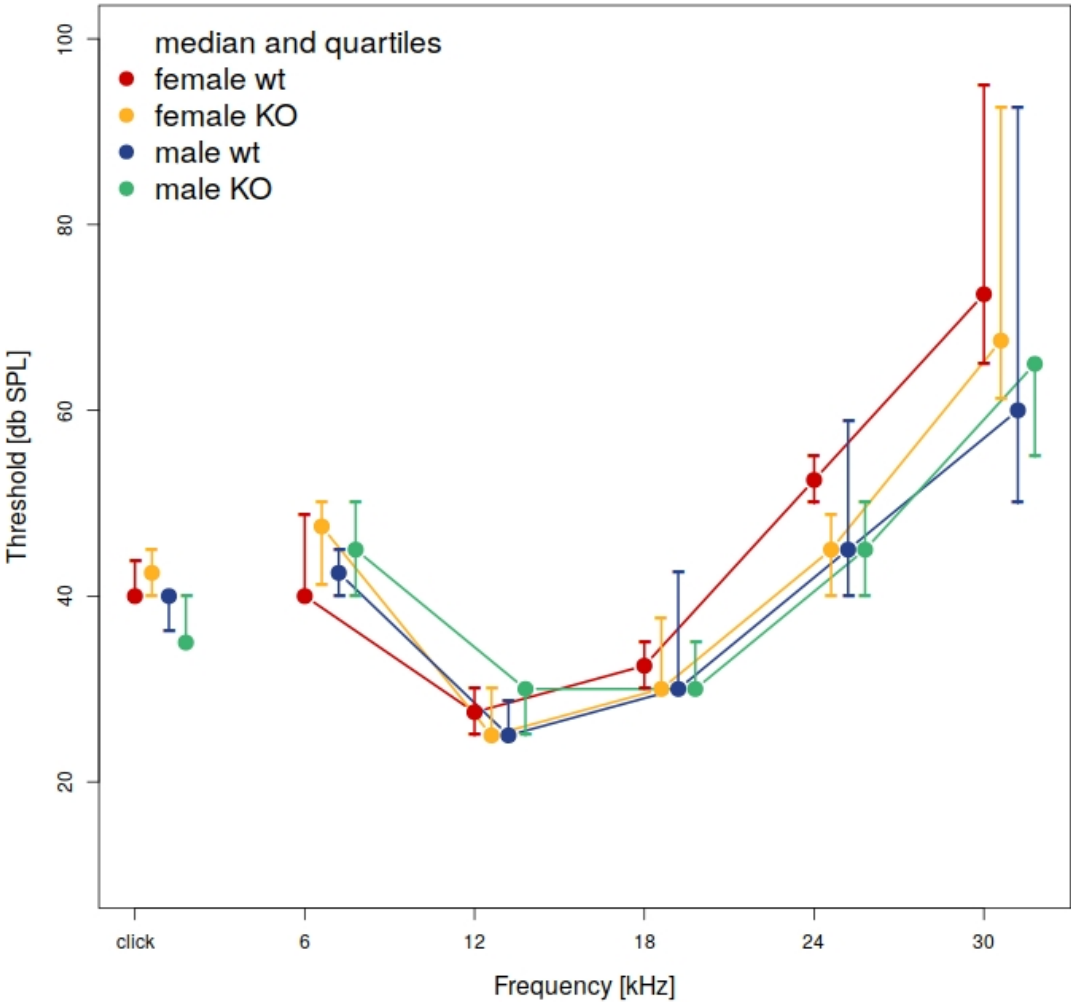
Fundus and retinal main blood vessels are similar to the ones of the control littermates.



Retinal layers are developed properly and the total retinal thickness is similar to the control littermate retina.



No alteration of the visual function was detected for the *U90926 KO* mutant mouse.

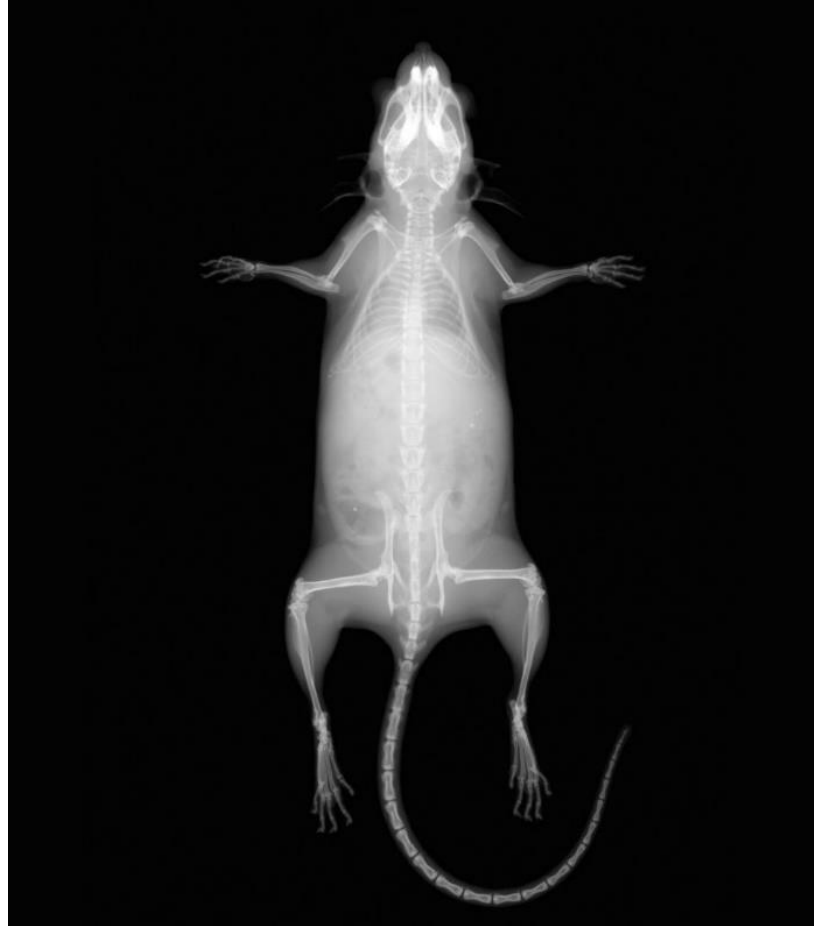


No differences for ABR thresholds

wt



U90926 KO



After X-ray analyses, no anatomical alterations were detected in U90926 KO mice

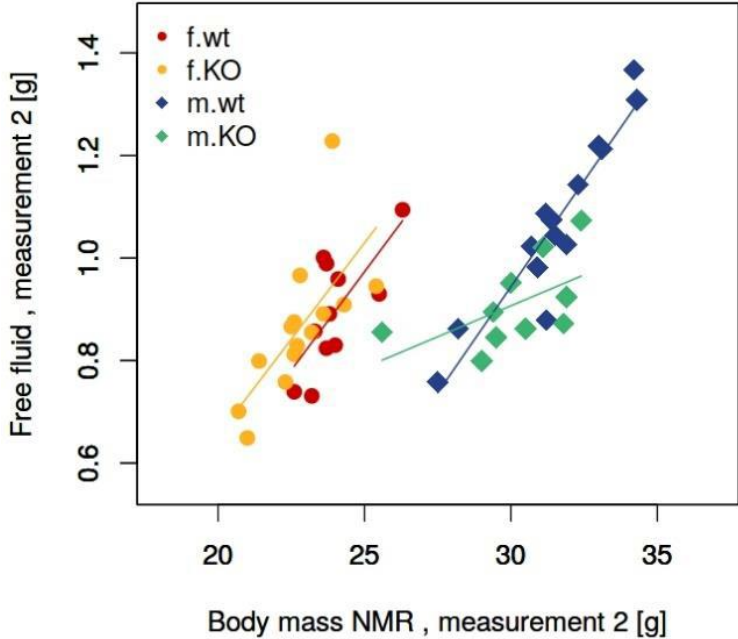
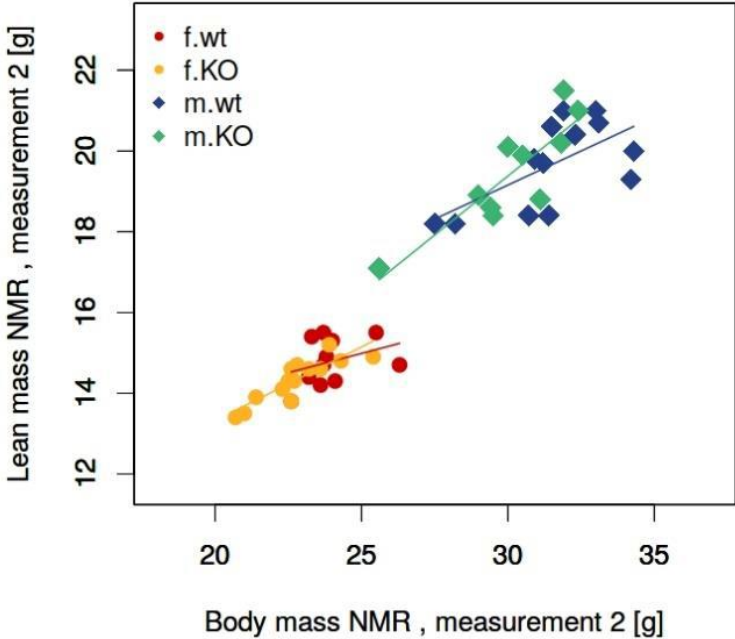
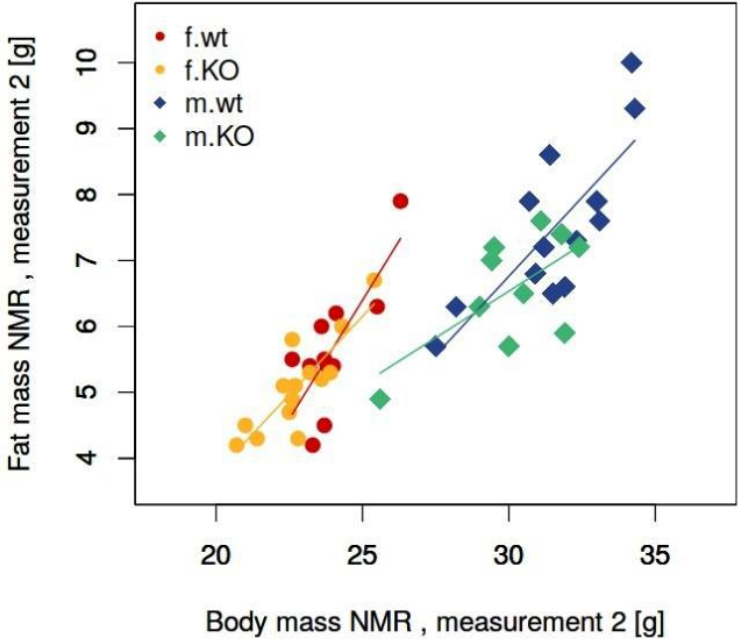
U90926 line: Dual-Energy X-Ray Absorptiometry (DEXA) (17 weeks)

	mean ± sd	mean ± sd	Δ %	ANOVA		mean ± sd	mean ± sd	Δ %	ANOVA
	female wt	female KO	KO-wt/wt	genotype		male wt	male KO	KO-wt/wt	genotype
	N=11	N=14		p-value		N=13	N=9		p-value
Body weight [g]	23.9 ± 0.9	23.4 ± 1.3	-2.1	0.307	Body weight [g]	31.4 ± 1.9	30.7 ± 2.2	-2.2	0.431
Total weight whole mouse DXA [g]	23.4 ± 1.0	23.0 ± 1.3	-1.7	0.379	Total weight whole mouse DXA [g]	31.2 ± 1.9	30.5 ± 2.3	-2.2	0.437
Bone area whole mouse [cm²]	8.17 ± 0.25	7.88 ± 0.24	-3.5	0.008	Bone area whole mouse [cm²]	8.68 ± 0.27	8.48 ± 0.46	-2.3	0.219
BMC whole mouse [mg]	527.481 ± 23.354	501.166 ± 28.784	-5	0.022	BMC whole mouse [mg]	580.105 ± 29.791	576.303 ± 47.167	-0.7	0.819
BMD whole mouse [mg/cm²]	64.5 ± 1.7	63.5 ± 2.4	-1.6	0.249	BMD whole mouse [mg/cm²]	66.8 ± 2.1	67.9 ± 2.4	1.6	0.287
vBMD whole mouse [mg/cm³]	22.6 ± 0.6	22.6 ± 0.8	0	0.807	vBMD whole mouse [mg/cm³]	22.7 ± 0.7	23.3 ± 0.5	2.6	0.031
Bone area ROI [cm²]	0.49 ± 0.03	0.47 ± 0.02	-4.1	0.01	Bone area ROI [cm²]	0.51 ± 0.03	0.53 ± 0.05	3.9	0.39
BMC ROI [mg]	35.368 ± 3.075	32.571 ± 3.174	-7.9	0.037	BMC ROI [mg]	35.991 ± 4.098	37.478 ± 5.530	4.1	0.476
BMD ROI [mg/cm²]	72.0 ± 4.2	70.0 ± 5.6	-2.8	0.342	BMD ROI [mg/cm²]	70.0 ± 5.0	71.0 ± 6.8	1.4	0.688
vBMD ROI [mg/cm³]	92.2 ± 2.8	93.3 ± 3.5	1.2	0.418	vBMD ROI [mg/cm³]	93.3 ± 3.2	93.7 ± 3.5	0.4	0.795

Decreased bone mineral content (BMC) in female mutants and slightly increased volumetric bone mineral density (vBMD) in male KO mice were detected by DEXA

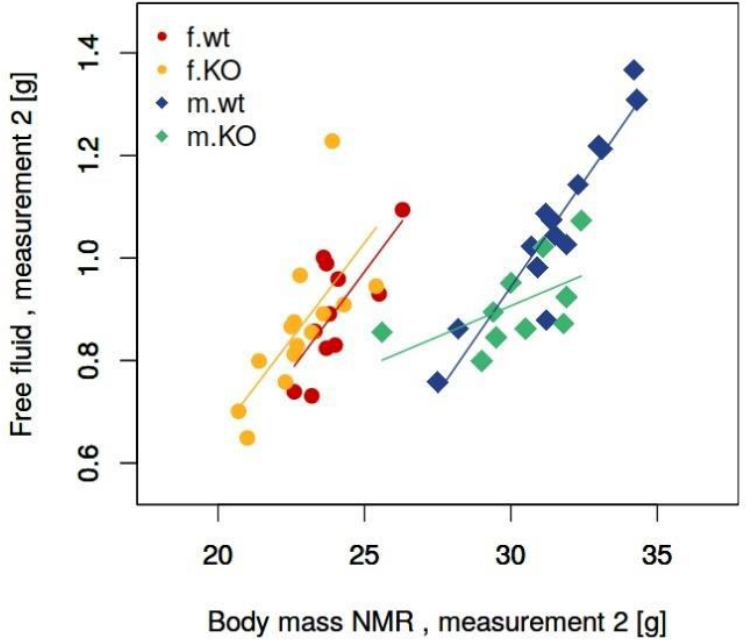
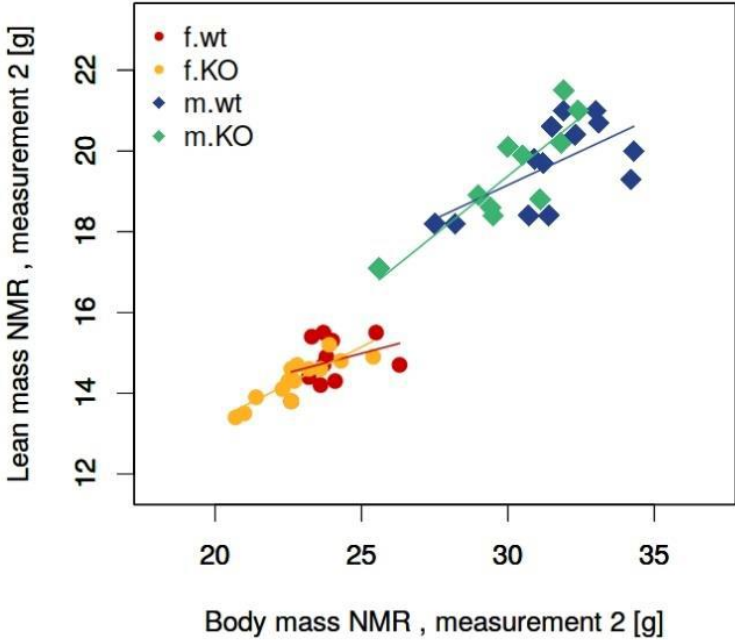
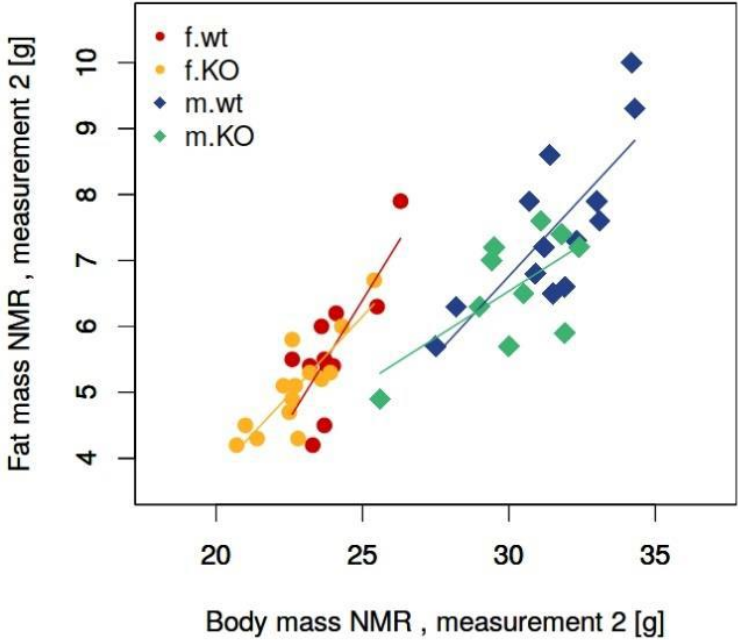
Body composition analysis II (18 weeks old)

	female		male		linear model	linear model	linear model	linear model
	wt	KO	wt	KO	sex	genotype	Bodymass	sex:genotype
	n=11	n=14	n=14	n=10				
	mean ± sd	mean ± sd	mean ± sd	mean ± sd	p-value	p-value	p-value	p-value
Body mass NMR	24 ± 1	22.8 ± 1.3	31.5 ± 1.9	30.1 ± 2	< 0.001	0.007	NA	0.82
Fat mass NMR	5.7 ± 1	5.1 ± 0.7	7.5 ± 1.2	6.6 ± 0.9	0.002	0.415	< 0.001	0.484
Lean mass NMR	14.8 ± 0.6	14.3 ± 0.5	19.7 ± 1	19.4 ± 1.3	< 0.001	0.356	< 0.001	0.392
Free fluid	0.9 ± 0.1	0.9 ± 0.1	1.1 ± 0.2	0.9 ± 0.1	< 0.001	0.621	< 0.001	0.032
Adiposity Index	0.4 ± 0.1	0.4 ± 0	0.4 ± 0.1	0.3 ± 0	0.001	0.419	< 0.001	0.658



Body composition analysis II (18 weeks old)

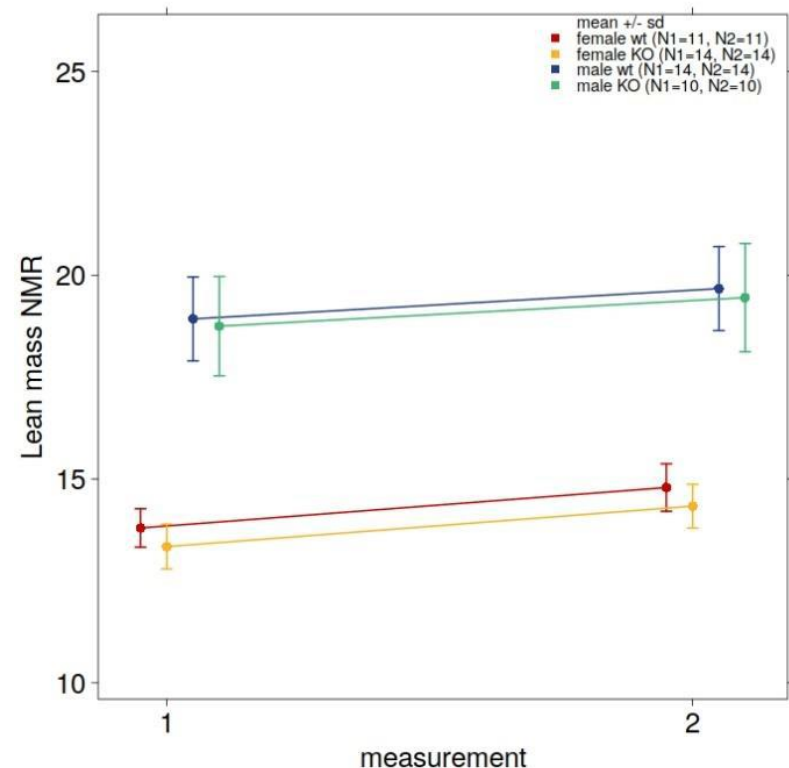
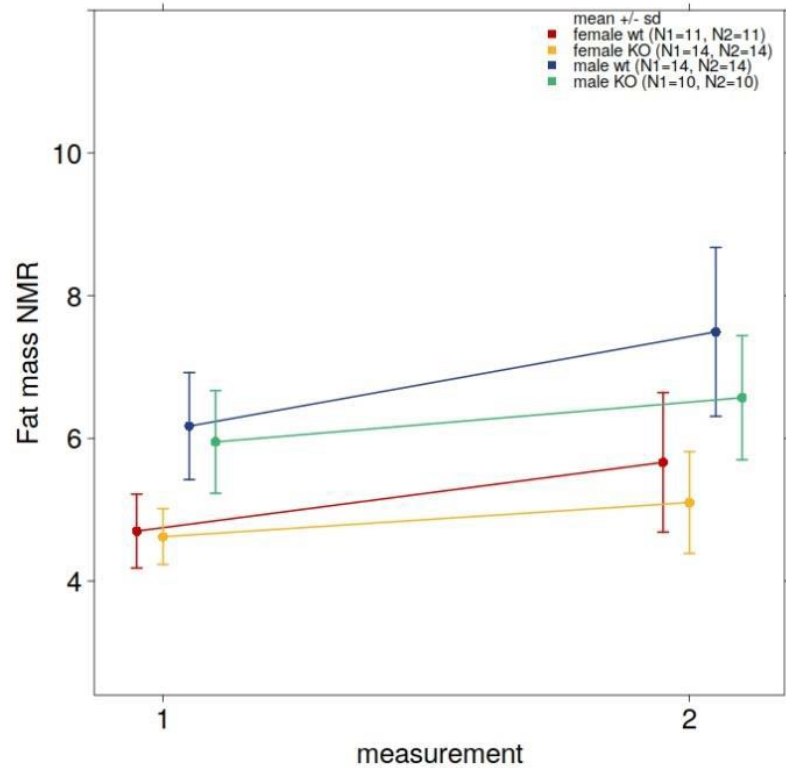
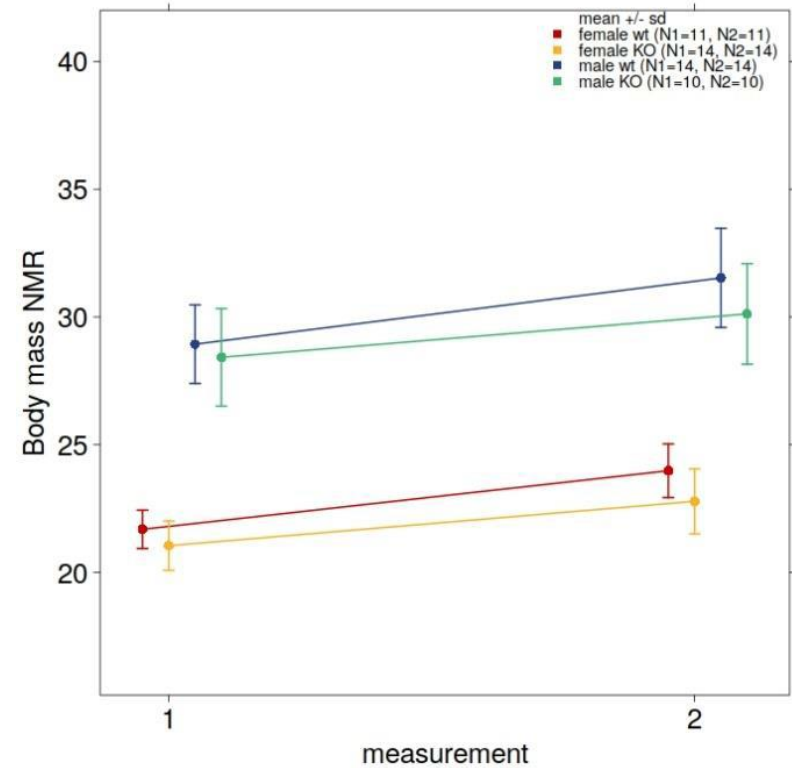
	female		male		linear model	linear model	linear model	linear model
	wt	KO	wt	KO	sex	genotype	Bodymass	sex:genotype
	n=11	n=14	n=14	n=10				
	mean ± sd	mean ± sd	mean ± sd	mean ± sd	p-value	p-value	p-value	p-value
Body mass NMR	24 ± 1	22.8 ± 1.3	31.5 ± 1.9	30.1 ± 2	< 0.001	0.007	NA	0.82
Fat mass NMR	5.7 ± 1	5.1 ± 0.7	7.5 ± 1.2	6.6 ± 0.9	0.002	0.415	< 0.001	0.484
Lean mass NMR	14.8 ± 0.6	14.3 ± 0.5	19.7 ± 1	19.4 ± 1.3	< 0.001	0.356	< 0.001	0.392
Free fluid	0.9 ± 0.1	0.9 ± 0.1	1.1 ± 0.2	0.9 ± 0.1	< 0.001	0.621	< 0.001	0.032
Adiposity Index	0.4 ± 0.1	0.4 ± 0	0.4 ± 0.1	0.3 ± 0	0.001	0.419	< 0.001	0.658



Mutants showed a subtle genotype-dependent body weight reduction

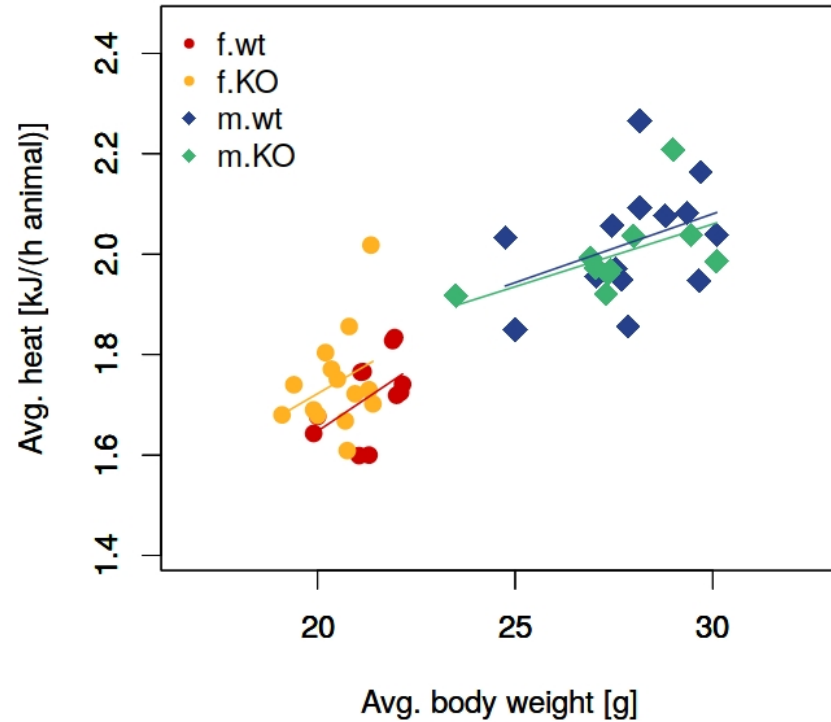
Body composition analysis (13-18 weeks old)

	sex	genotype	measurement	Bodymass	genotype:measurement
Body mass NMR	< 0.001	0.027	< 0.001	NA	< 0.001
Fat mass NMR	< 0.001	0.905	0.438	< 0.001	0.044
Lean mass NMR	< 0.001	0.744	0.923	< 0.001	0.026



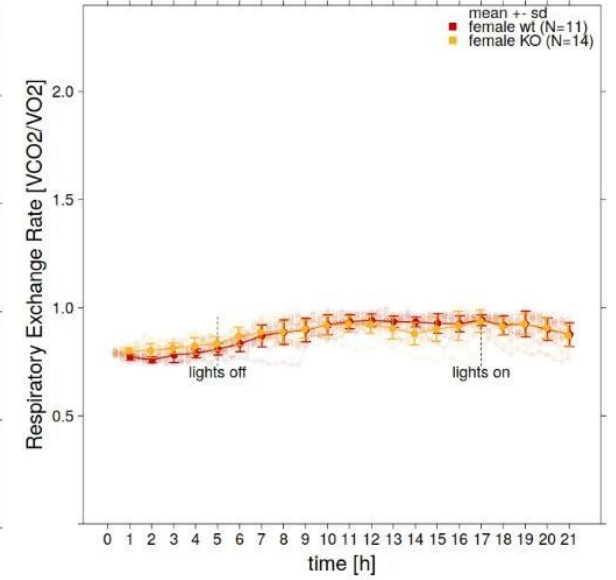
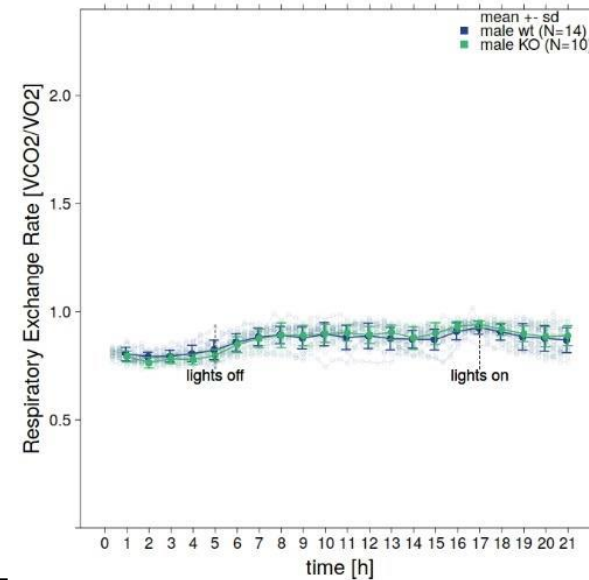
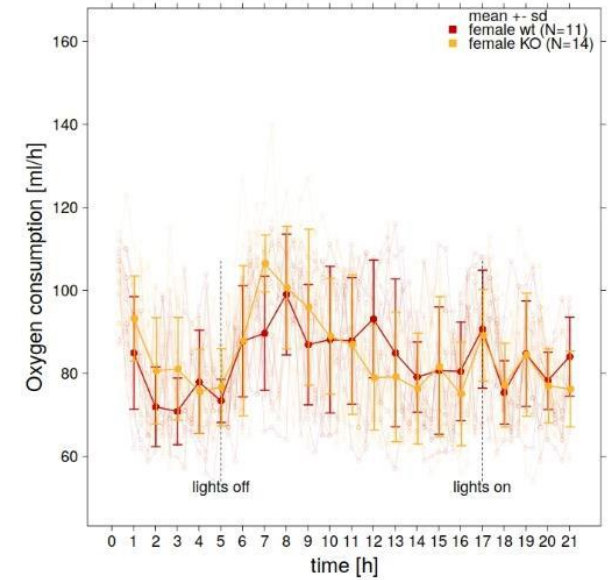
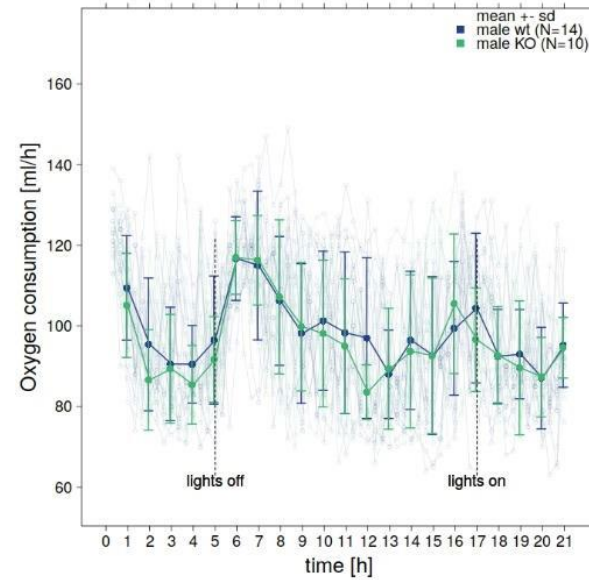
Tendency in gaining less fat amount with ageing

Indirect Calorimetry – substrate oxidation rates



Slightly higher metabolic rate in females

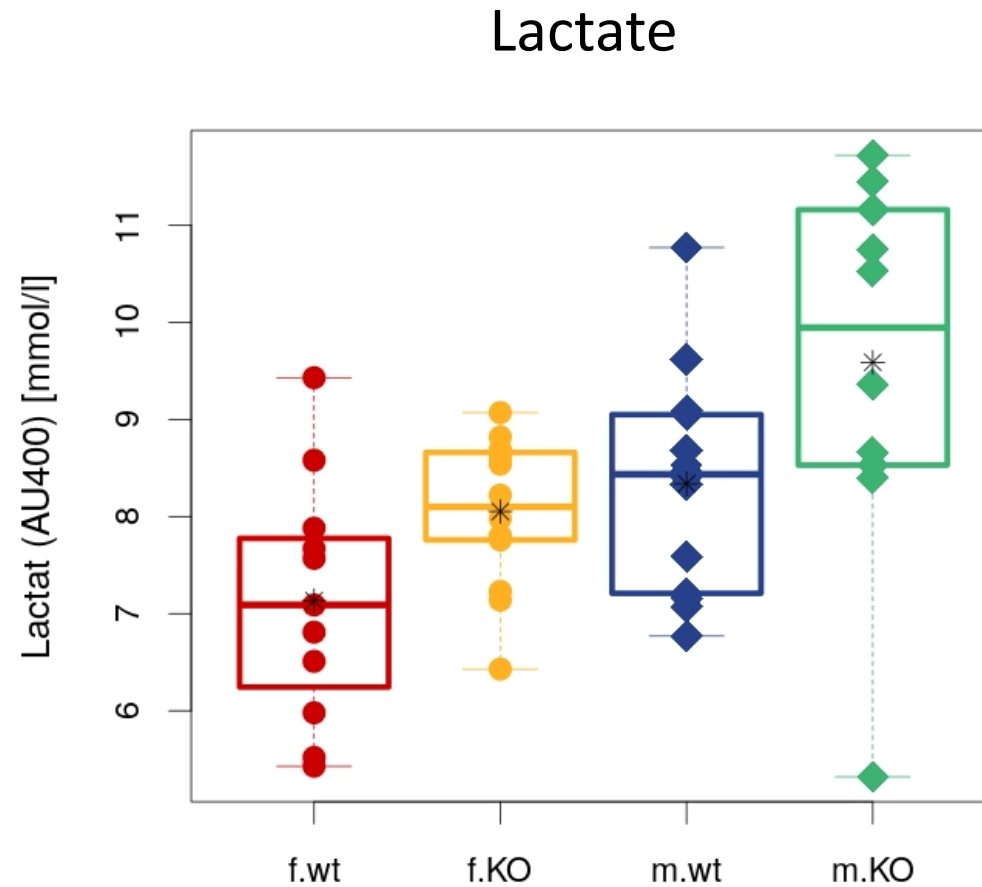
Matching max oxygen consumption rates



Results hematology (19 weeks)

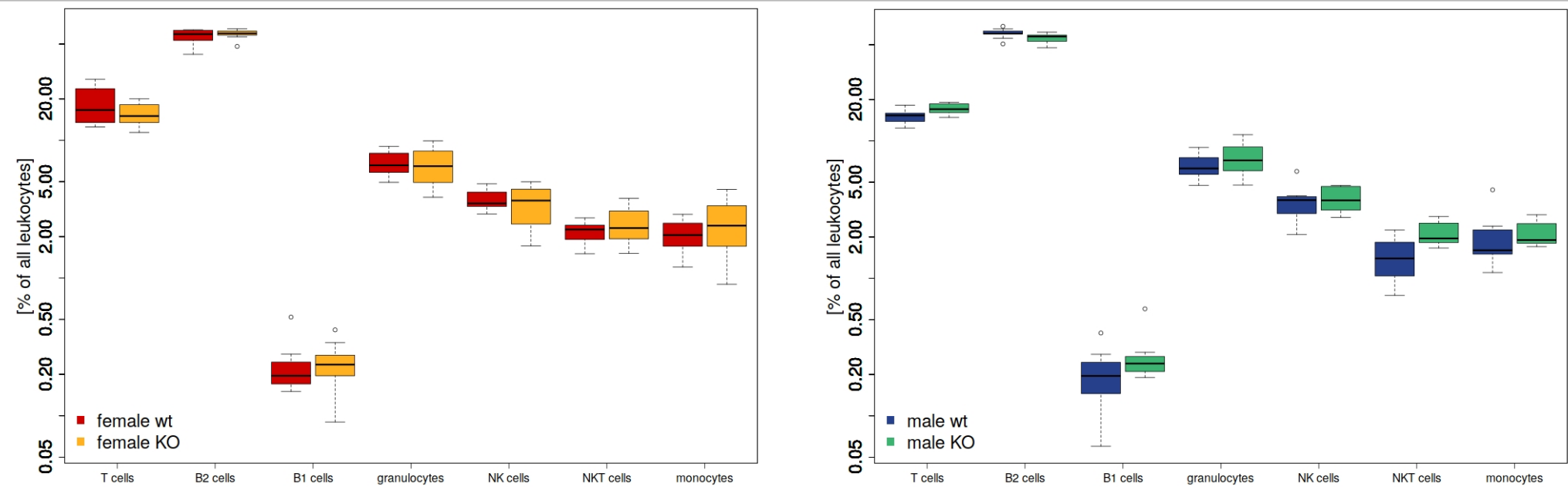
U90926_KO	female		male		linear model	linear model	linear model
	wt	KO	wt	KO	genotype	sex	genotype:sex
	n=11	n=14	n=14	n=10			
	mean ± sd	mean ± sd	mean ± sd	mean ± sd	p-value	p-value	p-value
RBC [Mio/mm ³]	10.45 ± 0.41	10.4 ± 0.53	10.17 ± 0.36	10.12 ± 0.69	0.738	0.059	0.97
HGB [g/dl]	16.38 ± 0.78	16.25 ± 0.84	15.56 ± 0.52	15.52 ± 1.05	0.704	0.002	0.85
HCT [%]	50.29 ± 2.01	49.36 ± 2.5	47.79 ± 1.5	47.7 ± 2.89	0.438	0.002	0.519
MCV [fl]	48.18 ± 0.98	47.57 ± 1.55	47.14 ± 1.1	47.1 ± 0.57	0.331	0.028	0.398
MCH [pg]	15.67 ± 0.55	15.62 ± 0.47	15.31 ± 0.42	15.36 ± 0.63	0.996	0.04	0.726
MCHC [g/dl]	32.57 ± 0.79	32.91 ± 0.59	32.59 ± 0.61	32.54 ± 1.21	0.526	0.439	0.407
RDW [%]	13.32 ± 0.32	14.24 ± 3.73	14.47 ± 0.98	14.75 ± 0.57	0.329	0.175	0.6
WBC [10 ³ /mm ³]	4.99 ± 1.86	4.94 ± 1.29	6.87 ± 2.12	7.11 ± 1.5	0.855	< 0.001	0.77
PLT [10 ³ /mm ³]	973.36 ± 130.33	981.43 ± 188.33	1234.86 ± 115.8	1232.9 ± 145.08	0.944	< 0.001	0.908
MPV [fl]	6.55 ± 0.25	6.51 ± 0.17	6.29 ± 0.13	6.27 ± 0.16	0.561	< 0.001	0.883
PDW [fL]	6.03 ± 0.41	5.99 ± 0.3	5.61 ± 0.22	5.59 ± 0.25	0.738	< 0.001	0.889
PLCR [%]	2.97 ± 0.72	2.69 ± 0.57	2.05 ± 0.36	2.09 ± 0.46	0.431	< 0.001	0.298
PCT [%]	0.64 ± 0.08	0.64 ± 0.13	0.78 ± 0.08	0.77 ± 0.08	0.914	< 0.001	0.863

No evidence of genotype-related effects on hematological parameters.



Slightly elevated lactate levels in mutant animals as compared to controls.
Linear model, genotype effect $p = 0,005$

Results flow cytometry_main leukocyte lineages (19 weeks)

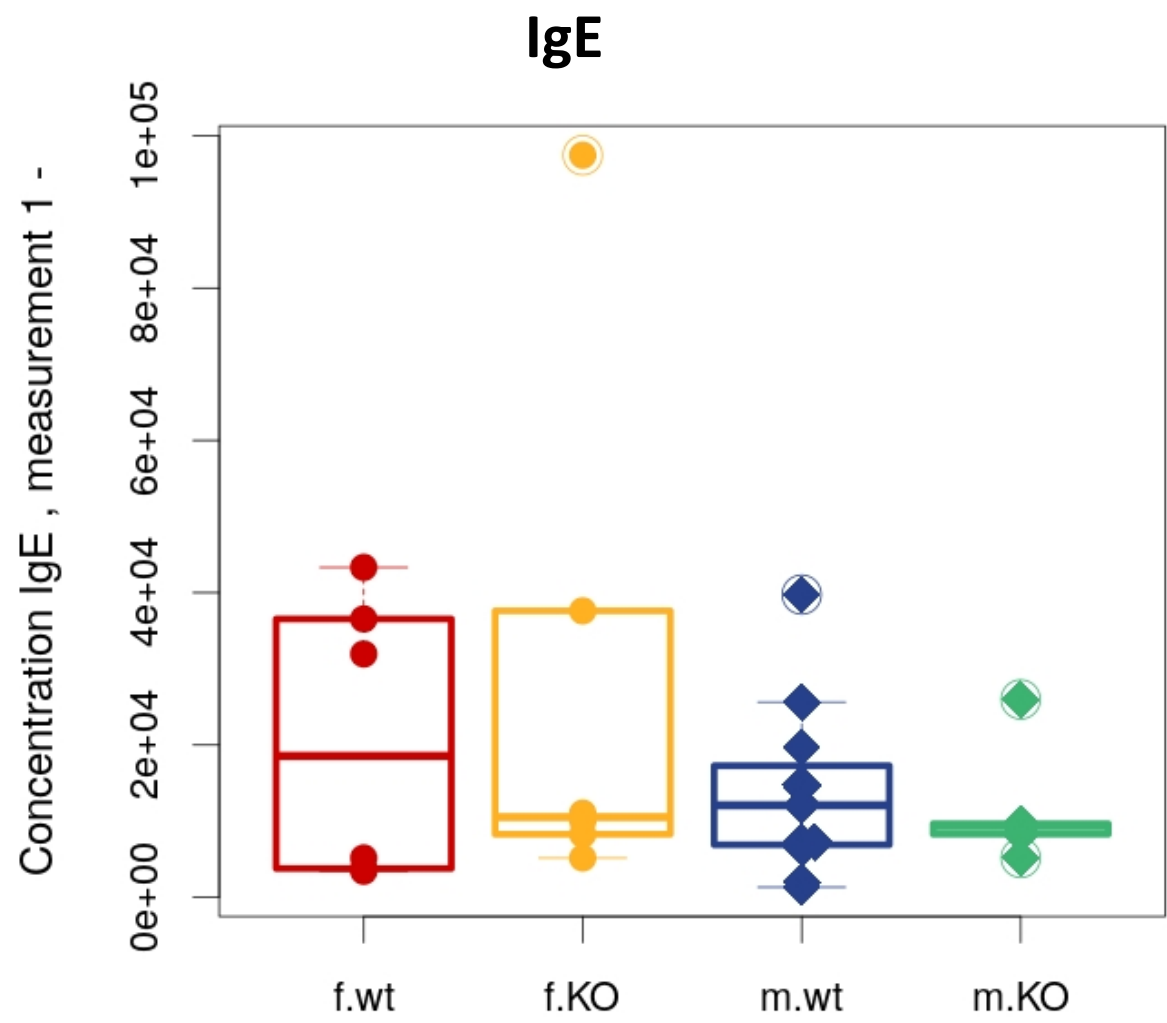


	female		male		female	male	overall
	wt	KO	wt	KO			
	n=8	n=12	n=12	n=7			
	median	median	median	median	p-value	p-value	p-value
	[25%, 75%]	[25%, 75%]	[25%, 75%]	[25%, 75%]			
T cells	16.6	15	15.3	17	0.353	0.017	0.545
	[13.88 , 23.2]	[13.97 , 17.62]	[14.03 , 15.8]	[16.05 , 18.6]			
B2 cells	59.1	59.75	60.3	57.4	0.72	0.027	0.222
	[54.27 , 62.95]	[58.33 , 61.9]	[59.95 , 62.45]	[52.95 , 58.8]			
B1 cells	0.2	0.24	0.2	0.24	0.314	0.104	0.047
	[0.18 , 0.23]	[0.2 , 0.27]	[0.15 , 0.23]	[0.21 , 0.27]			
granulocytes	6.58	6.49	6.3	7.21	0.571	0.34	0.829
	[6.06 , 7.7]	[4.97 , 8.32]	[5.76 , 7.34]	[6.06 , 9.04]			
NK cells	3.48	3.65	3.7	3.69	0.851	0.522	0.873
	[3.37 , 4.19]	[2.51 , 4.27]	[3.08 , 3.92]	[3.13 , 4.66]			
NKT cells	2.25	2.31	1.4	1.95	0.508	0.014	0.007
	[1.98 , 2.42]	[1.96 , 3.03]	[1.04 , 1.82]	[1.82 , 2.52]			
monocytes	2	2.4	1.6	1.9	0.415	0.112	0.101
	[1.7 , 2.4]	[1.8 , 3.3]	[1.5 , 2.2]	[1.8 , 2.5]			

Results flow cytometry_sub-populations (19 weeks)

	female		male		female	male	overall
	wt	KO	wt	KO			
	n=8	n=12	n=12	n=7			
	median	median	median	median	p-value	p-value	p-value
	[25%, 75%]	[25%, 75%]	[25%, 75%]	[25%, 75%]			
T/CD4+	55.1	54.05	54.7	54.5	0.851	0.837	0.776
	[52.92 , 56.3]	[52.3 , 57.67]	[52.9 , 55.88]	[52.55 , 54.9]			
T/CD8+	41.5	41.25	42.4	42.5	0.836	0.664	0.873
	[39.55 , 43.83]	[38.85 , 42.83]	[41.02 , 43.3]	[41.6 , 44.55]			
T/DP	0.2	0.32	0.29	0.43	0.314	0.047	0.177
	[0.18 , 0.27]	[0.22 , 0.38]	[0.26 , 0.37]	[0.31 , 0.46]			
T/DN	3.67	4.13	3.06	2.51	0.215	0.261	0.518
	[2.84 , 3.9]	[3.54 , 5.09]	[2.55 , 3.59]	[2.34 , 2.94]			
T/gdTCR+	2.25	2.96	2.04	1.96	0.175	0.419	0.448
	[2.03 , 2.75]	[2.6 , 3.42]	[1.94 , 2.28]	[1.83 , 2.1]			
gdTCR+/DN	84.7	89.7	87.25	88.9	0.129	0.853	0.177
	[81.38 , 89.83]	[88.4 , 92.58]	[84.8 , 91.25]	[84.75 , 91.45]			

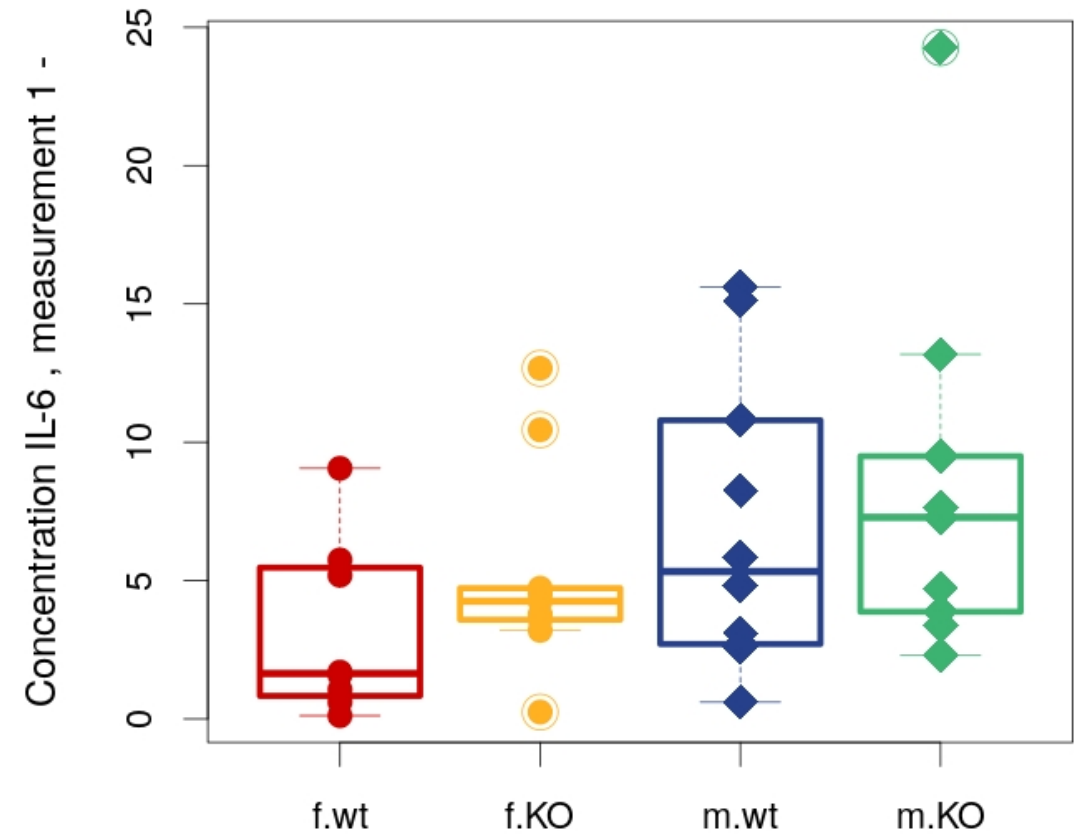
	female		male		female	male	overall
	wt	KO	wt	KO			
	n=8	n=12	n=12	n=7			
	median	median	median	median	p-value	p-value	p-value
	[25%, 75%]	[25%, 75%]	[25%, 75%]	[25%, 75%]			
Ly6C low monocytes	26.6	26.1	22.4	18.5	0.91	0.261	0.923
	[23.1 , 30.3]	[21.4 , 37]	[16 , 30.5]	[13.3 , 19.9]			
Ly6C intermediate monocytes	16.6	19.6	15.9	16.9	0.262	0.983	0.261
	[13.6 , 19.4]	[15.3 , 21.9]	[12.5 , 18.3]	[11.9 , 17.9]			
Ly6C high monocytes	36	33.2	38.8	44.6	0.97	0.711	0.972
	[23.2 , 40.8]	[20.6 , 46]	[31 , 53.4]	[40.8 , 48]			



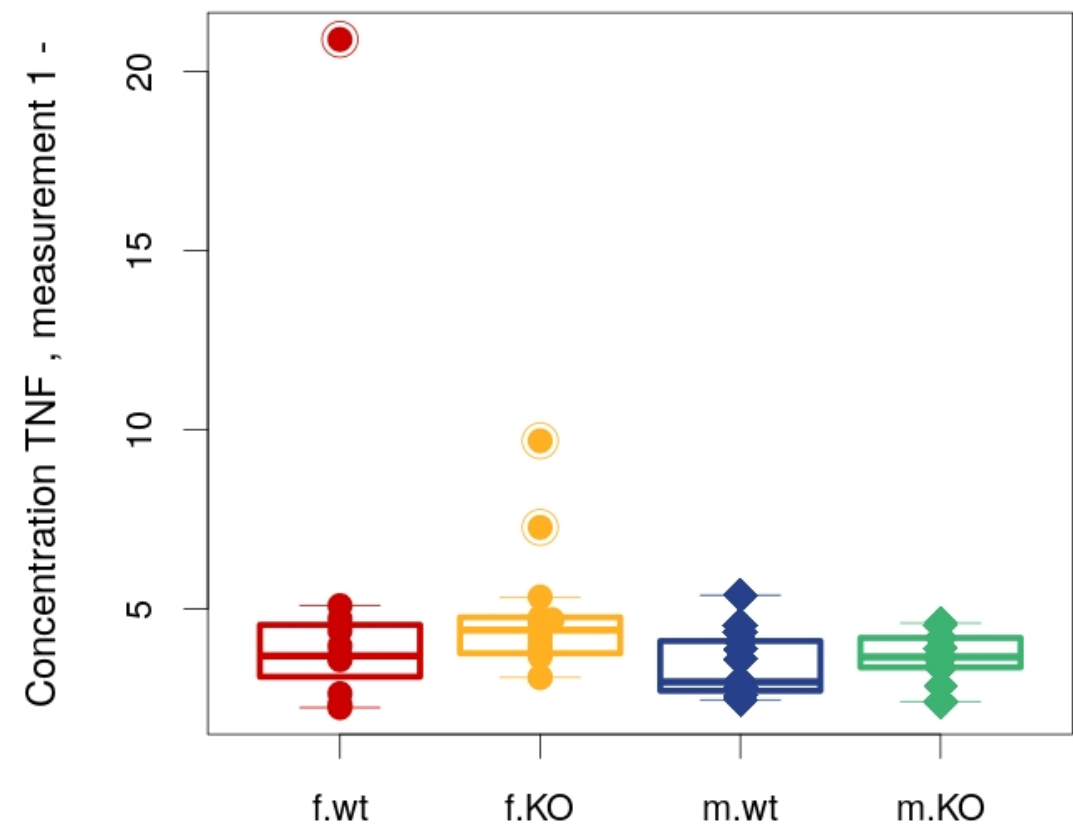
No phenotype

Means, Standard deviations and p-values of a Wilcoxon test.

IL-6



TNFa



Means, Standard deviations and p-values of a Wilcoxon test.

Macroscopy visceral organs weight (19 weeks)

Means, standard deviation and p-values calculated by a linear model (parameter ~ genotype * sex + body weight)

	female		male		linear model	linear model	linear model	linear model
	wt	KO	wt	KO	genotype	sex	bodyWeight	genotype:sex
	n=5	n=5	n=5	n=5				
	mean ± sd	mean ± sd	mean ± sd	mean ± sd	p-value	p-value	p-value	p-value
Heart weight [mg]	134 ± 19.1	137.2 ± 10.2	164.8 ± 20.4	184.4 ± 28.7	0.499	0.578	0.081	0.803
Tibia length [mm]	18.22 ± 0.47	18.19 ± 0.48	18.6 ± 0.18	18.78 ± 0.47	0.732	0.27	0.924	0.635
Age of mice when culled [day]	141 ± 2	141 ± 2	143 ± 2	140 ± 1	0.08	0.739	0.951	0.18
Liver weight [g]	1.291 ± 0.233	1.226 ± 0.191	1.694 ± 0.109	1.705 ± 0.115	0.652	0.031	0.679	0.761
Spleen weight [g]	0.099 ± 0.025	0.086 ± 0.007	0.079 ± 0.009	0.088 ± 0.018	0.796	0.429	0.81	0.232

Histological findings – genotype-specific differences (19 weeks)

Skin	NAD	Oesophagus	NAD
Brain	NAD	Stomach	NAD
Cervical lymph node	NAD	Small intestine	NAD
Salivary glands	NAD	Large intestine	NAD
Trachea	NAD	Pancreas	NAD
Thyroid	NAD	Testes	NAD
Parathyroid	NAD	Epididymides	NAD
Heart	NAD	Funiculus spermaticus	NAD
Lung	NAD	Prostate	NAD
Thymus	NAD	Male accessory glands	NAD
Spleen	NAD	Ovaries	NAD
liver	NAD	Uterus	NAD
Adrenals	NAD	Vagina	NAD
Kidney	NAD	Urinary bladder	NAD
WAT	NAD	BAT	NAD

NAD: no alterations determined