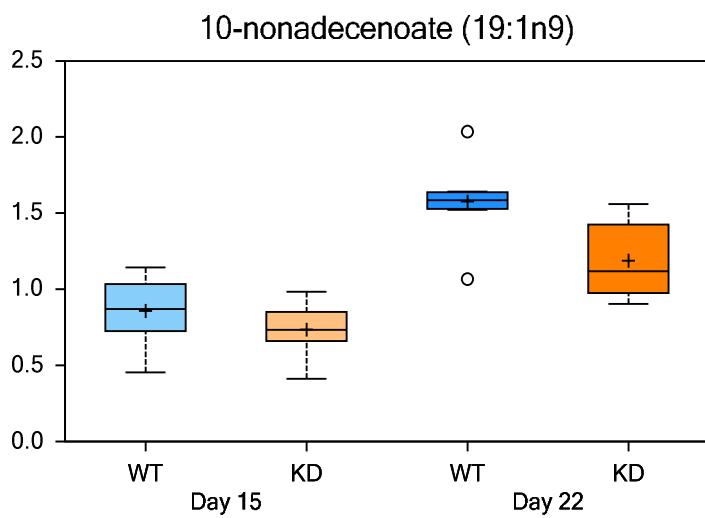
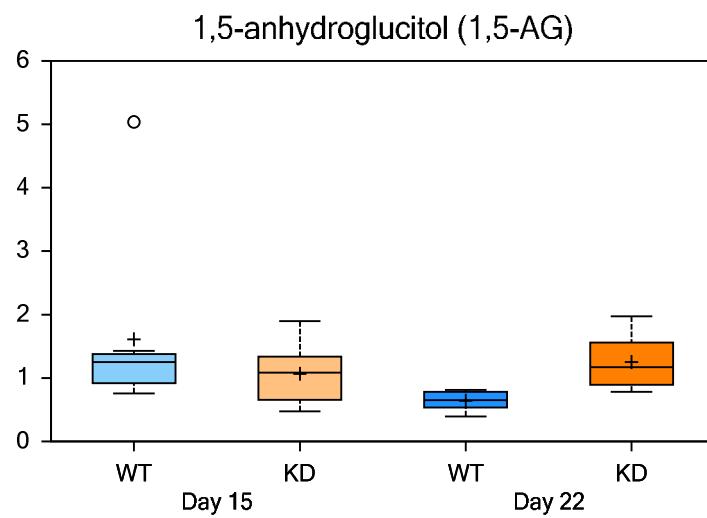
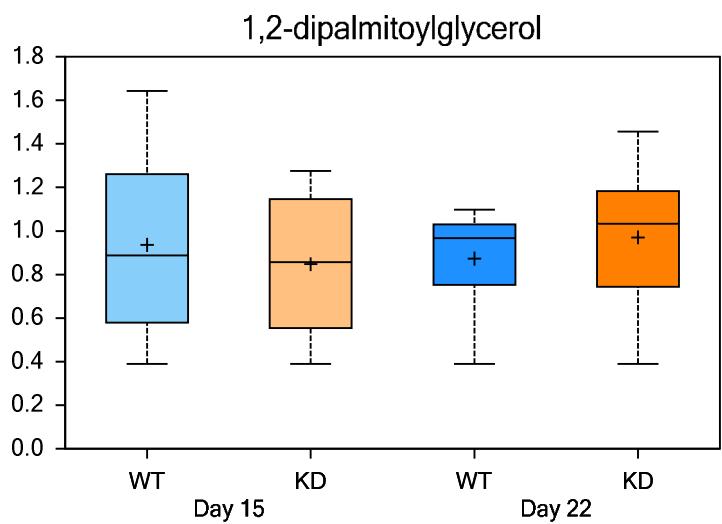
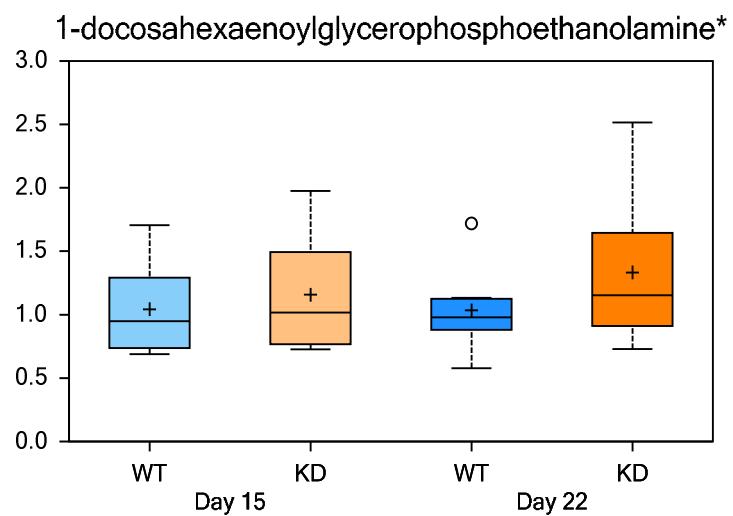
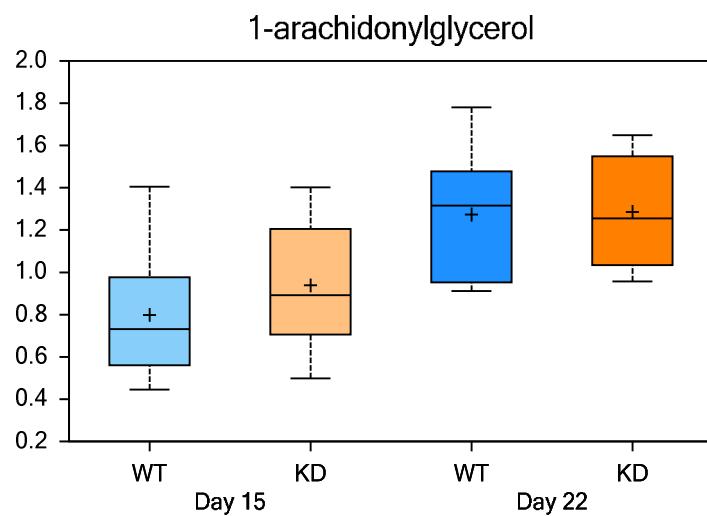
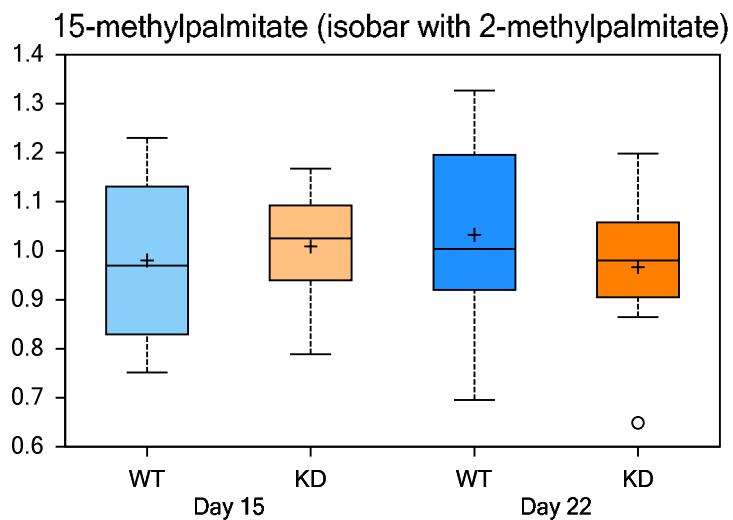


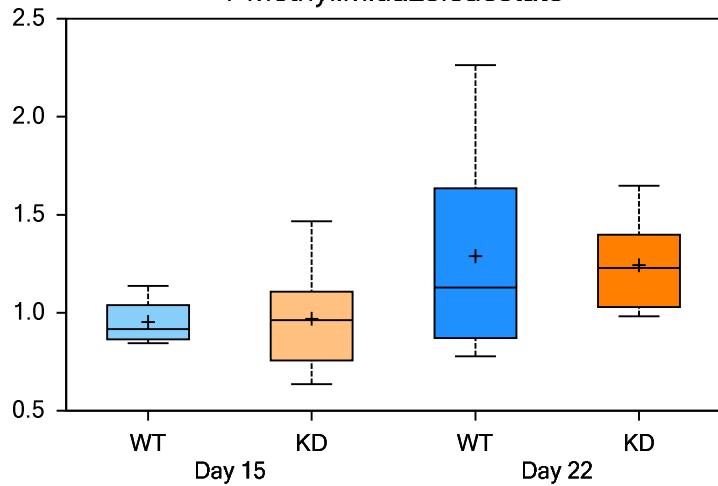
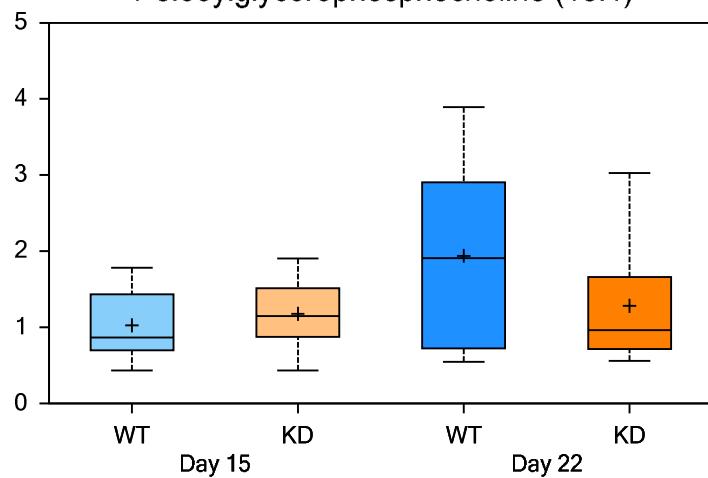
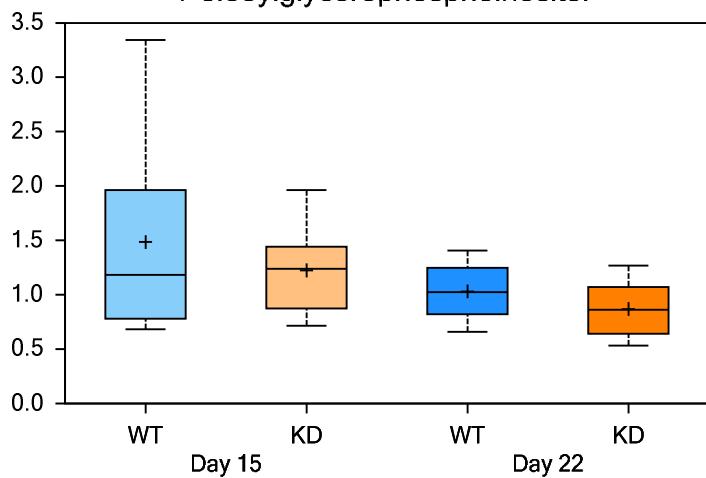
Supplementary Table 1. Heat map of all 314 metabolites profiled in this study. Red and blue shaded cells indicate $p \leq 0.05$ (red indicates that the mean values are significantly higher for that comparison; blue values significantly lower). Light red and light blue shaded cells indicate $0.05 < p < 0.10$ (light red indicates that the mean values trend higher for that comparison; light green values trend lower).

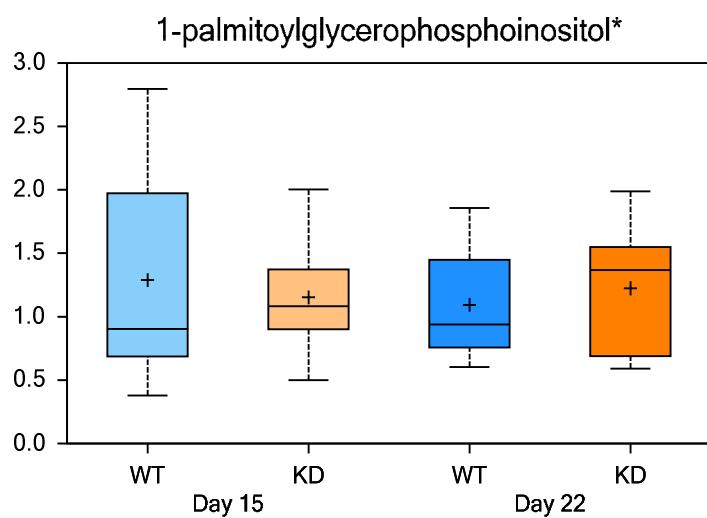
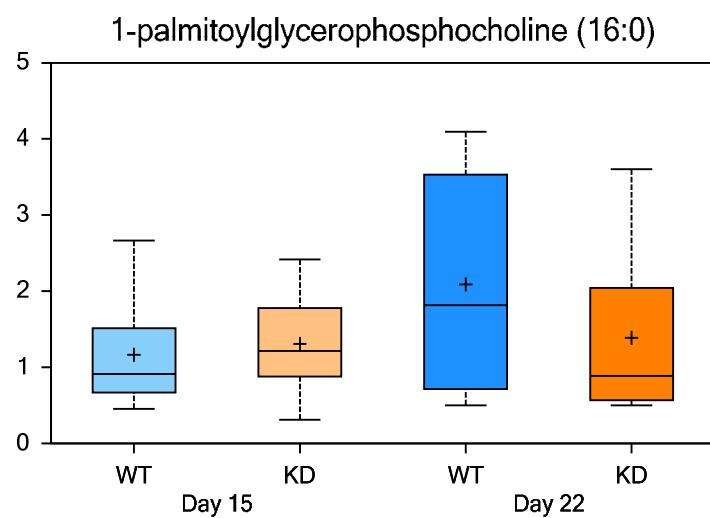
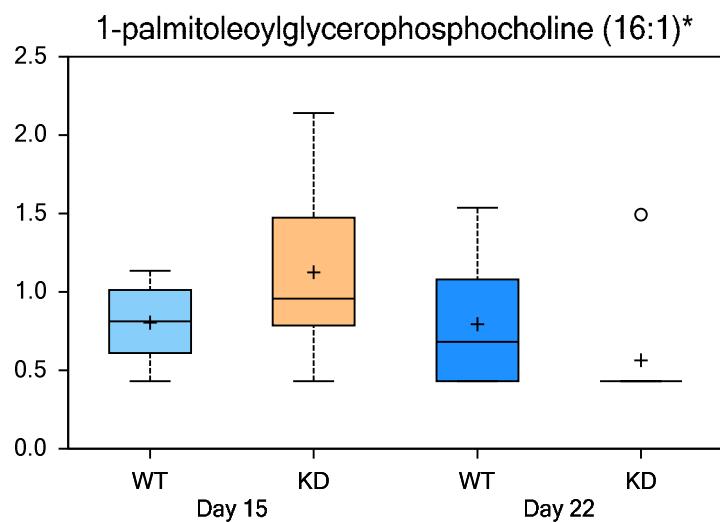
Supplementary Table 2. Box plots of all 314 metabolites profiled in this study. The top and bottom bars with whiskers represent the entire spread of the data points for the samples, excluding extreme points, which are indicated with small circles. Within the boxplot, the plus (+) indicates the mean value, and the horizontal dividing line is the median value. The top and bottom of the box represent the seventy-fifth and twenty-fifth percentile, with the whiskers indicating the maximum and minimum points. The *p-values* for all comparisons are referenced in Supplementary Table 1.

cytidine 5'-monophosphate (5'-CMP)	6131	0.71	0.77	0.89	0.96	2.11E-06	4.62E-06	8.69E-05	0.0002	0.0531	0.9698	0.5181	0.7996
cytidine	6175	0.7	0.68	0.95	0.92	0.0008	0.0007	0.0004	0.0008	0.6523	0.9841	0.471	0.782
methylphosphate	13130	1.42	1.47	0.9	0.93	0.0001	0.0001	2.95E-05	9.77E-05	0.1655	0.9698	0.3829	0.7342
nicotinamide	936	1.07	1.05	0.99	0.96	0.0749	0.032	0.2361	0.1638	0.731	0.9841	0.3325	0.7055
nicotinamide adenine dinucleotide (NAD+)	5893	1.51	1.33	0.91	0.8	0.1088	0.0432	0.3696	0.2355	0.7044	0.9841	0.2688	0.6536
riboflavin (Vitamin B2)	493570	1.12	1.13	1.12	1.13	0.2596	0.0815	0.2551	0.1715	0.2176	0.9698	0.2136	0.6072
flavin adenine dinucleotide (FAD)	643975	1.33	1.35	0.96	0.98	0.0006	0.0006	0.0003	0.0006	0.5286	0.9698	0.7357	0.849
flavin mononucleotide (FMN)	710	0.82	0.67	1.11	0.91	0.0988	0.0407	0.001	0.0018	0.3267	0.9698	0.3332	0.7055
pantothenate	6613	0.78	0.86	1	1.11	2.95E-05	3.57E-05	0.0055	0.0073	0.989	0.9997	0.0574	0.2896
phosphopantetheine	987	1.01	0.96	1.02	0.97	0.8433	0.1889	0.6974	0.3621	0.809	0.9997	0.7302	0.849
3'-dephosphocoenzyme A	444485	1.14	1.09	0.98	0.93	0.1594	0.0569	0.4804	0.285	0.8412	0.9997	0.6015	0.8195
coenzyme A	317	1.42	0.98	1.05	0.72	0.0033	0.0025	0.8928	0.4128	0.6249	0.9841	0.0081	0.0689
glucarate (saccharate)	33037	0.74	0.58	1.01	0.79	0.0142	0.0089	1.06E-05	4.20E-05	0.7988	0.9997	0.0193	0.1396
ascorbate (Vitamin C)		0.74	0.92	0.91	1.13	0.0078	0.0053	0.4319	0.2647	0.3615	0.9698	0.2626	0.6536
dehydroascorbate	835	1.06	0.8	1.1	0.83	0.6235	0.1496	0.1678	0.1226	0.316	0.9698	0.3803	0.7342
oxalate (ethanedioate)	971	0.86	0.89	0.97	1.01	0.2816	0.0857	0.6017	0.3271	0.6123	0.9841	0.9547	0.8846
alpha-tocopherol	14985	0.95	2.97	0.76	2.36	0.8346	0.188	0.0059	0.0077	0.7173	0.9841	0.0229	0.1535
pyridoxal	1050	1.07	0.88	1.03	0.85	0.3924	0.1074	0.3139	0.207	0.6607	0.9841	0.158	0.54
1,6-anhydroglucose	2724705	0.72	0.94	0.73	0.95	0.1421	0.0529	0.724	0.3664	0.1272	0.9698	0.6794	0.8451
ergothioneine	3032311	1.18	1.11	1.14	1.07	0.3595	0.1013	0.5874	0.3218	0.4932	0.9698	0.7575	0.8511
erythritol	222285	1.12	1.25	0.85	0.94	0.3727	0.1037	0.1041	0.0837	0.1463	0.9698	0.4775	0.782
phosphoglycolate	529	0.71	1	0.77	1.09	0.2248	0.0727	0.7154	0.3664	0.318	0.9698	0.5581	0.8195
stachydrine	115244	3.05	2.75	0.95	0.86	1.52E-09	1.14E-08	2.59E-08	2.41E-07	0.8747	0.9997	0.1968	0.5815
2-pyrrolidinone	12025	1.26	1.35	0.96	1.03	0.0376	0.0179	0.0129	0.0149	0.7009	0.9841	0.9334	0.8846
2-ethylhexanoate (isobar with 2-propylpentanoate)	4072356	0.9	0.86	1.03	0.99	0.2486	0.0789	0.1081	0.0865	0.6855	0.9841	0.9429	0.8846
glycerol 2-phosphate	2526	1.29	1	1	0.77	0.017	0.0097	0.9497	0.4293	0.882	0.9997	0.0207	0.1424
trizma acetate	6503	0.28	0.77	2.5	6.89	0.5787	0.1413	0.506	0.2934	0.4498	0.9698	0.5181	0.7996

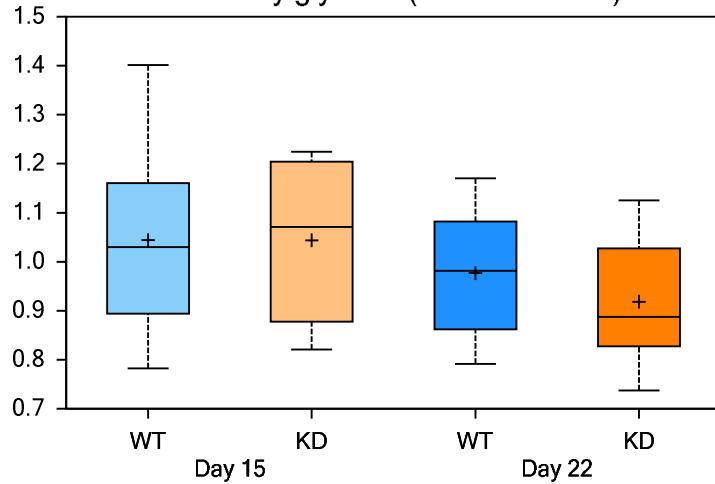




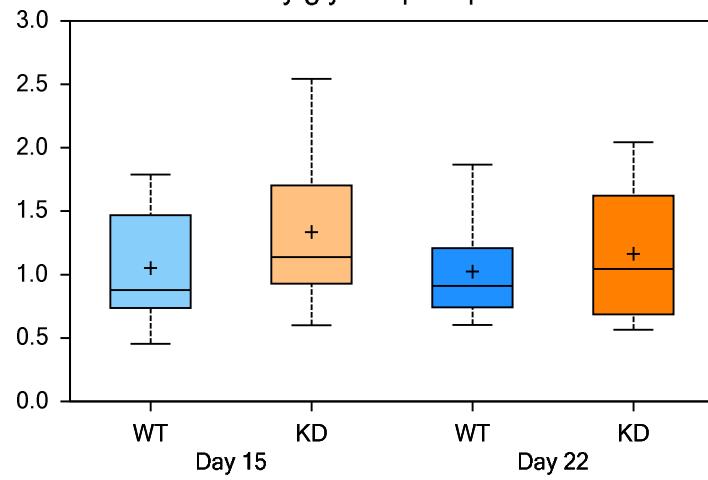
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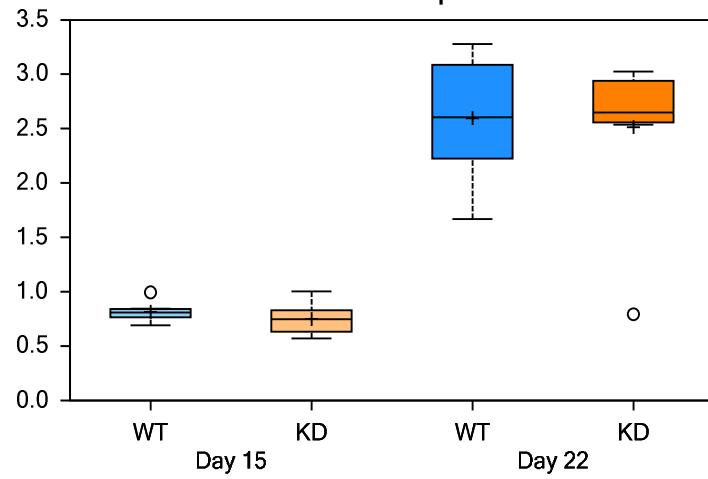
1-stearoylglycerol (1-monostearin)



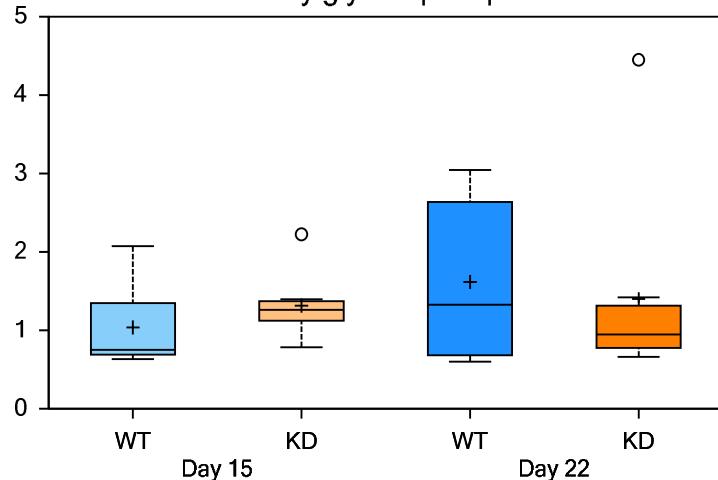
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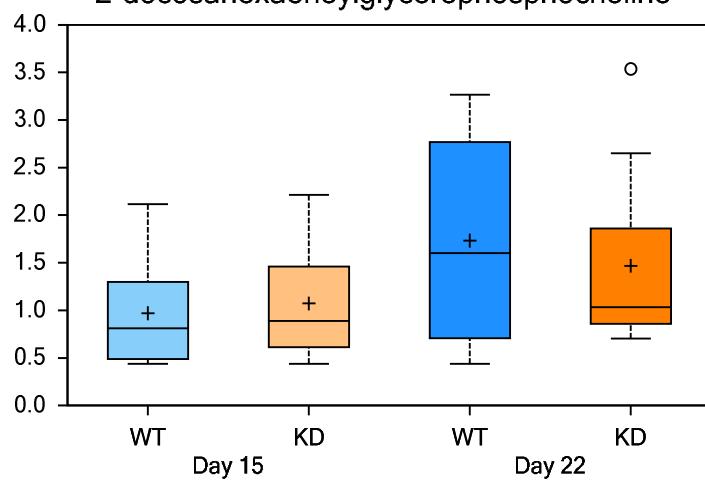
2-aminoadipate



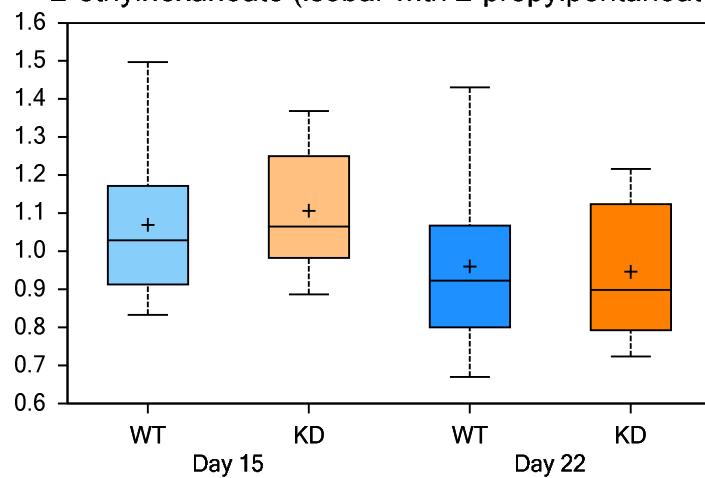
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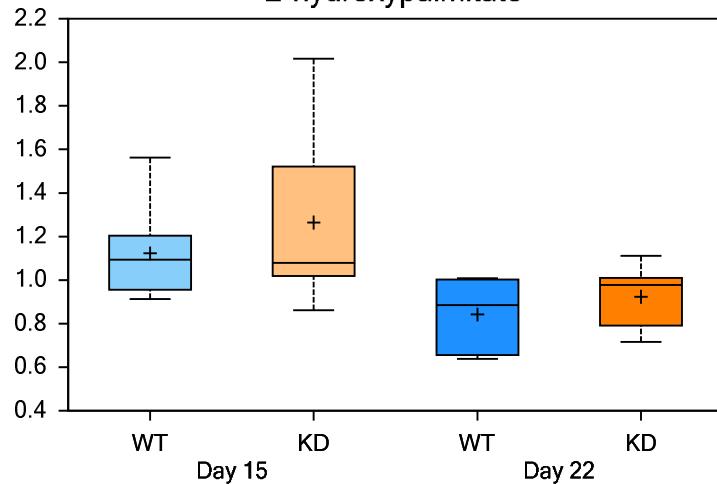
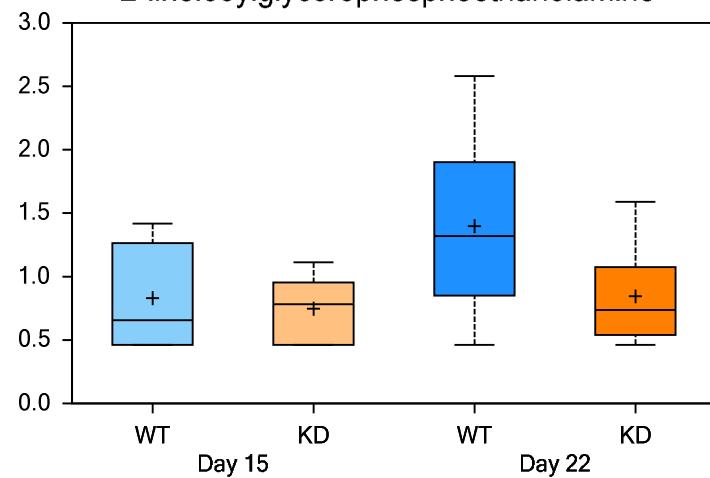
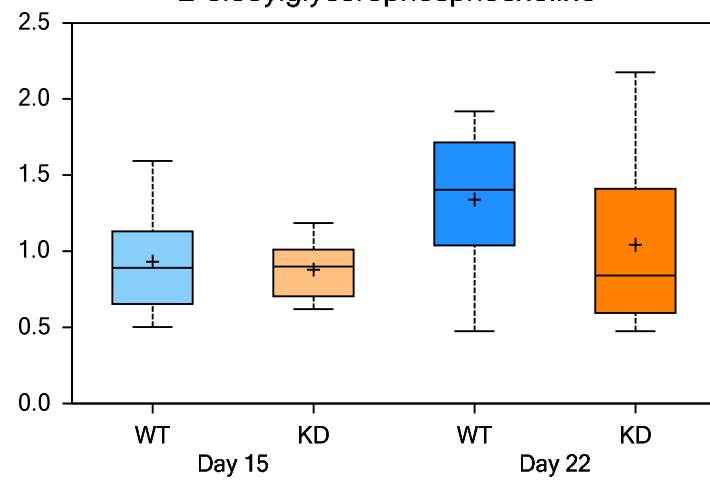


2-docosahexaenoylglycerophosphocholine*

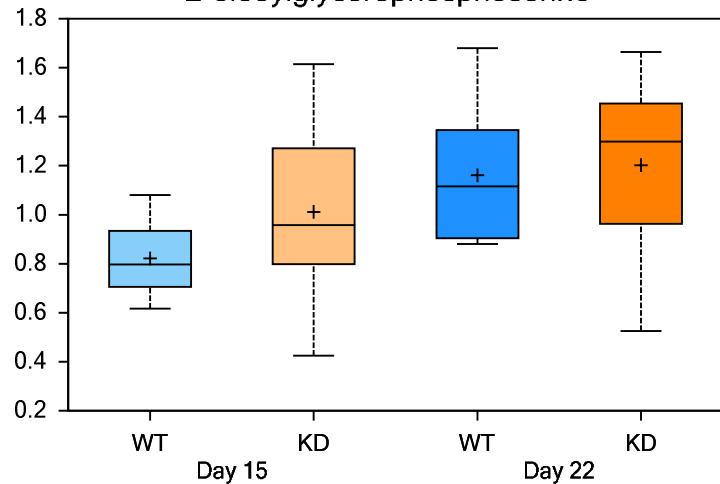


2-ethylhexanoate (isobar with 2-propylpentanoate)

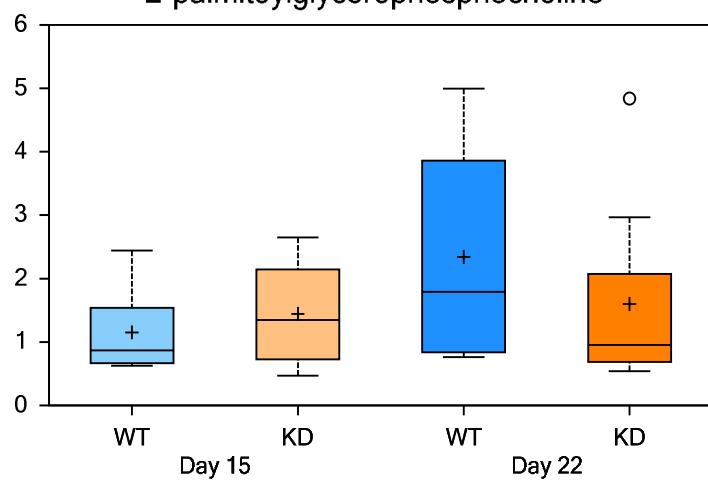


2-hydroxypalmitate**2-linoleoylglycerophosphoethanolamine*****2-oleoylglycerophosphocholine***

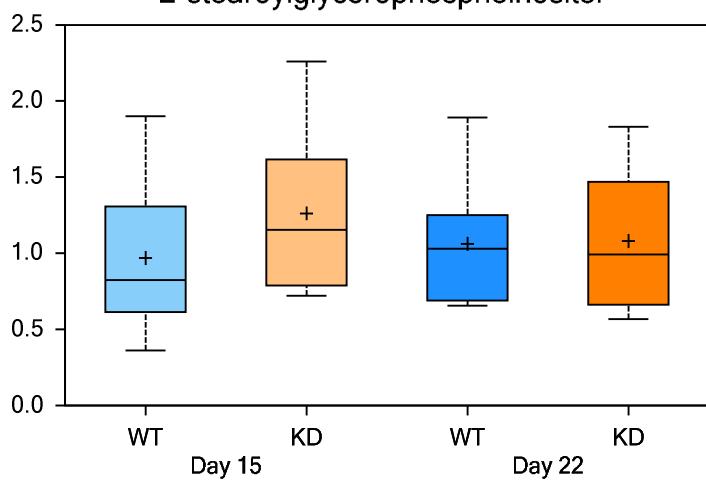
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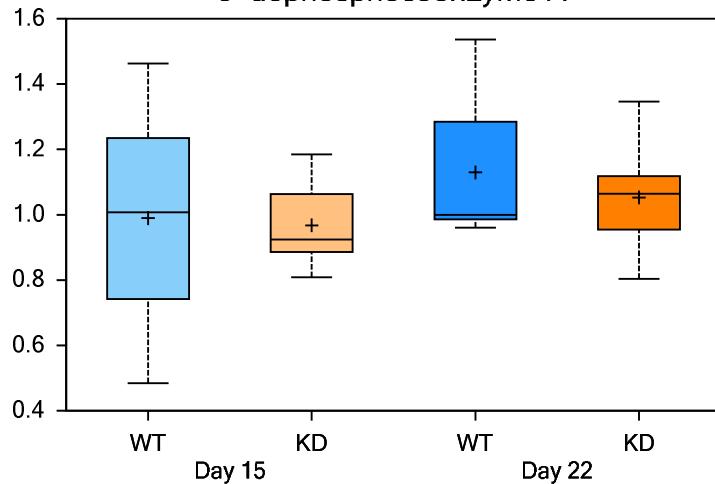
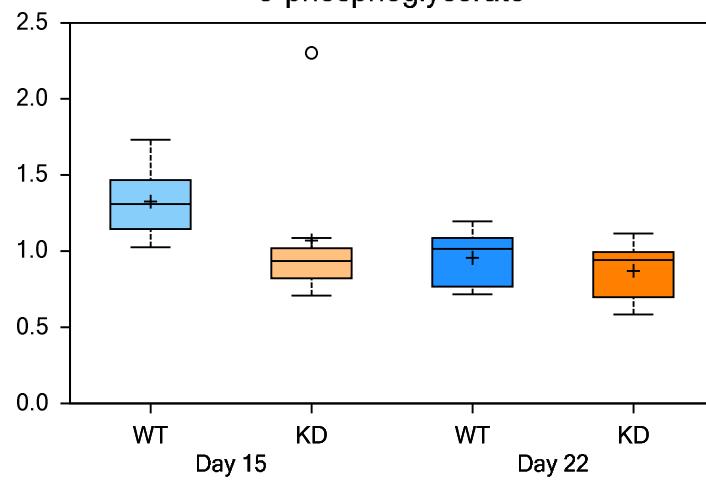
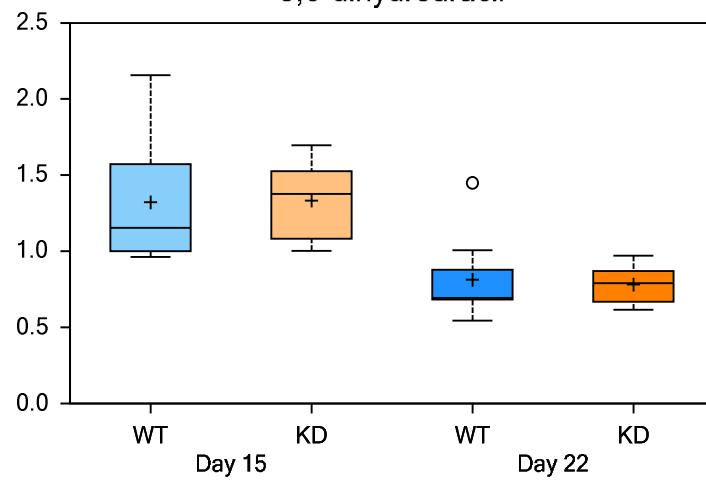


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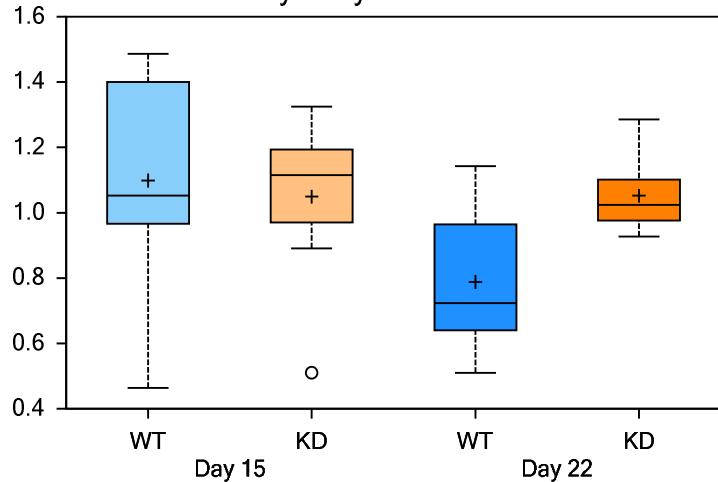


2-stearoylglycerophosphoinositol*

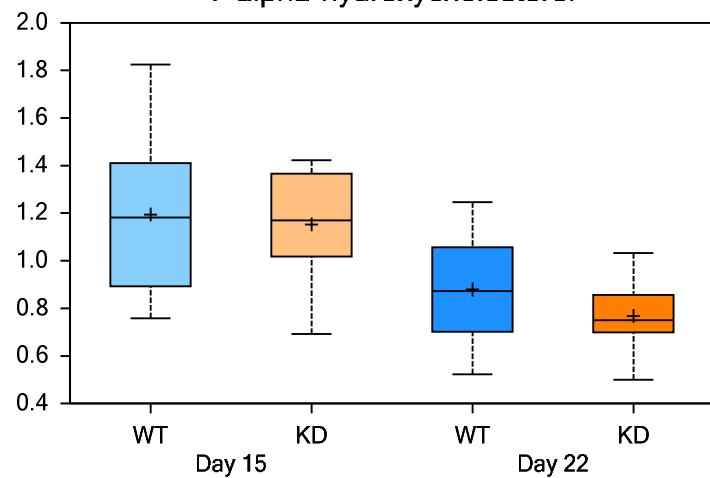


3'-dephosphocoenzyme A**3-phosphoglycerate****5,6-dihydrouracil**

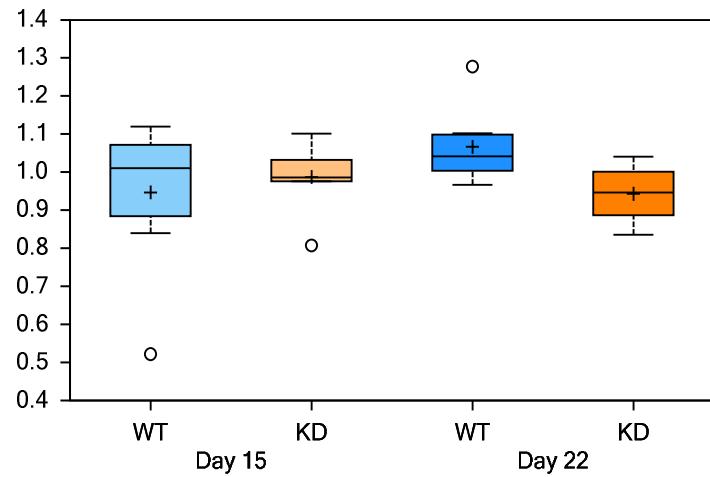
5-hydroxyindoleacetate



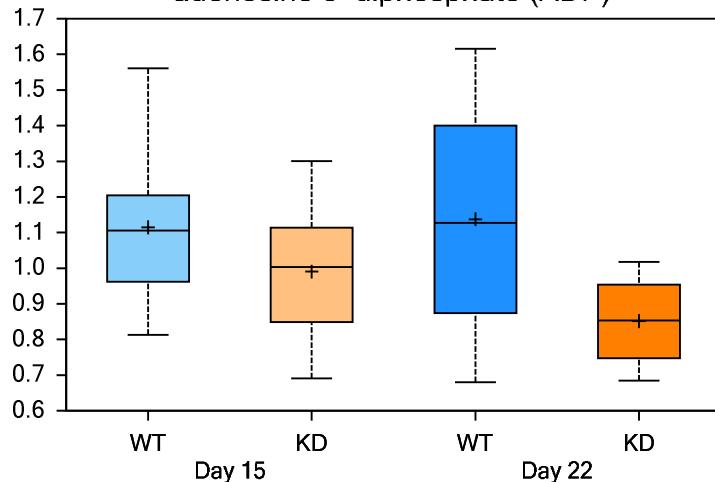
7-alpha-hydroxycholesterol



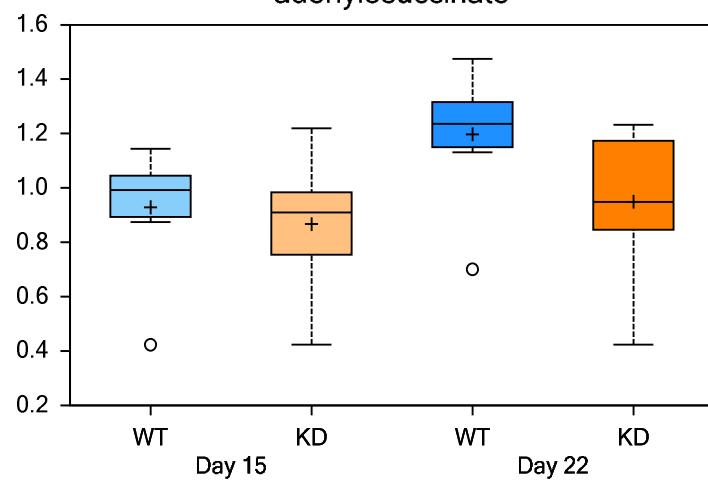
adenine



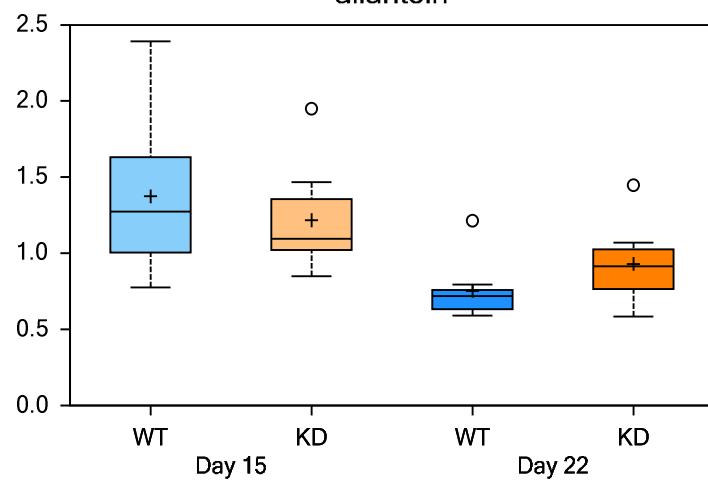
adenosine 5'-diphosphate (ADP)

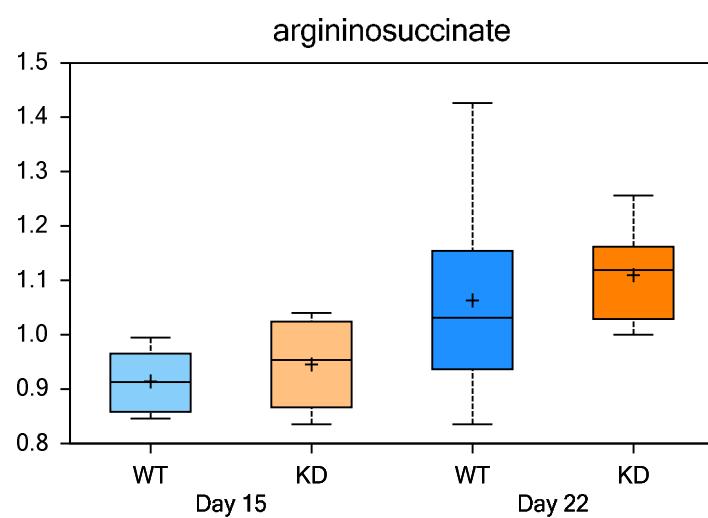
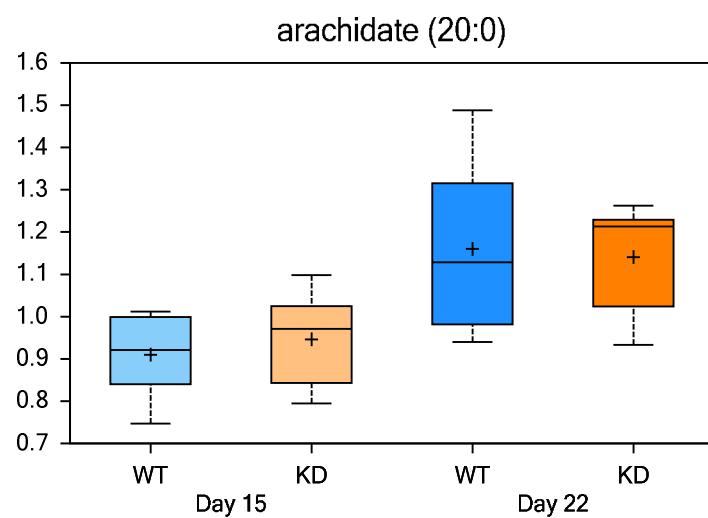
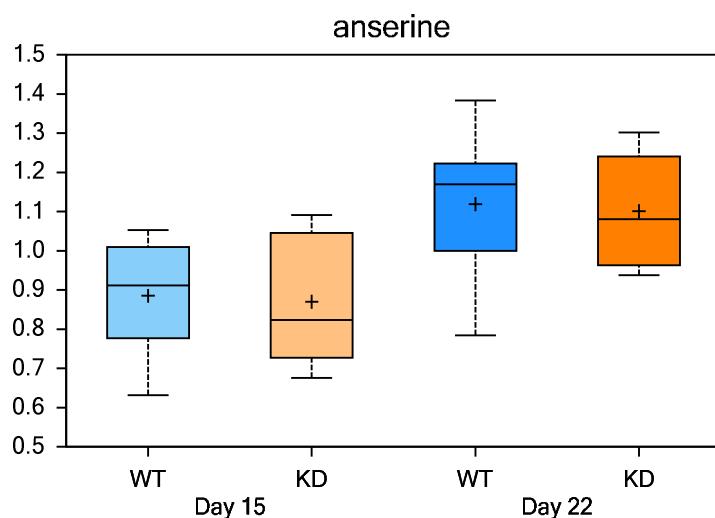


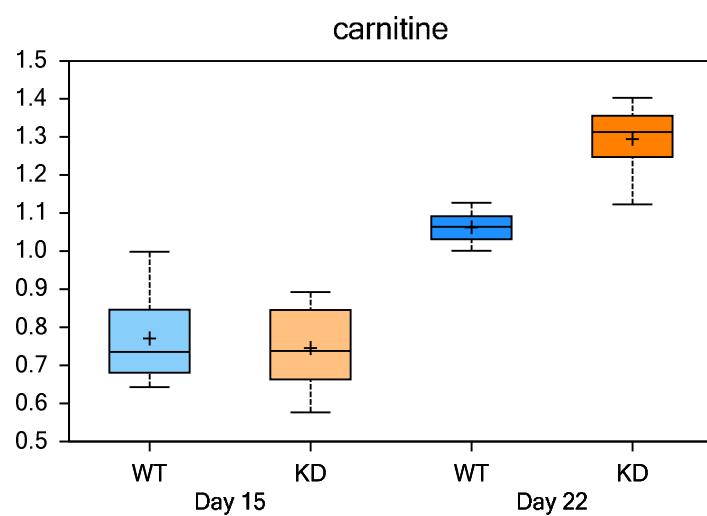
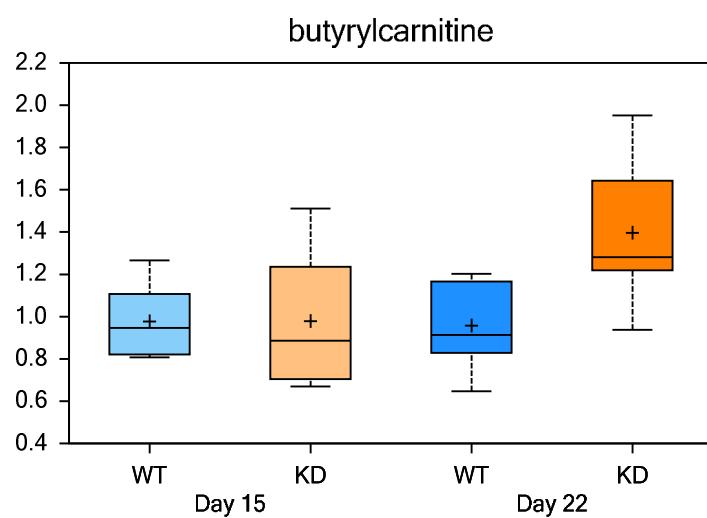
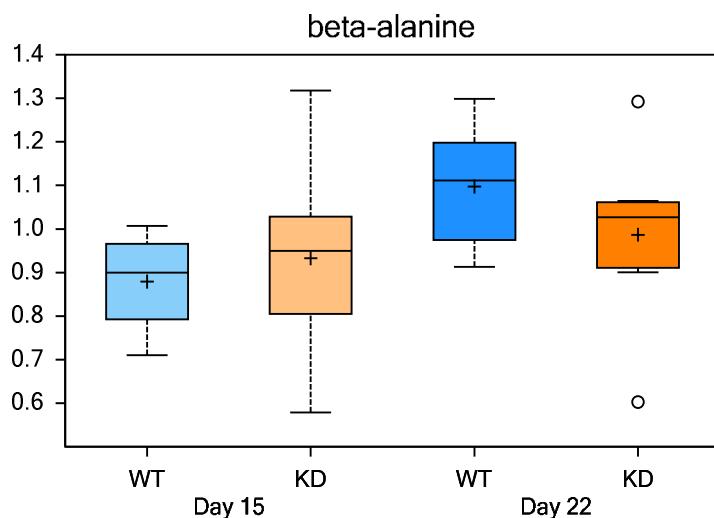
adenylosuccinate

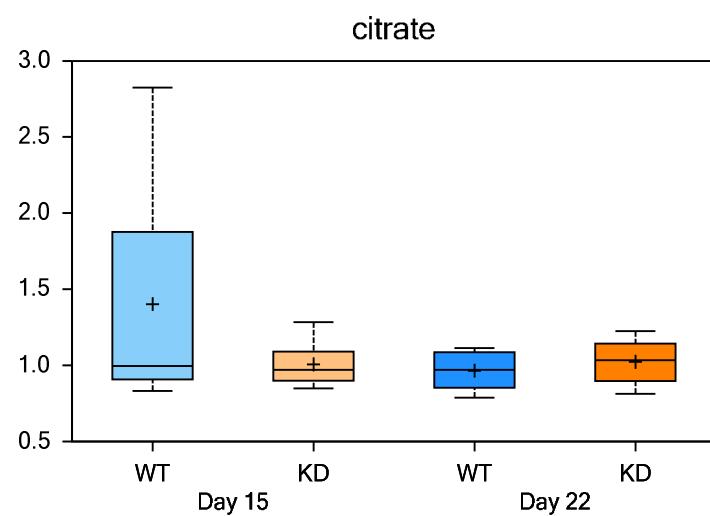
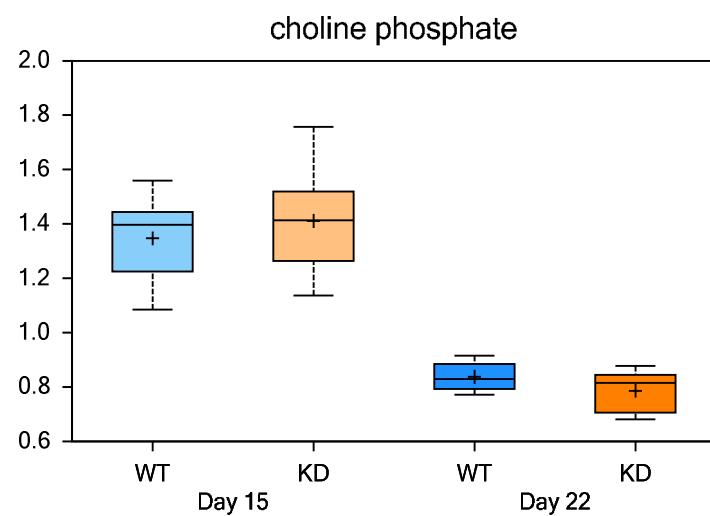
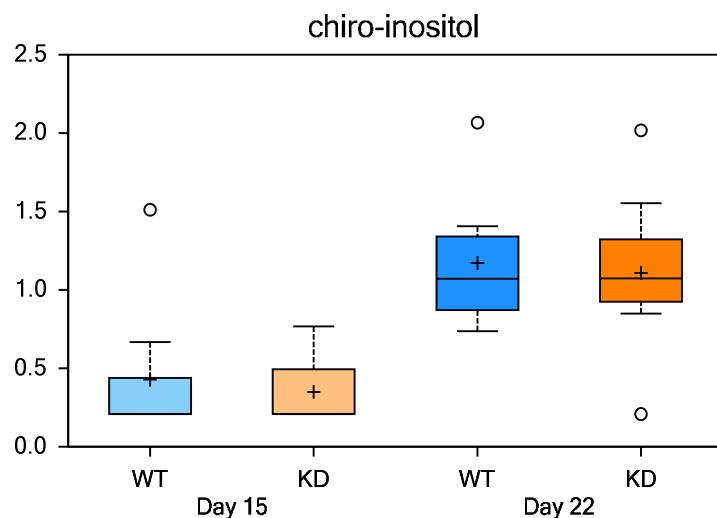


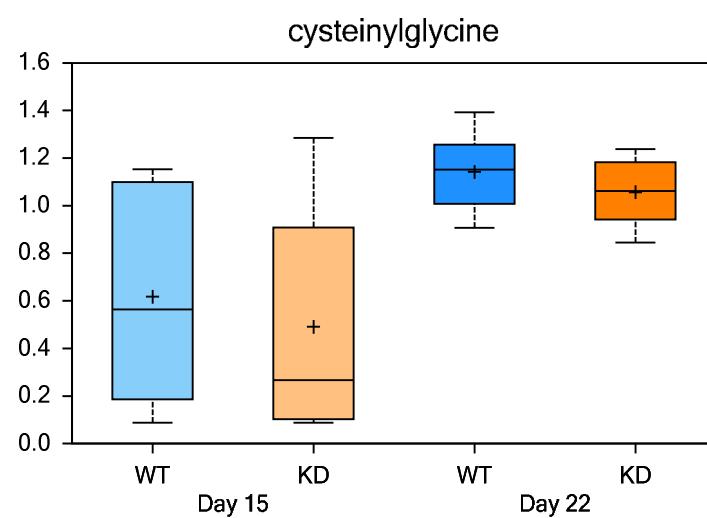
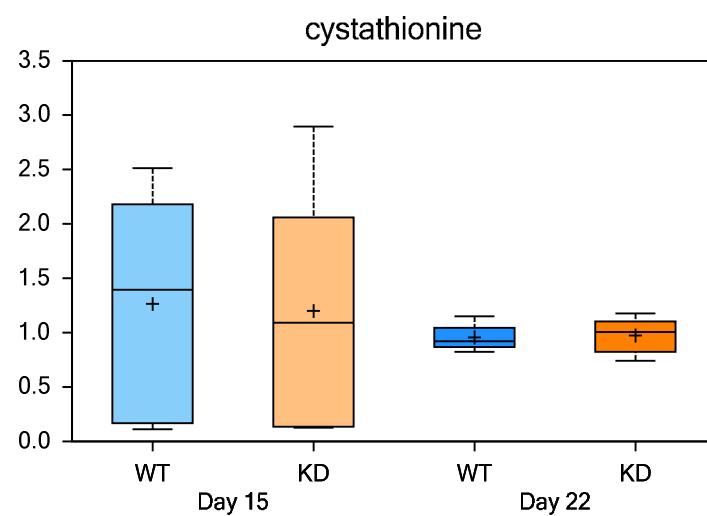
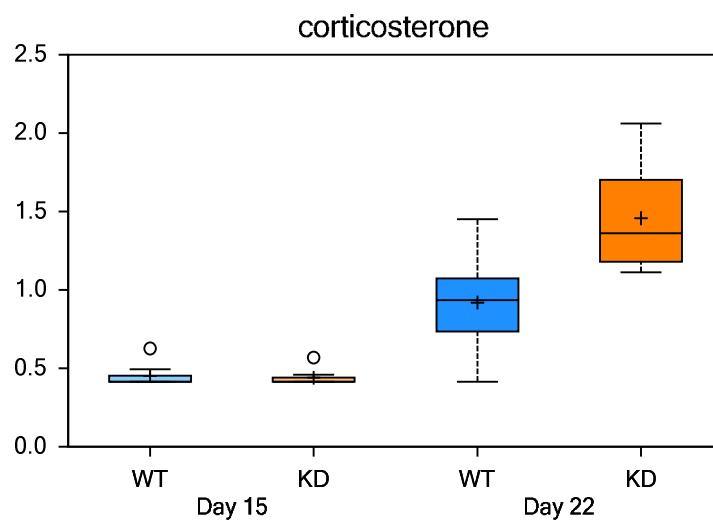
allantoin

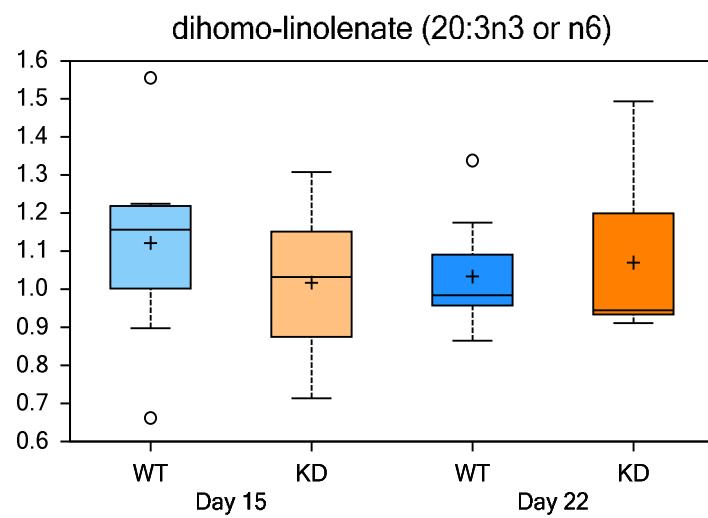
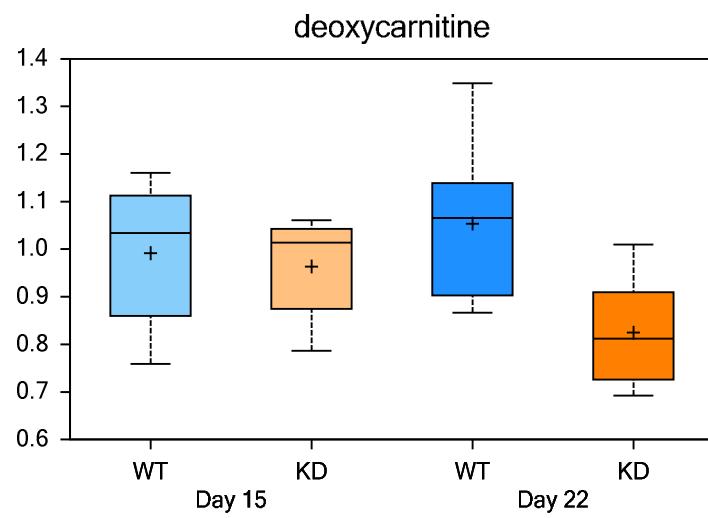
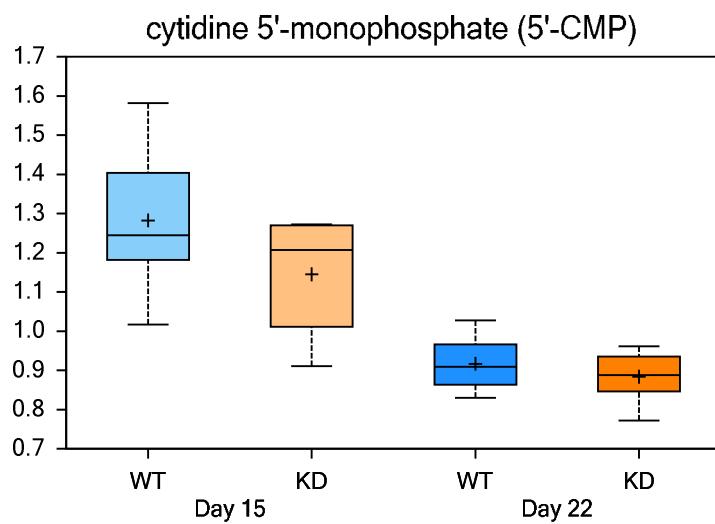


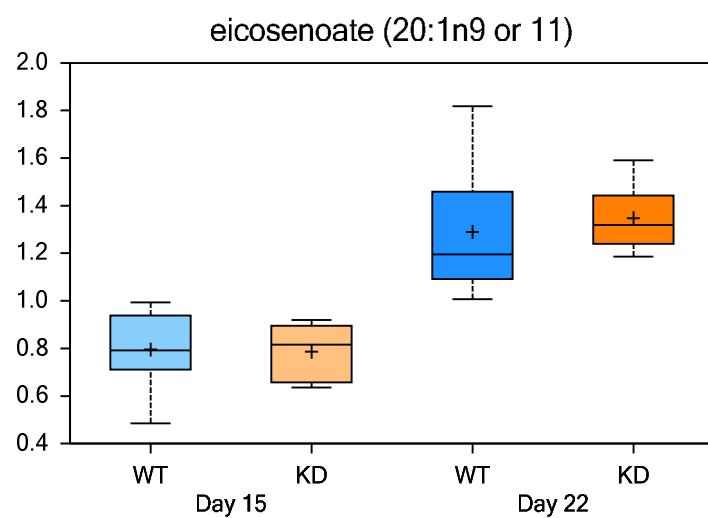
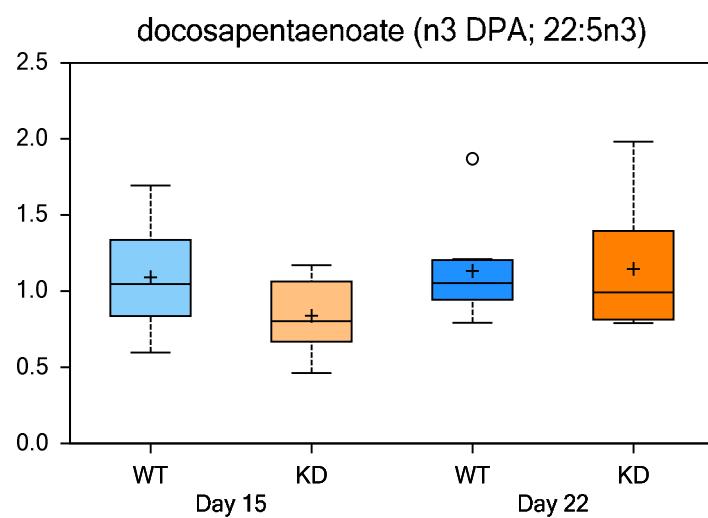
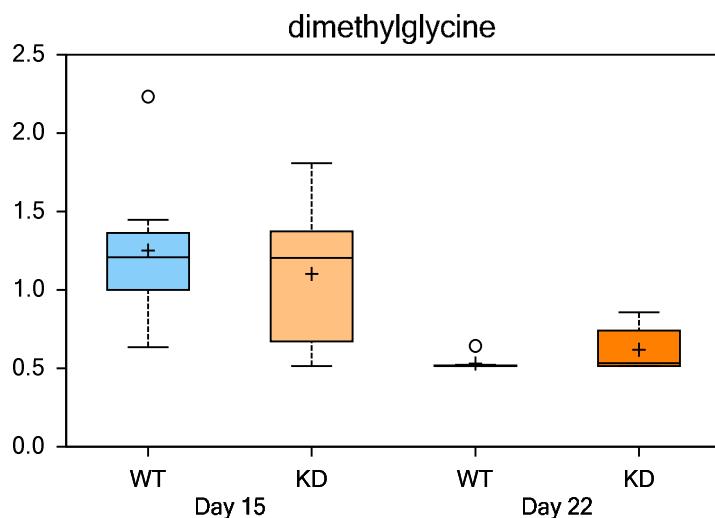


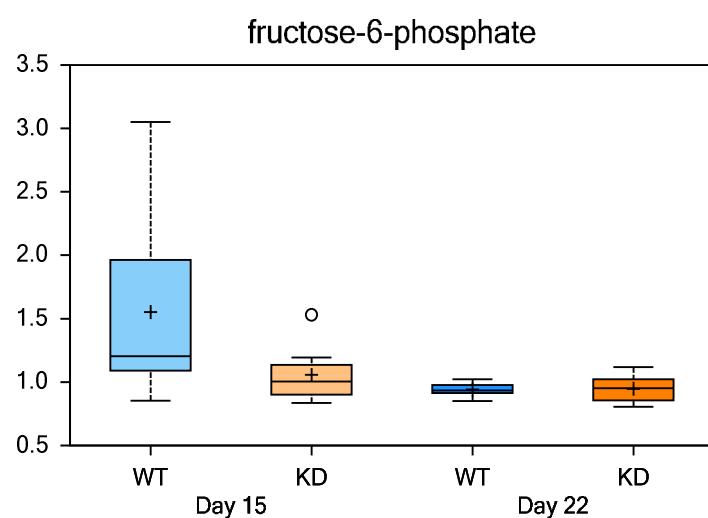
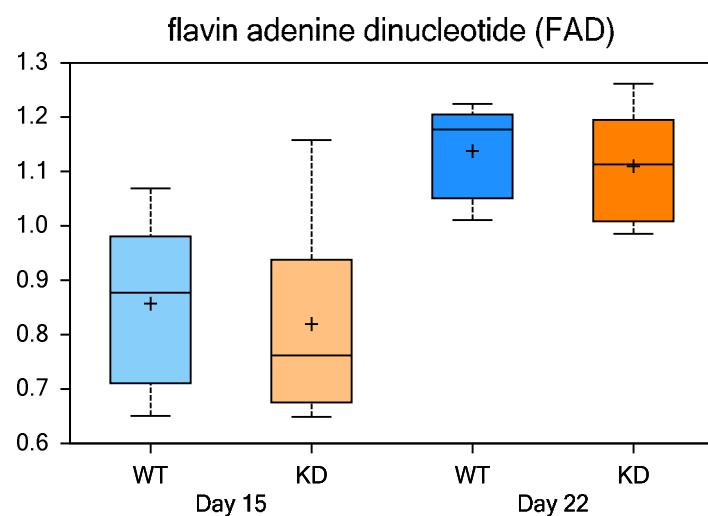
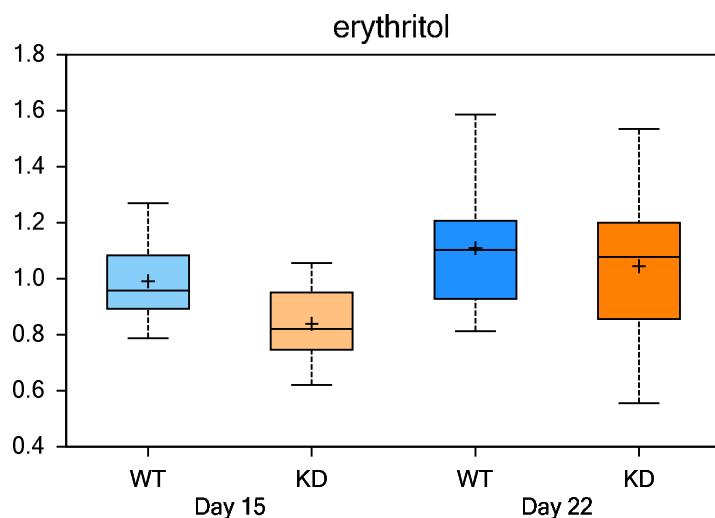


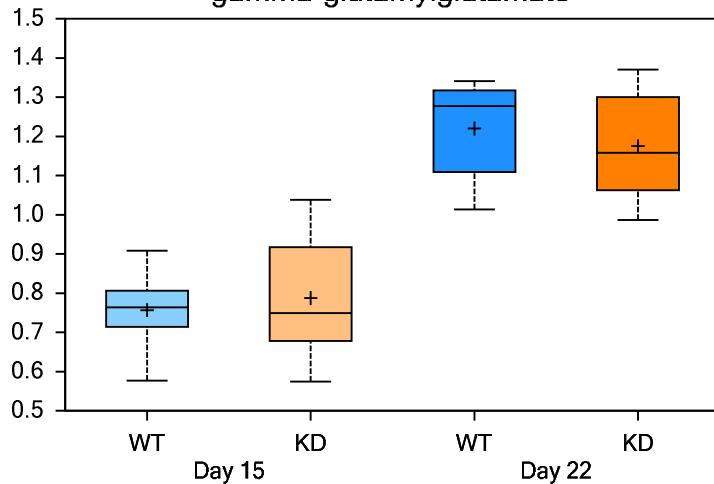
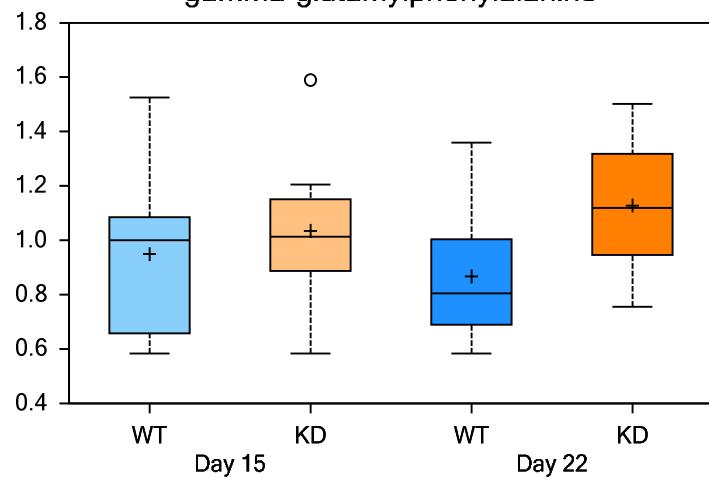
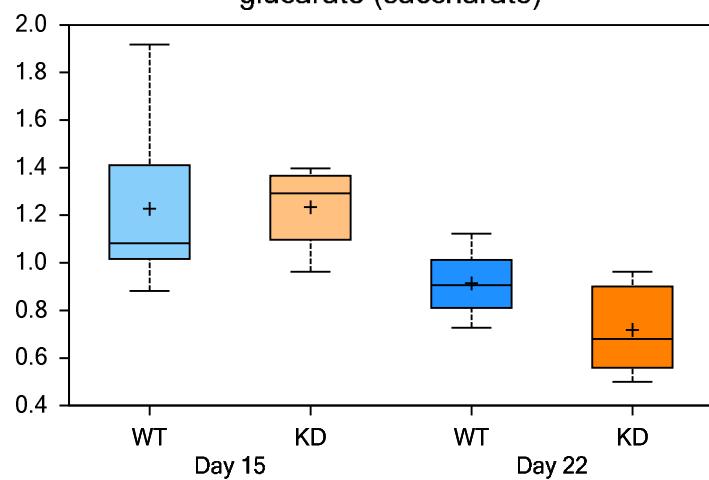


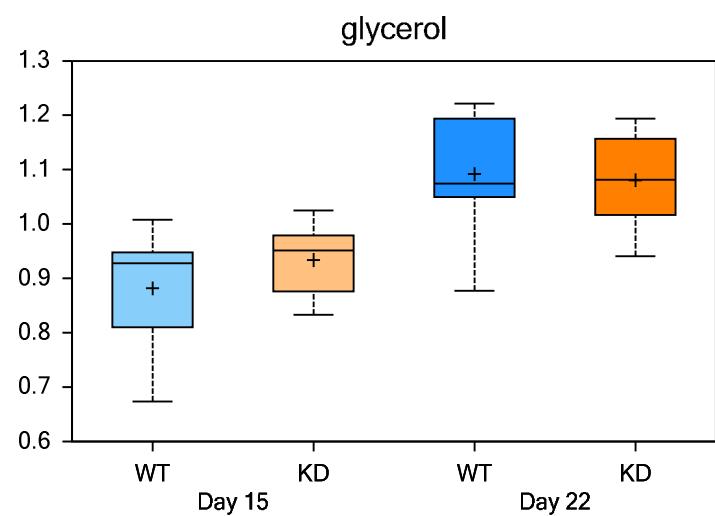
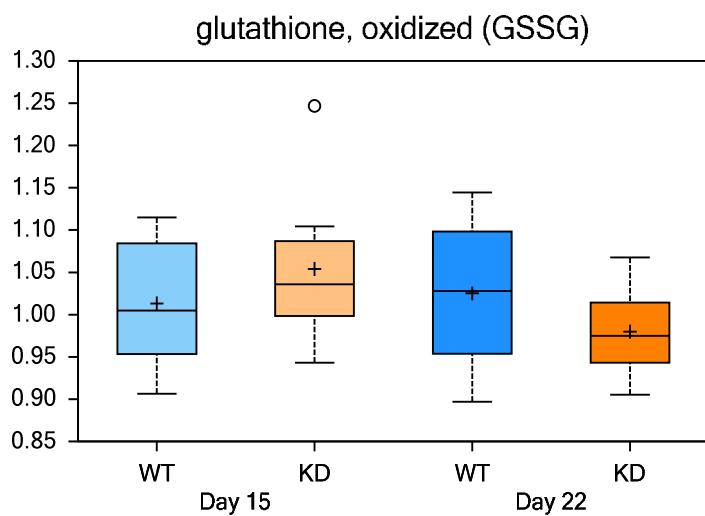
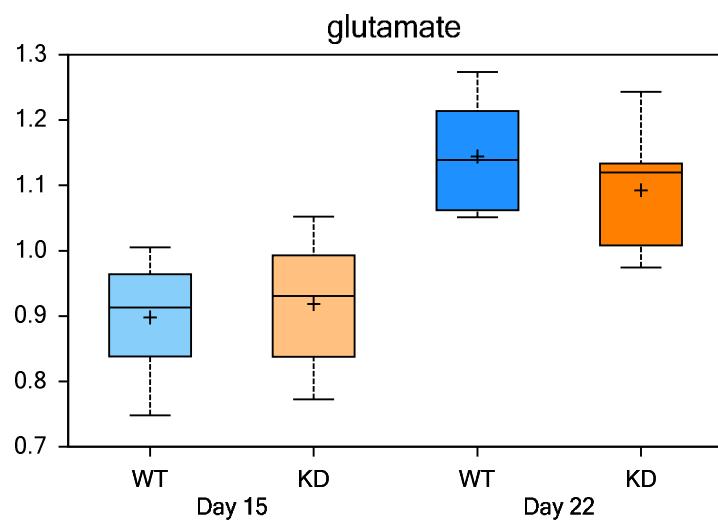


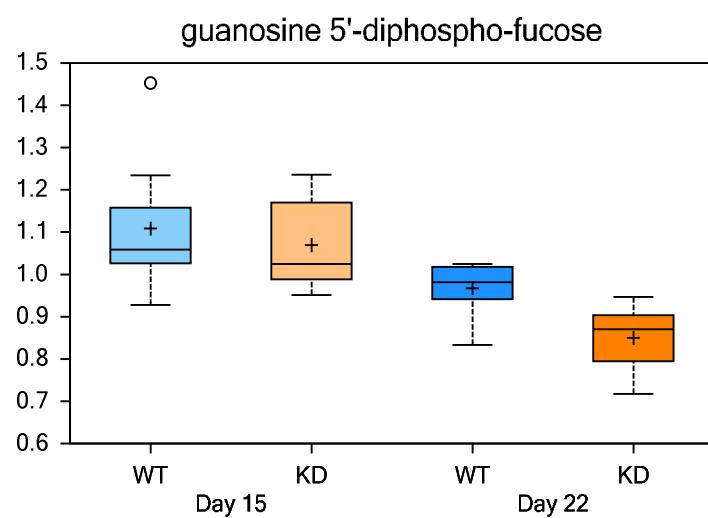
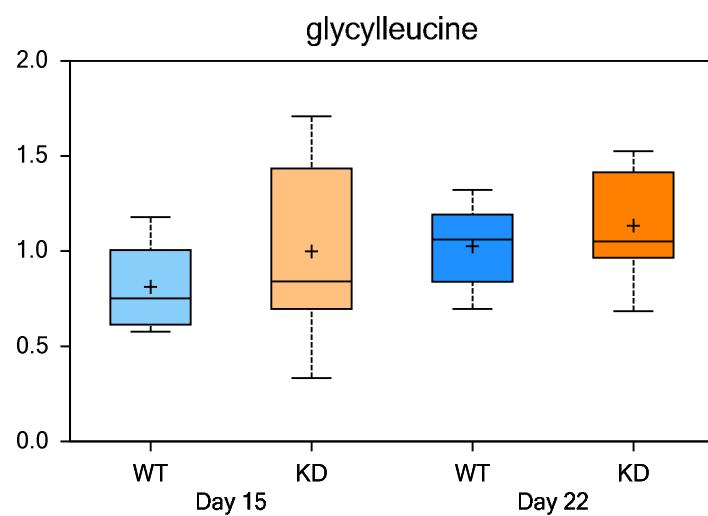
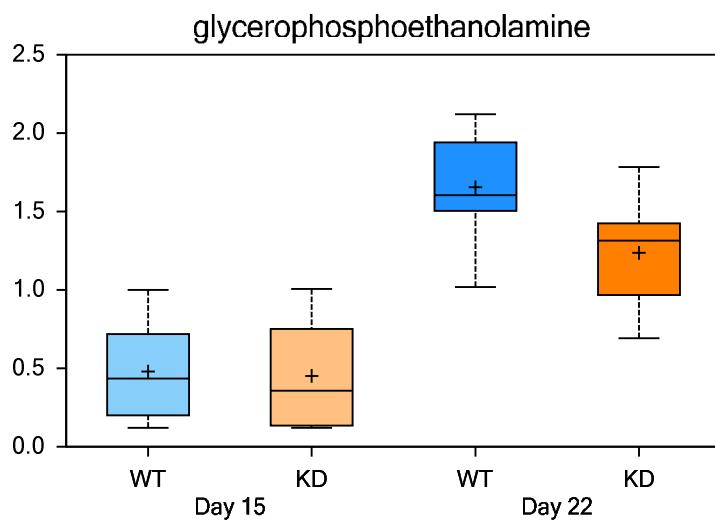




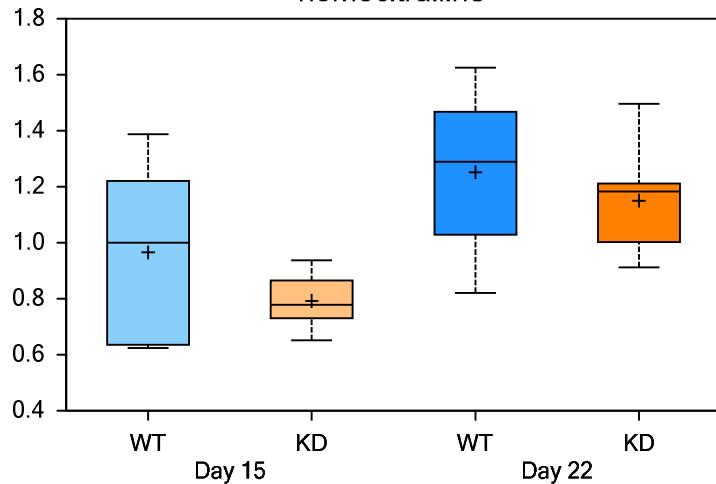


gamma-glutamylglutamate**gamma-glutamylphenylalanine****glucarate (saccharate)**

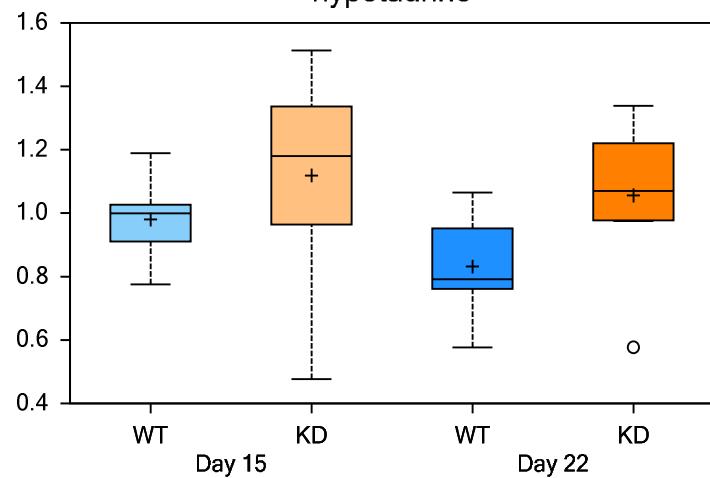




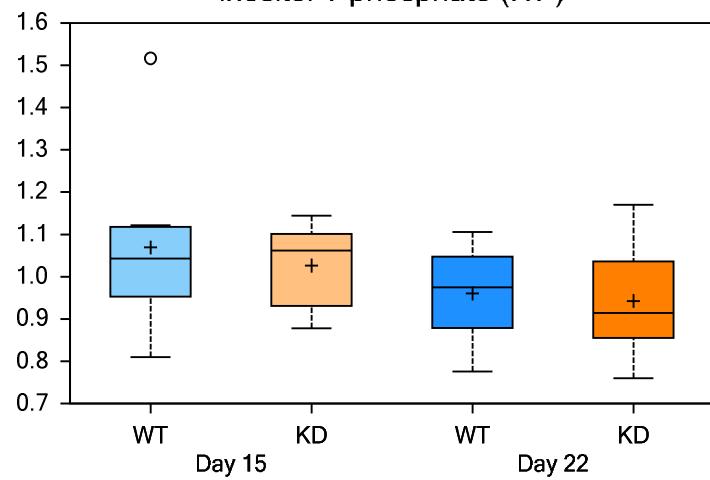
homocitrulline

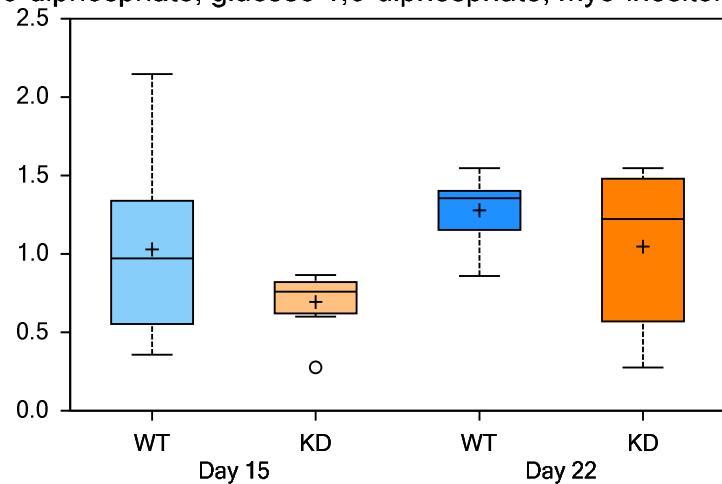
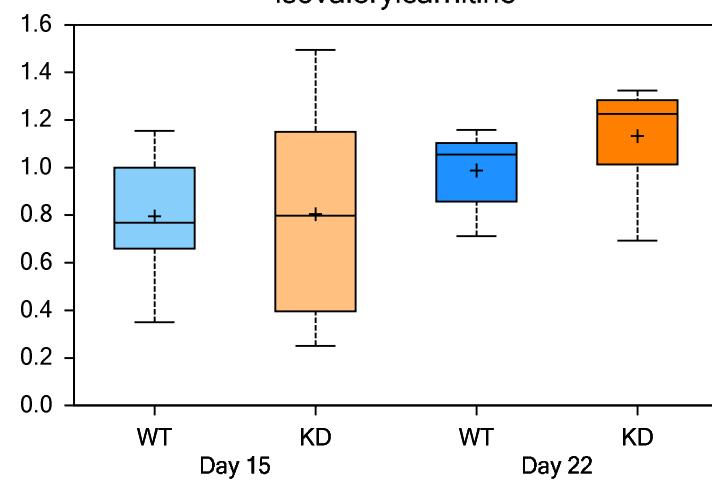
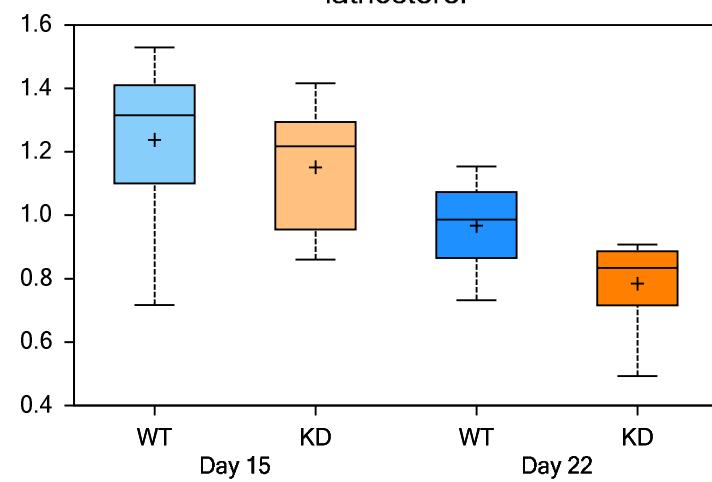


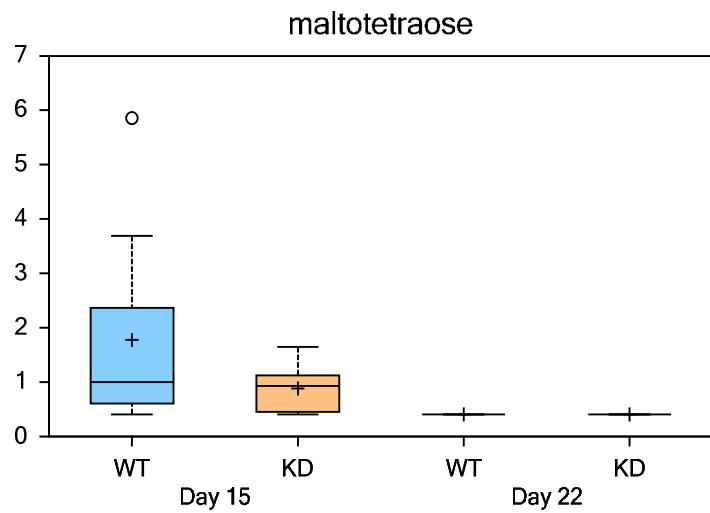
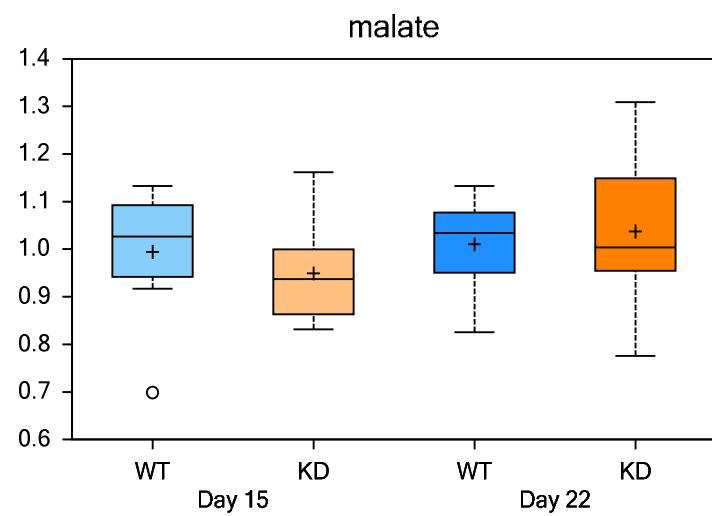
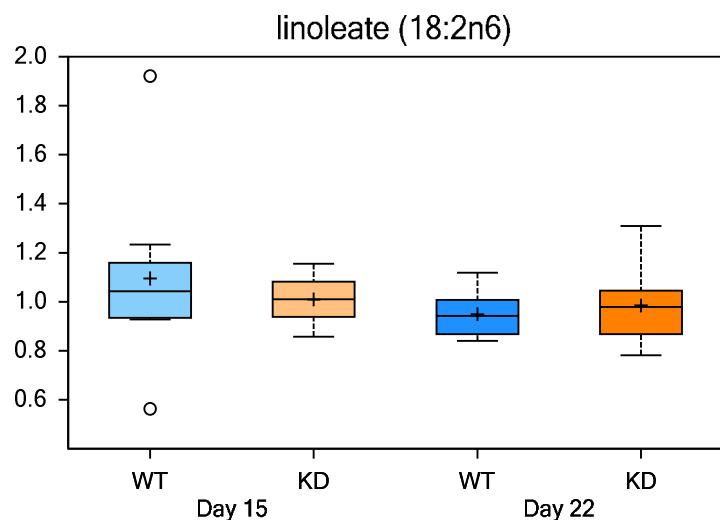
hypotaurine

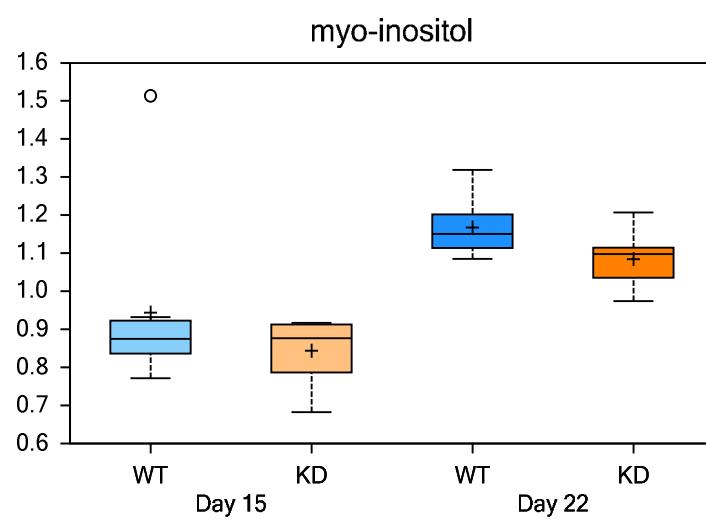
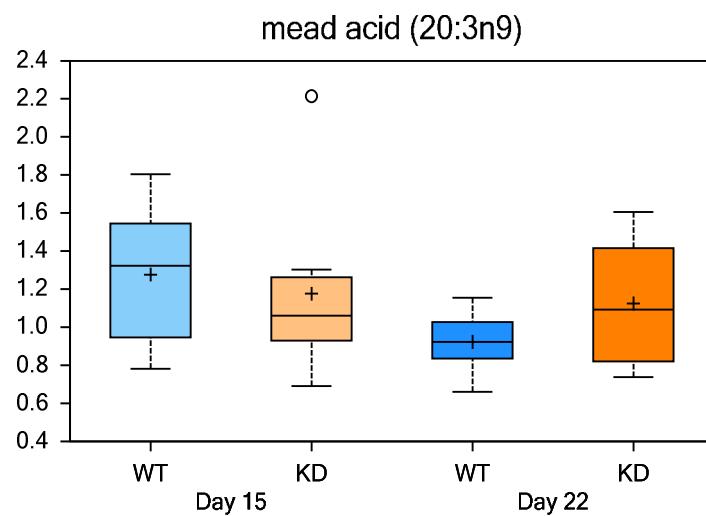
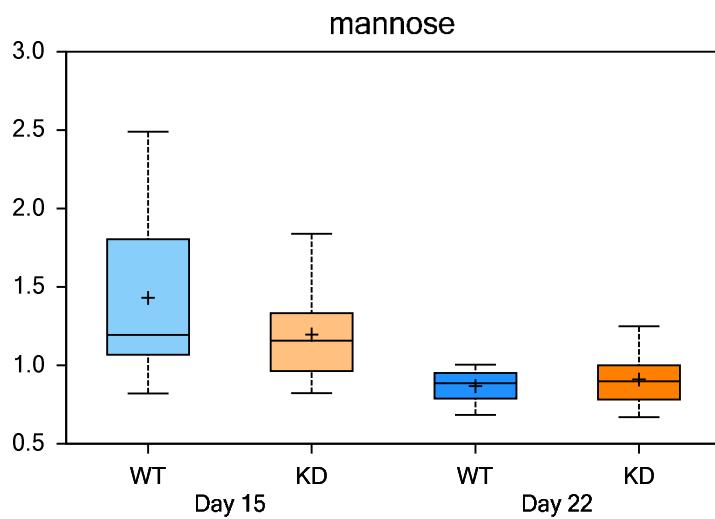


inositol 1-phosphate (I1P)

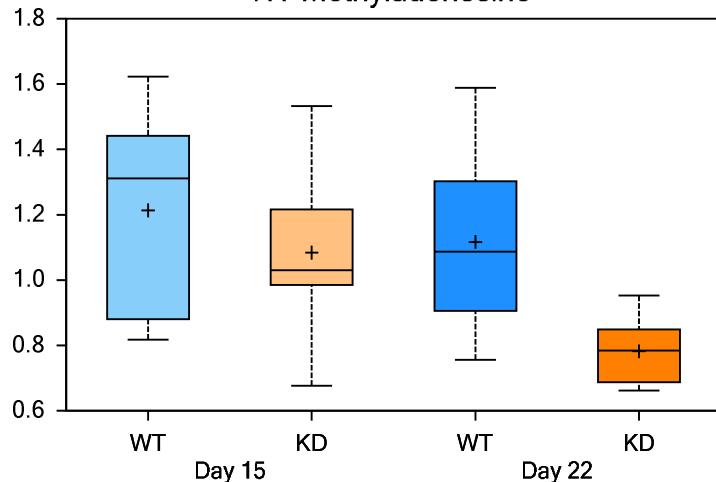


,6-diphosphate, glucose 1,6-diphosphate, myo-inositol 1**isovalerylcarnitine****lathosterol**

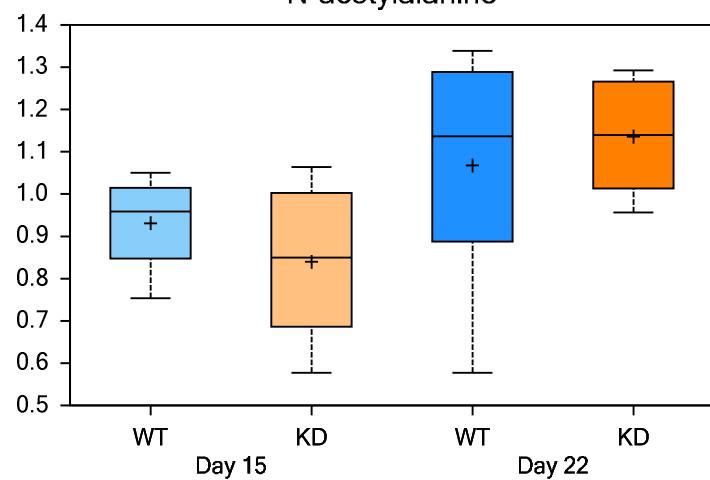




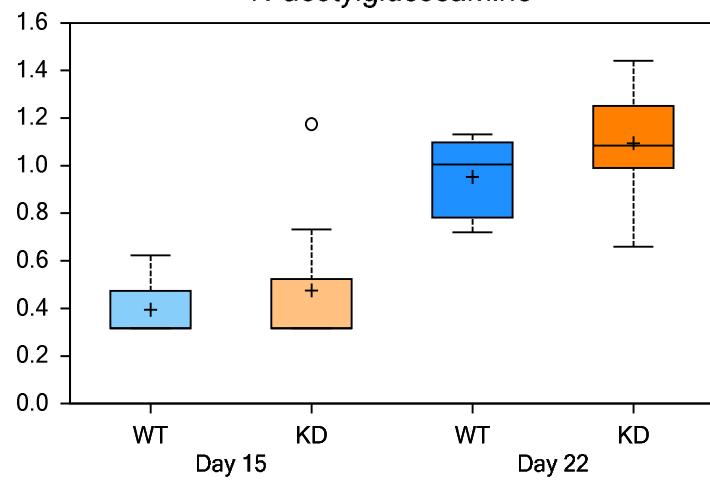
N1-methyladenosine

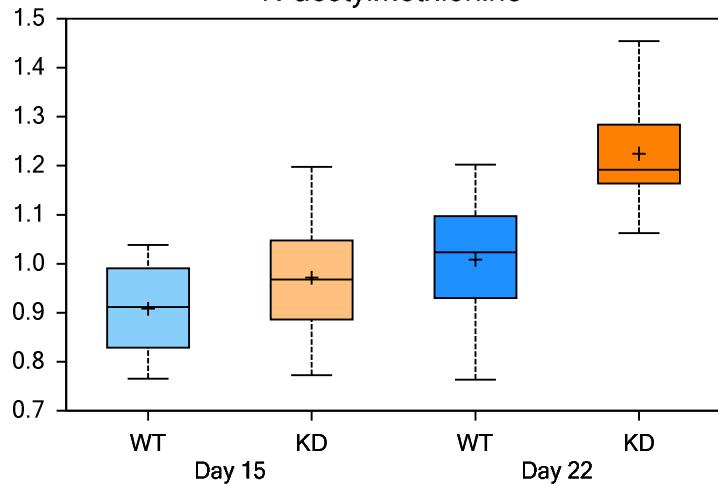
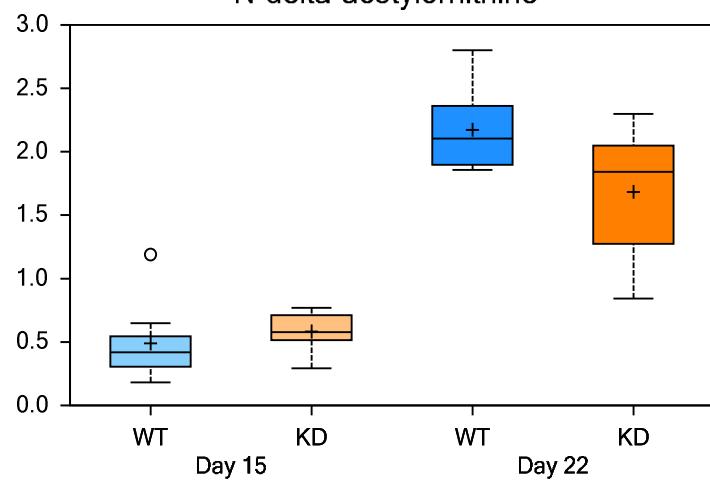
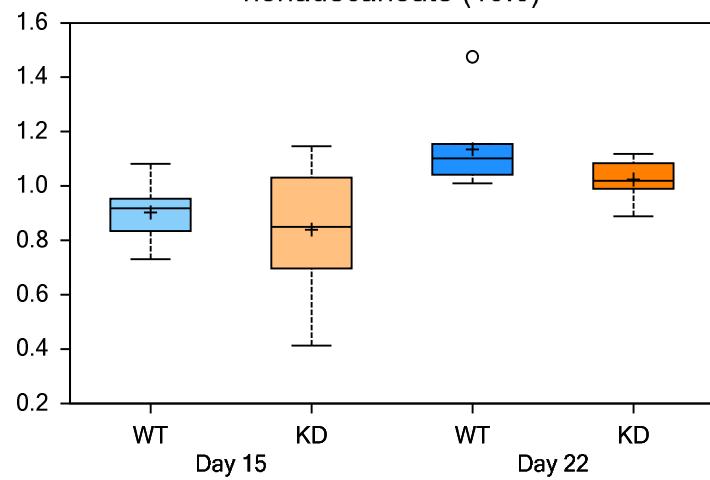


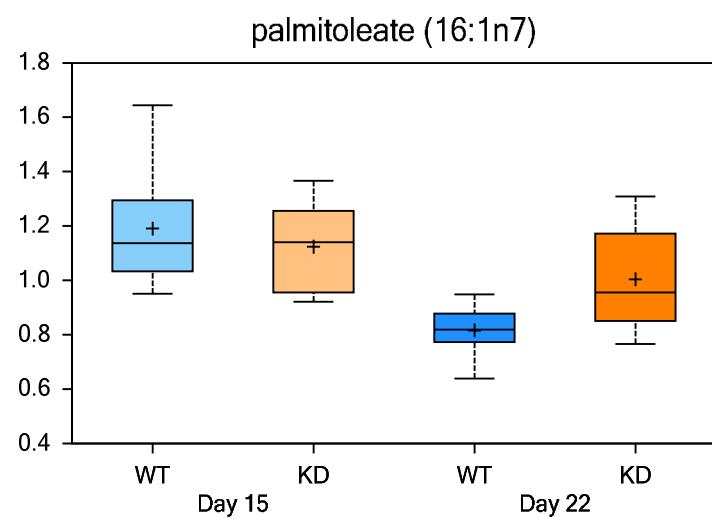
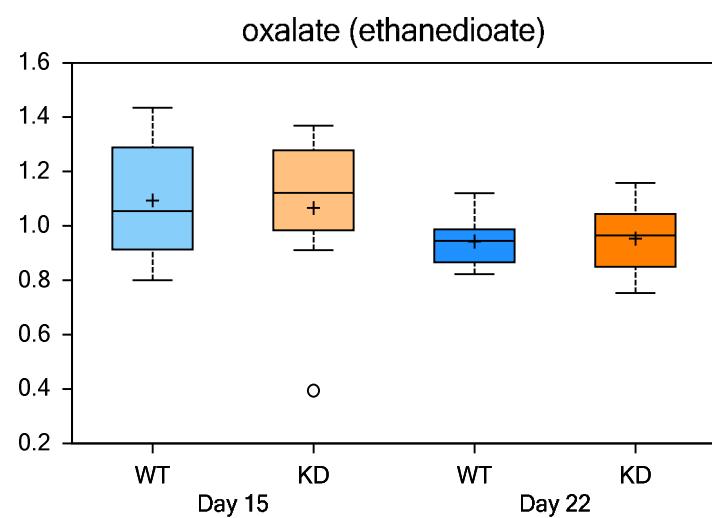
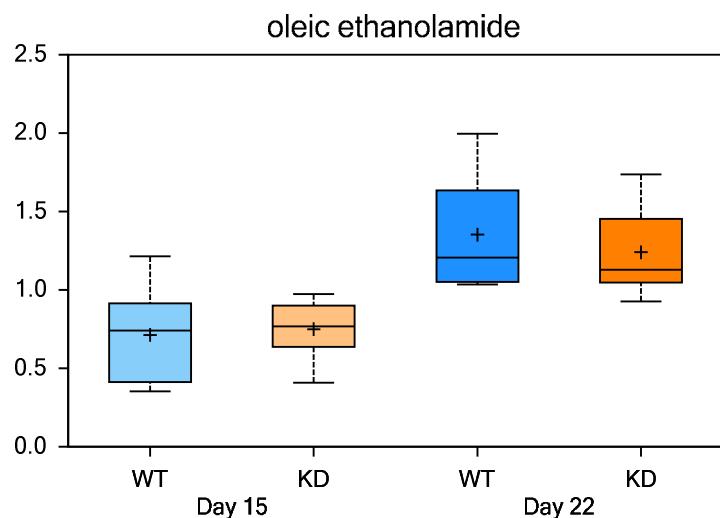
N-acetylalanine

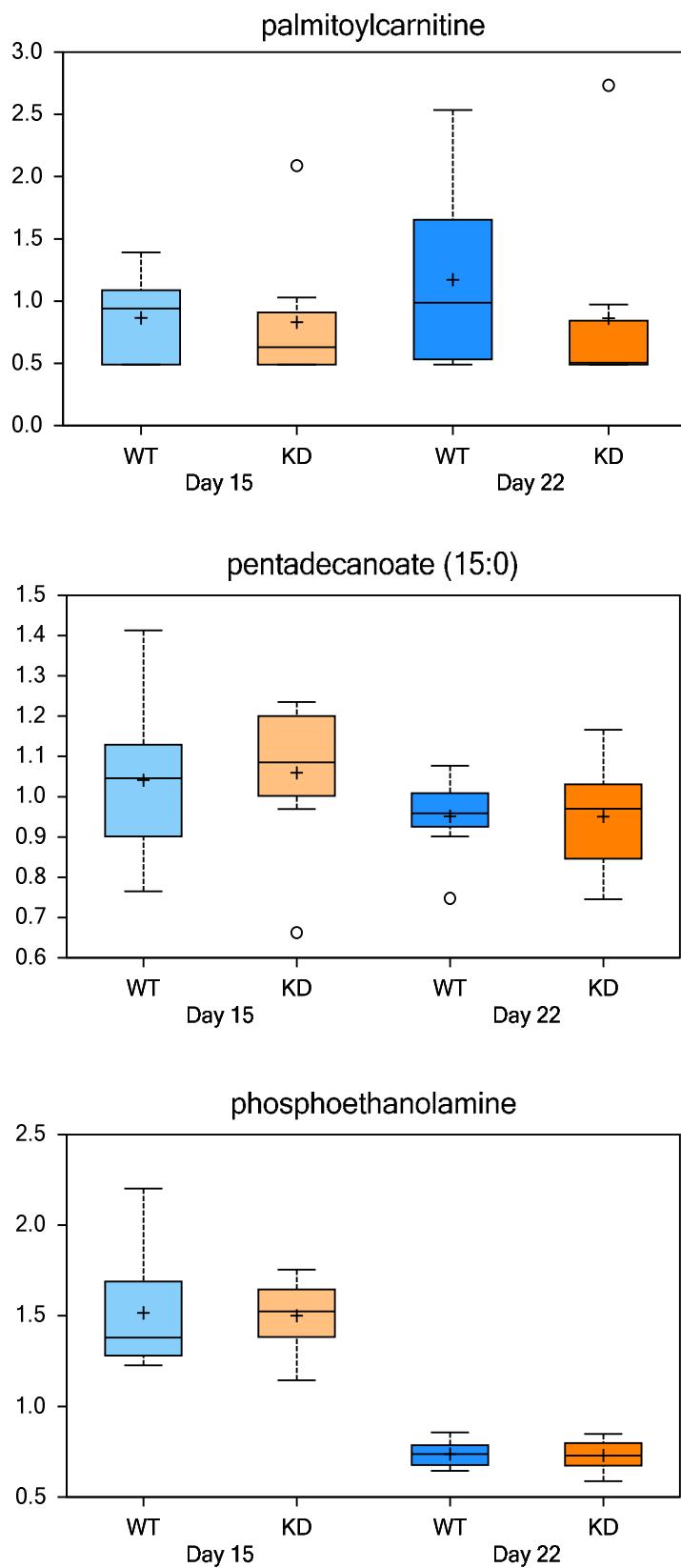


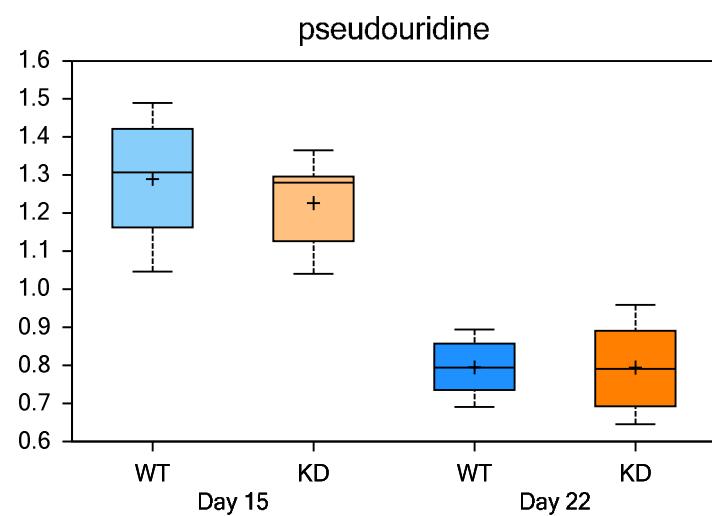
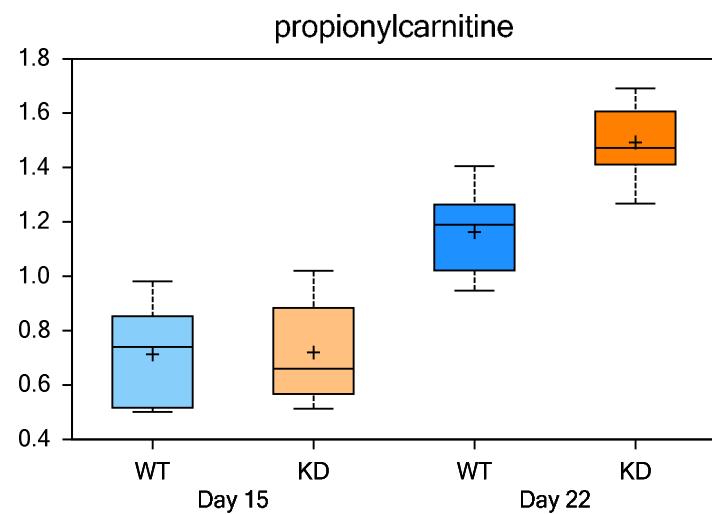
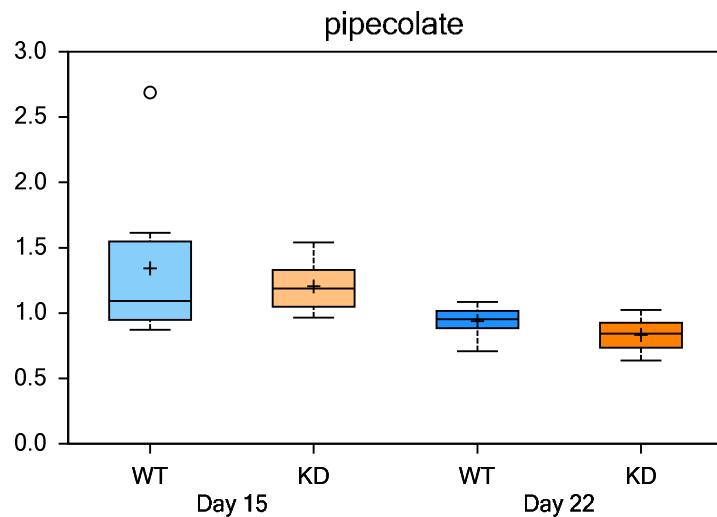
N-acetylglucosamine

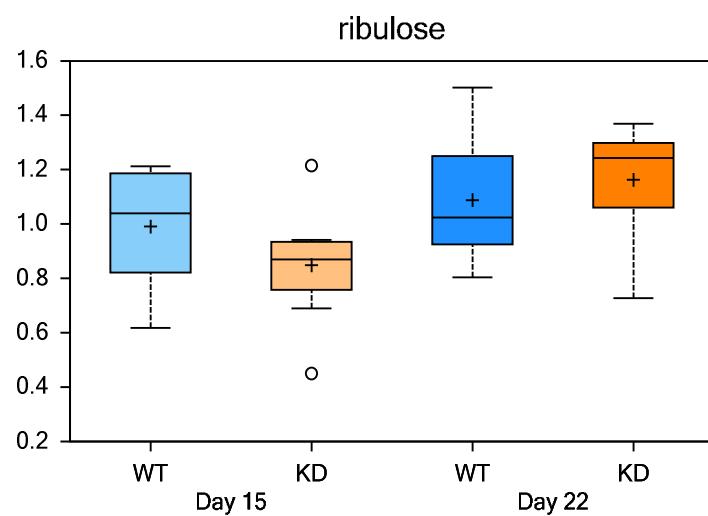
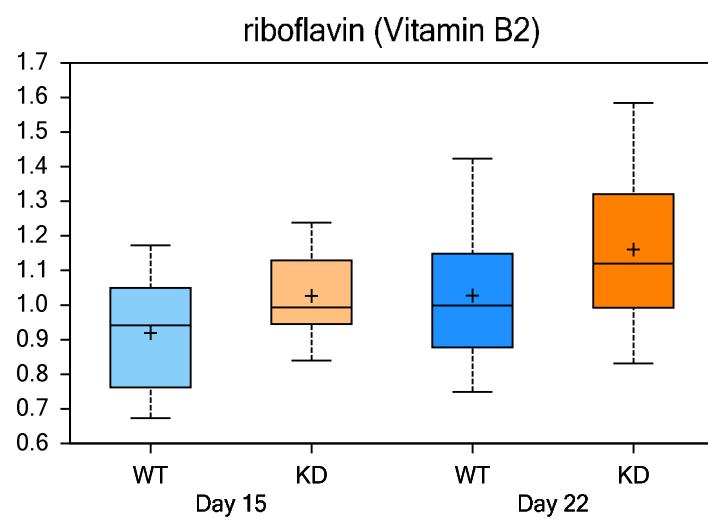
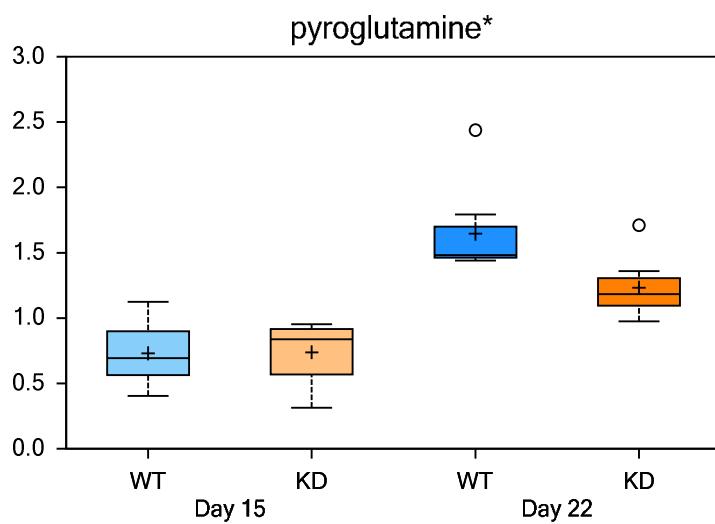


N-acetylmethionine**N-delta-acetylornithine*****nonadecanoate (19:0)**

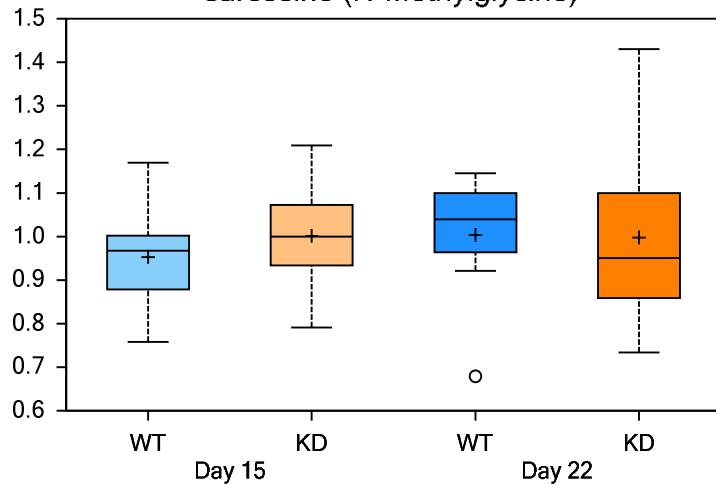




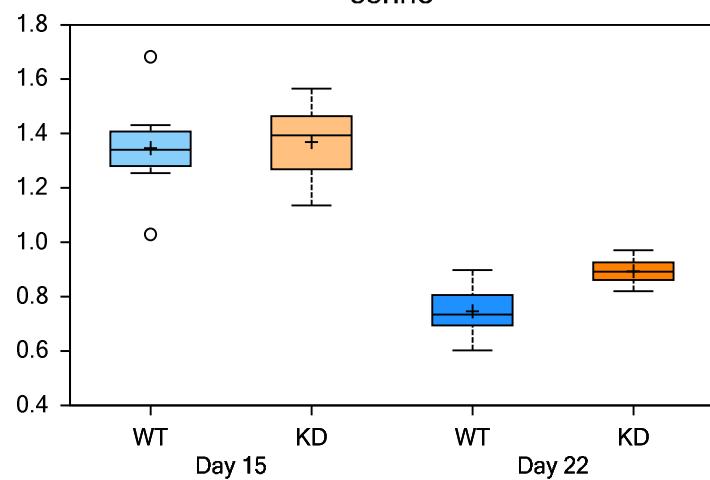




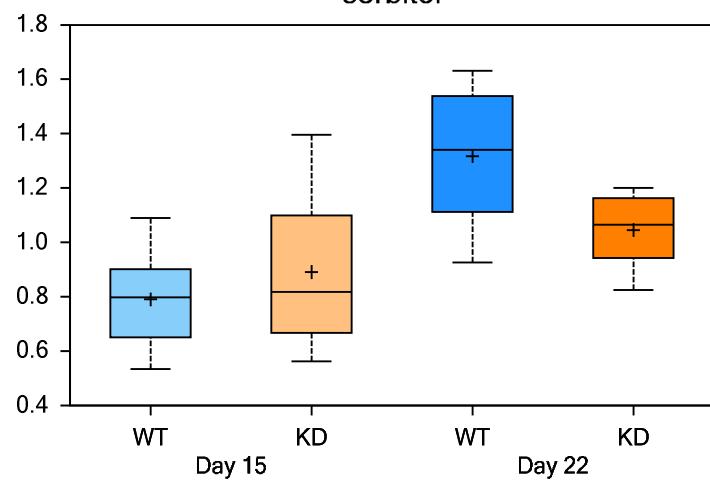
sarcosine (N-Methylglycine)



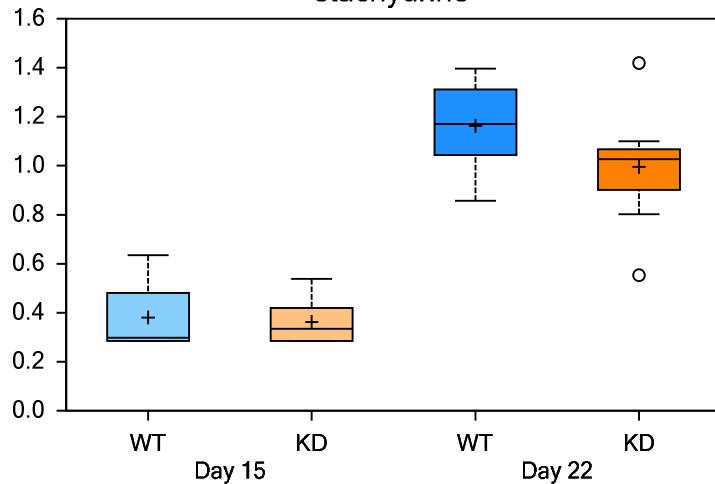
serine



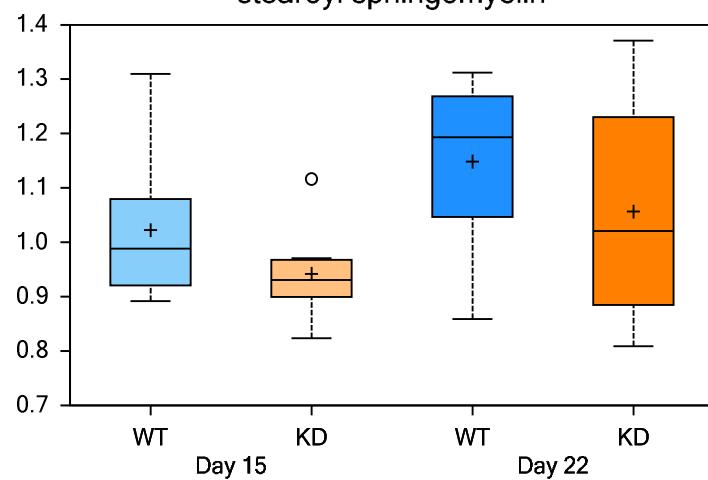
sorbitol



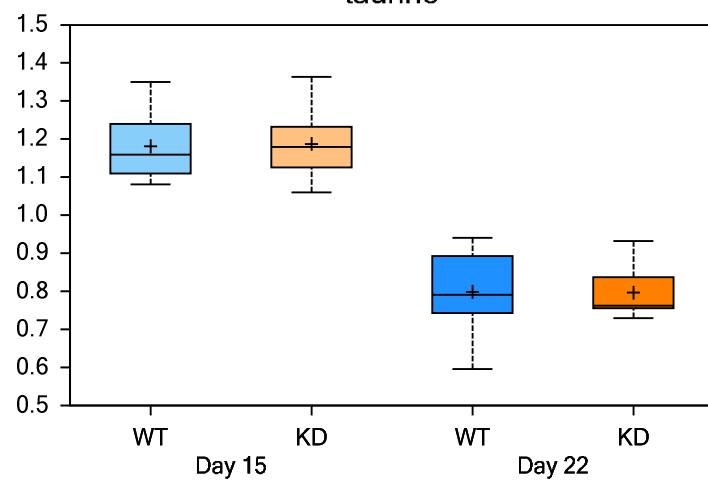
stachydrine

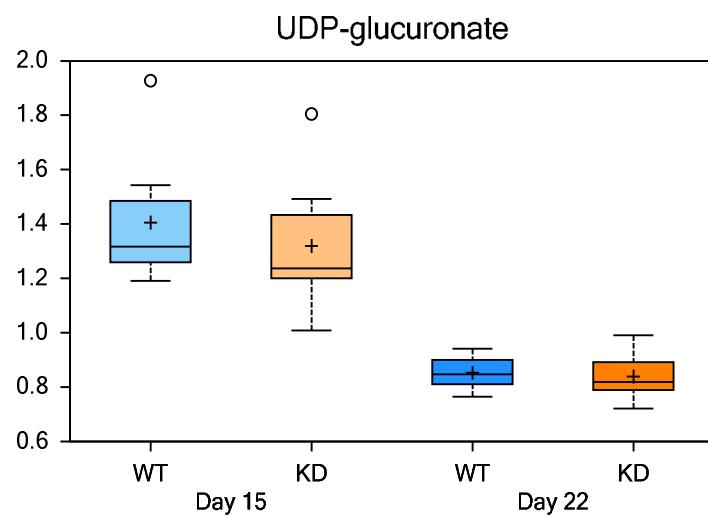
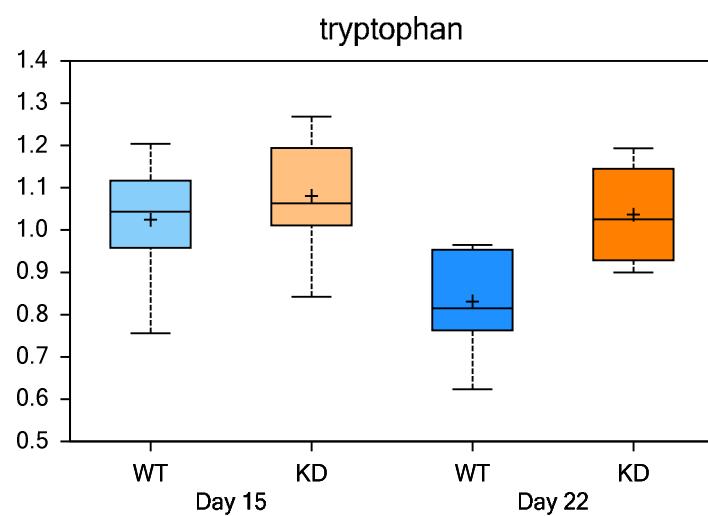
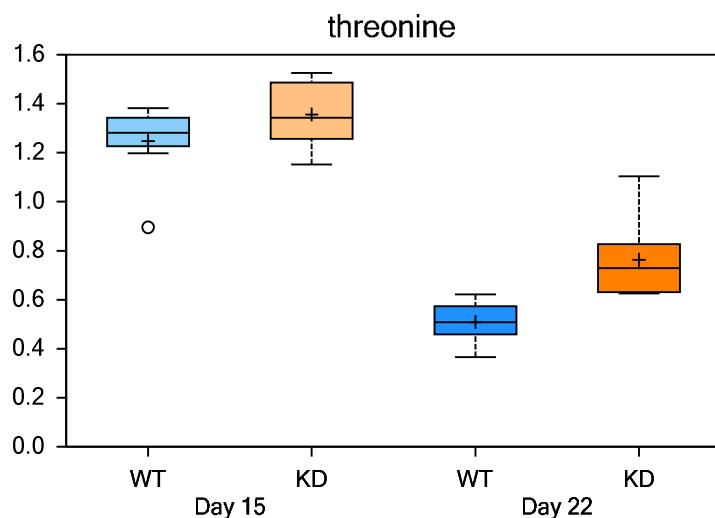


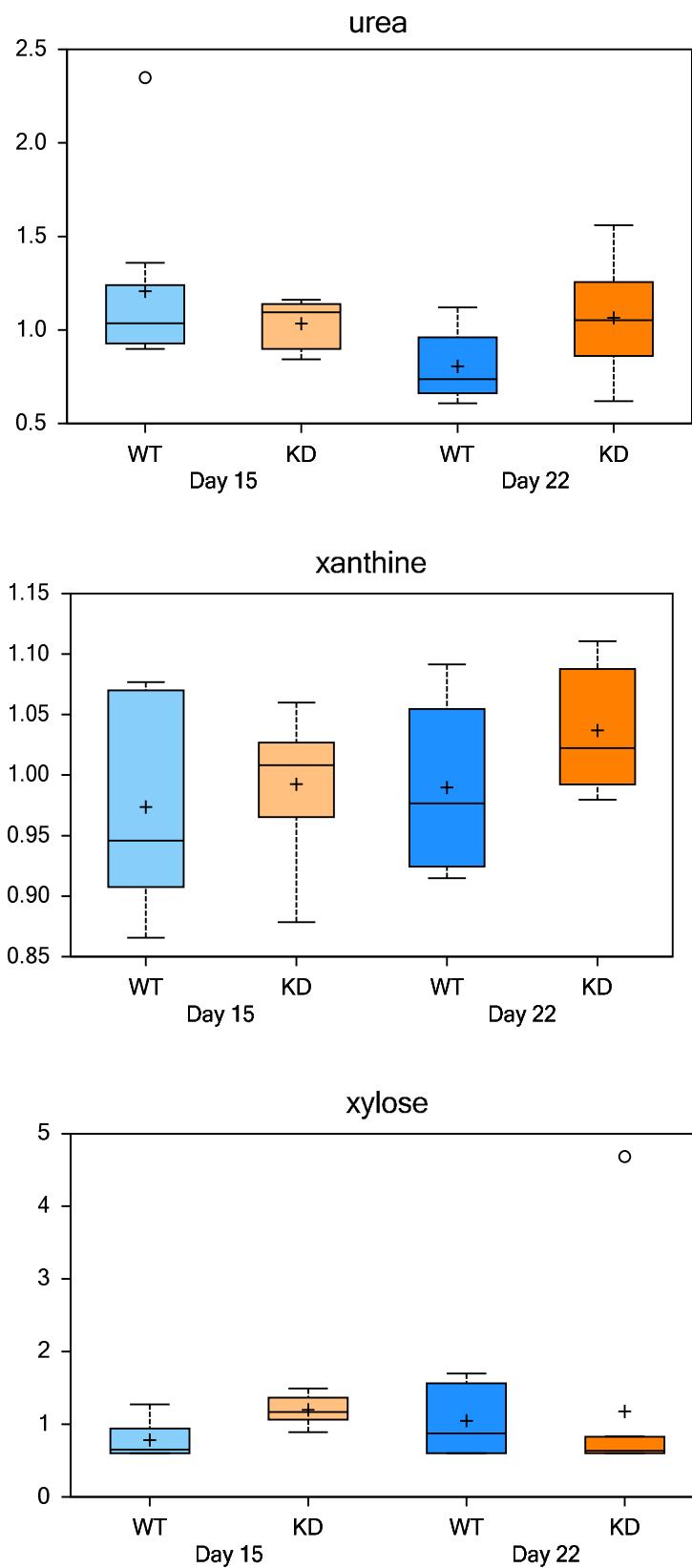
stearoyl sphingomyelin



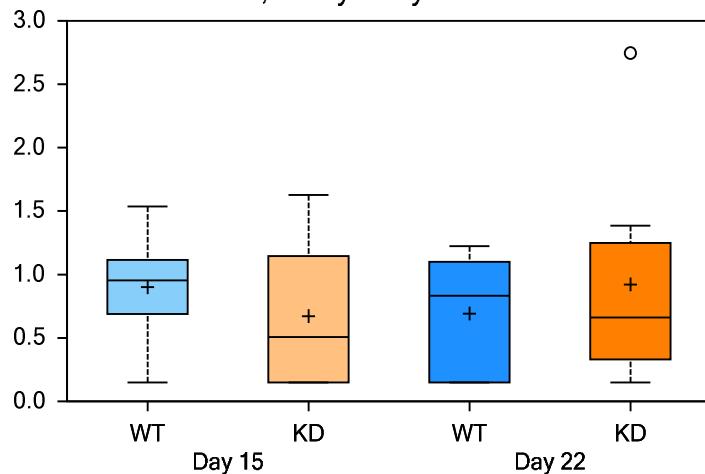
taurine



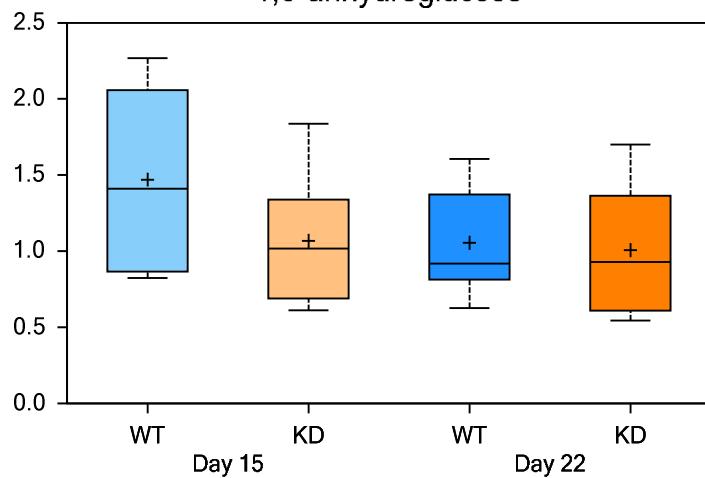




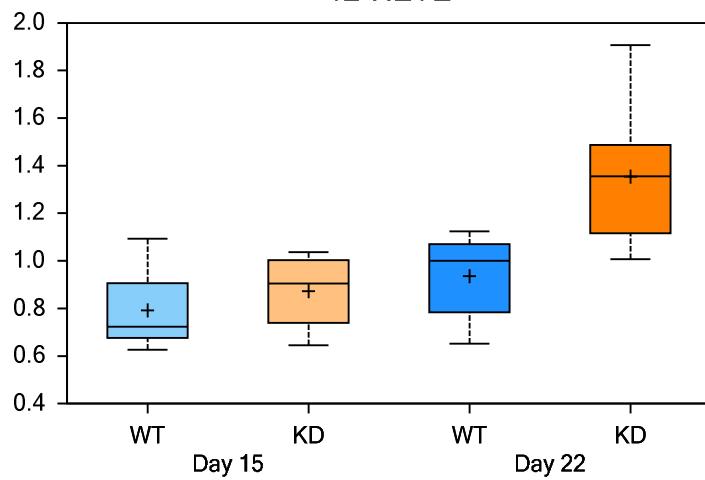
1,3-dihydroxyacetone



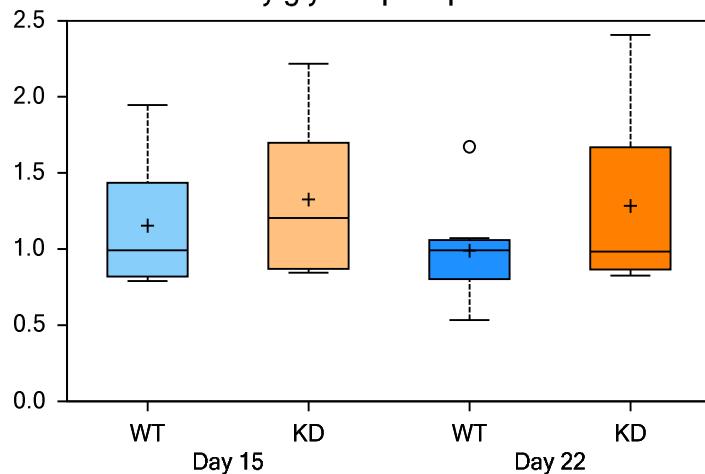
1,6-anhydroglucose



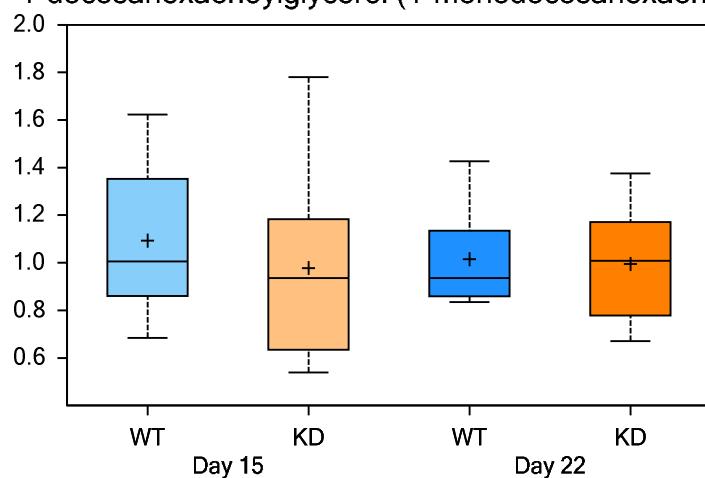
12-HETE



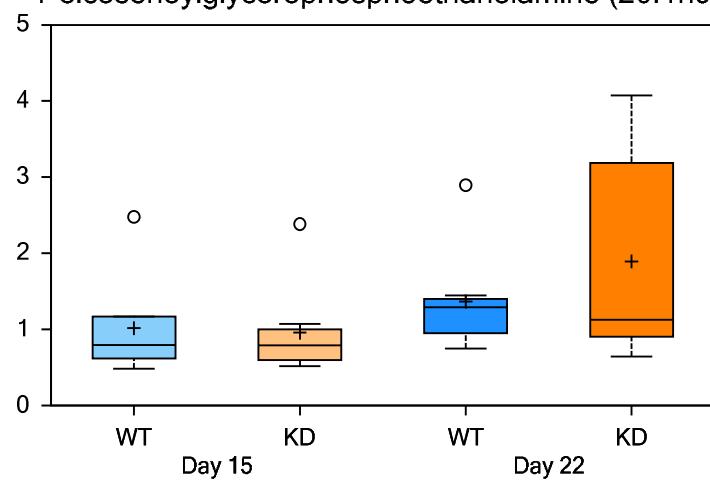
1-arachidonoylglycerophosphoethanolamine*



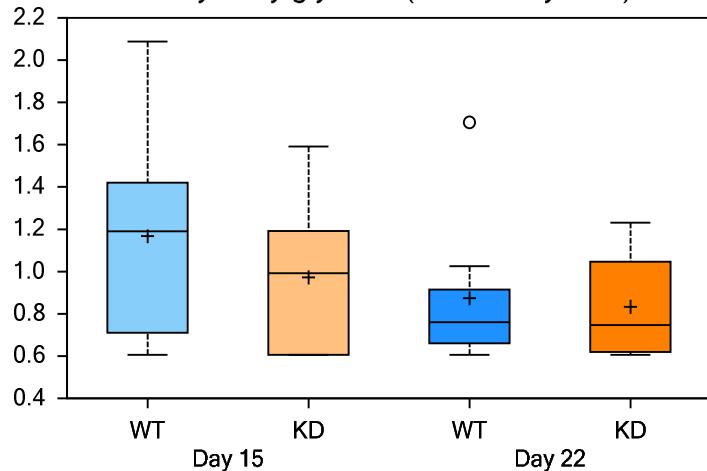
1-docosahexaenoylglycerol (1-monodocosahexaenoil)



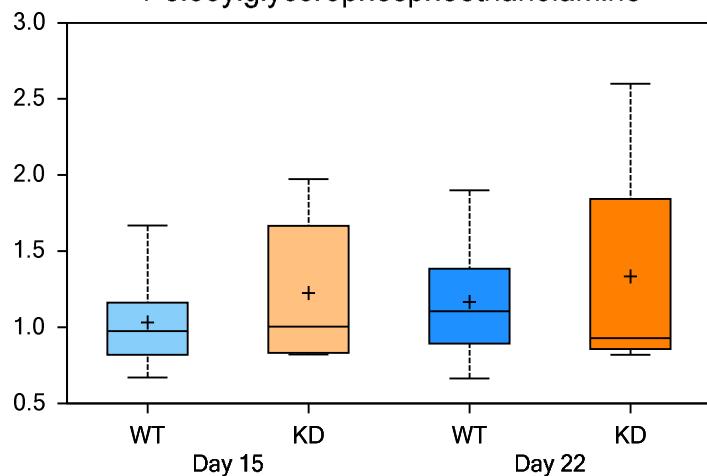
1-eicosenoylglycerophosphoethanolamine (20:1n9)



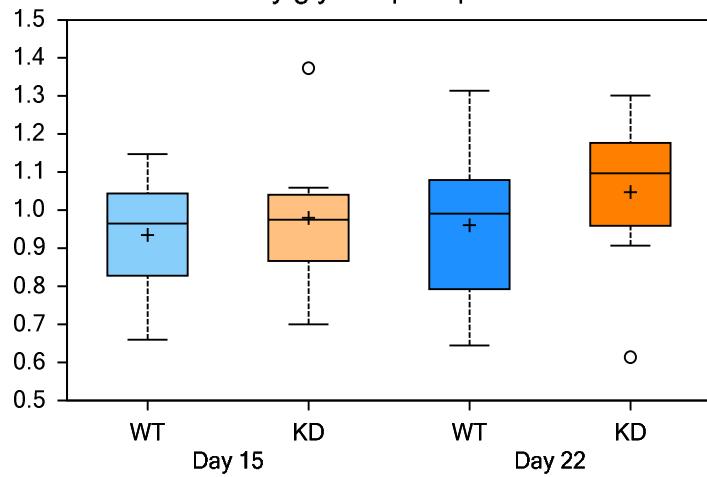
1-myristoylglycerol (1-monomyristin)



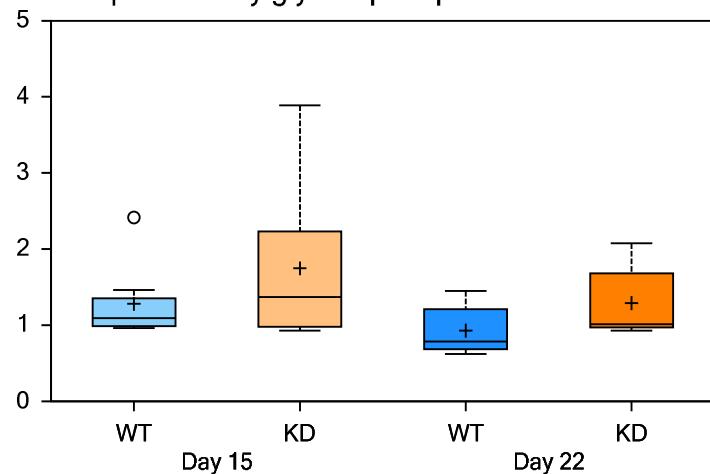
1-oleoylglycerophosphoethanolamine



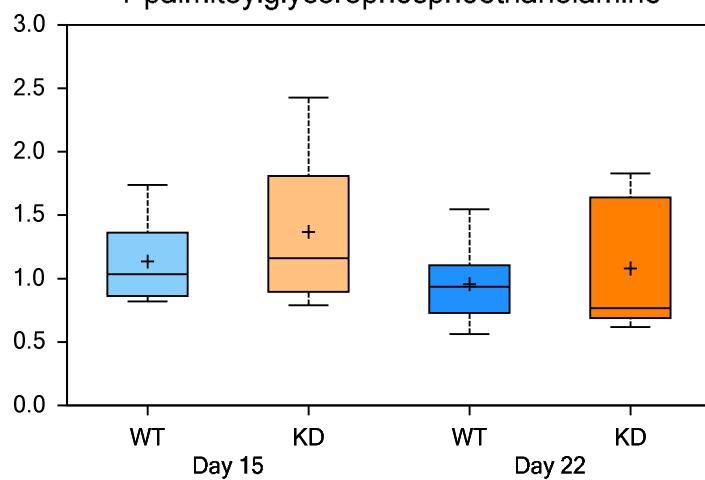
1-oleoylglycerophosphoserine



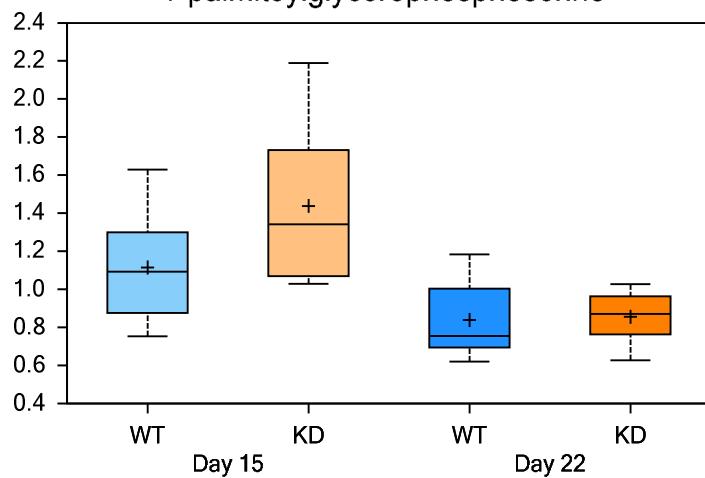
1-palmitoleoylglycerophosphoethanolamine*



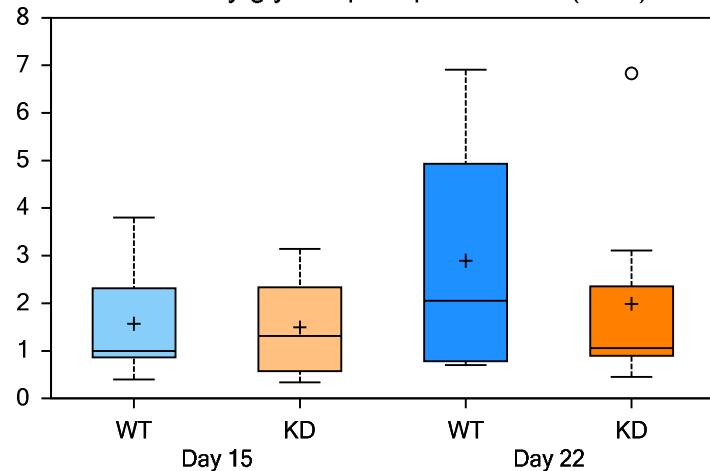
1-palmitoylglycerophosphoethanolamine



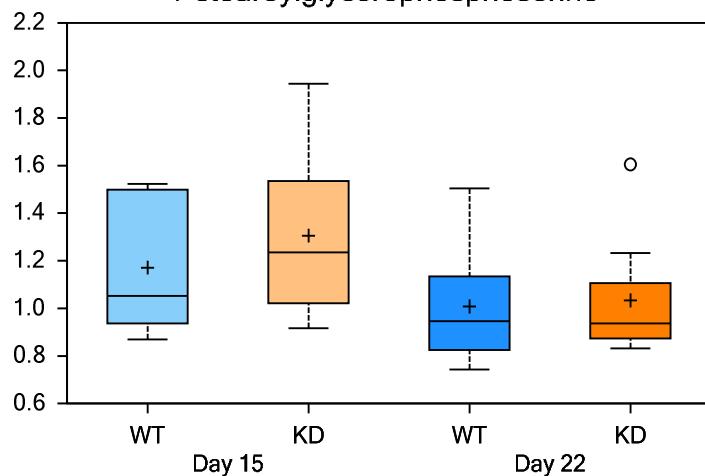
1-palmitoylglycerophosphoserine*



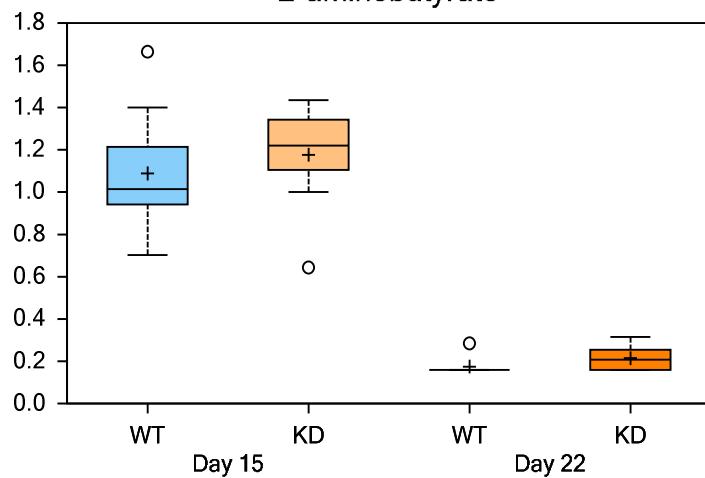
1-stearoylglycerophosphocholine (18:0)



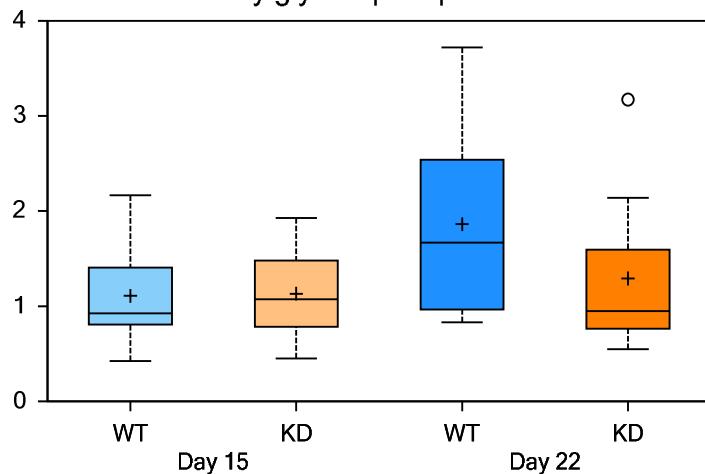
1-stearoylglycerophosphoserine*



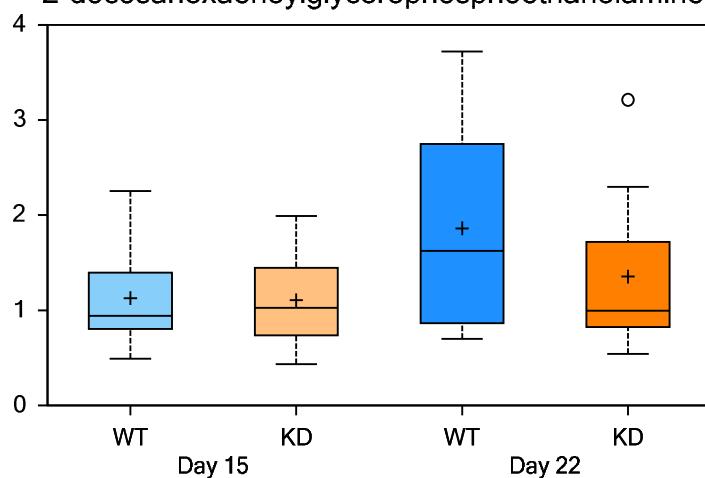
2-aminobutyrate



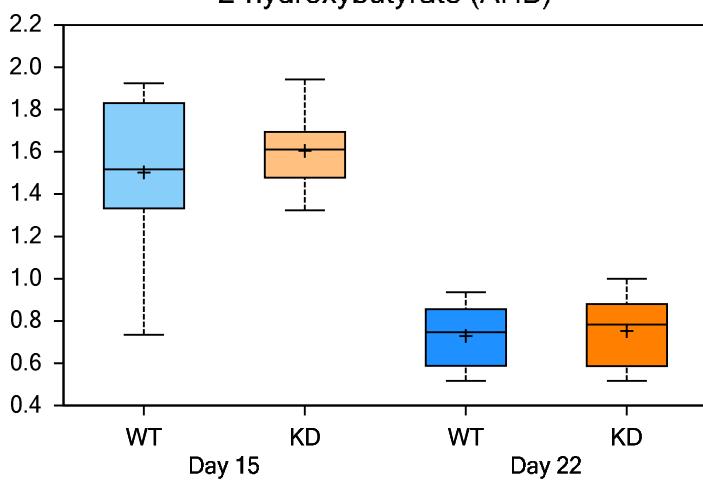
2-arachidonoylglycerophosphoethanolamine*



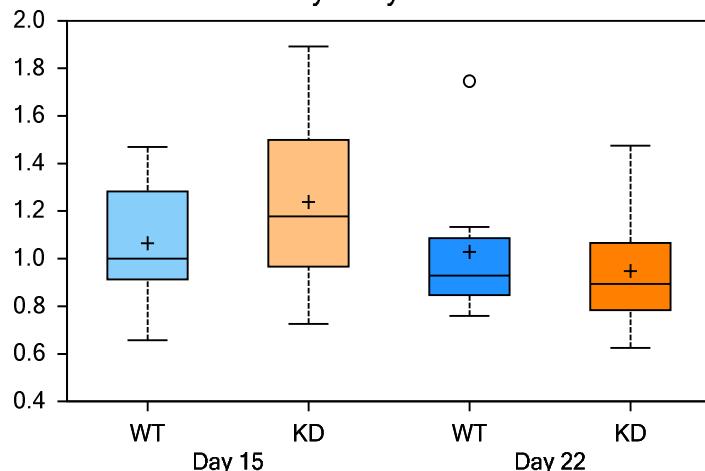
2-docosahexaenoylglycerophosphoethanolamine*



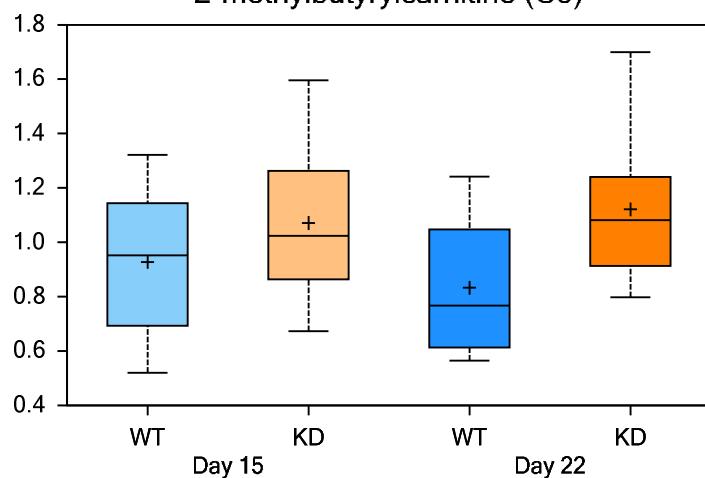
2-hydroxybutyrate (AHB)



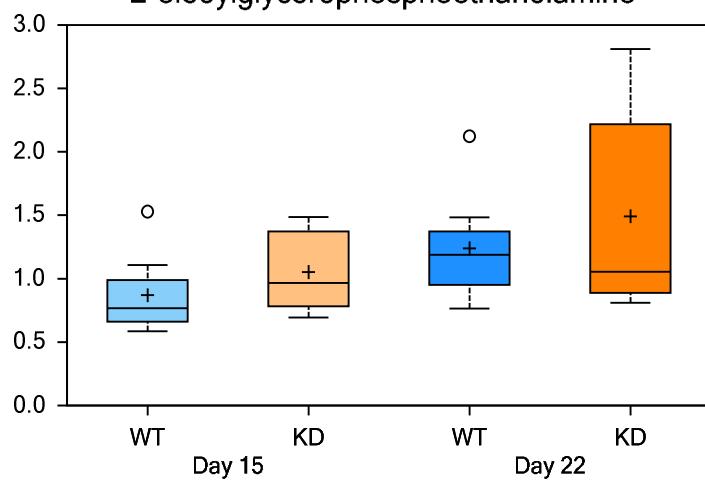
2-hydroxystearate



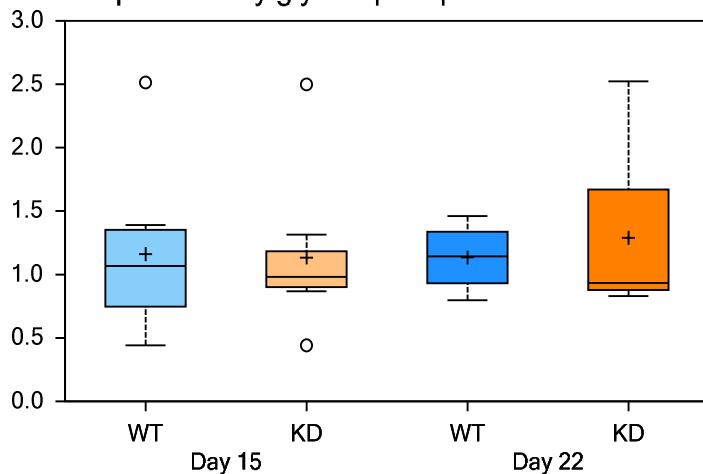
2-methylbutyrylcarnitine (C5)



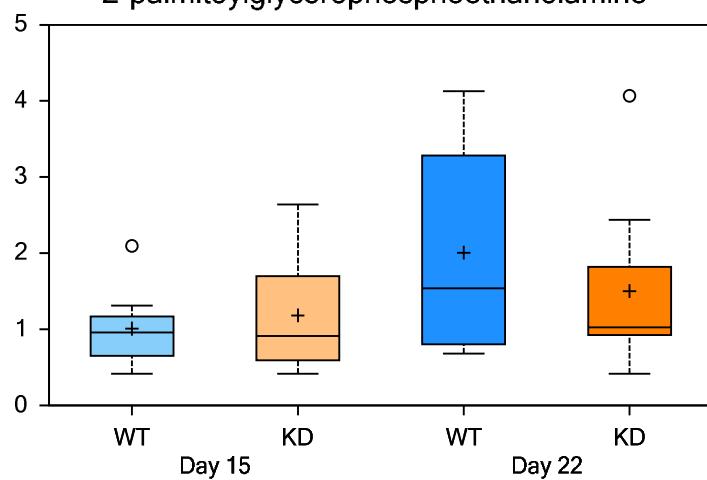
2-oleoylglycerophosphoethanolamine*



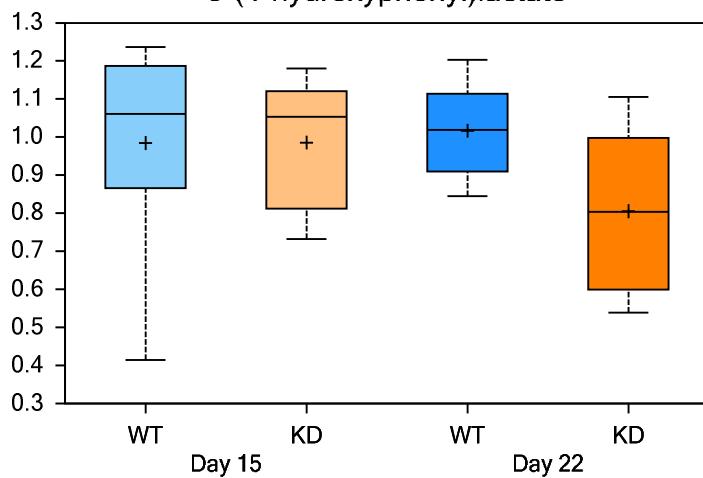
2-palmitoleoylglycerophosphoethanolamine*



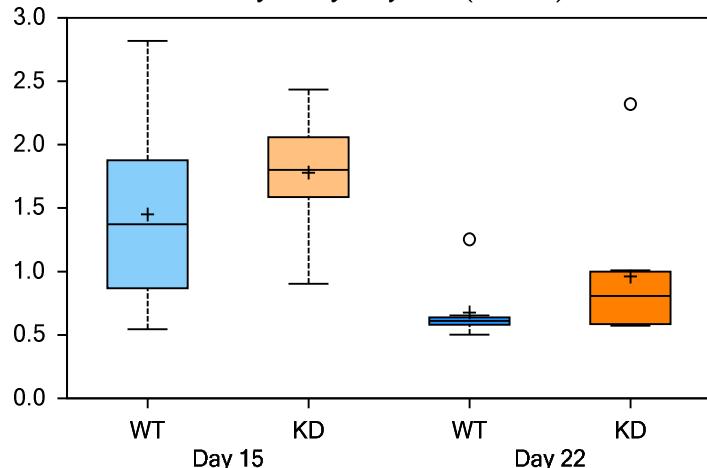
2-palmitoylglycerophosphoethanolamine*



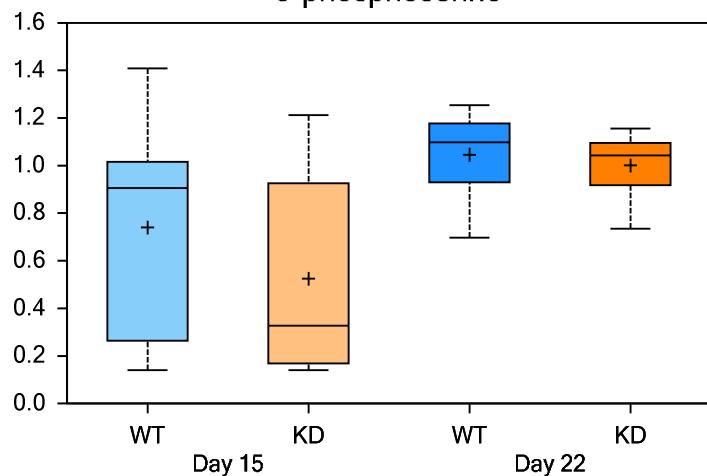
3-(4-hydroxyphenyl)lactate



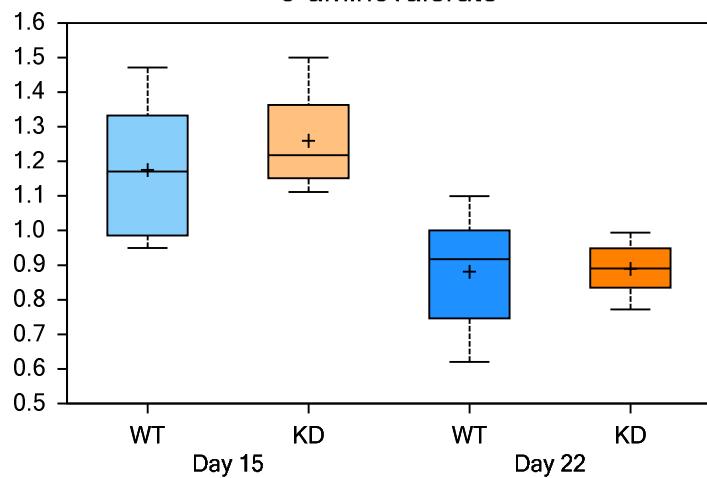
3-hydroxybutyrate (BHBA)

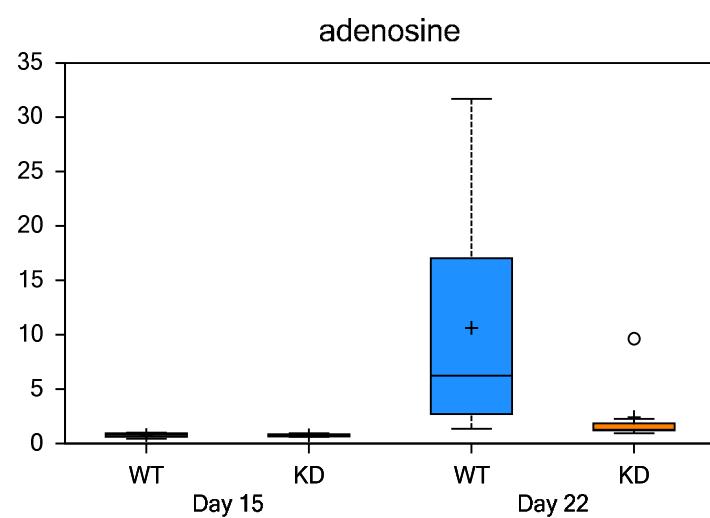
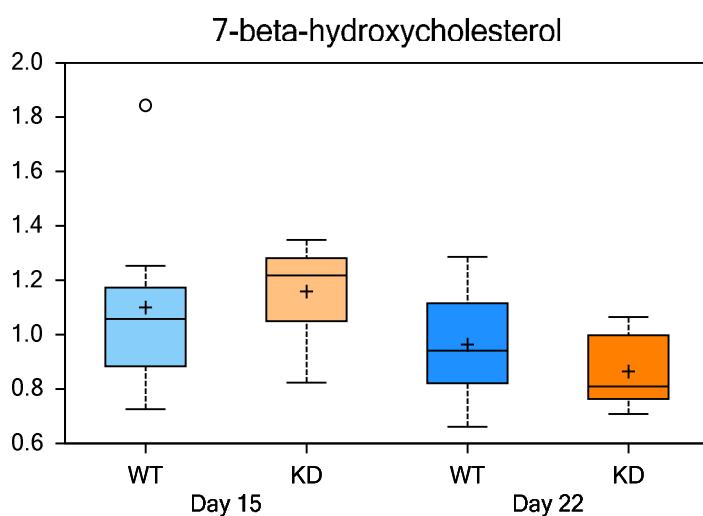
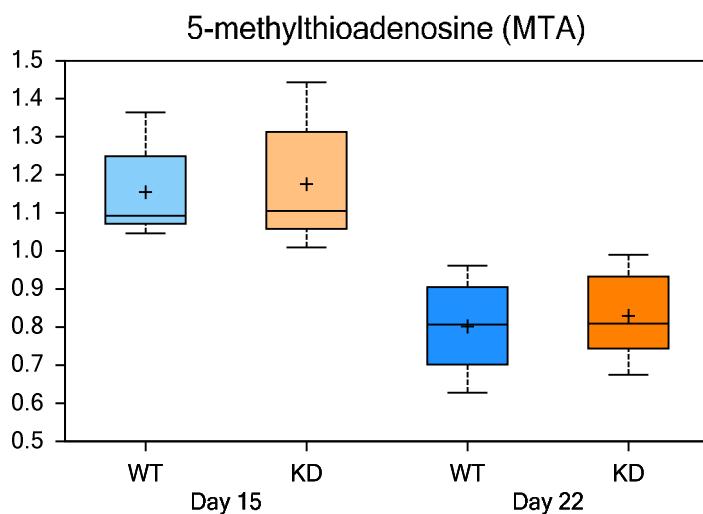


3-phosphoserine

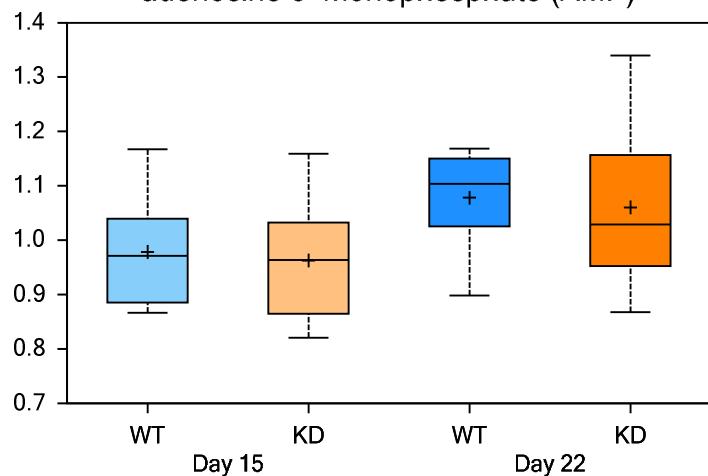


5-aminovalerate

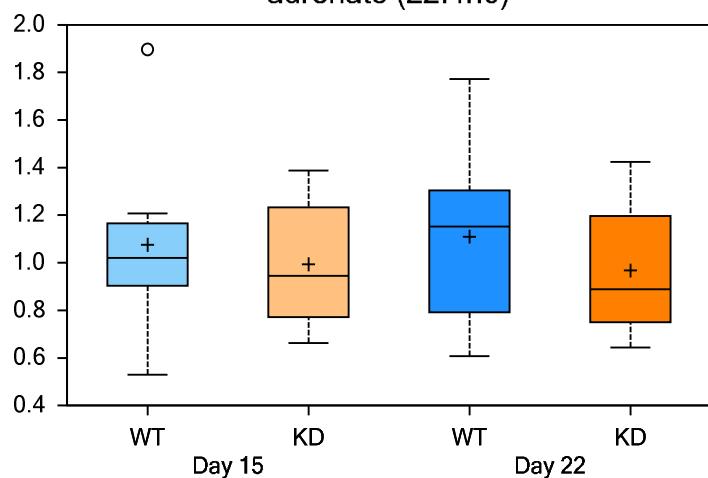




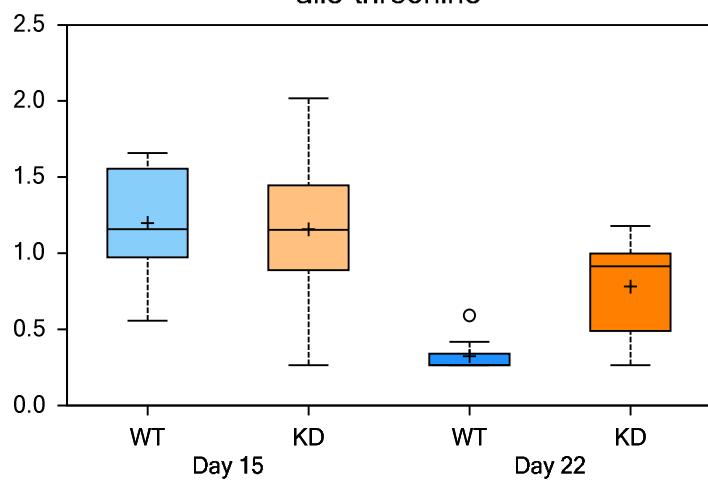
adenosine 5'-monophosphate (AMP)

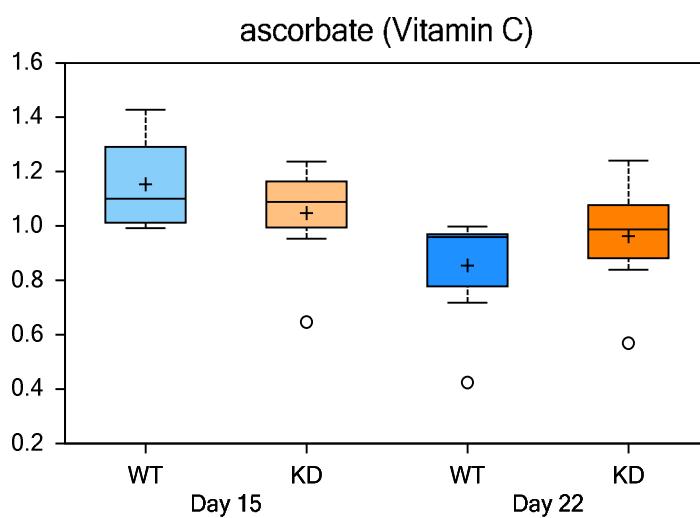
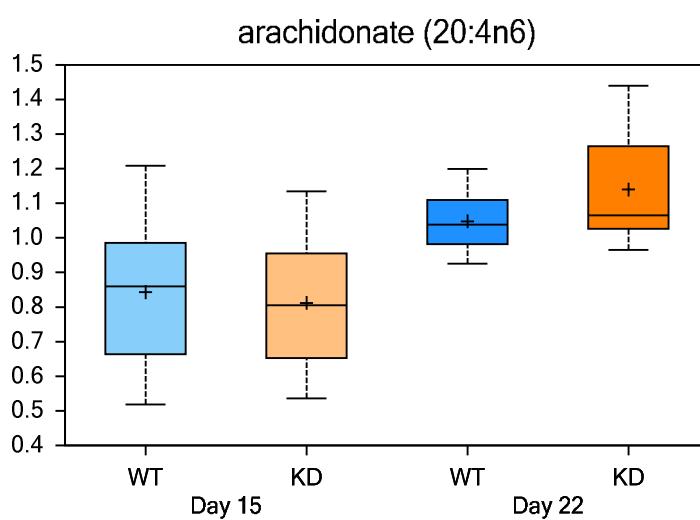
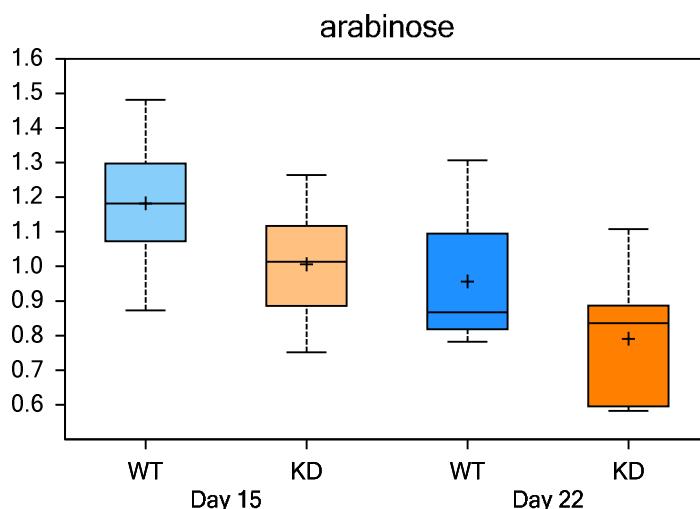


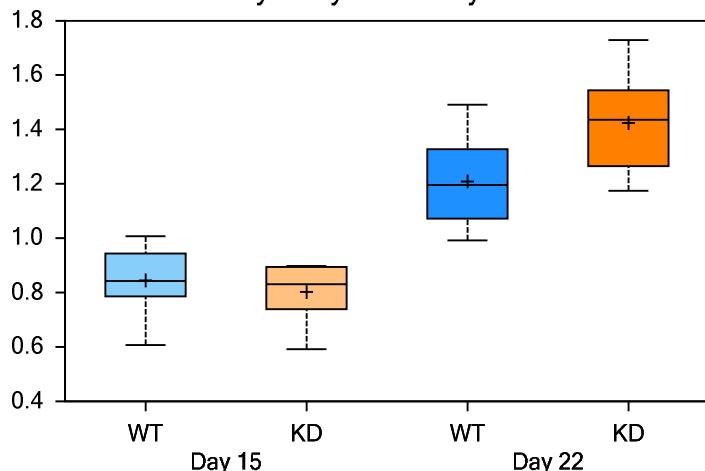
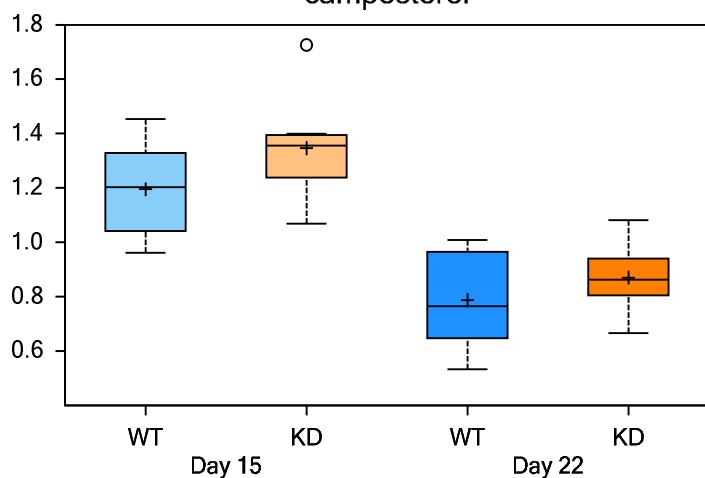
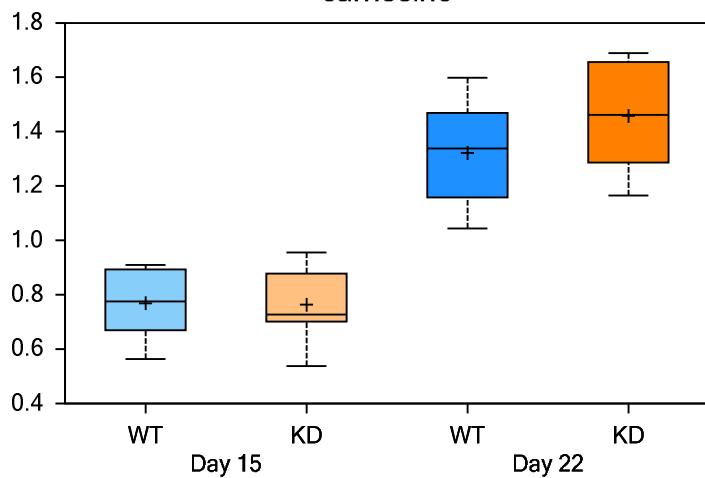
adrenate (22:4n6)

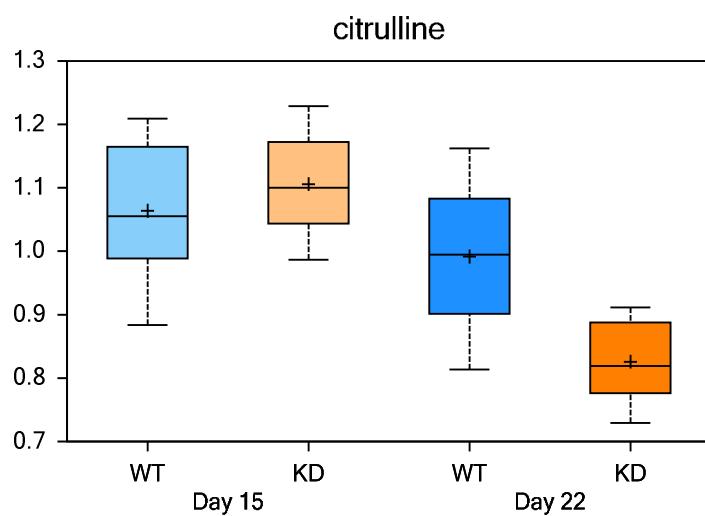
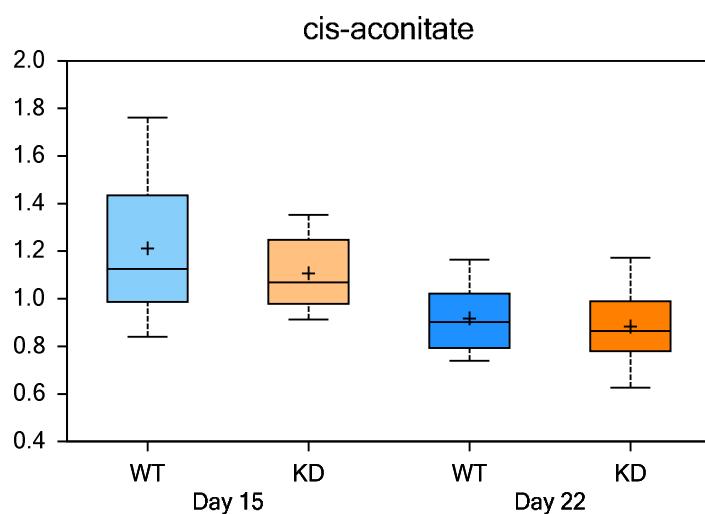
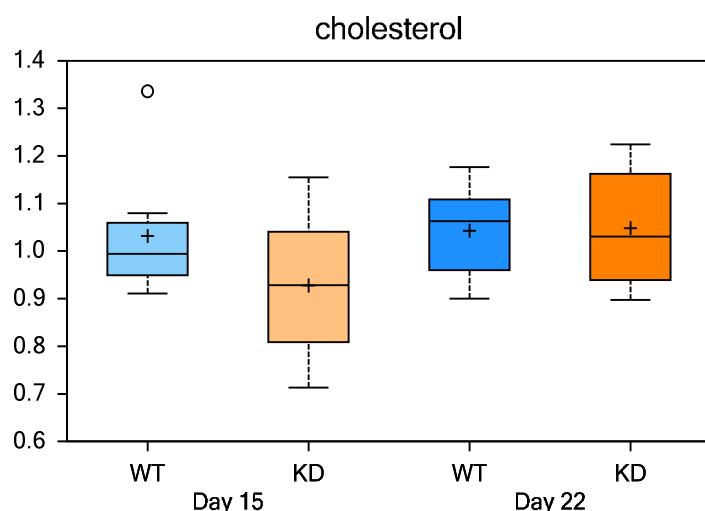


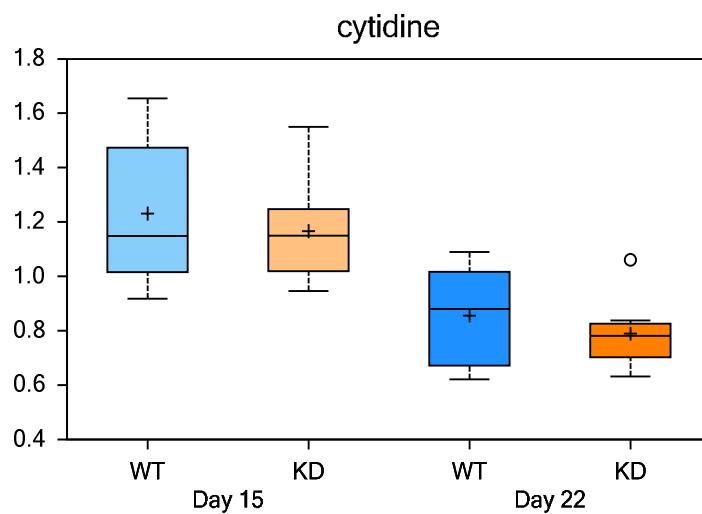
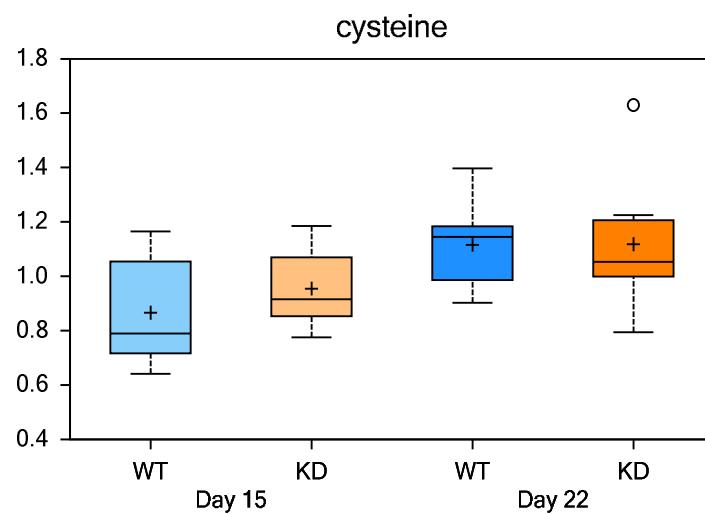
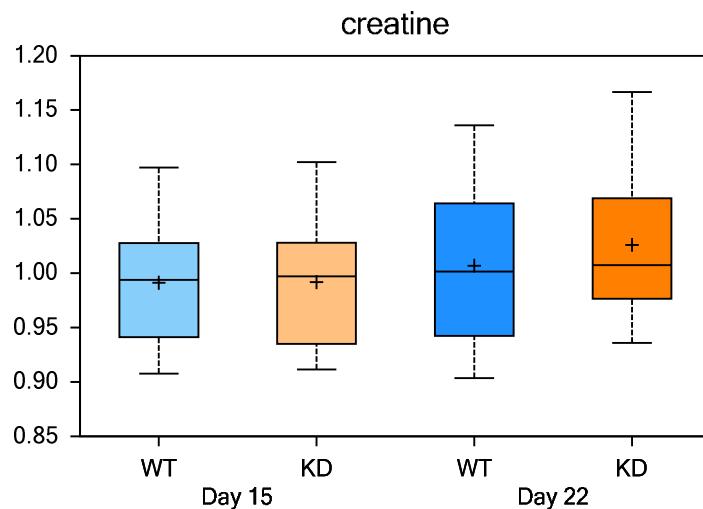
allo-threonine



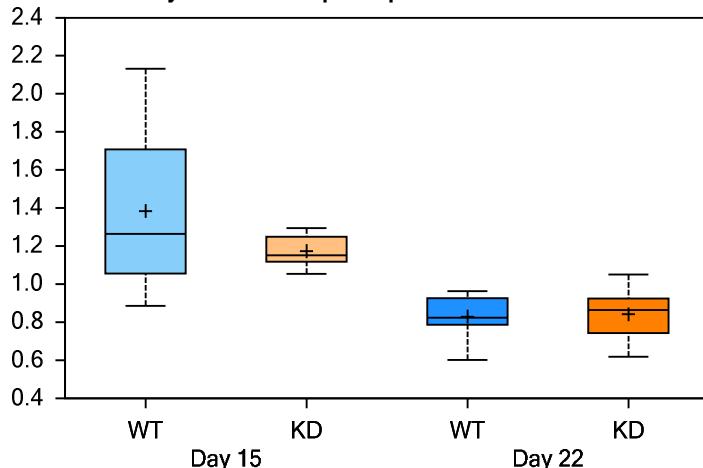


beta-hydroxyisovaleroylcarnitine**campesterol****carnosine**

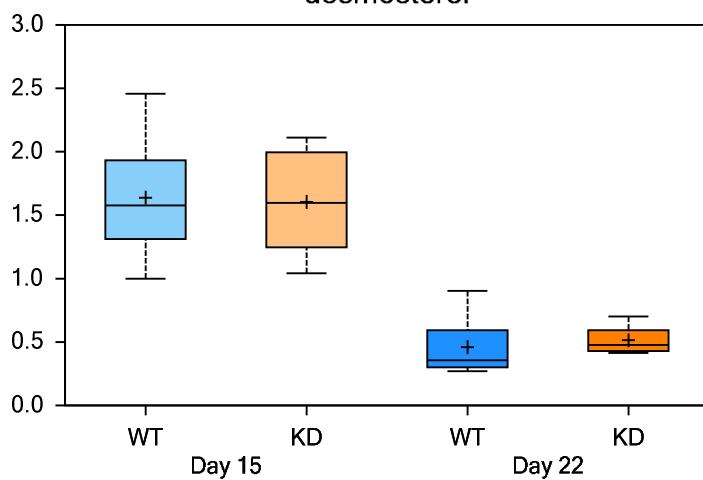




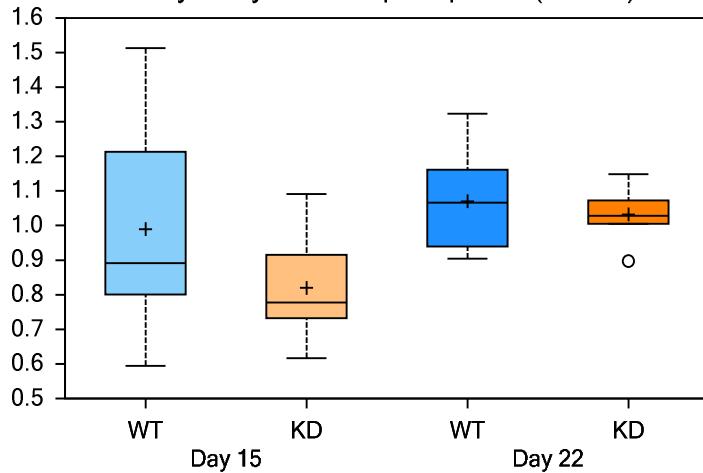
cytidine-5'-diphosphoethanolamine



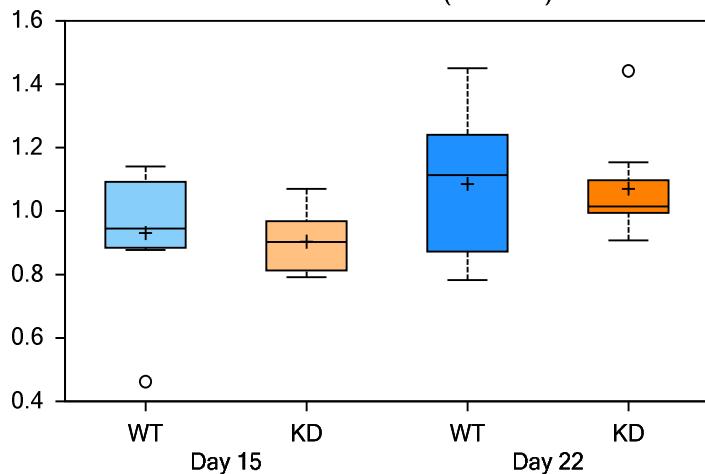
desmosterol



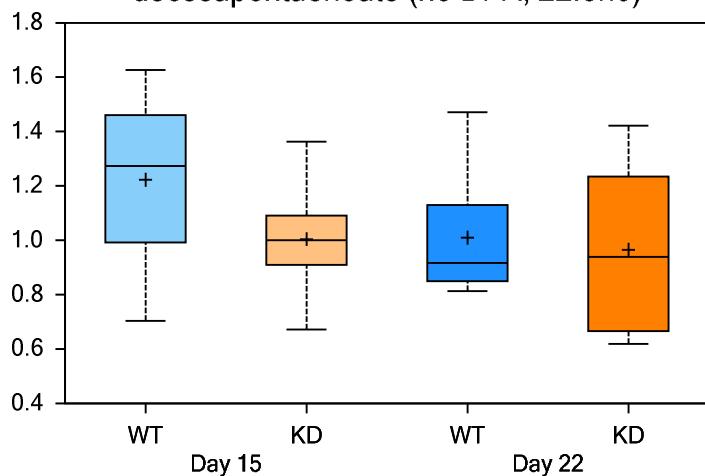
dihydroxyacetone phosphate (DHAP)



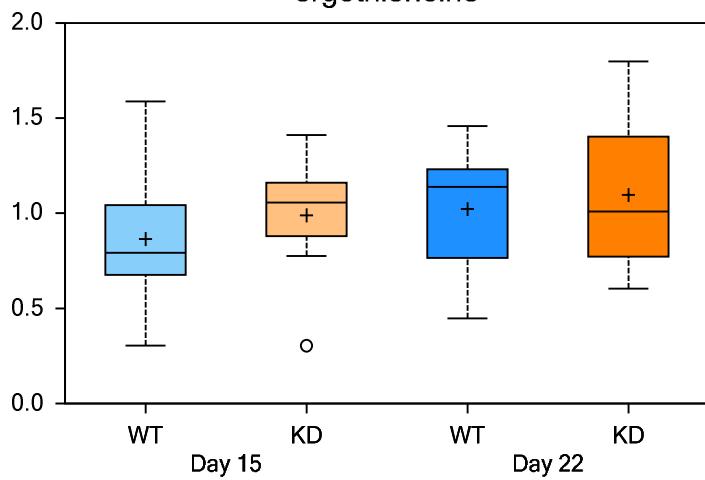
docosadienoate (22:2n6)

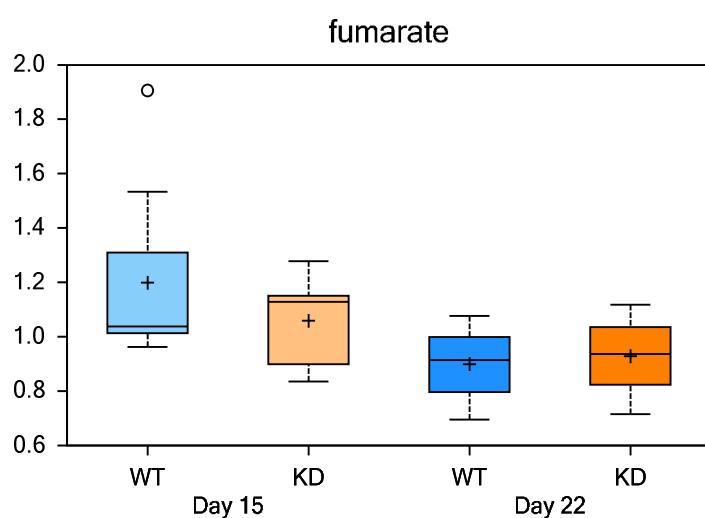
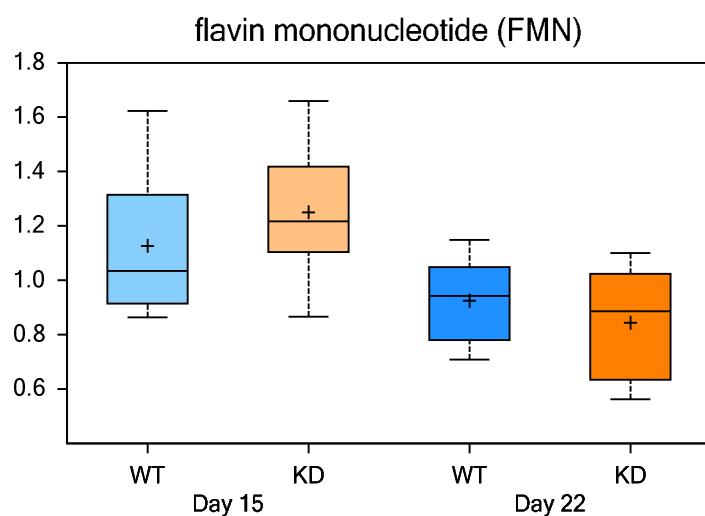
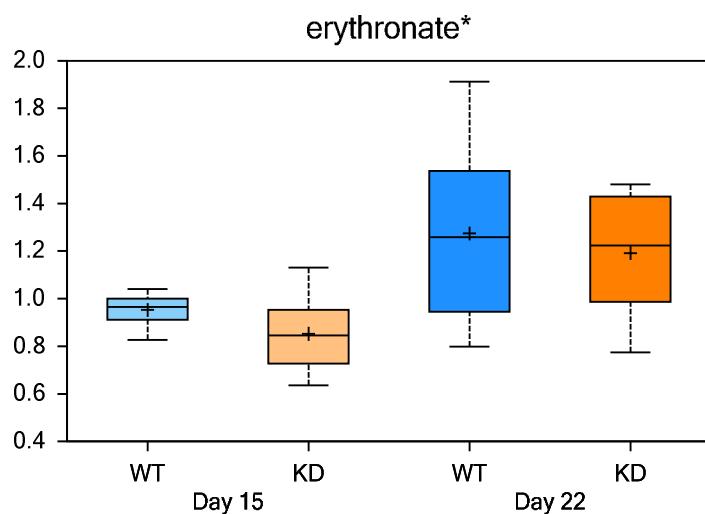


docosapentaenoate (n6 DPA; 22:5n6)

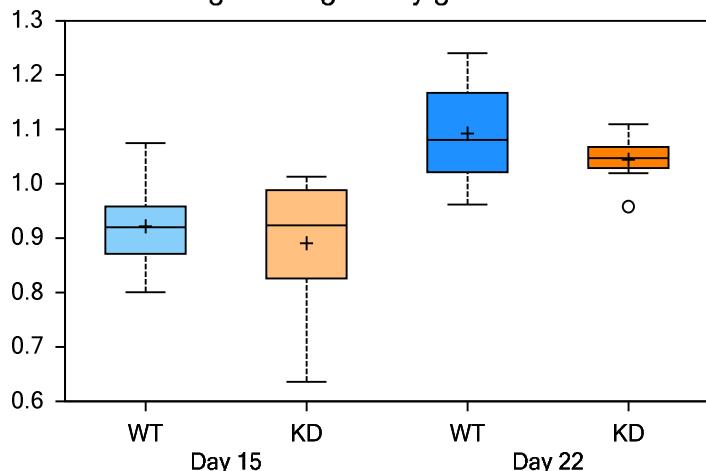


ergothioneine

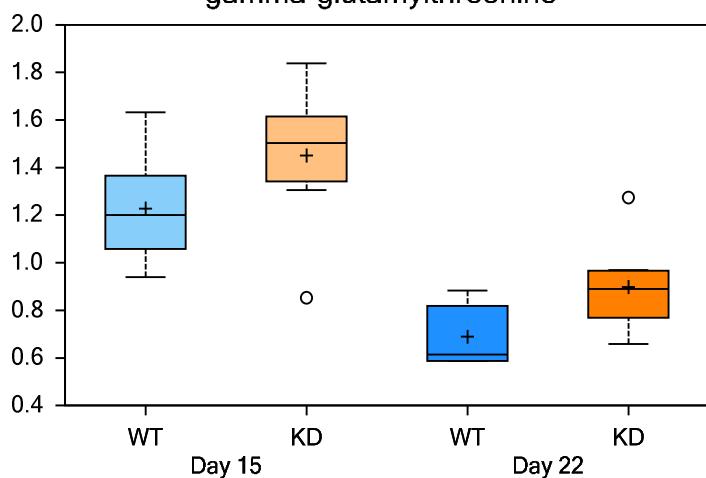




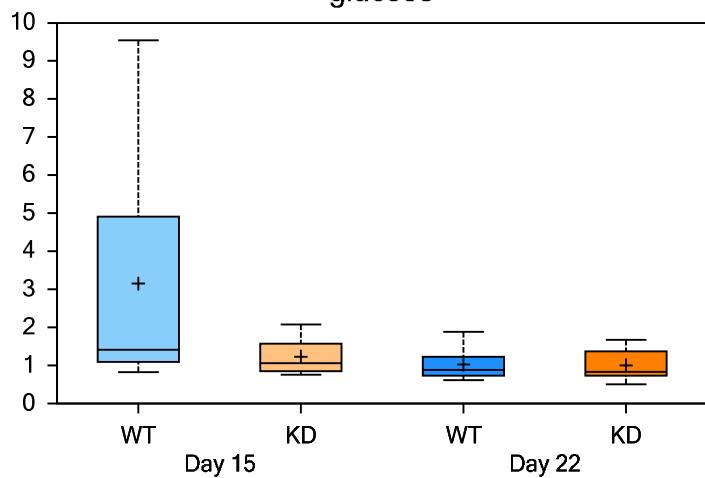
gamma-glutamylglutamine



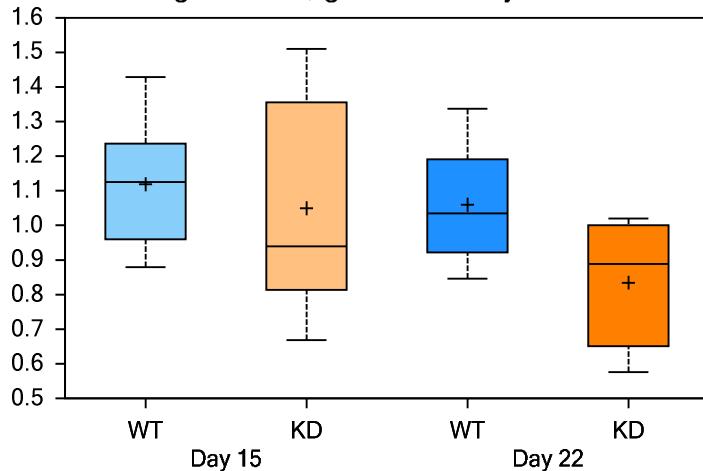
gamma-glutamylthreonine*



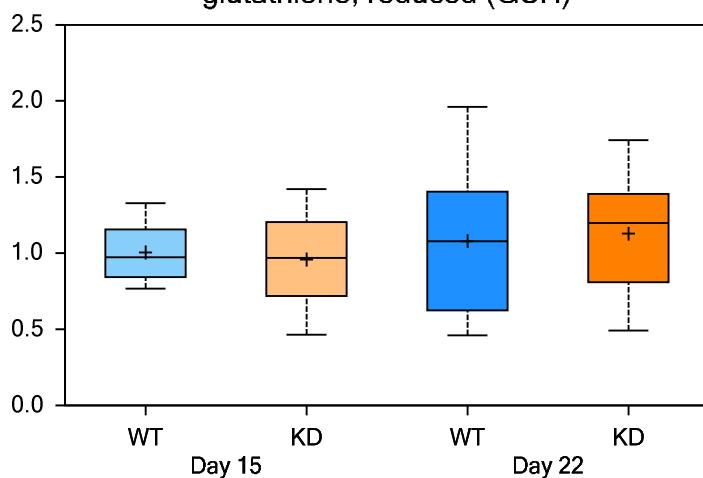
glucose



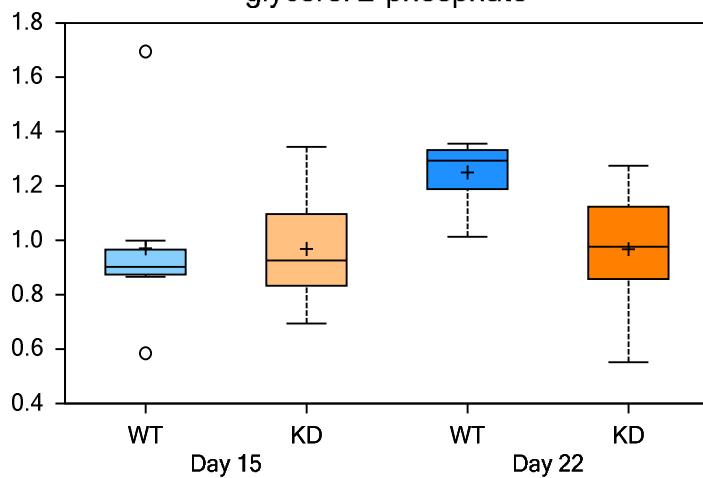
glutamate, gamma-methyl ester



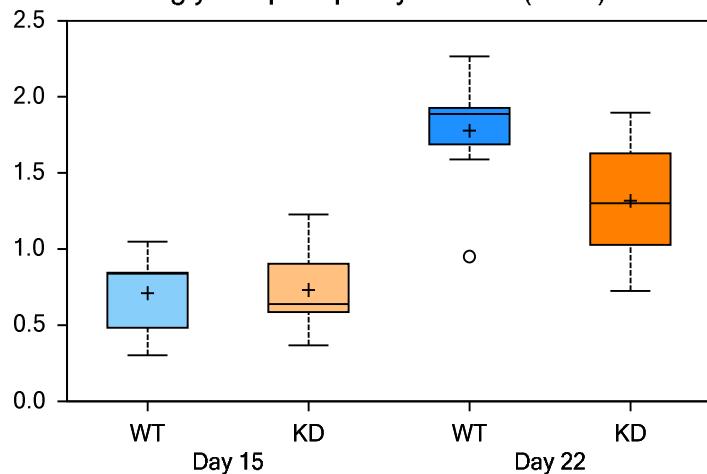
glutathione, reduced (GSH)



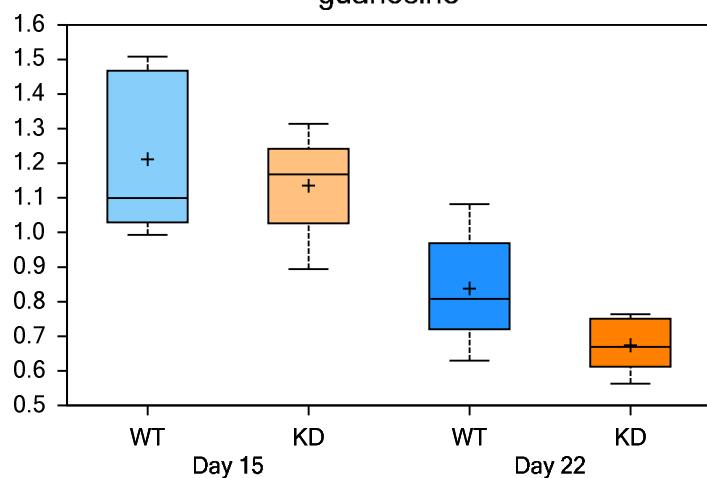
glycerol 2-phosphate



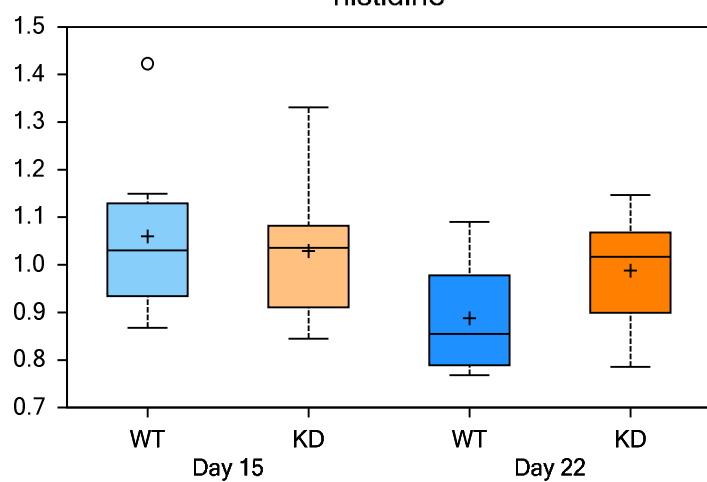
glycerophosphorylcholine (GPC)

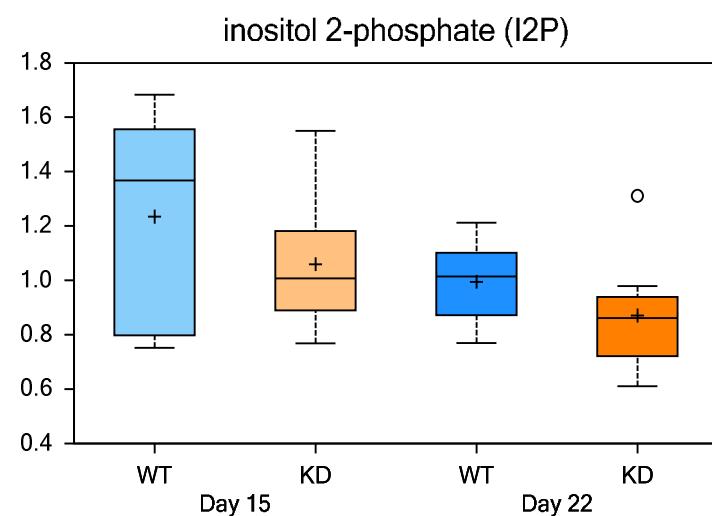
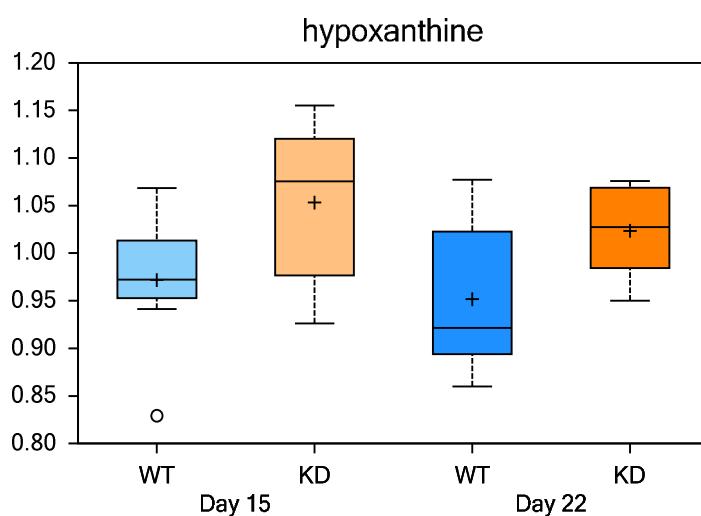
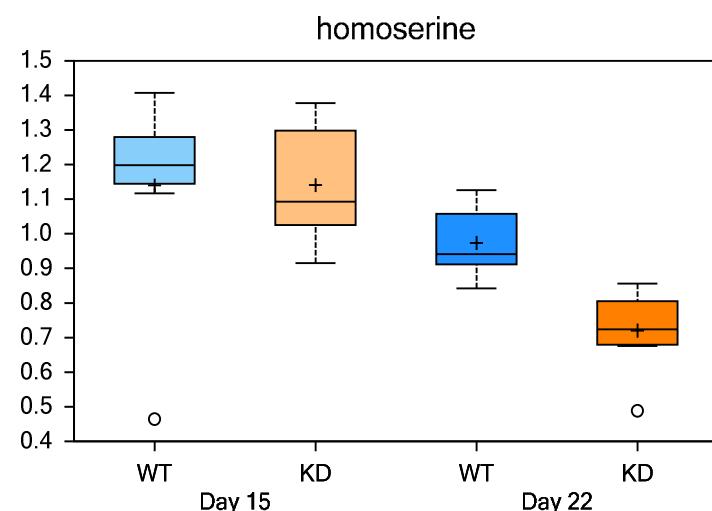


guanosine

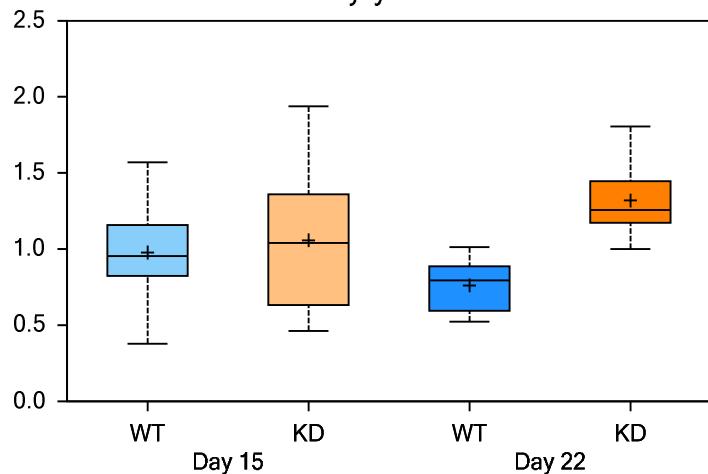


histidine

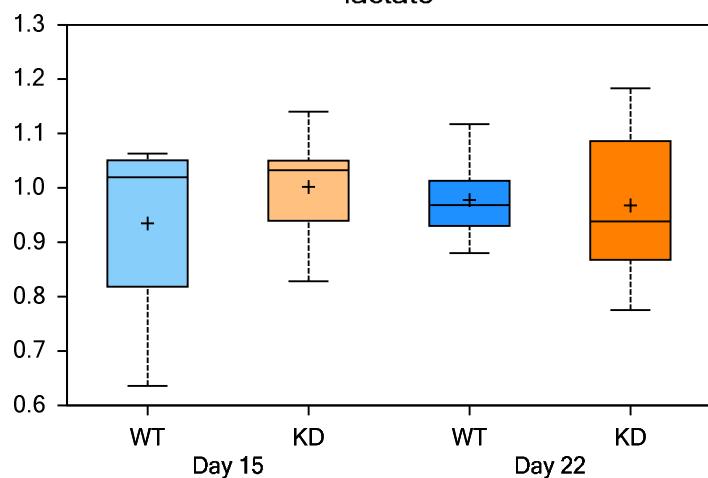




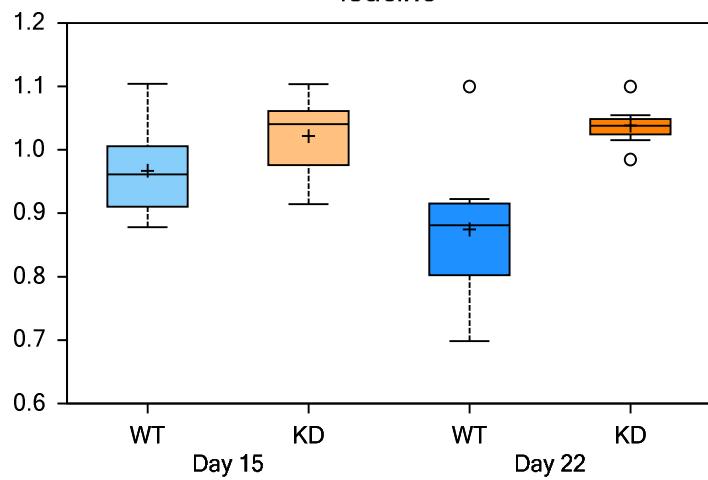
isobutyrylcarnitine



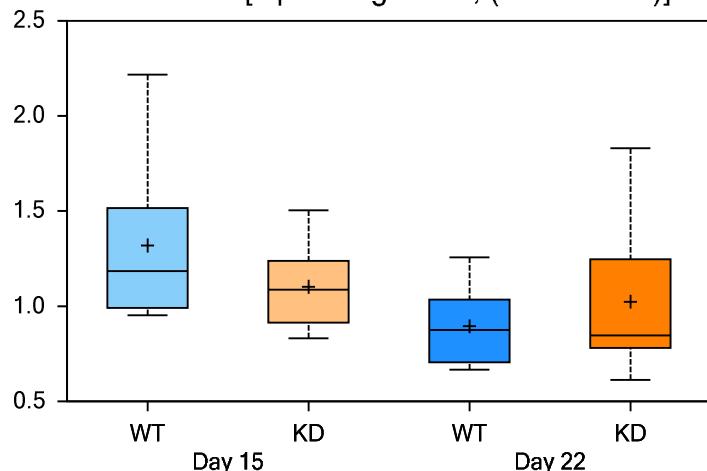
lactate



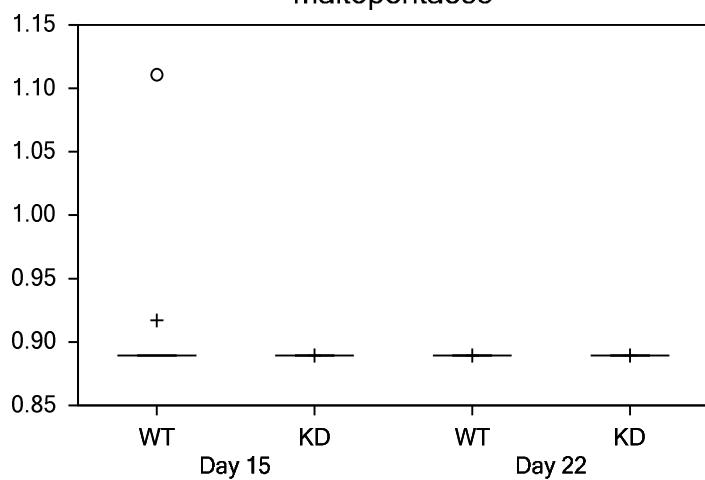
leucine



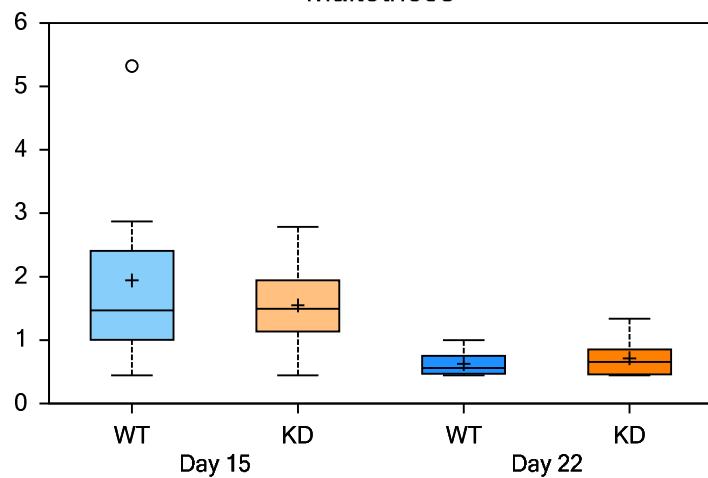
linolenate [alpha or gamma; (18:3n3 or 6)]



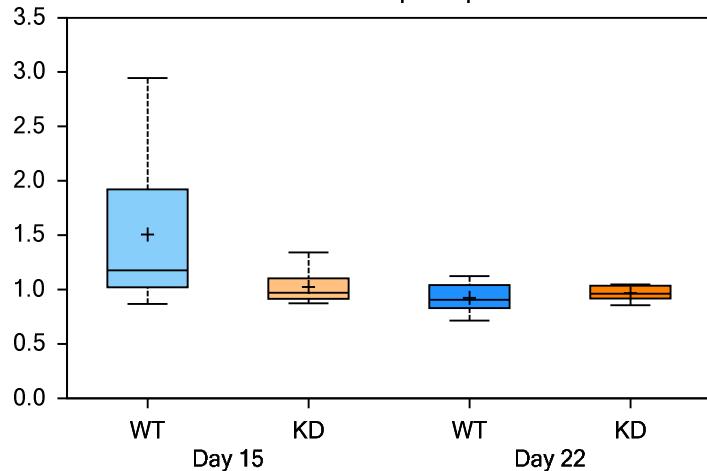
maltopentaose



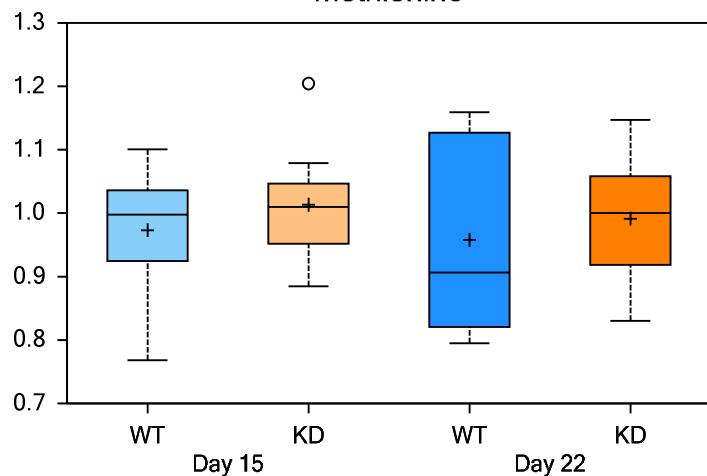
maltotriose



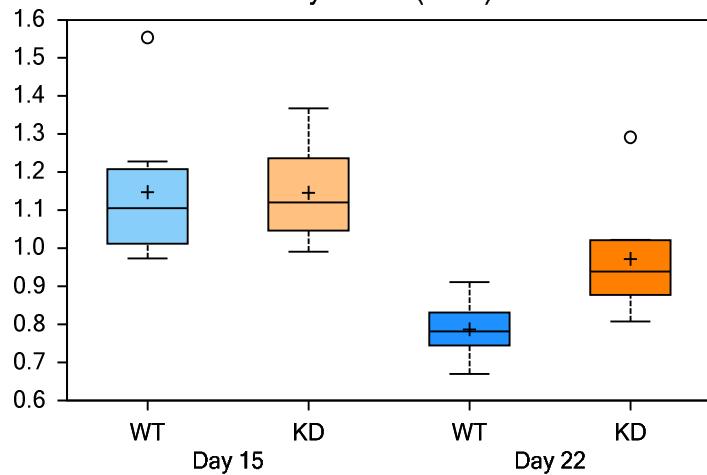
mannose-6-phosphate

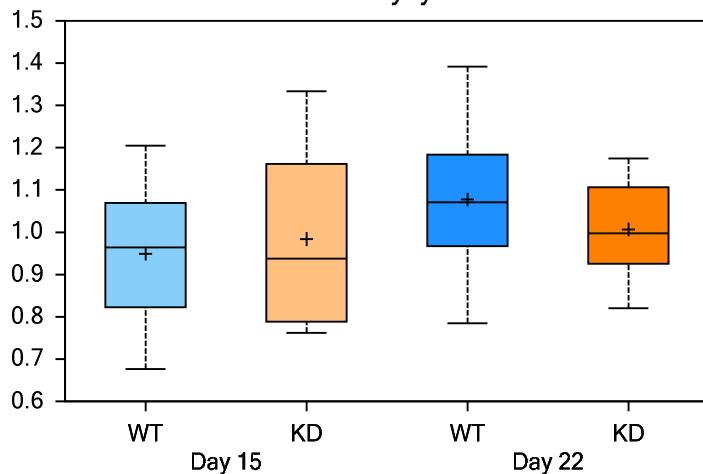
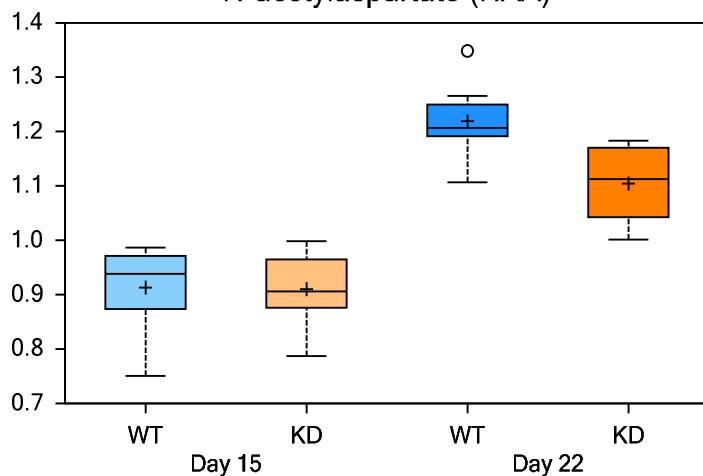
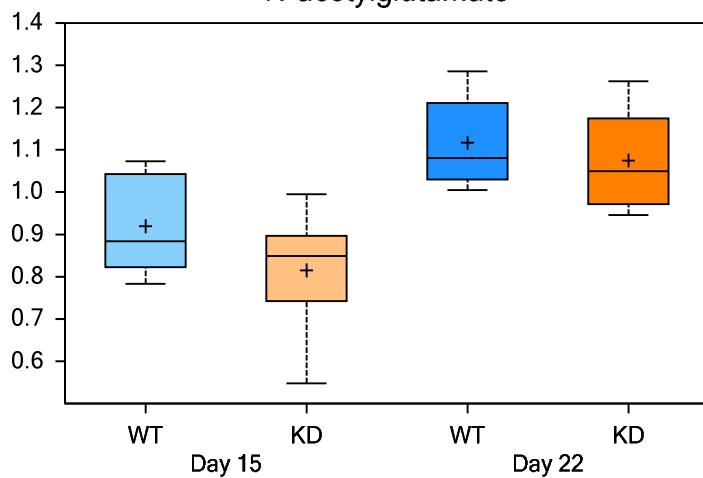


methionine

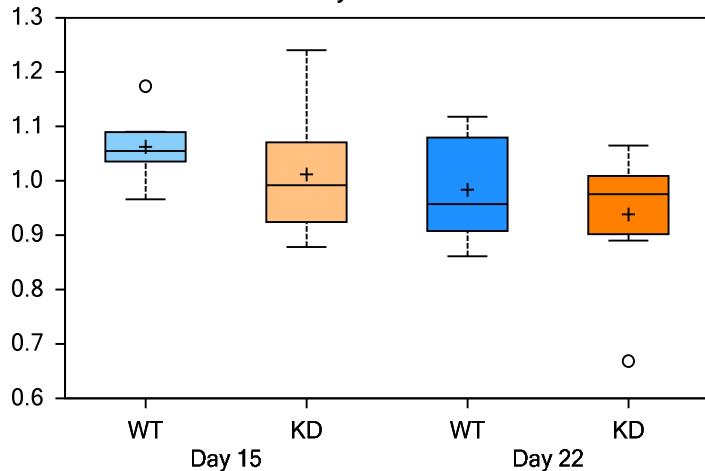


myristate (14:0)

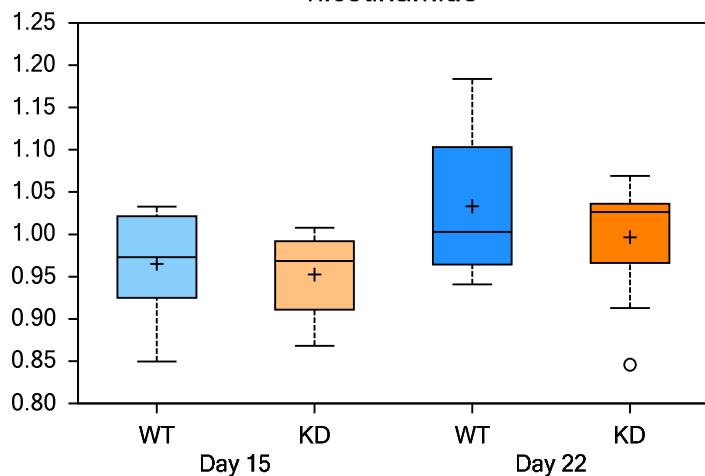


N6-acetyllysine**N-acetylaspartate (NAA)****N-acetylglutamate**

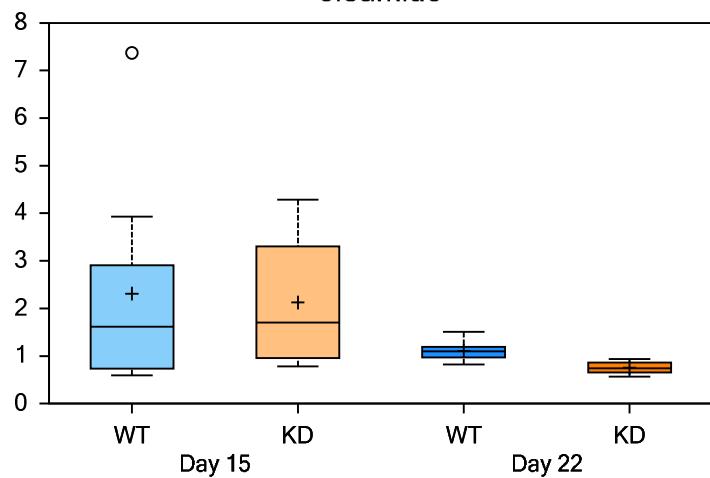
N-acetylneuraminate

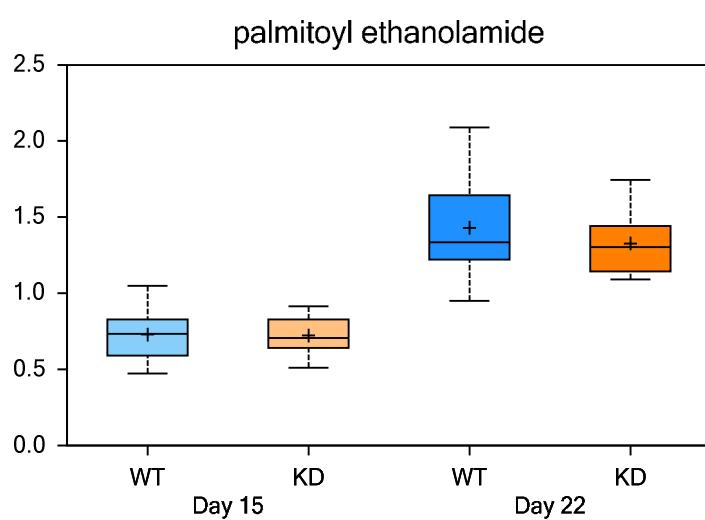
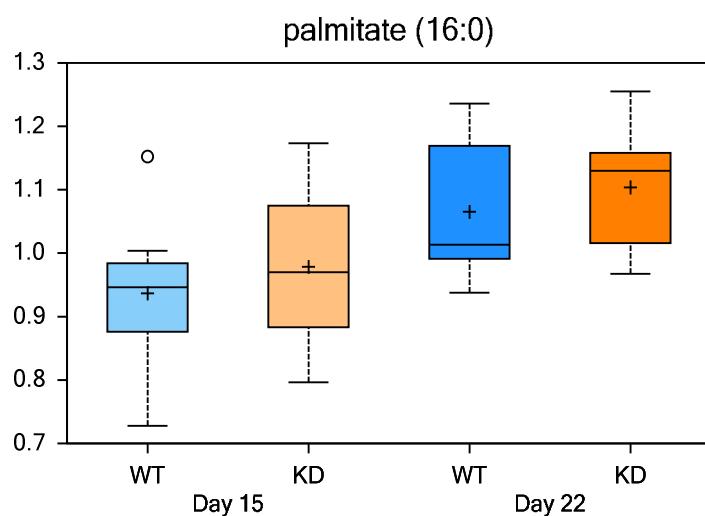
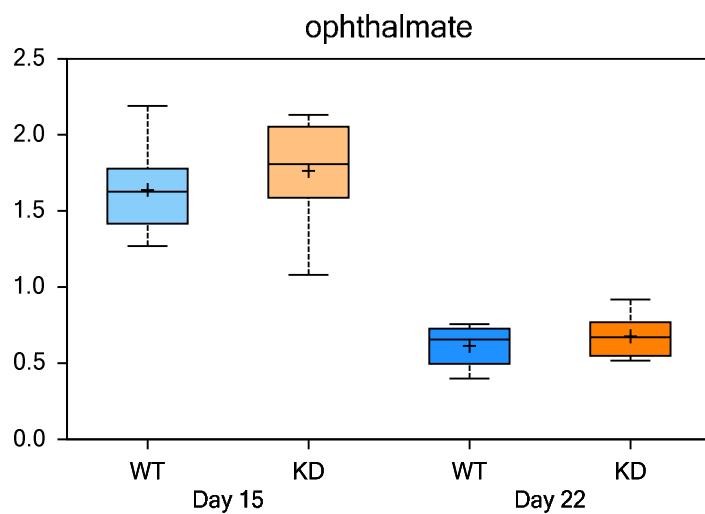


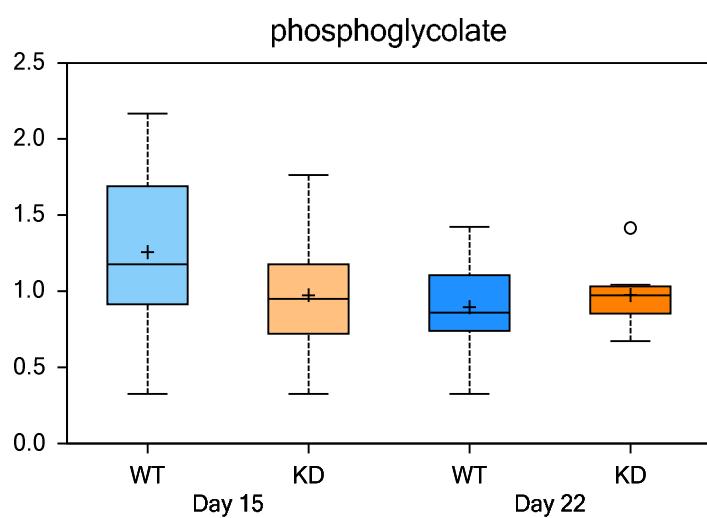
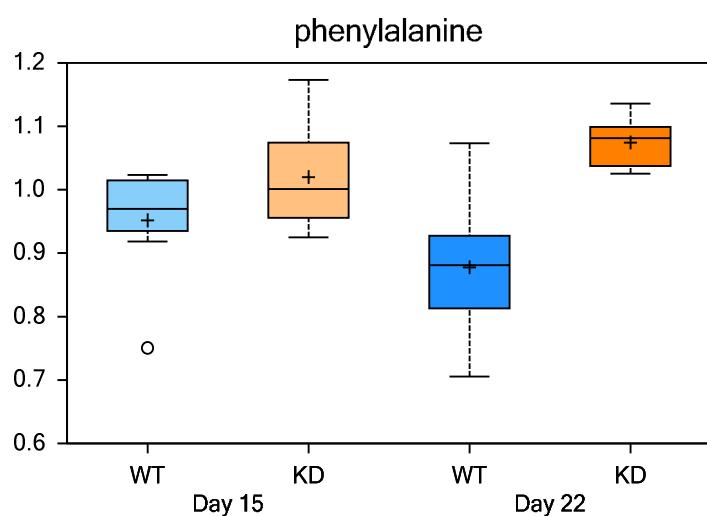
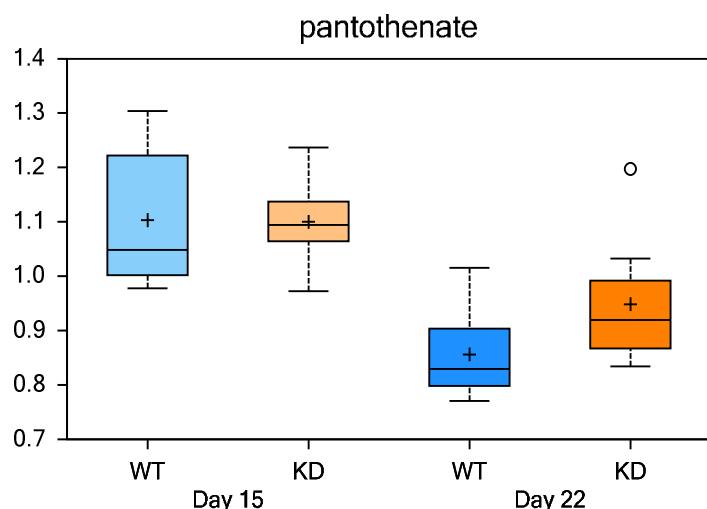
nicotinamide

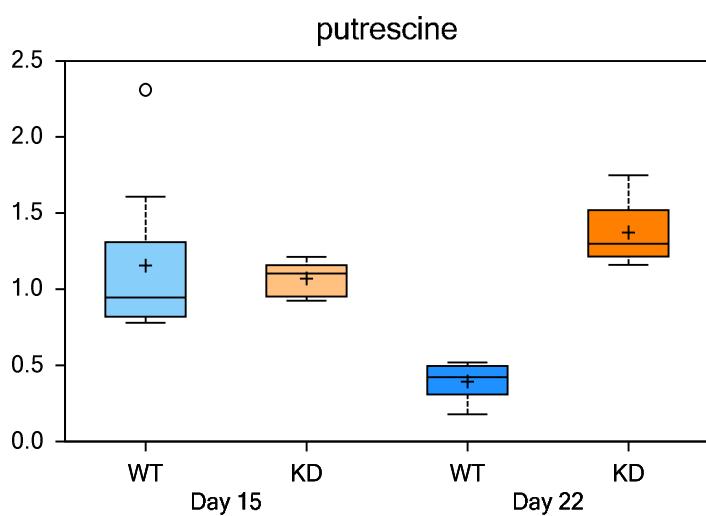
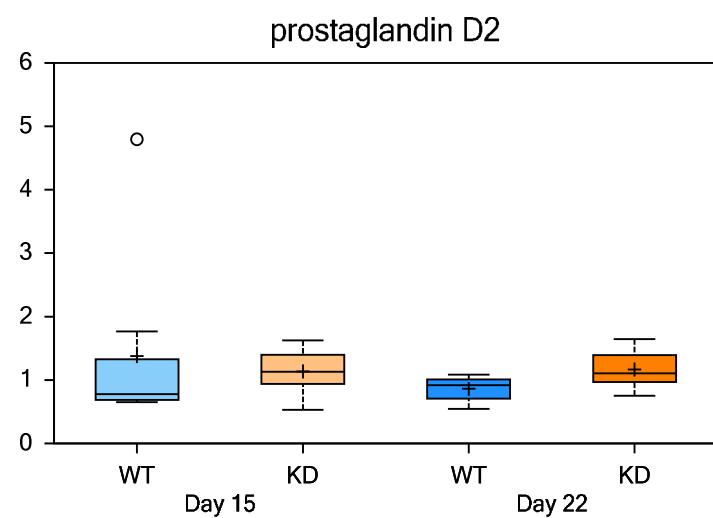
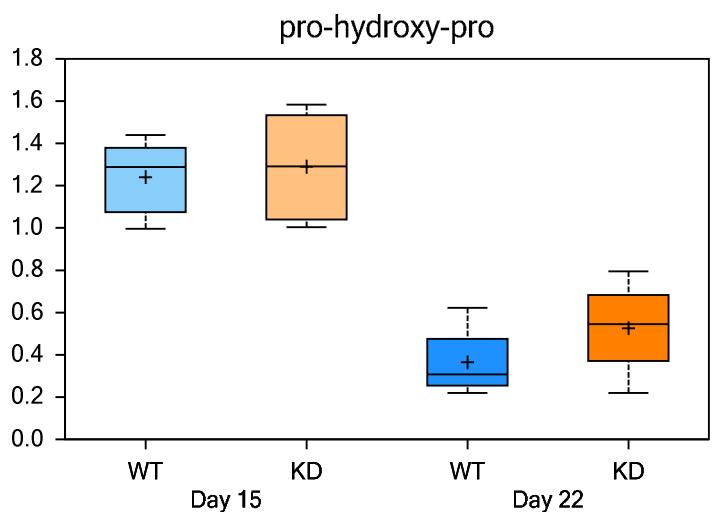


oleamide

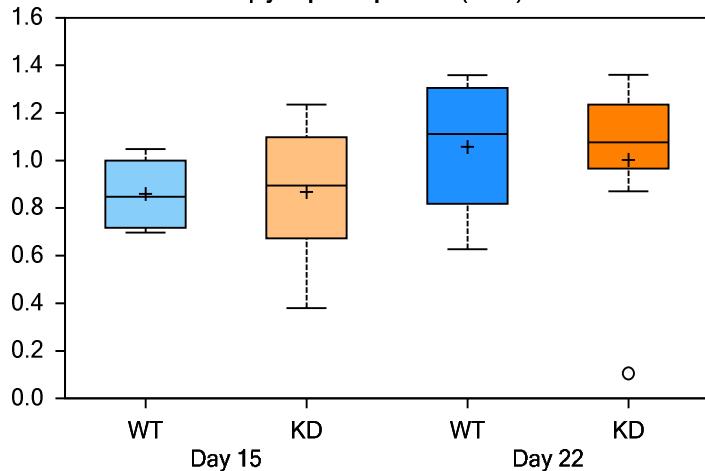




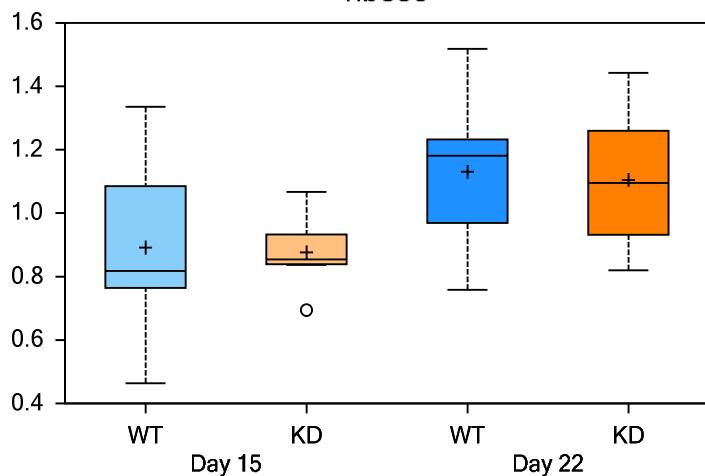




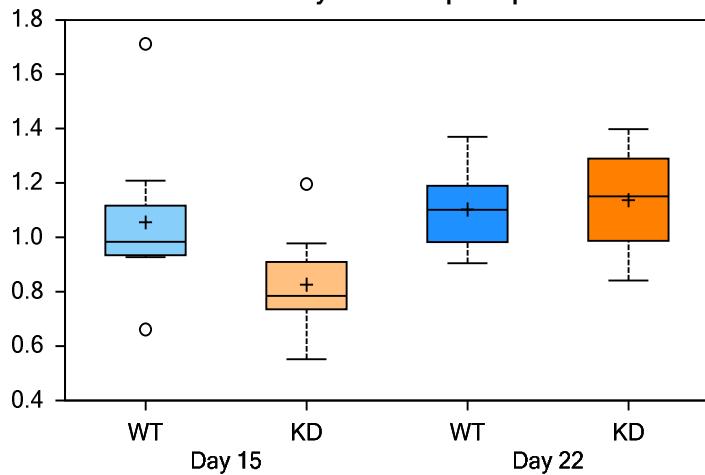
pyrophosphate (PPi)

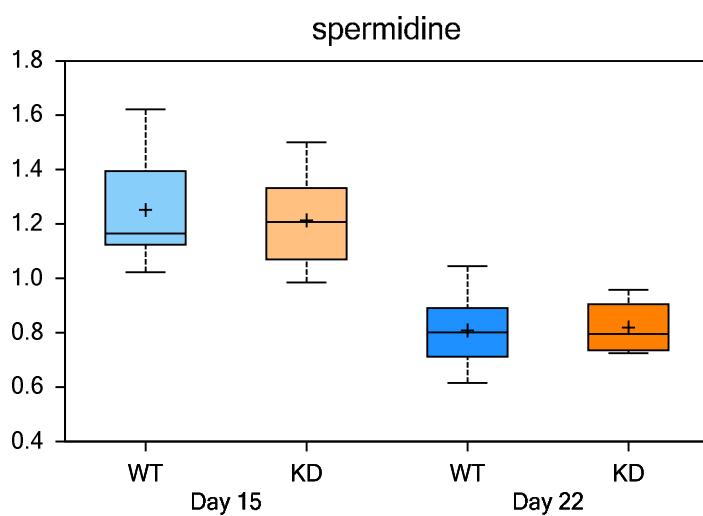
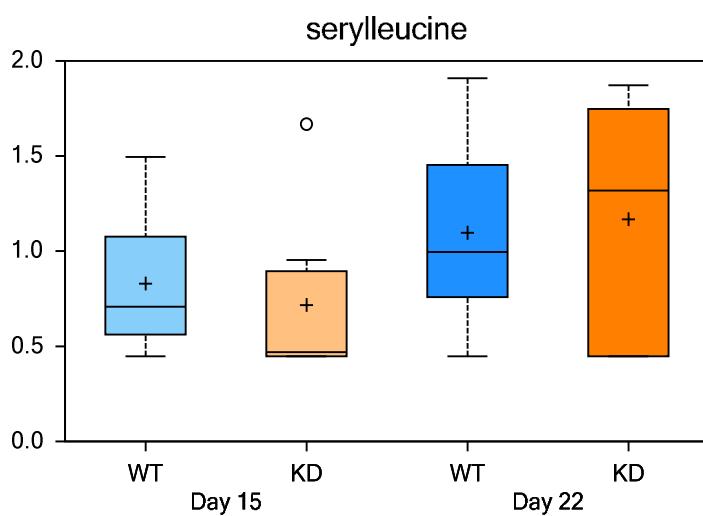
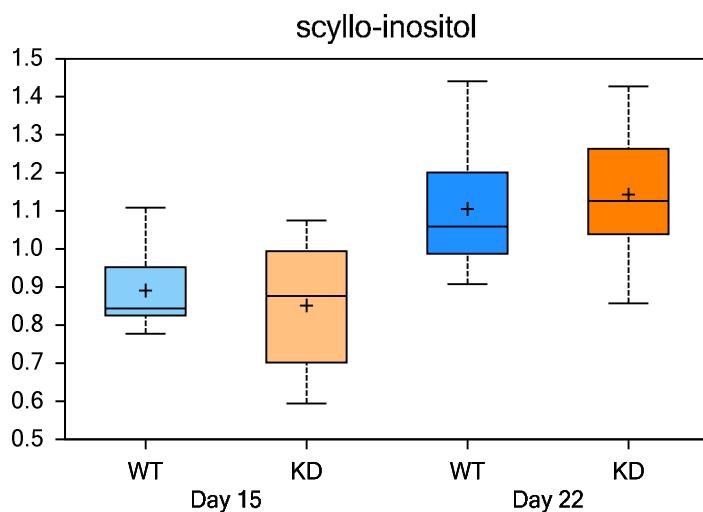


ribose

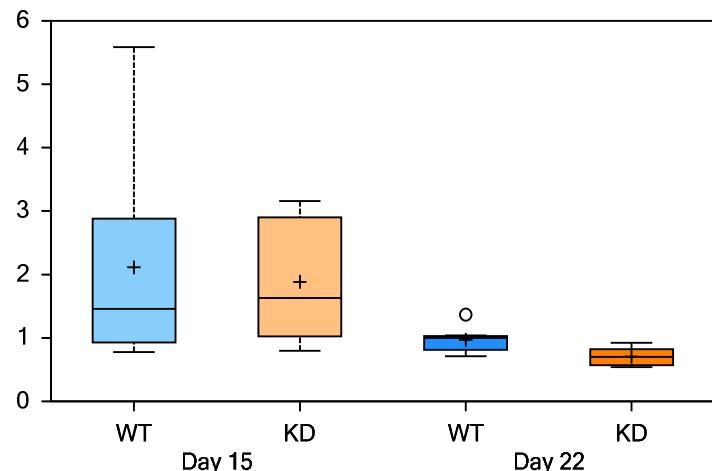


ribulose/xylulose 5-phosphate

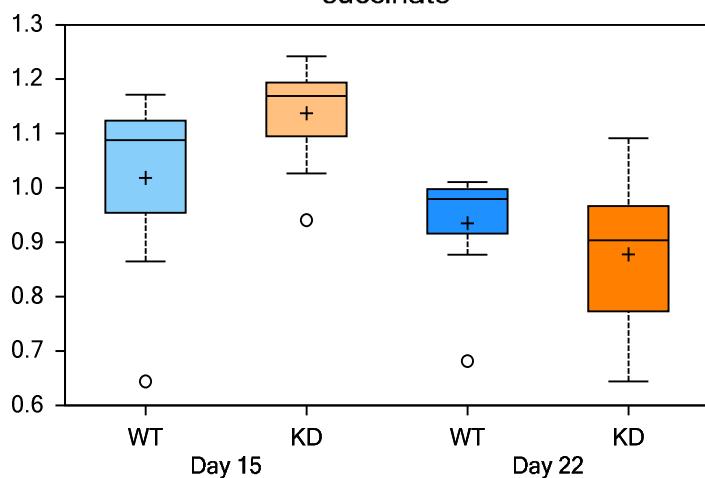




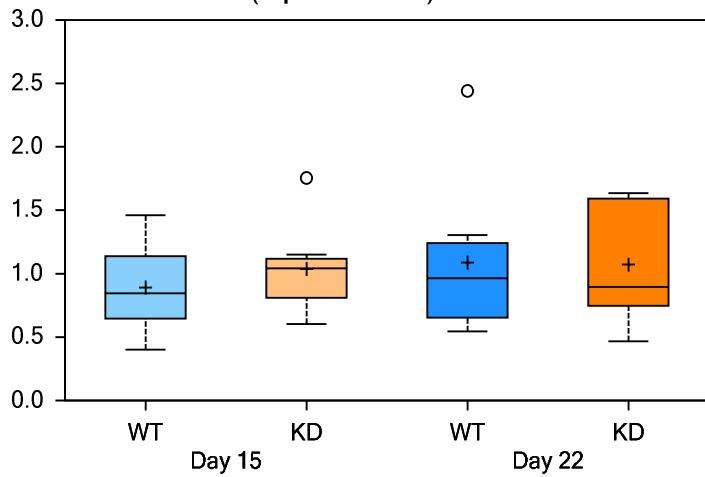
stearamide



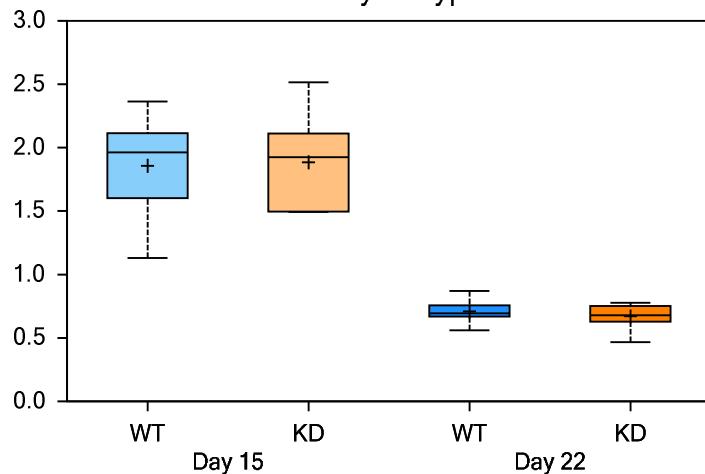
succinate



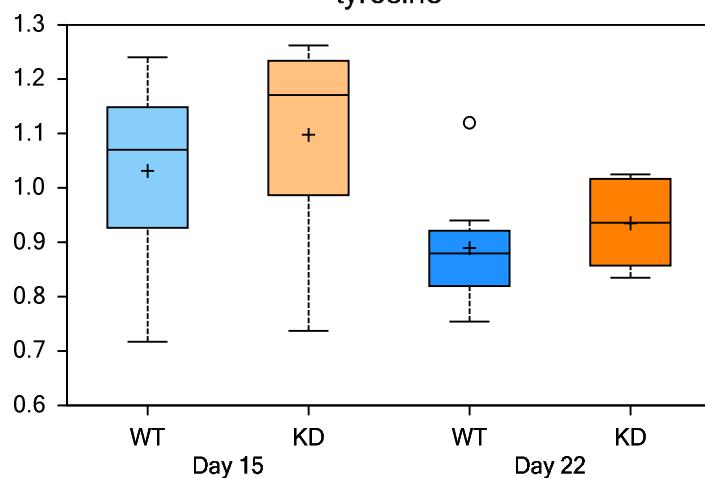
tauro(alpha + beta)muricholate



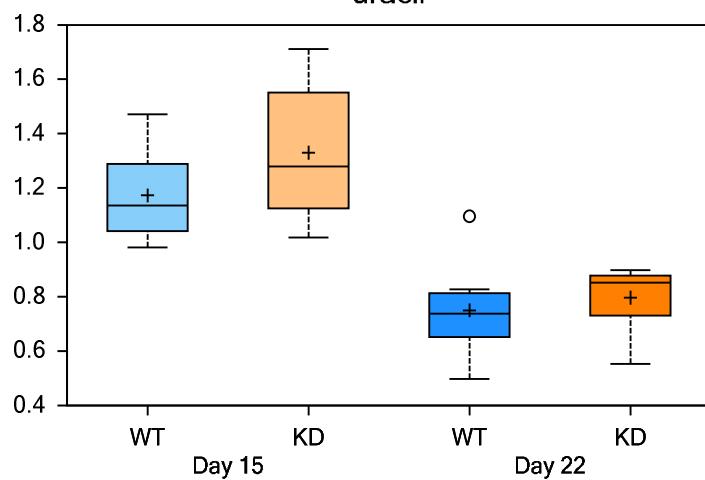
trans-4-hydroxyproline

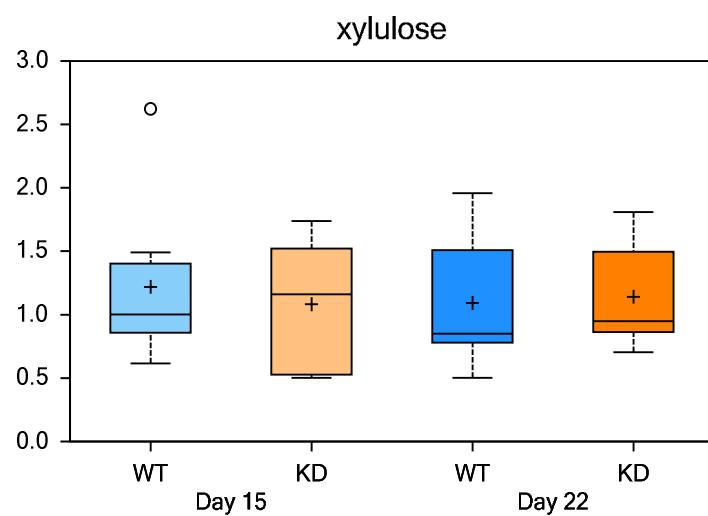
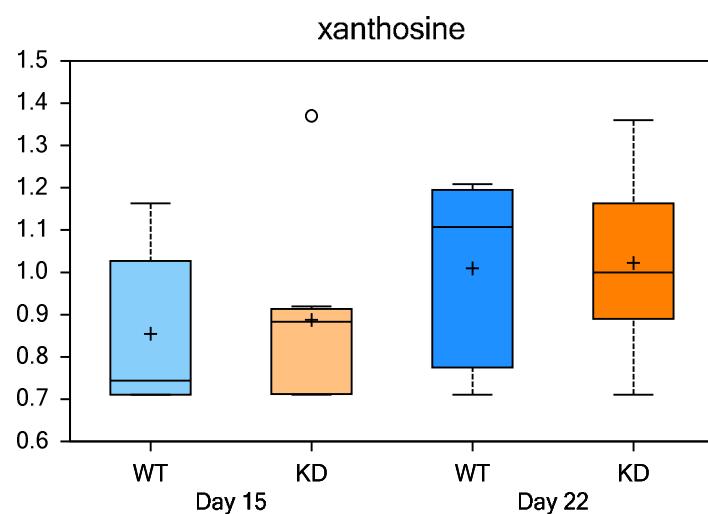
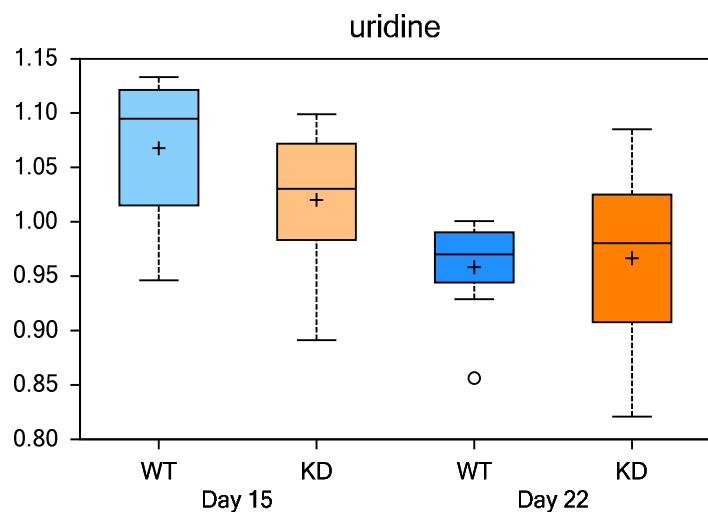


tyrosine



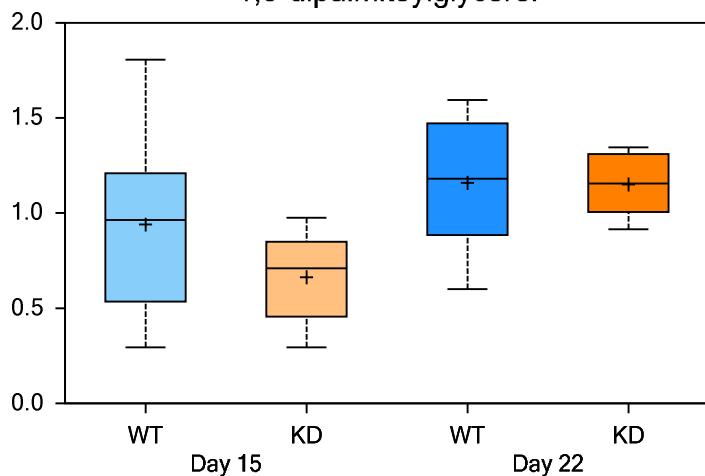
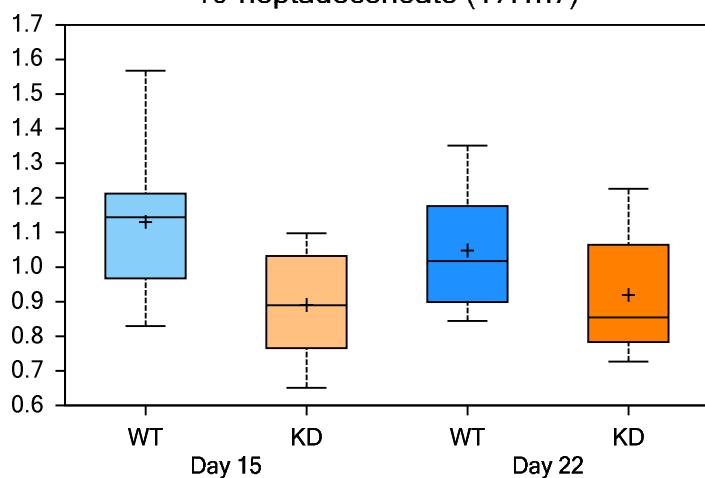
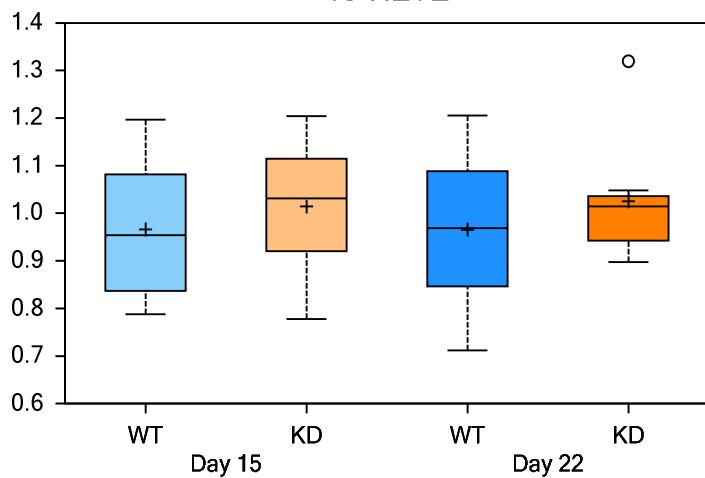
uracil

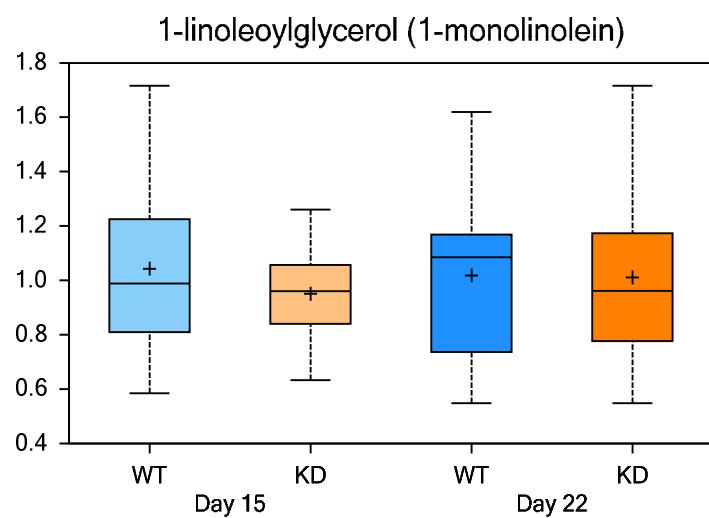
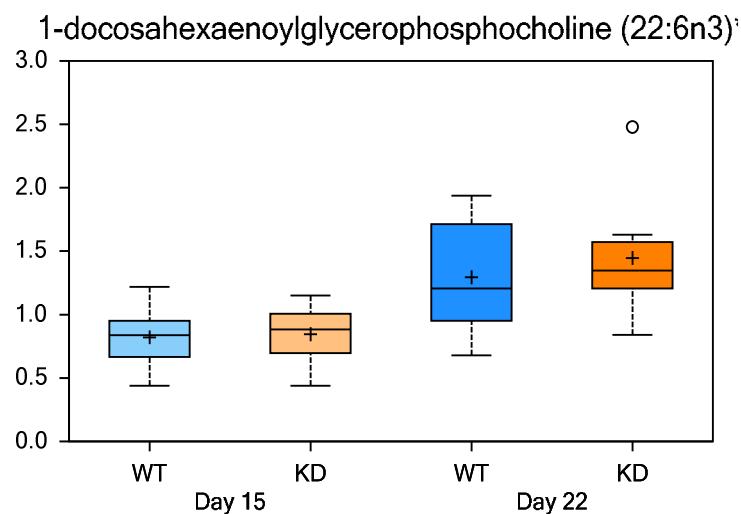
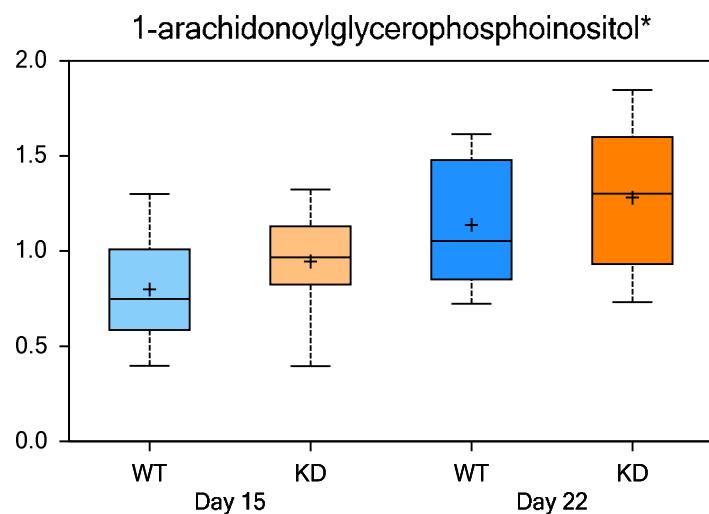




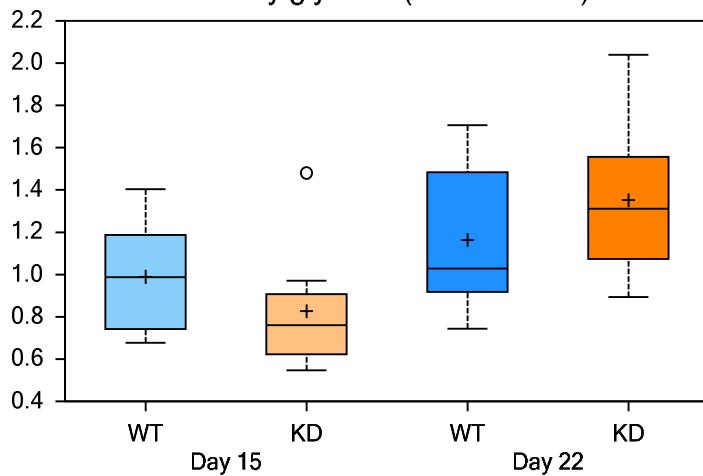
Box Plot Legend

- Wild type, day 15
- Twitcher, day 15
- Wild type, day 22
- Twitcher, day 22

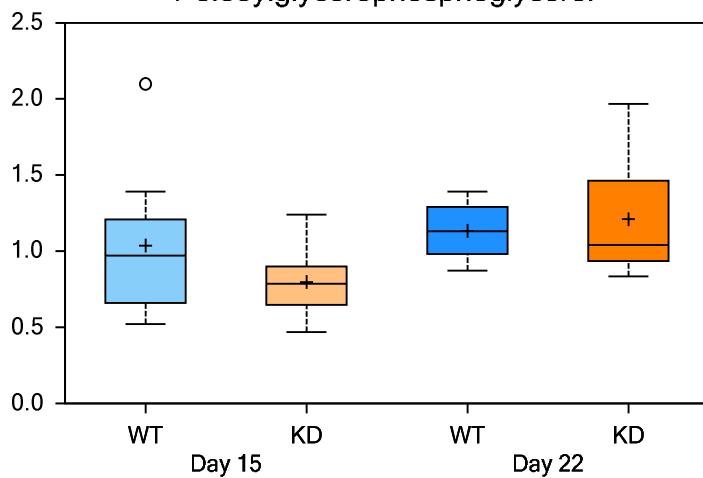
1,3-dipalmitoylglycerol**10-heptadecenoate (17:1n7)****15-HETE**



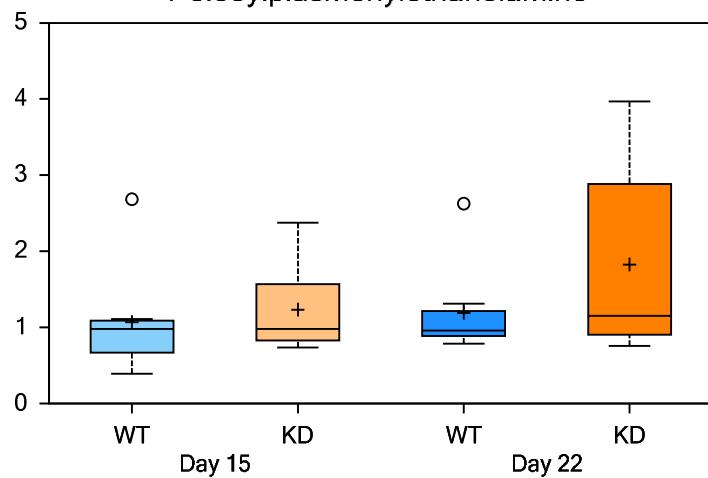
1-oleoylglycerol (1-monoolein)

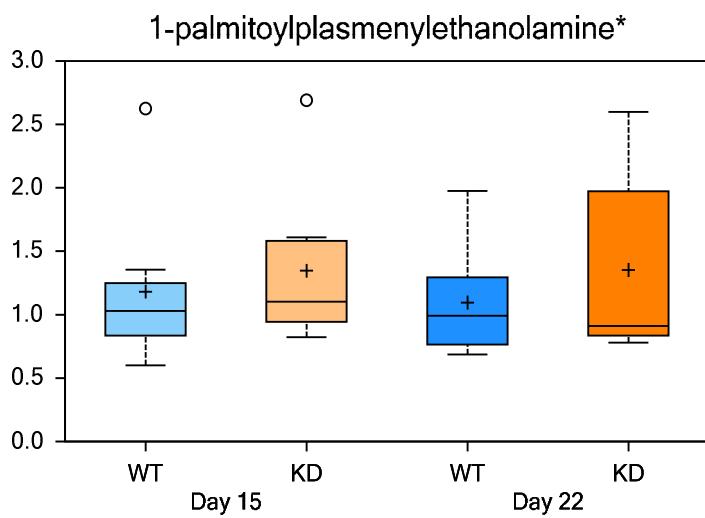
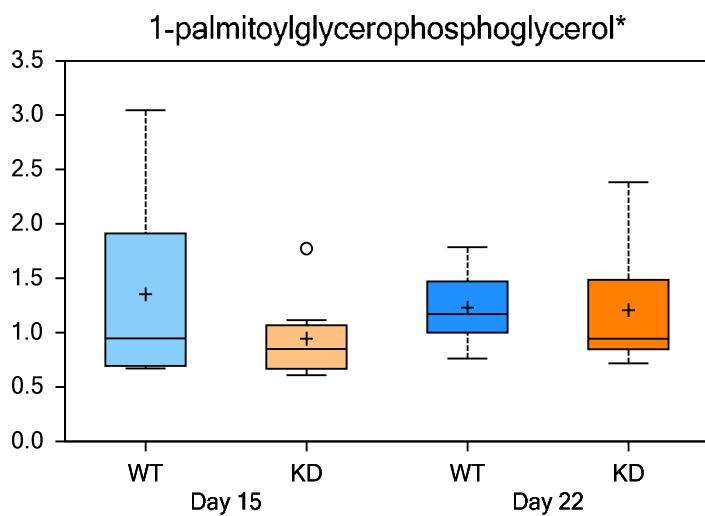
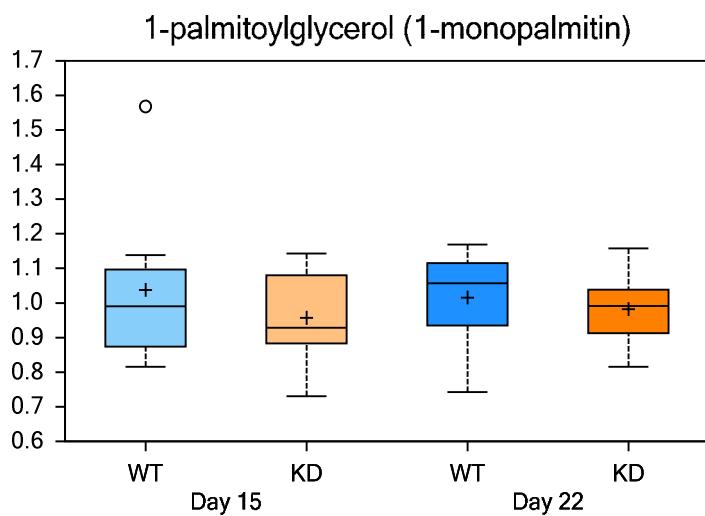


1-oleoylglycerophosphoglycerol*

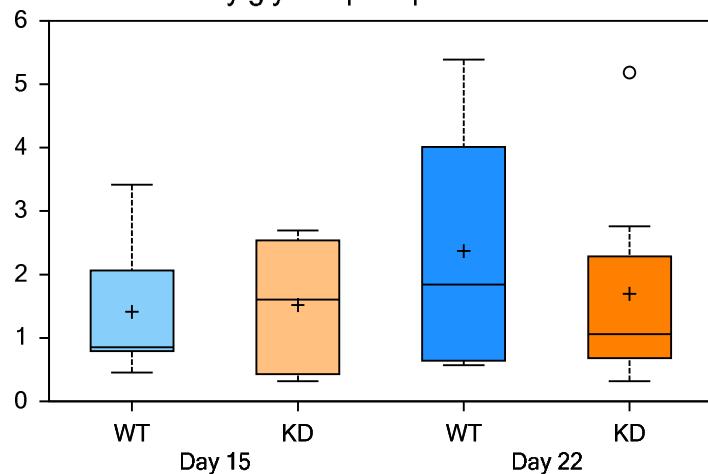


1-oleoylplasmenylethanolamine*

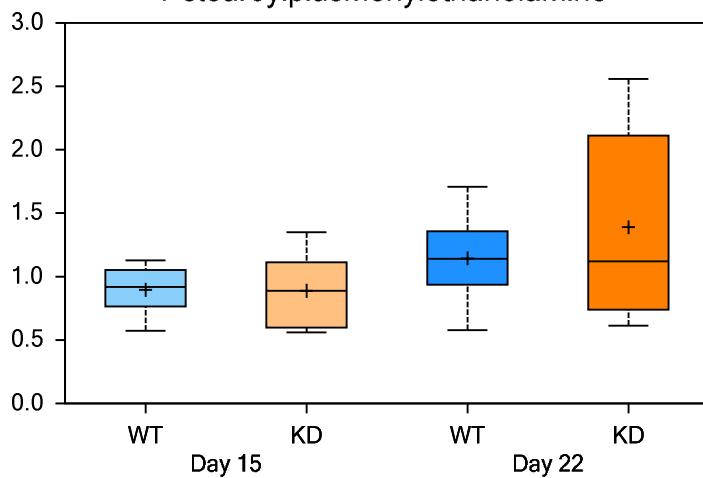




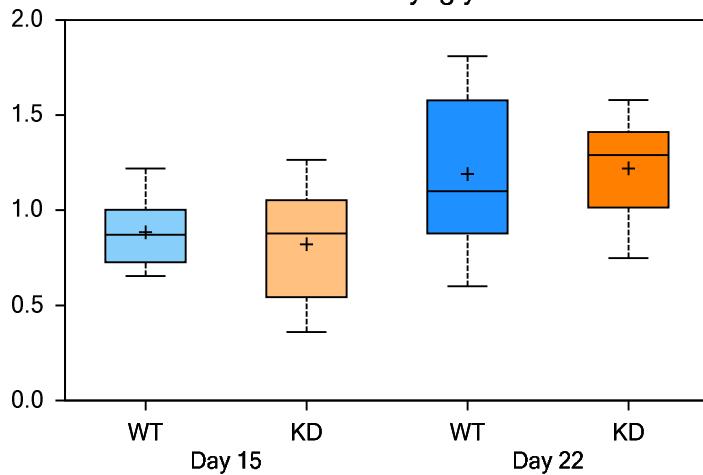
1-stearoylglycerophosphoethanolamine



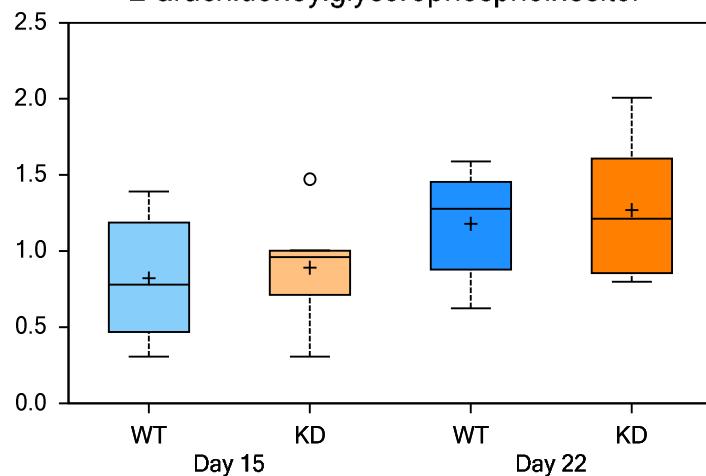
1-stearoylplasmenylethanolamine*



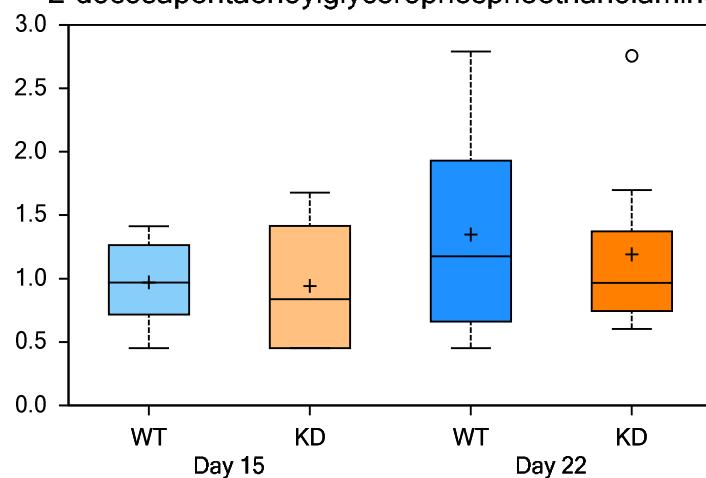
2-arachidonoyl glycerol



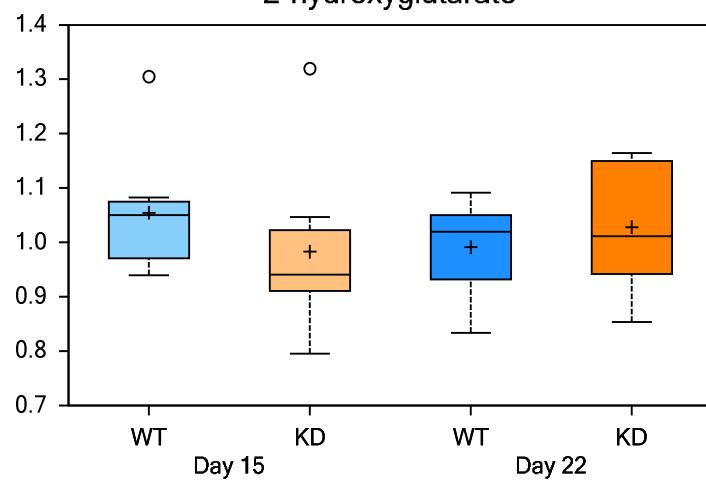
2-arachidonoylglycerophosphoinositil*

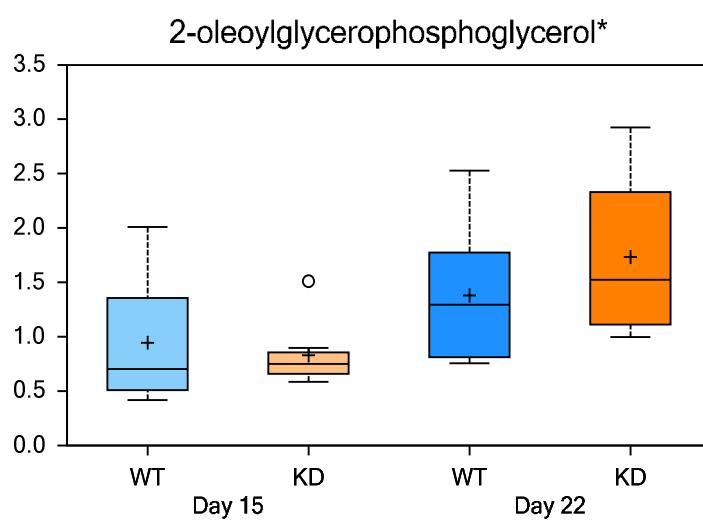
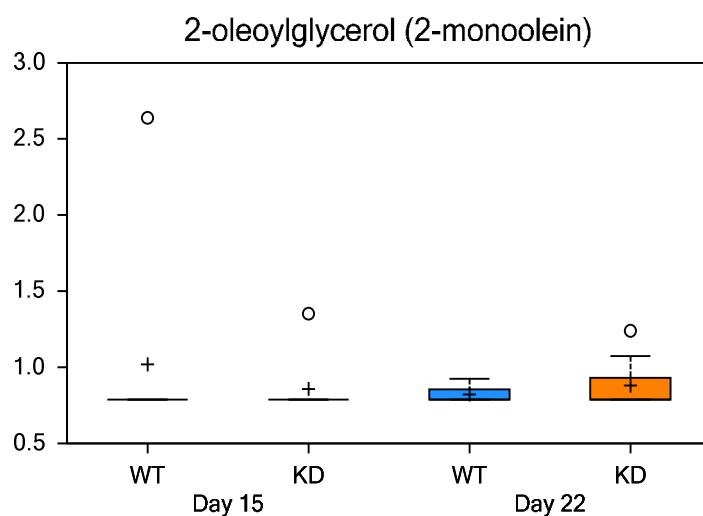
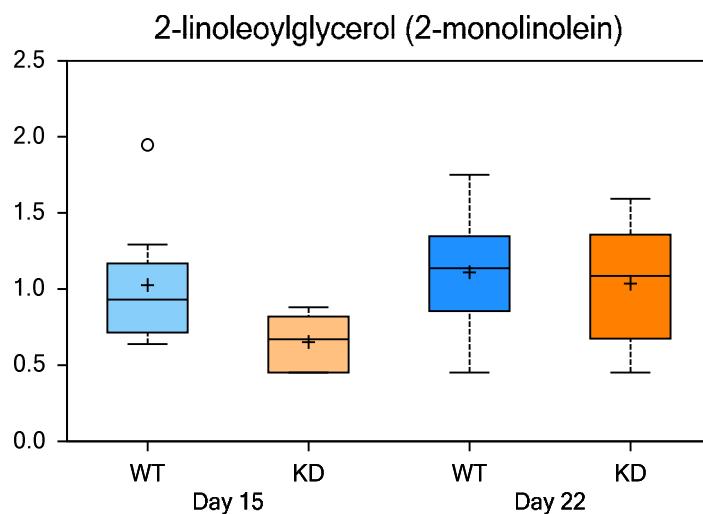


2-docosapentaenoylglycerophosphoethanolamine*

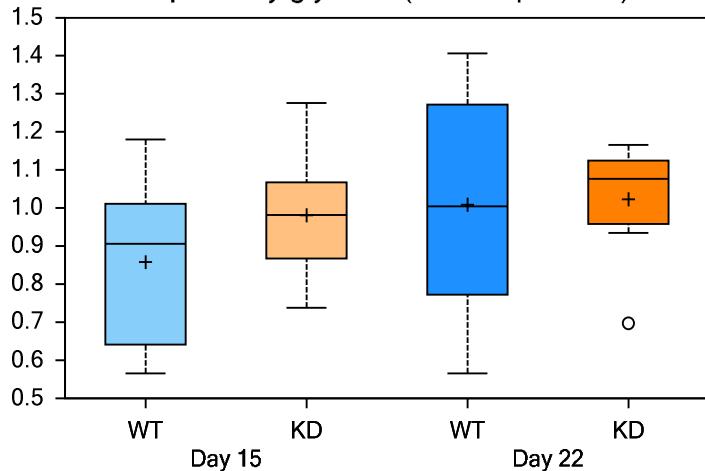


2-hydroxyglutarate

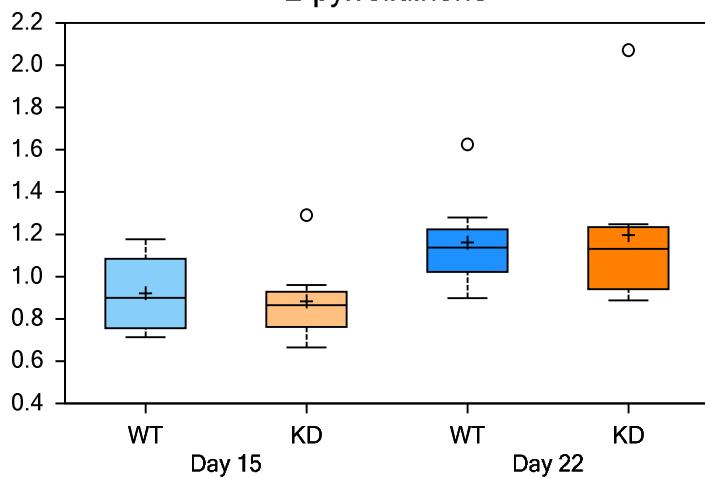




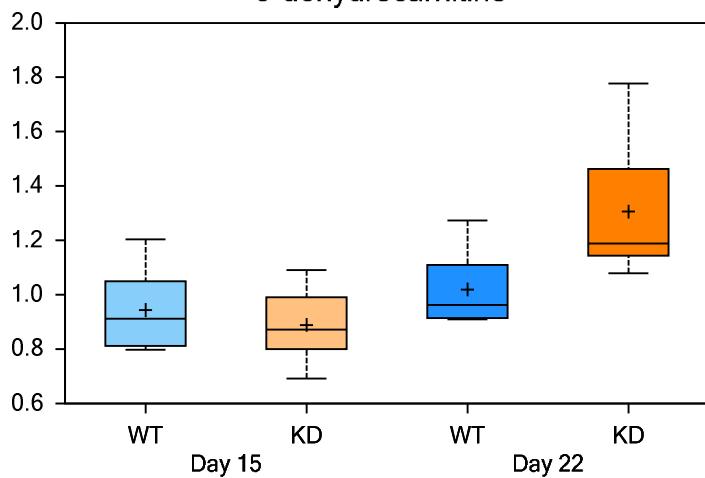
2-palmitoylglycerol (2-monopalmitin)



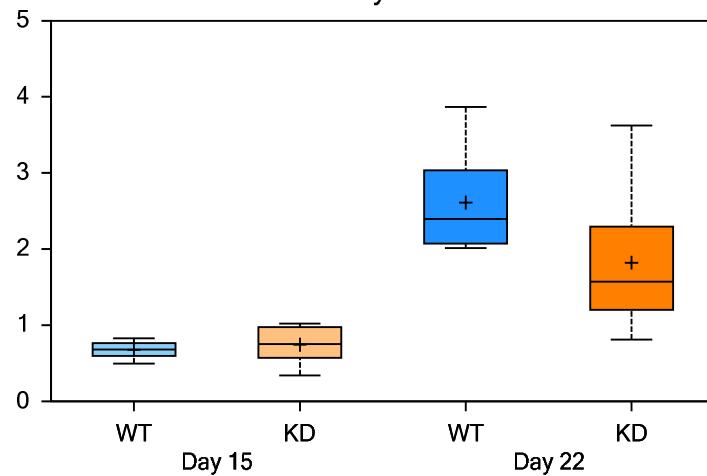
2-pyrrolidinone



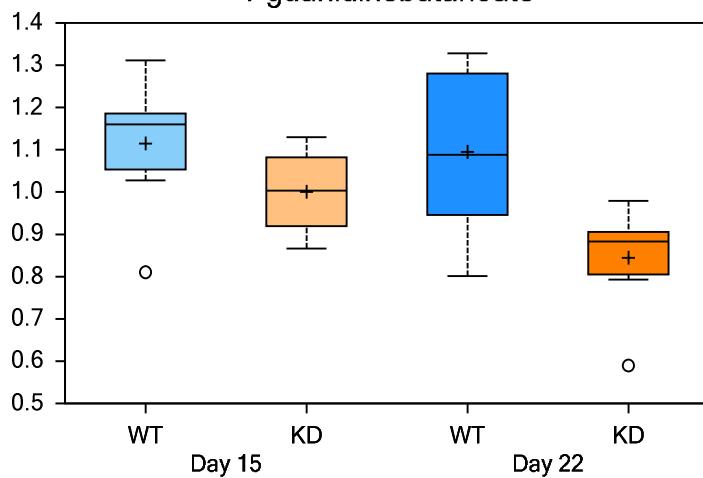
3-dehydrocarnitine*



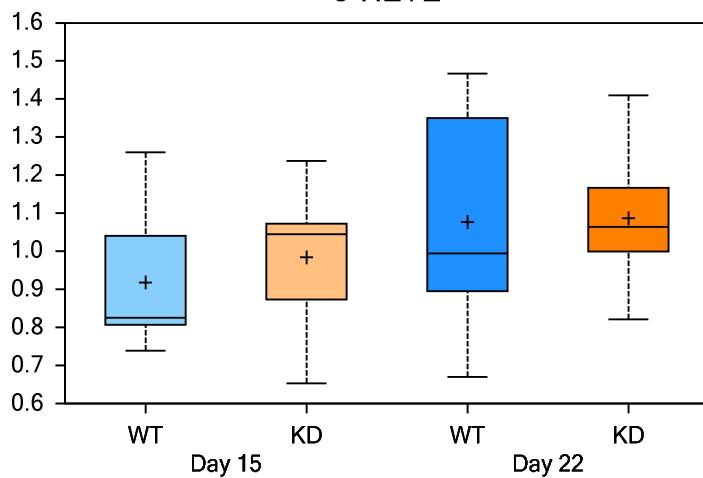
3-indoxyl sulfate



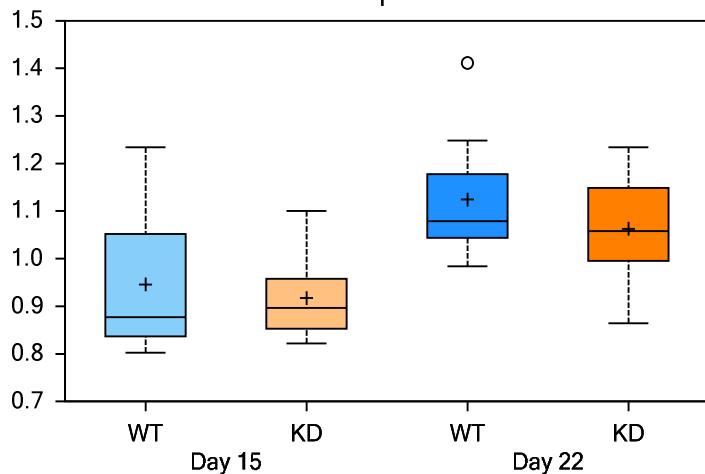
4-guanidinobutanoate



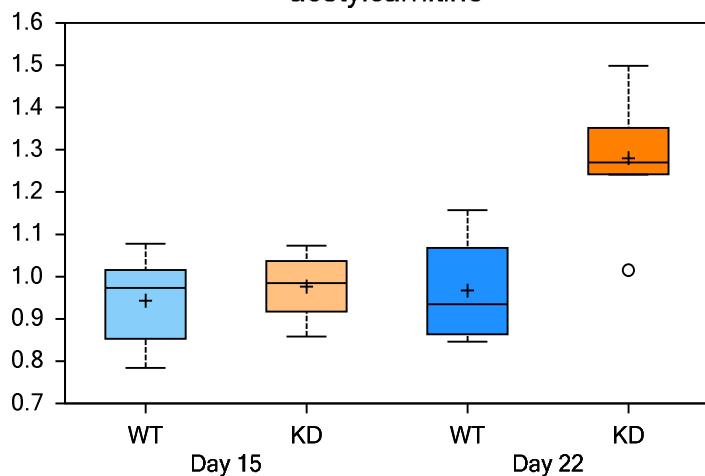
5-HETE



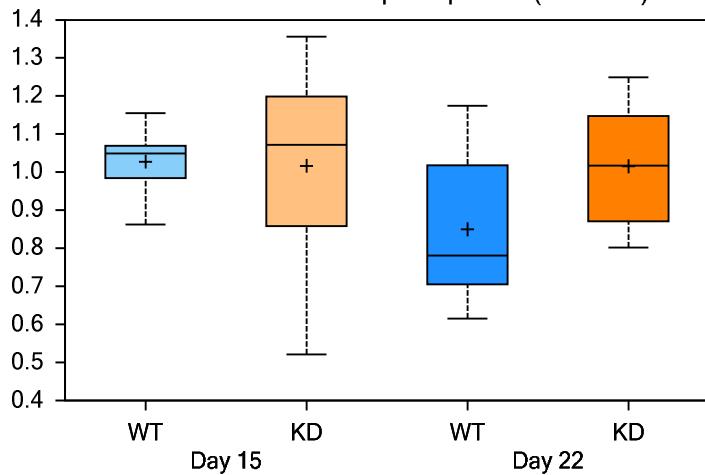
5-oxoproline



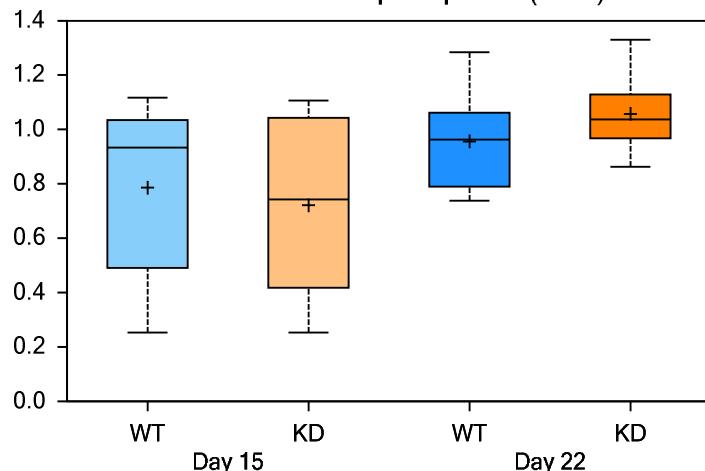
acetylcarnitine



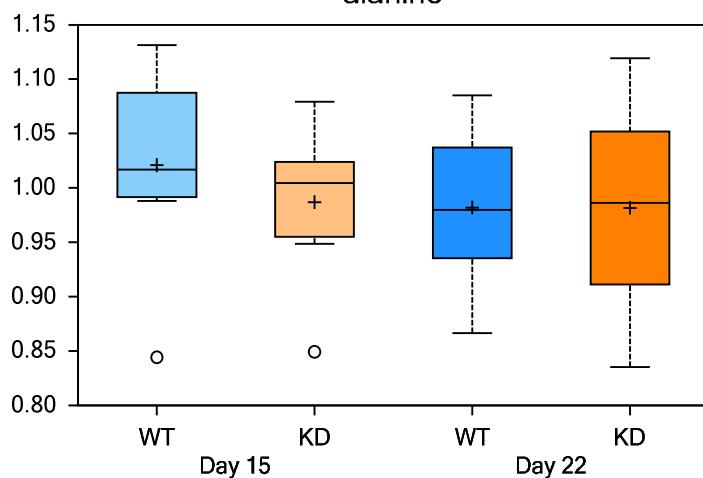
adenosine 2'-monophosphate (2'-AMP)



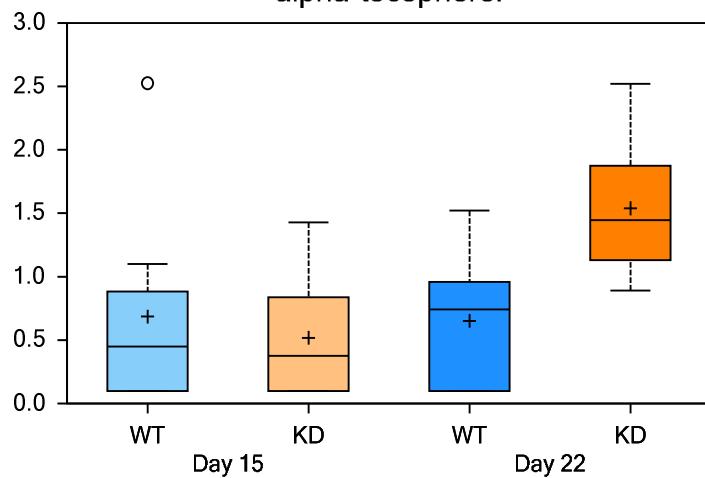
adenosine 5'-triphosphate (ATP)

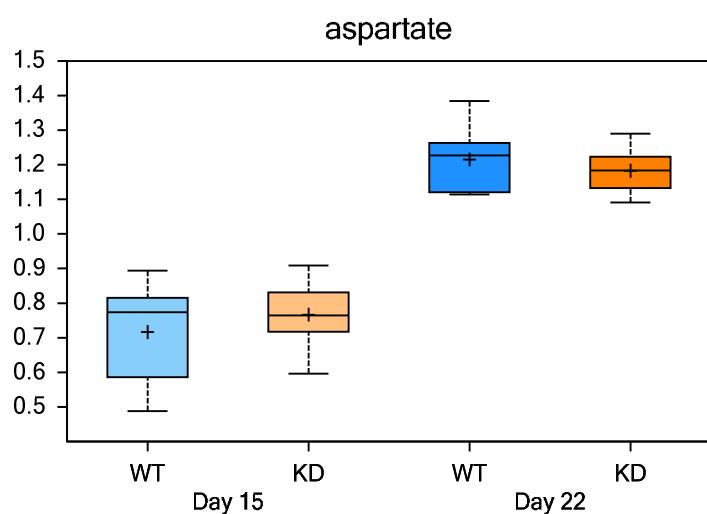
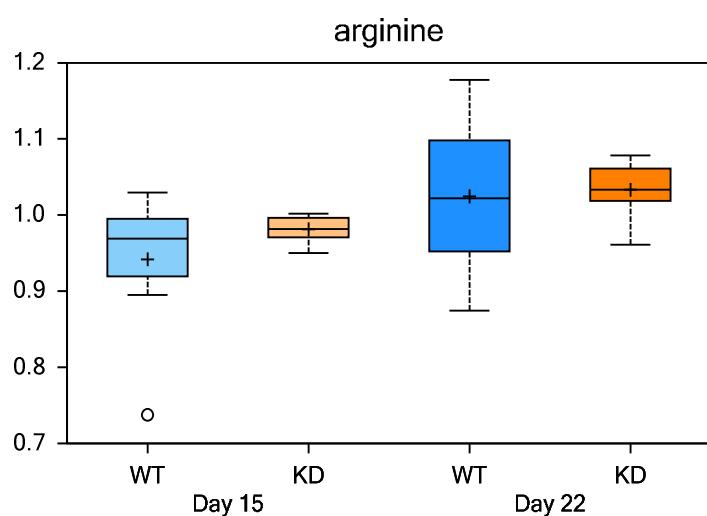
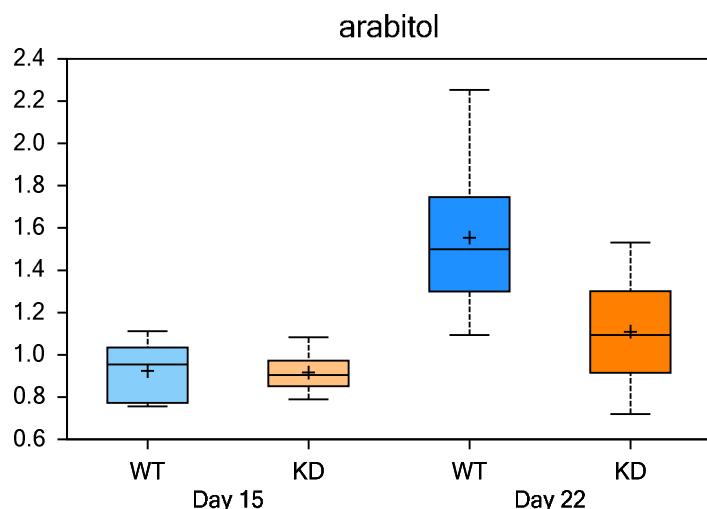


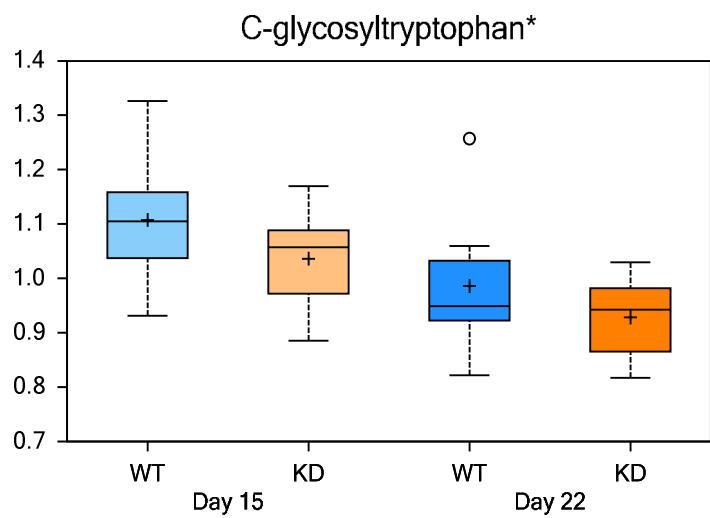
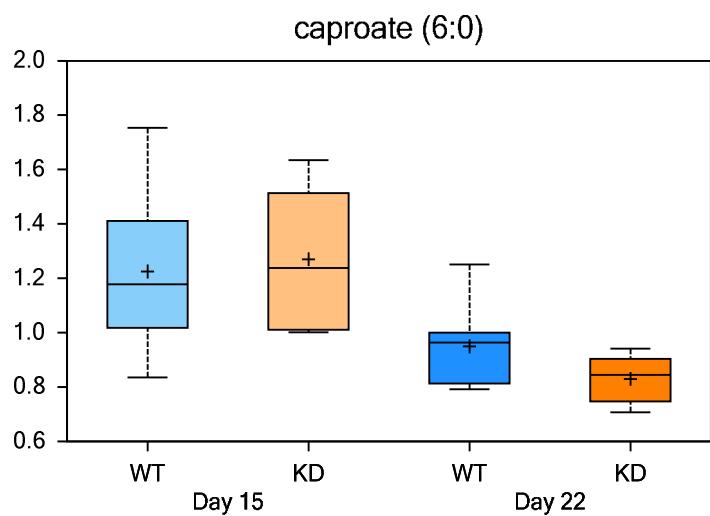
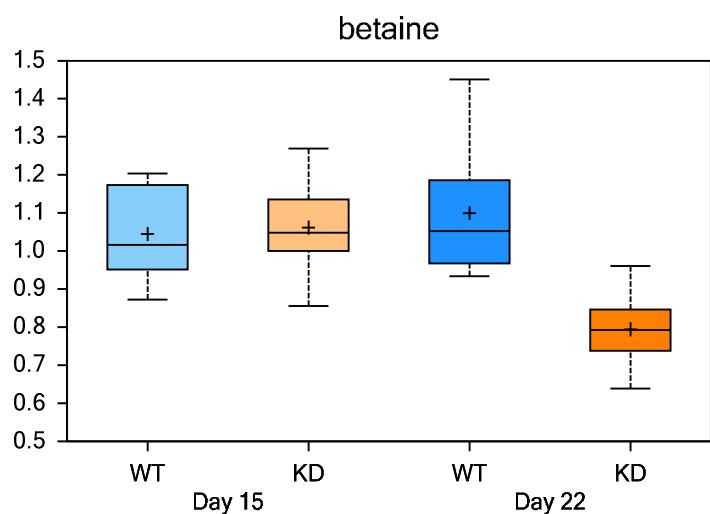
alanine

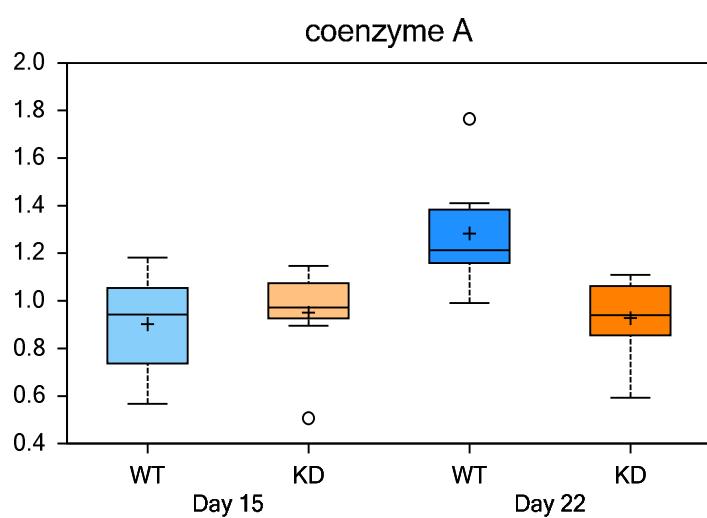
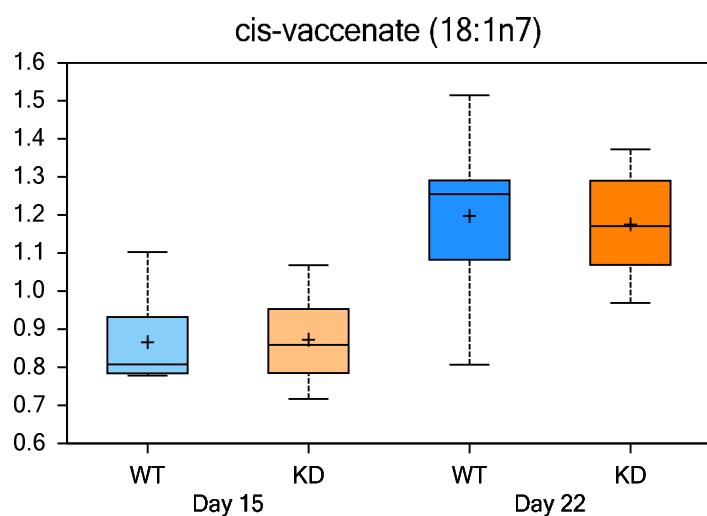
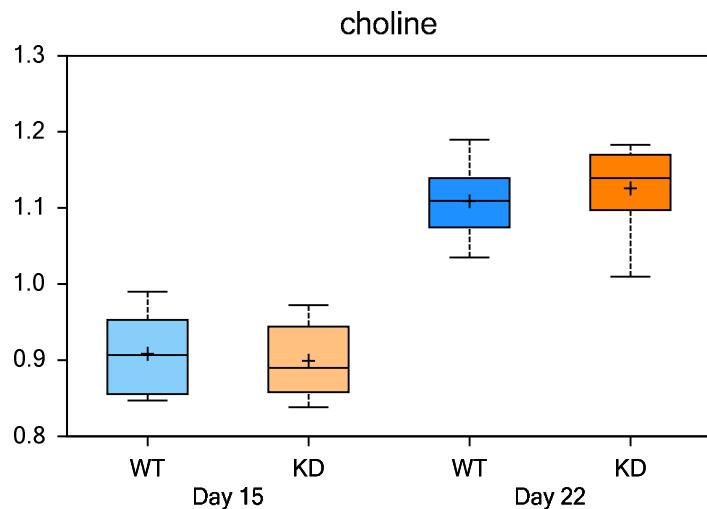


alpha-tocopherol

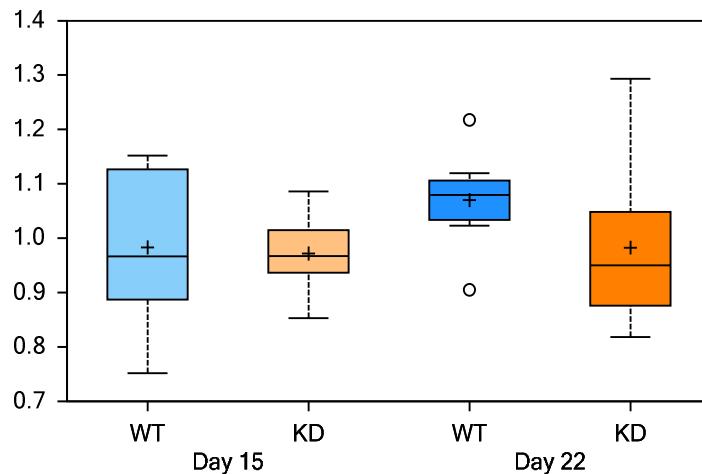




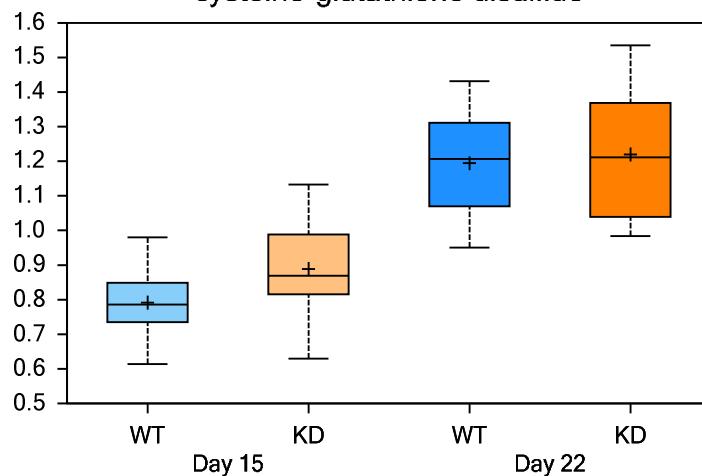




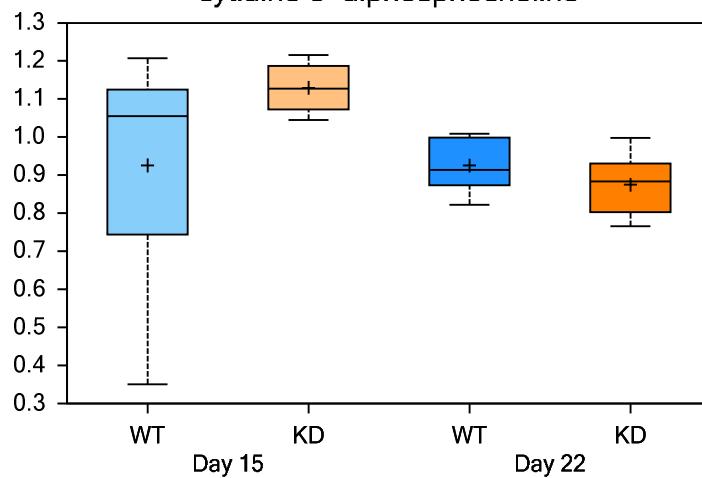
creatinine

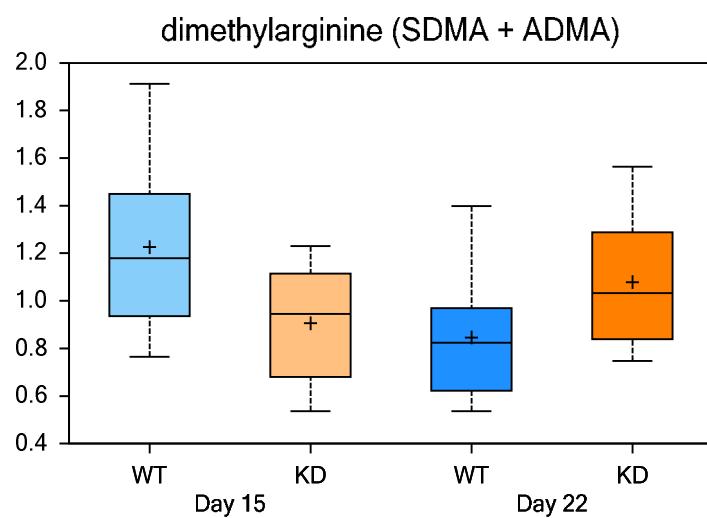
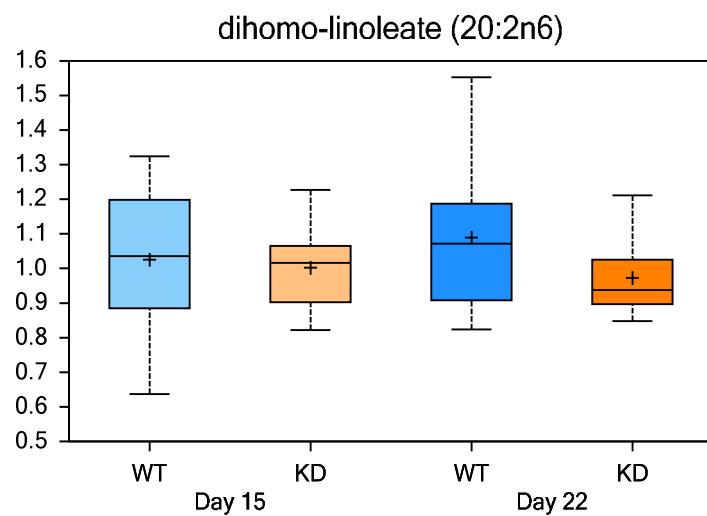
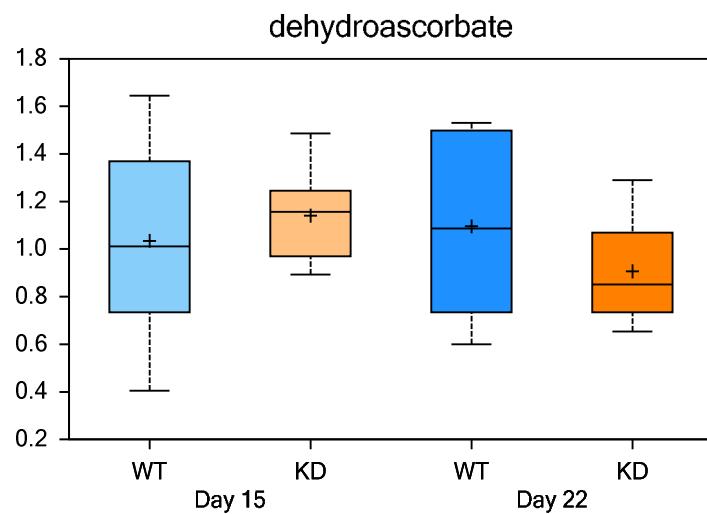


cysteine-glutathione disulfide

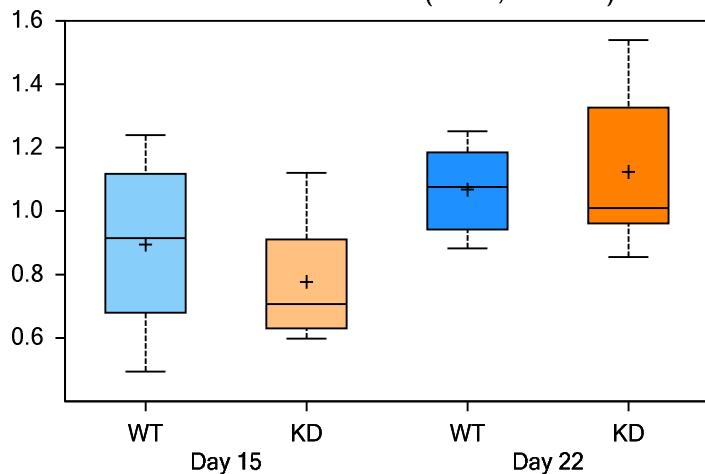


cytidine 5'-diphosphocholine

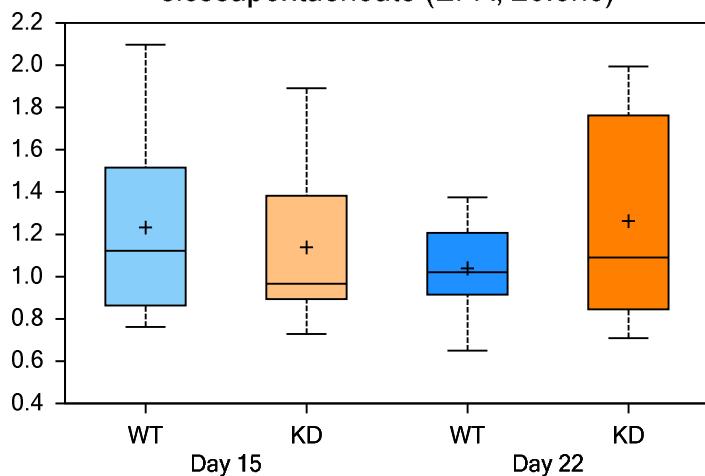




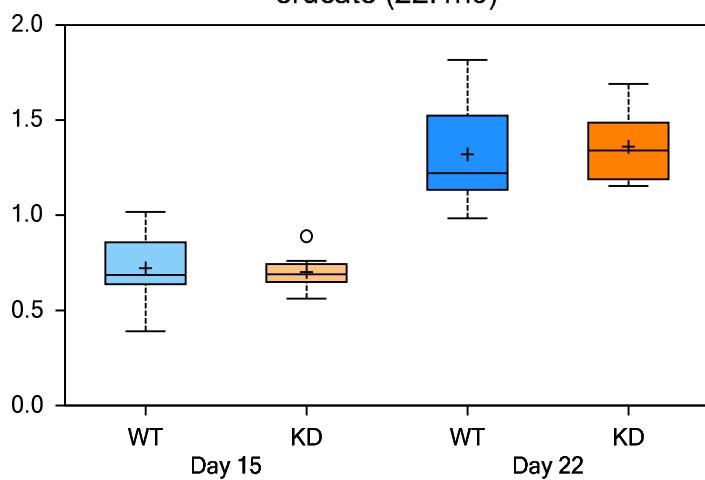
docosahexaenoate (DHA; 22:6n3)

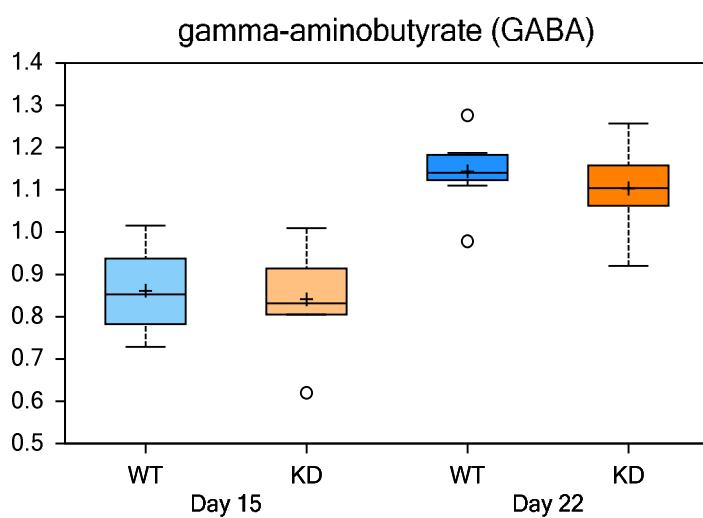
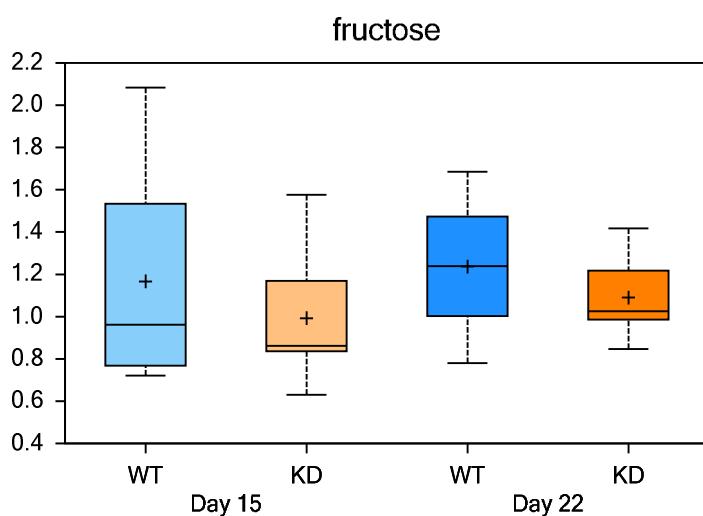
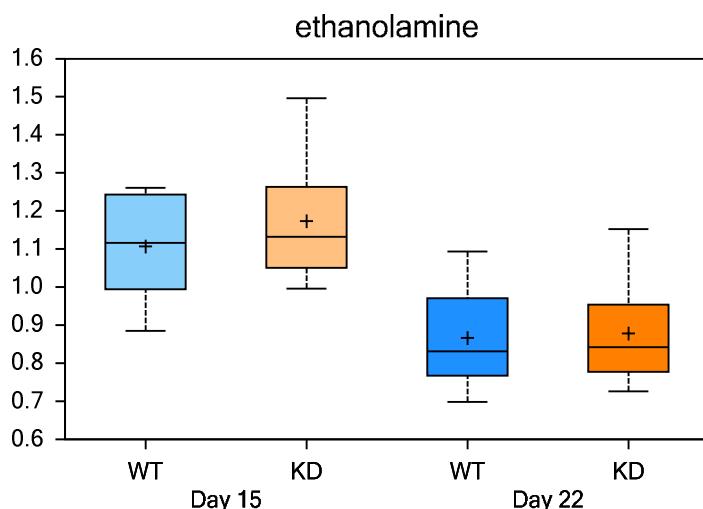


eicosapentaenoate (EPA; 20:5n3)

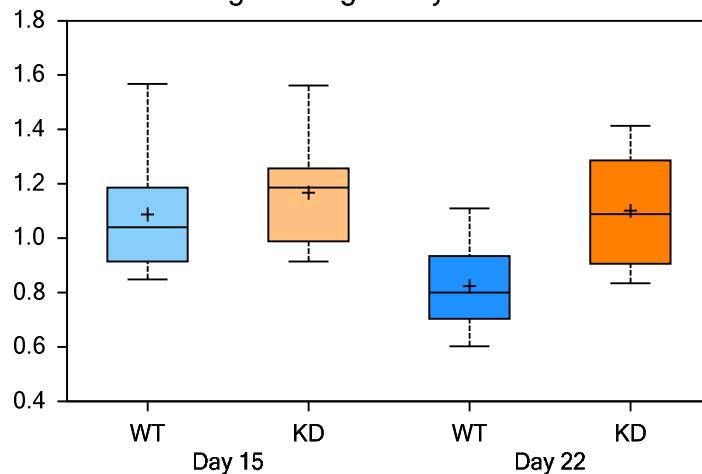


erucate (22:1n9)

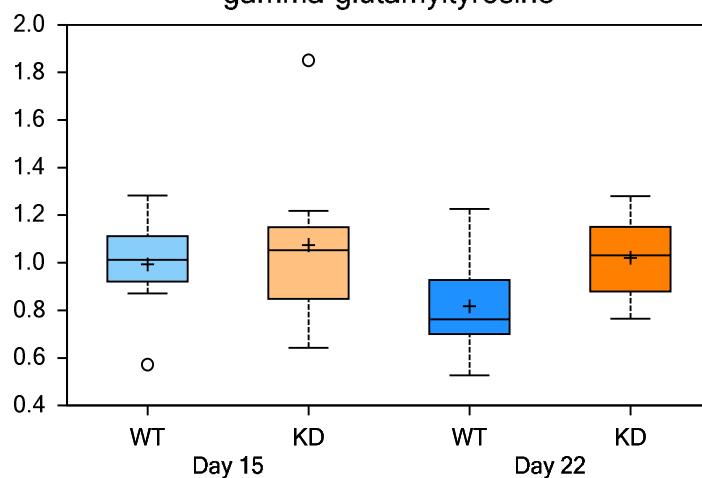




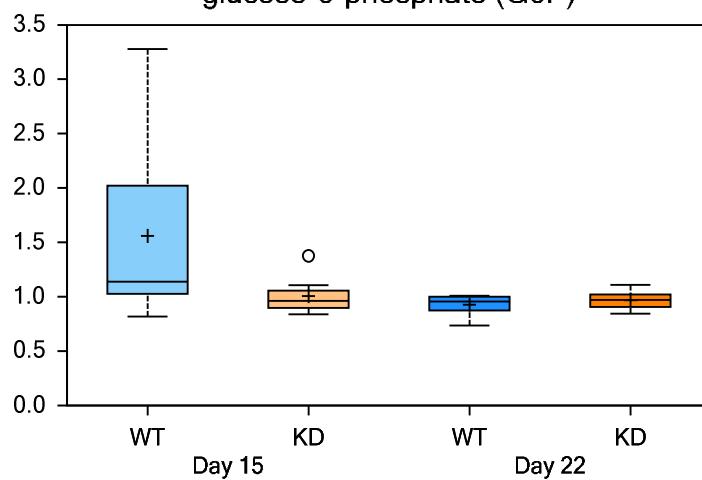
gamma-glutamylleucine

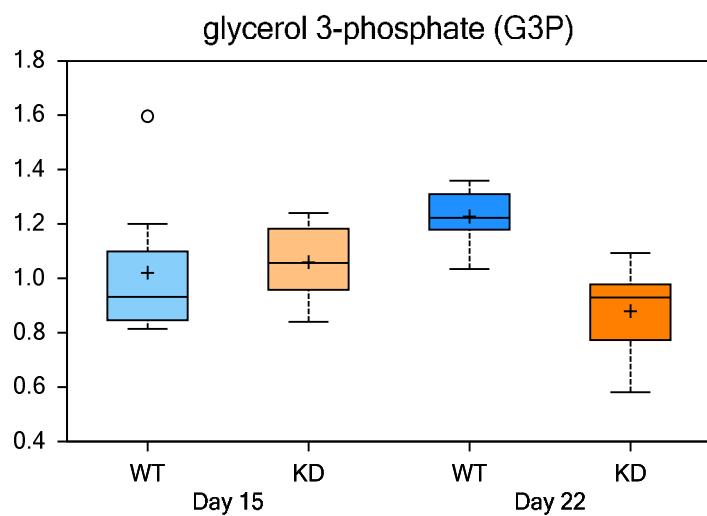
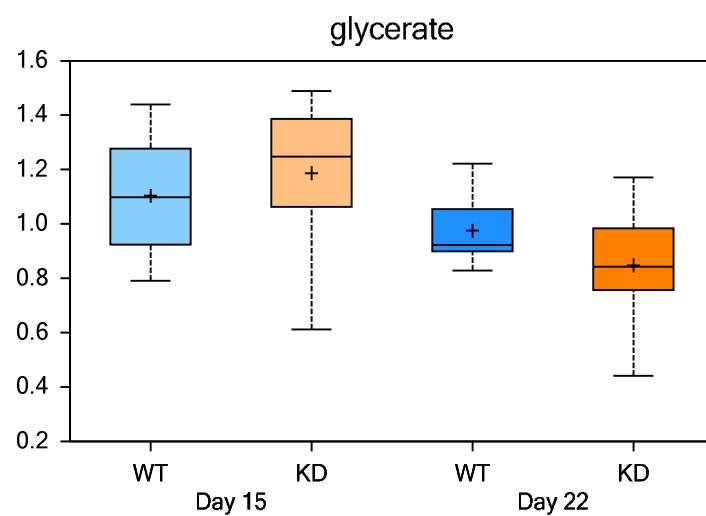
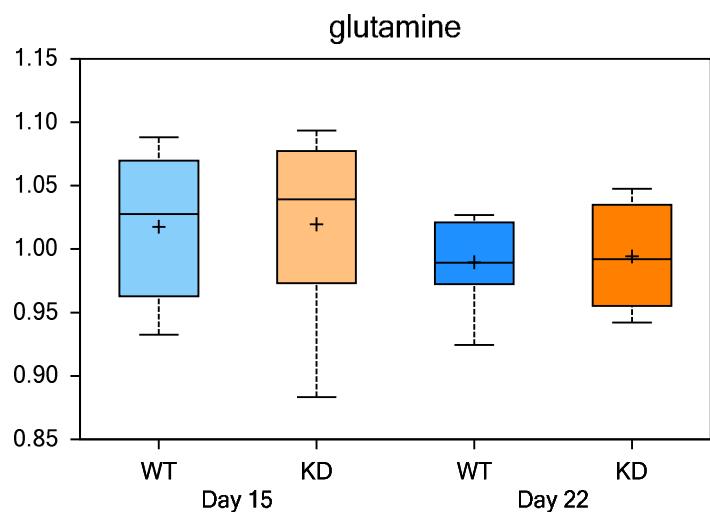


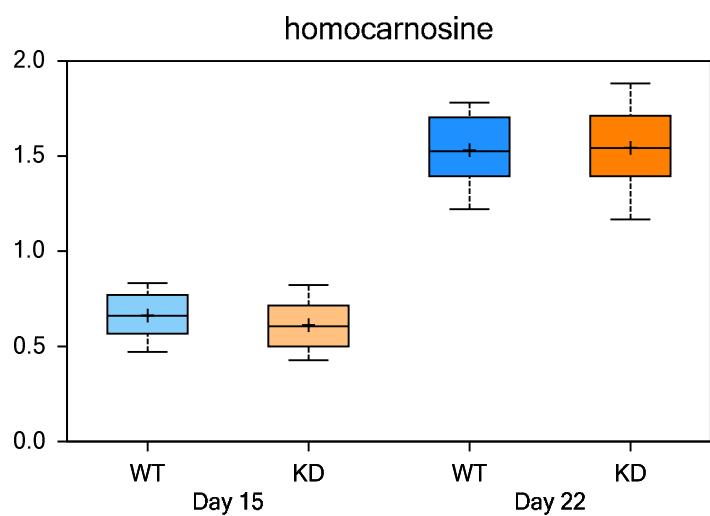
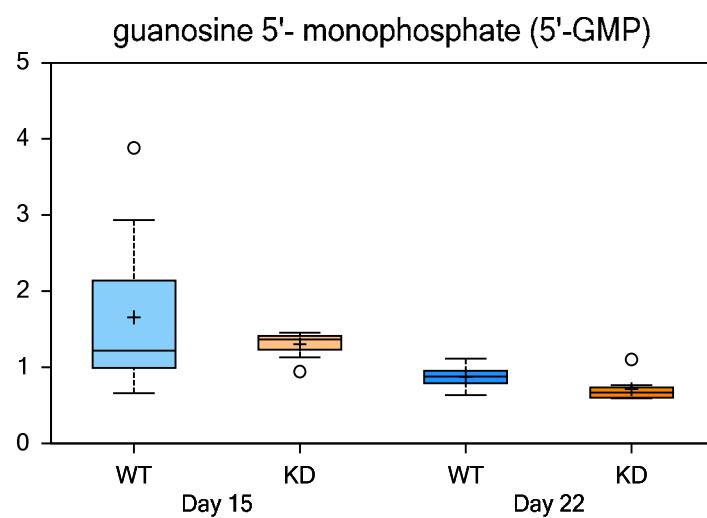
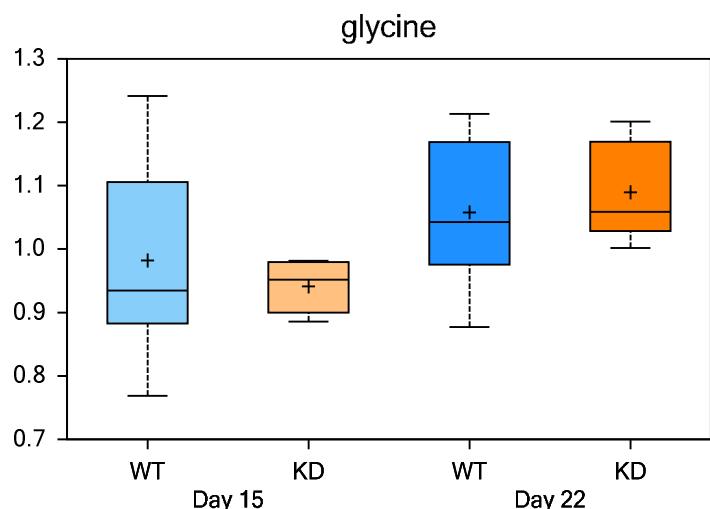
gamma-glutamyltyrosine



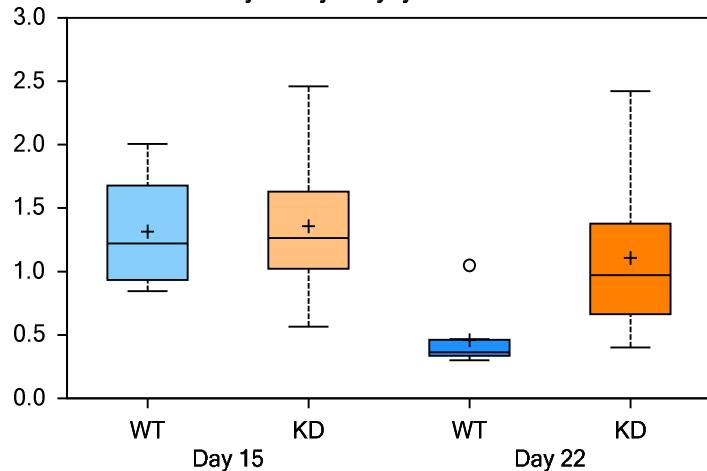
glucose-6-phosphate (G6P)



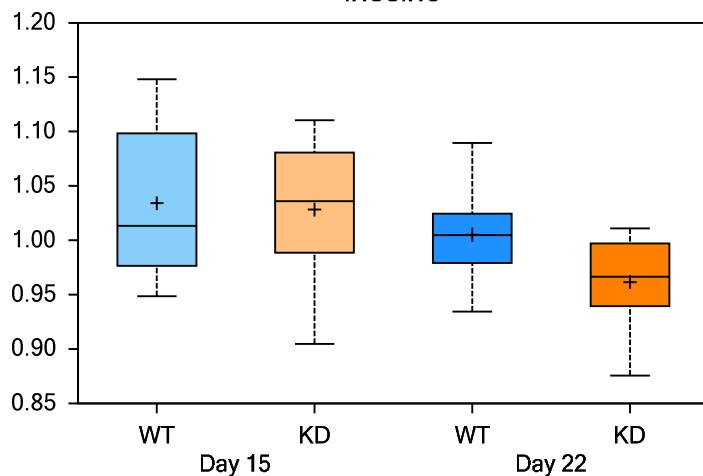




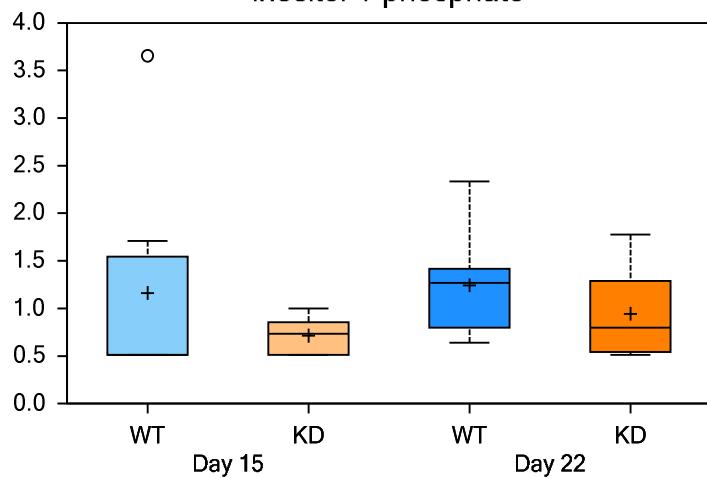
hydroxybutyrylcarnitine*

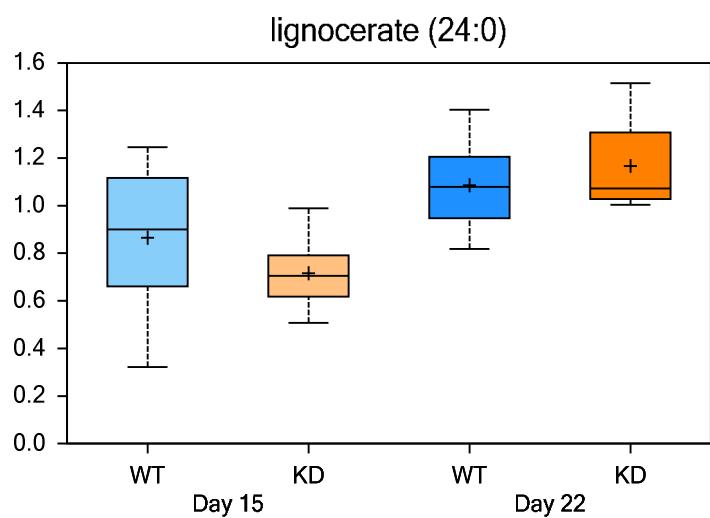
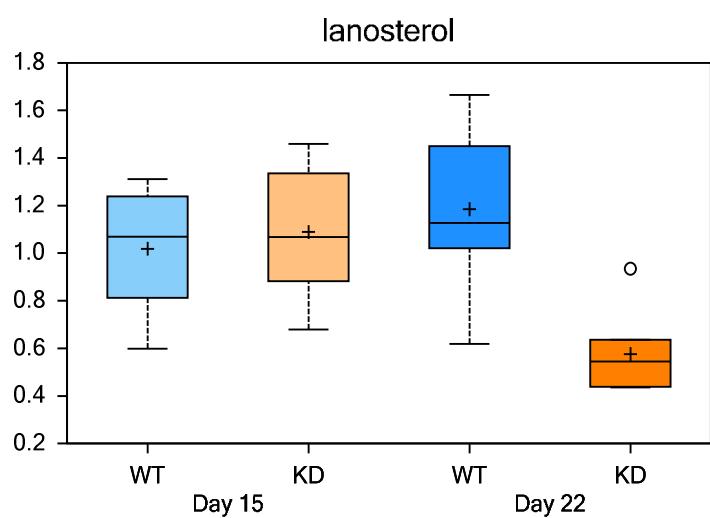
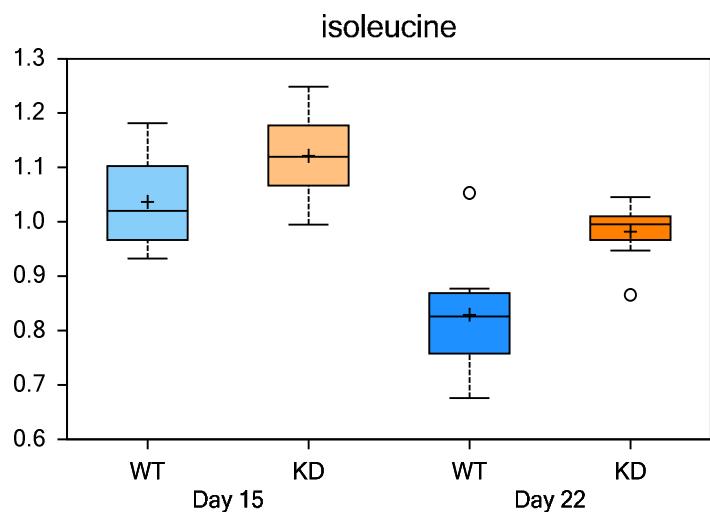


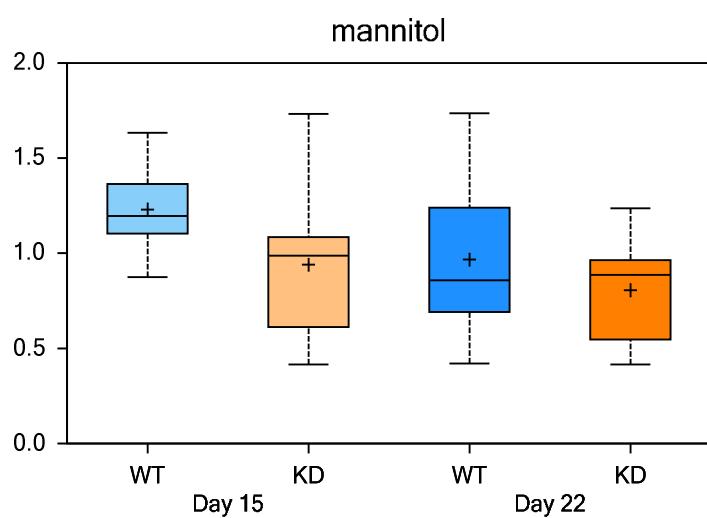
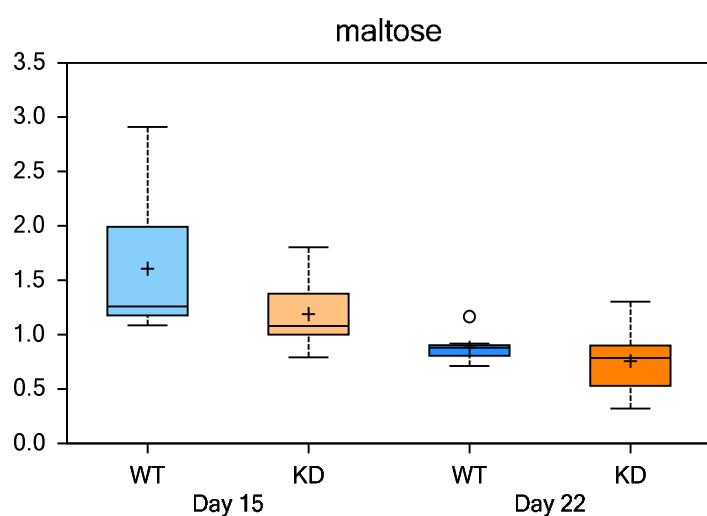
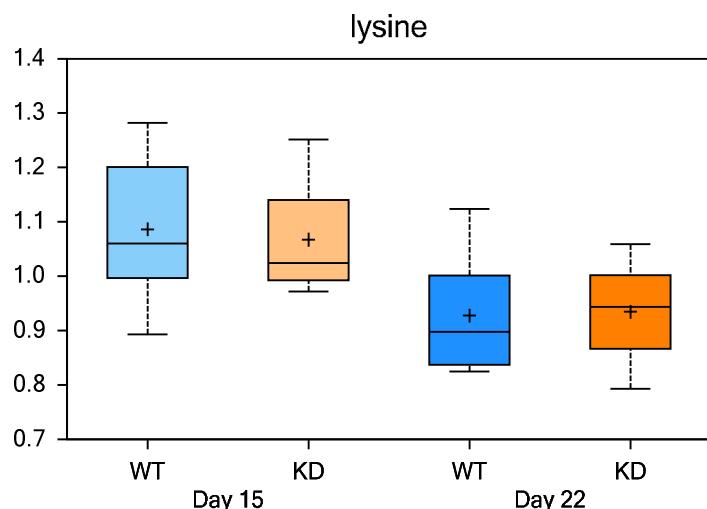
inosine



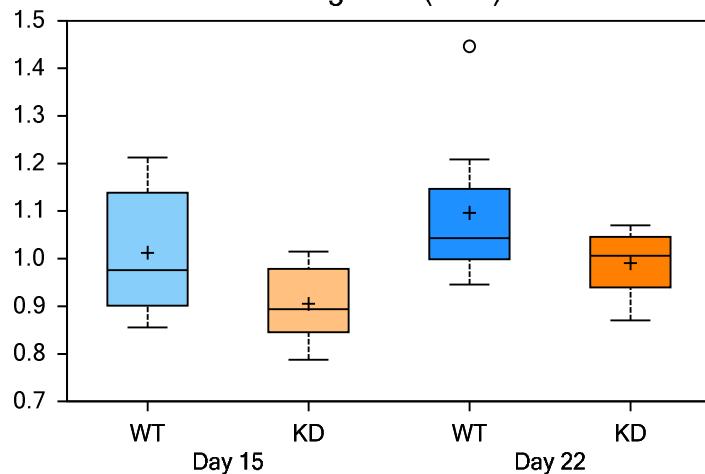
inositol 4-phosphate



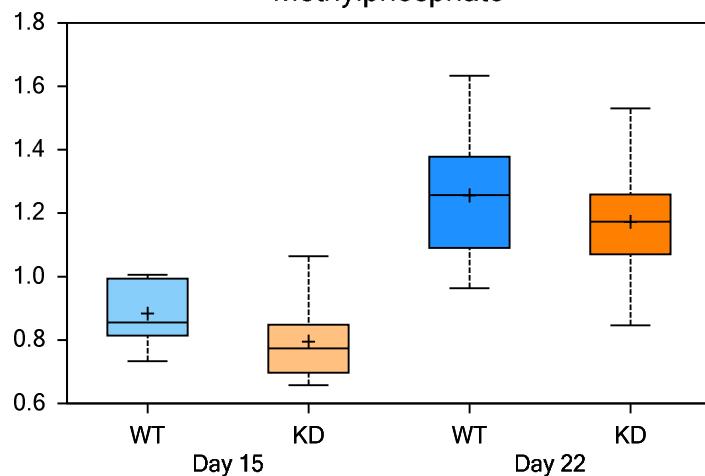




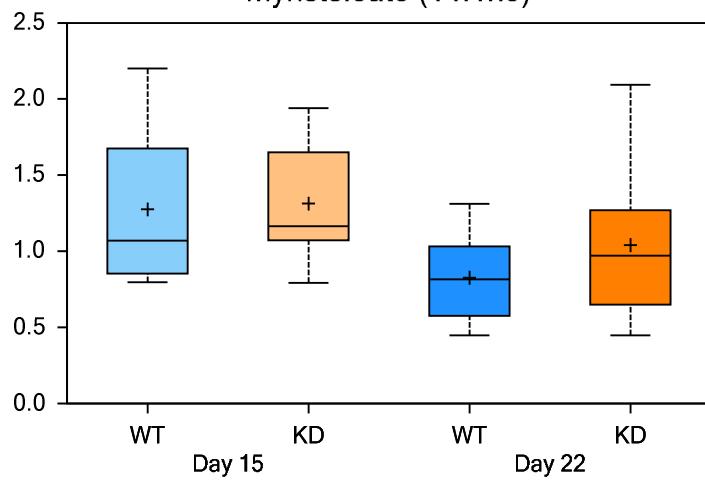
margarate (17:0)



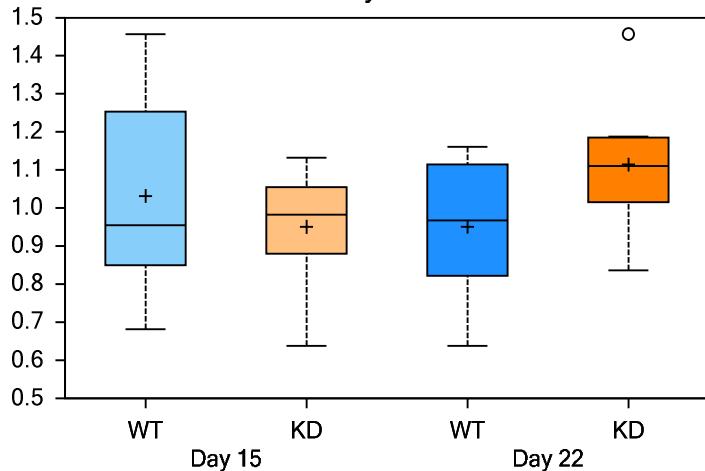
methylphosphate



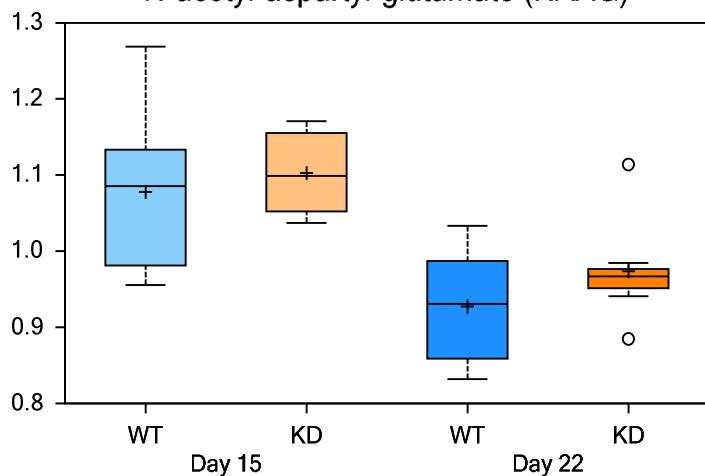
myristoleate (14:1n5)



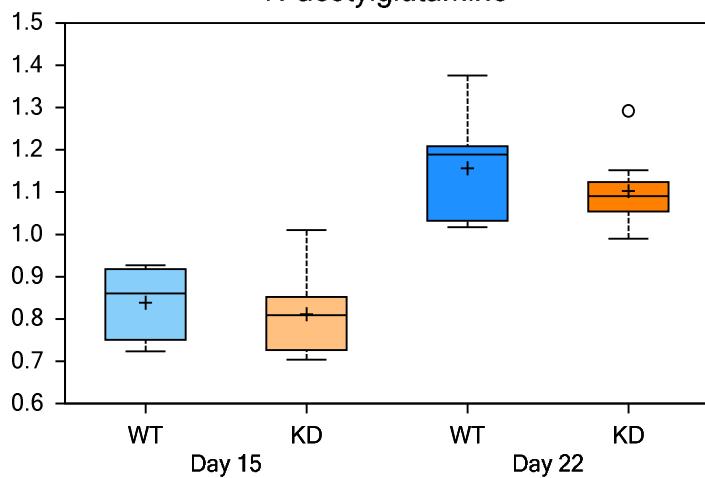
N6-methyladenosine

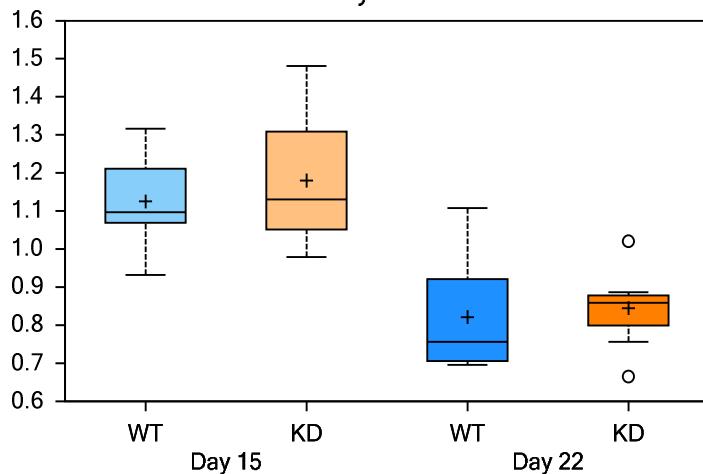
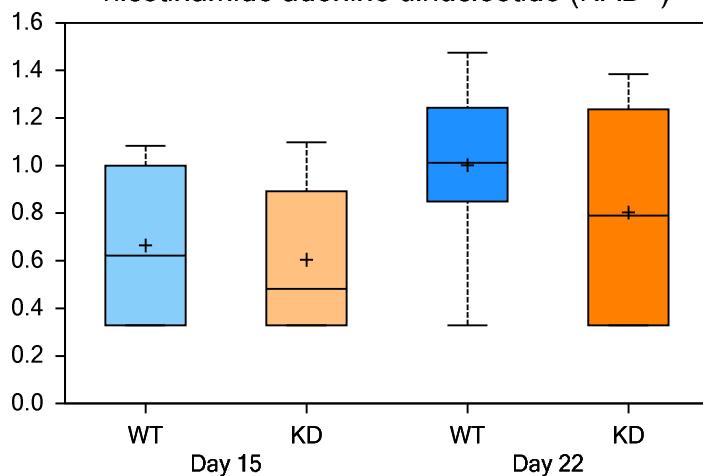
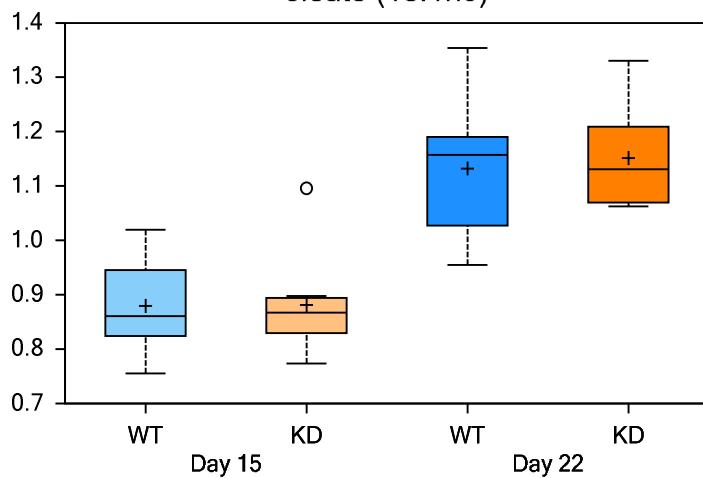


N-acetyl-aspartyl-glutamate (NAAG)

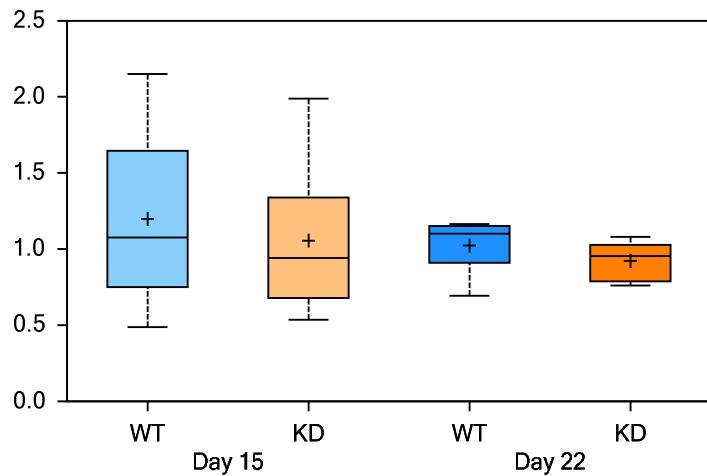


N-acetylglutamine

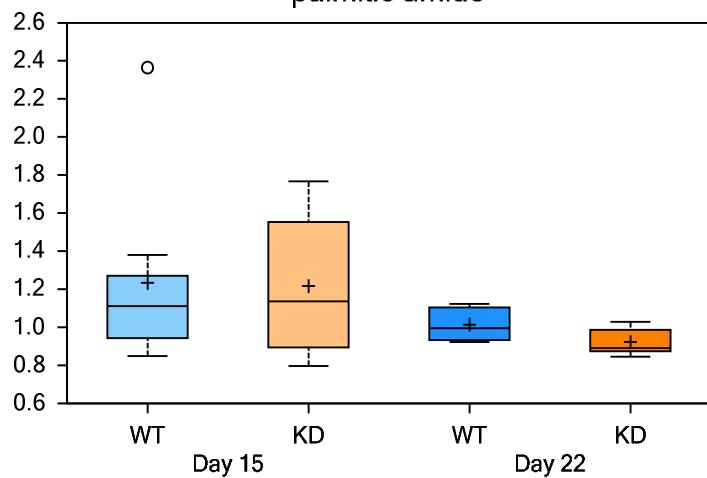


N-acetylthreonine**nicotinamide adenine dinucleotide (NAD⁺)****oleate (18:1n9)**

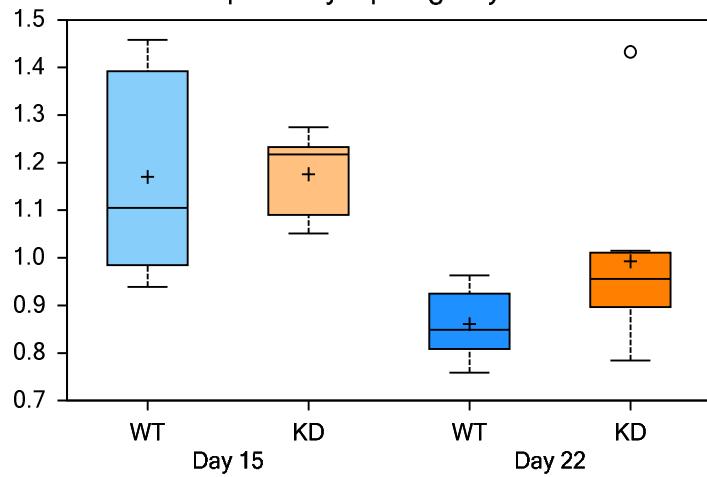
ornithine



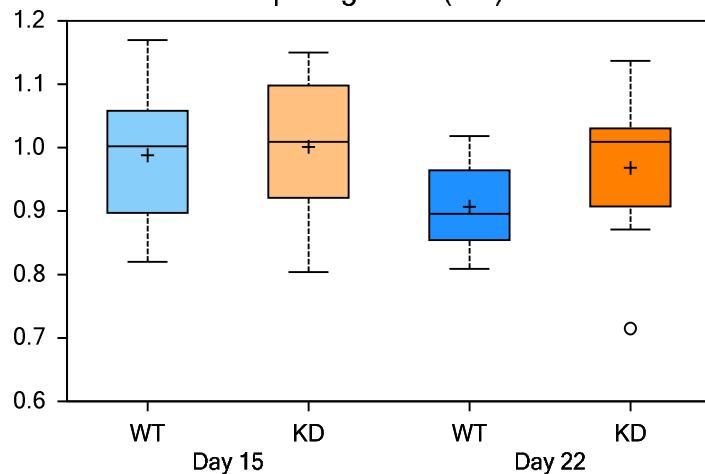
palmitic amide



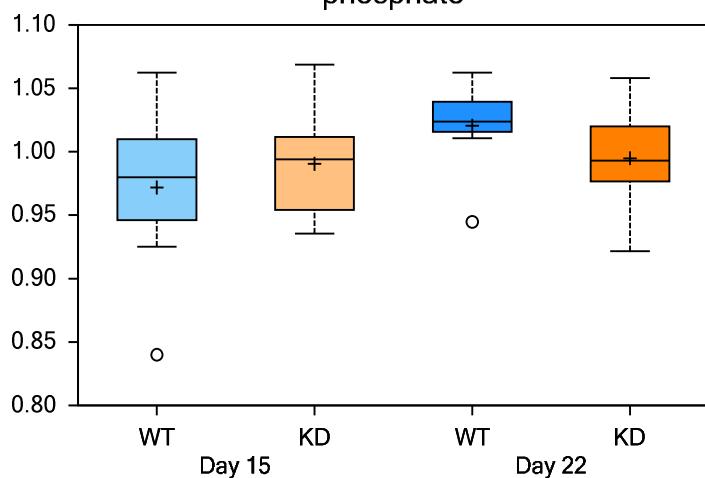
palmitoyl sphingomyelin



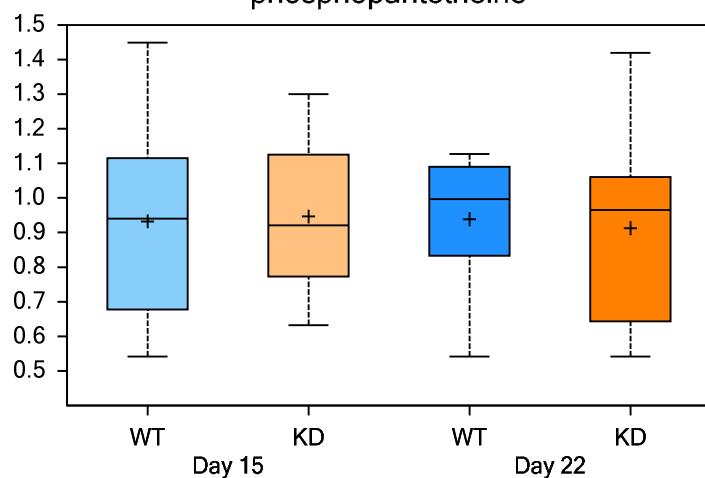
pelargonate (9:0)

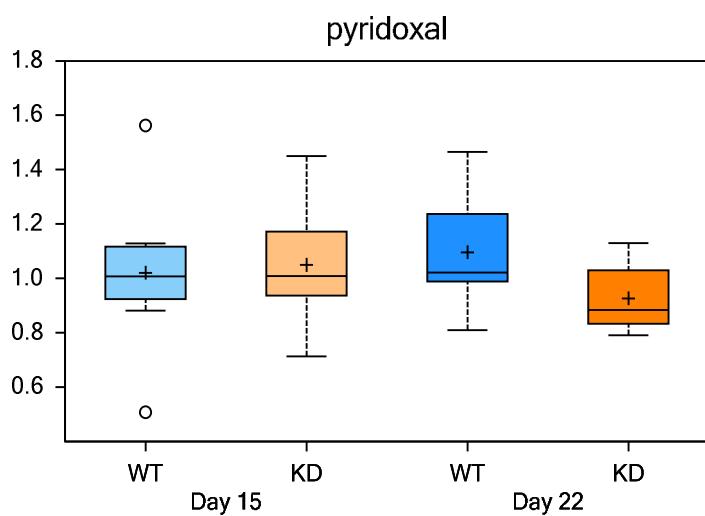
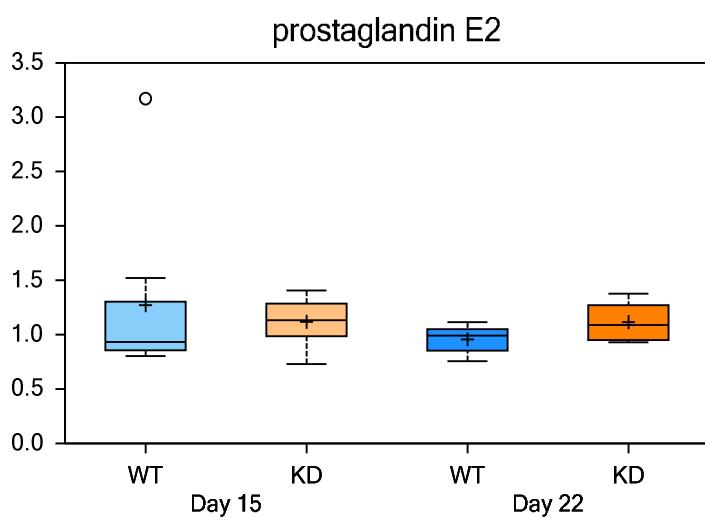
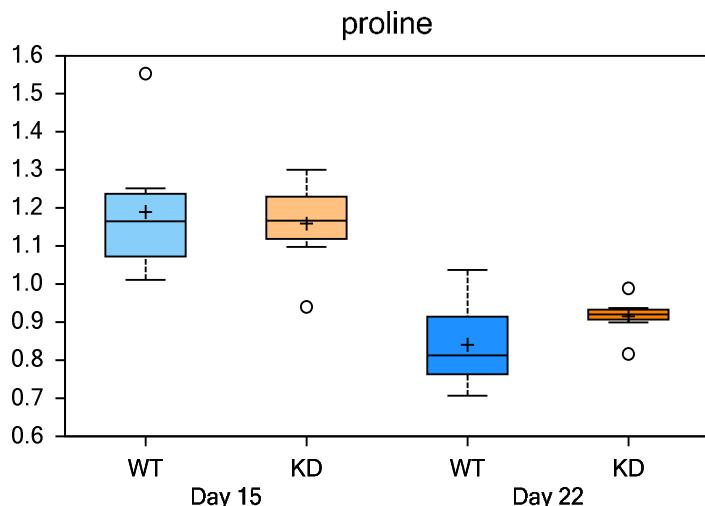


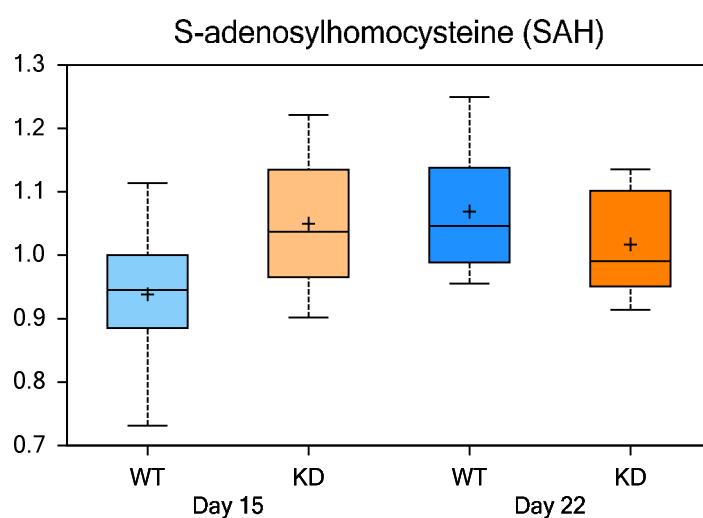
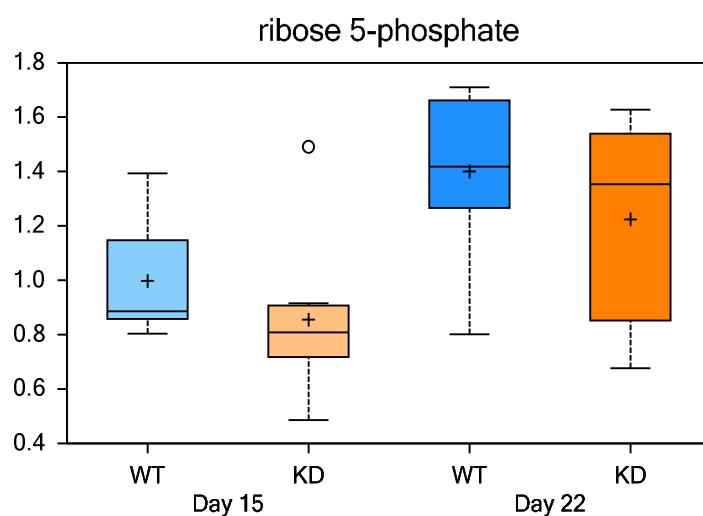
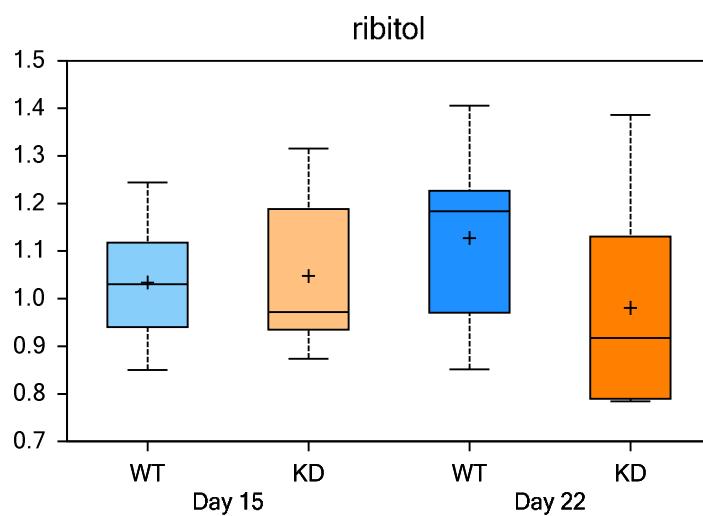
phosphate



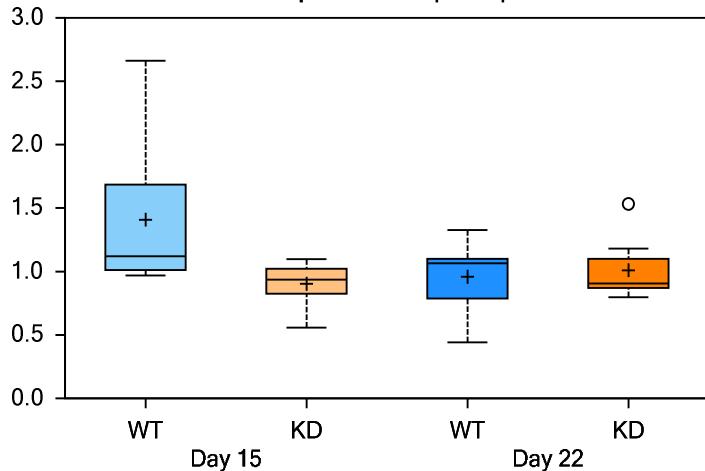
phosphopantetheine



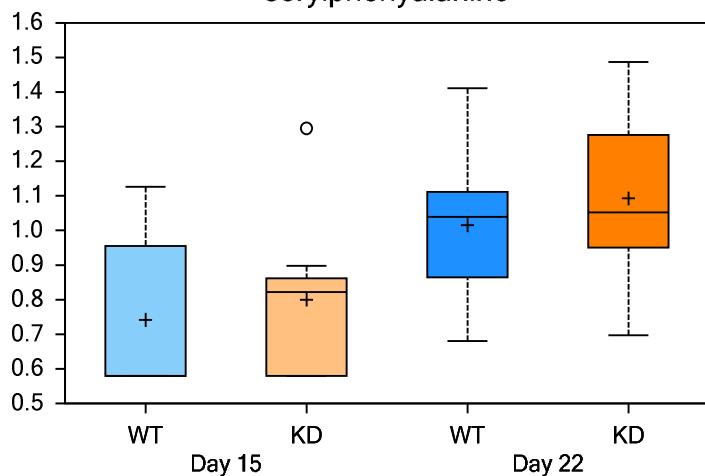




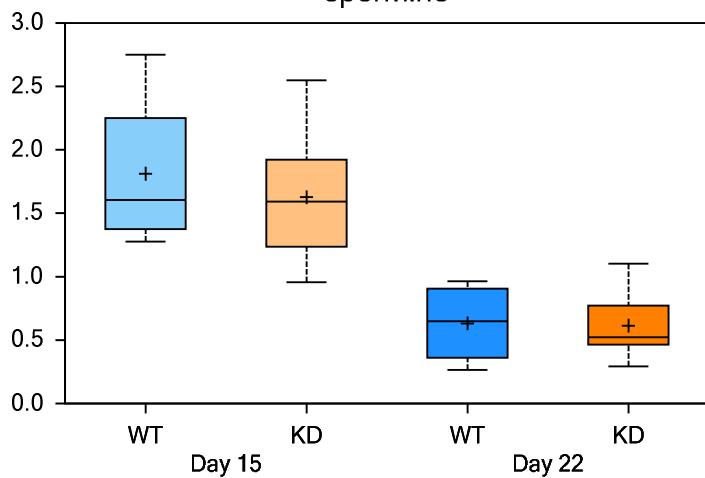
sedoheptulose-7-phosphate

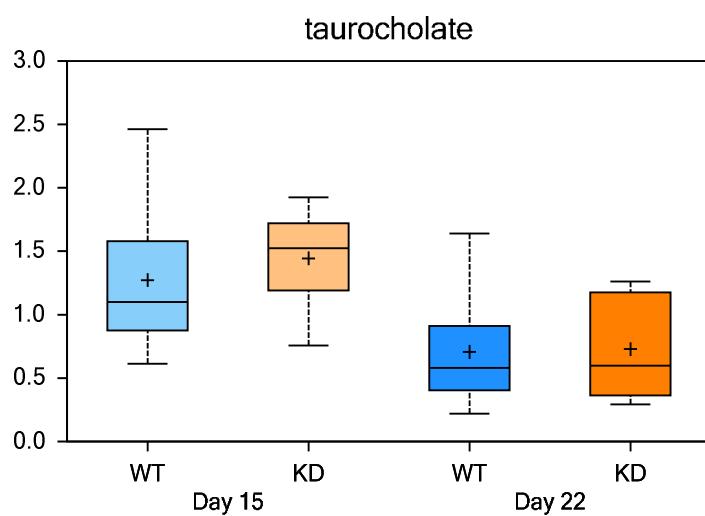
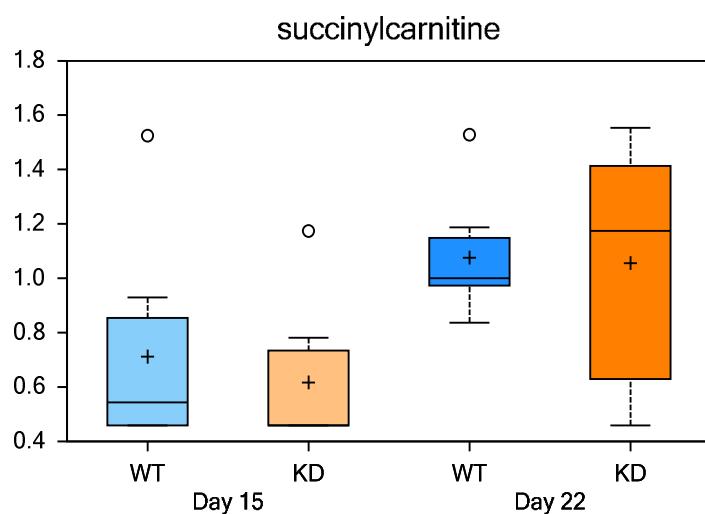
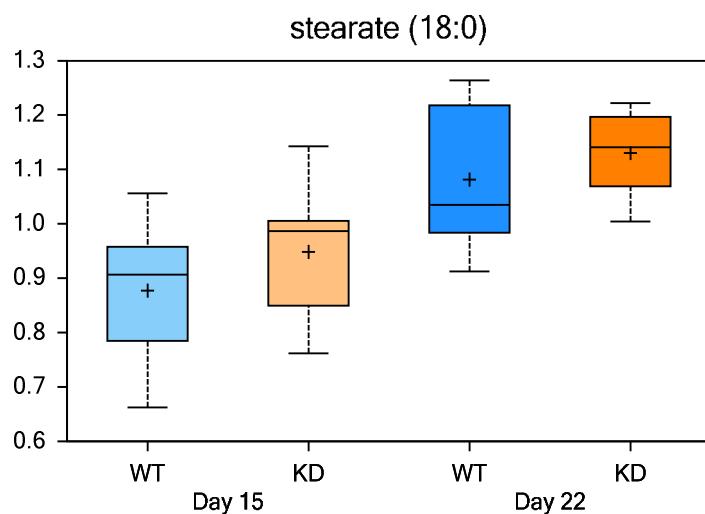


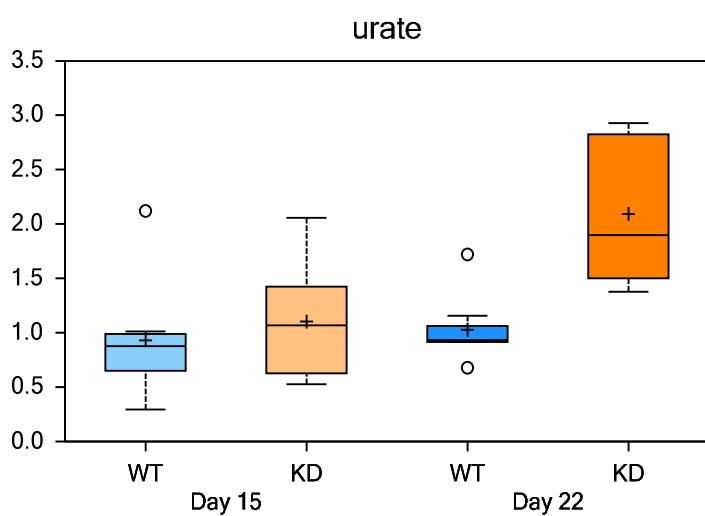
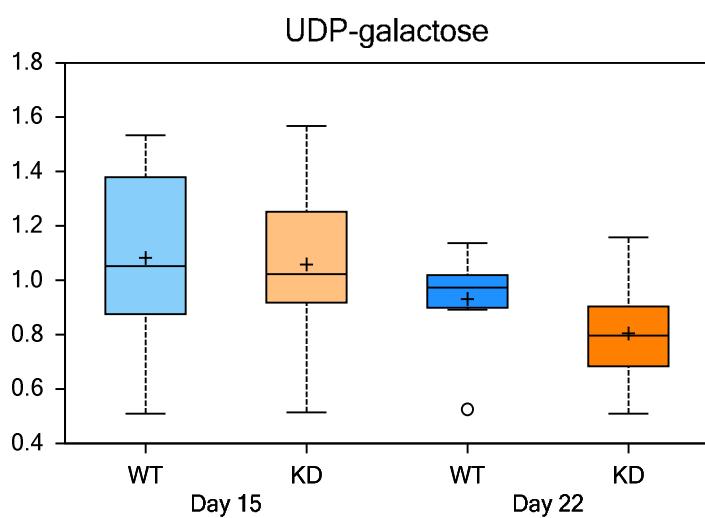
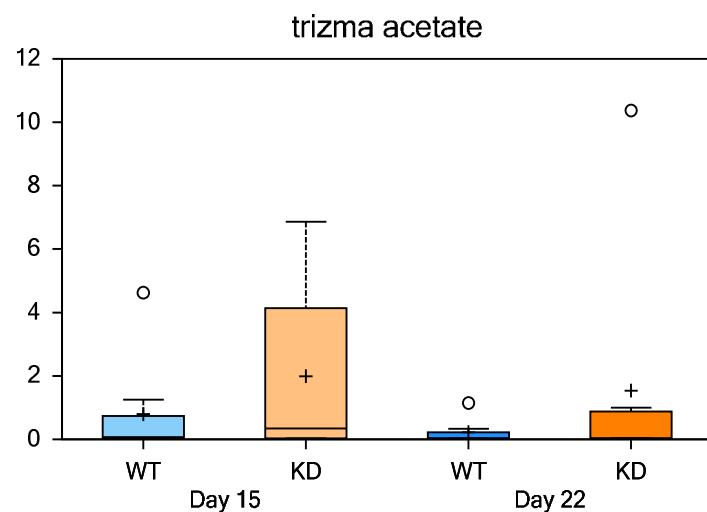
serylphenylalanine

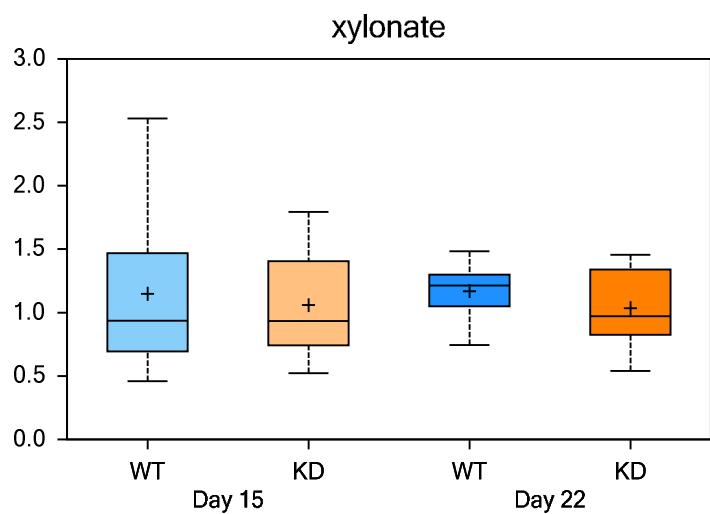
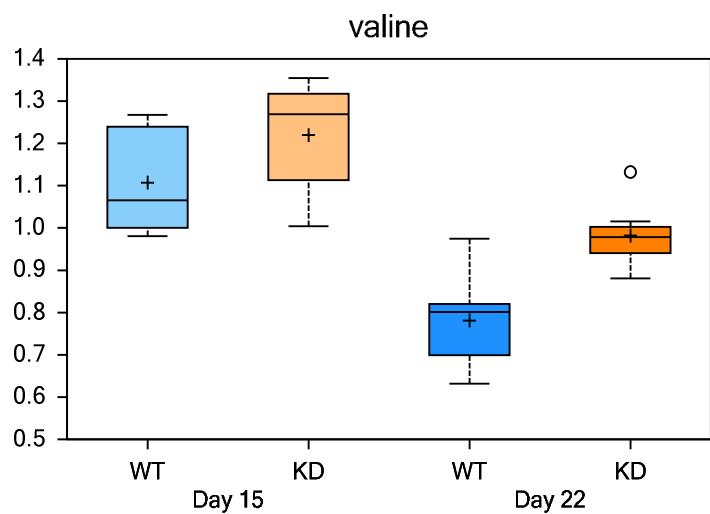


spermine

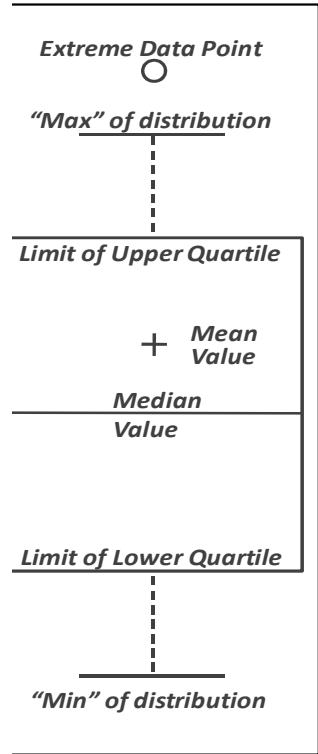


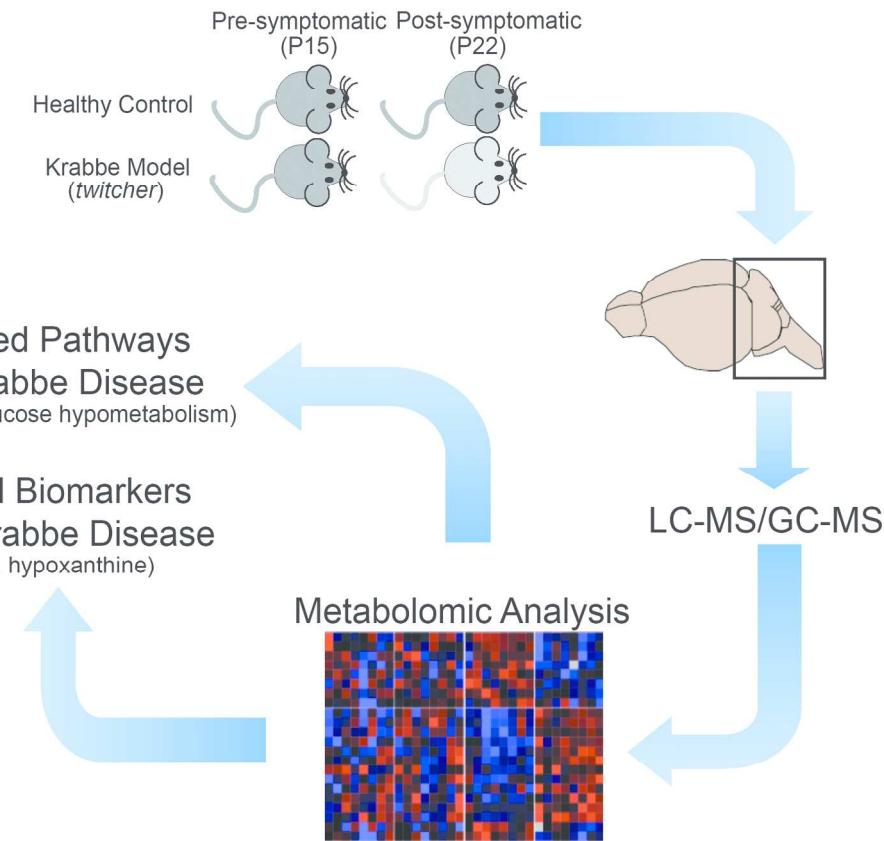






Legend





We performed a global metabolomic analysis from the hindbrains of pre-symptomatic and post-symptomatic Krabbe mice. We identified several altered metabolic pathways and a number of novel potential biomarkers that may be beneficial for patients with Krabbe disease.

173x150mm (300 x 300 DPI)

We performed a global metabolomic analysis from the hindbrains of pre-symptomatic and post-symptomatic Krabbe mice. We identified several altered metabolic pathways and a number of novel potential biomarkers that may be beneficial for patients with Krabbe disease.