

Analysis of Effects of ERR Agonist in Mouse Heart Post Pressure Overload

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Metabolon 

Study Overview



Study Objective

The goal of this study was to evaluate the metabolic effect of ERR agonists in mouse heart post pressure overload and in skeletal muscle.

Study Design

Group Name	Cohort	Description	n	
			Heart	Muscle
Vehicle Sham	1	Heart tissue vehicle, sham surgery	4	
Vehicle TAC	1	Heart tissue vehicle, TAC surgery	8	
SLU915 Sham	1	Heart tissue SLU915, sham surgery	4	
SLU915 TAC	1	Heart tissue SLU915, TAC surgery	6*	
WT	3	Heart tissue WT	5	
klf15	3	Heart tissue klf19	5	
Vehicle	2	Mouse quadricep Vehicle		7
SLU-PP-332	2	Mouse quadricep SLU-PP-332		7

*Note that 1 sample (Client ID: FB06212574) belonging to the SLU915 TAC group was excluded from the analysis due to it having a low response during data collection.

Statistical Summary (Heart)



Statistical Comparisons - Mouse Heart Tissue	
Welch's Two-Sample t-Test	<u>KLF15 MASS</u> WT MASS
Total biochemicals $p \leq 0.05$	10
Biochemicals (↑↓)	6 4
Total biochemicals $0.05 < p < 0.10$	21
Biochemicals (↑↓)	14 7

Statistical Comparisons - Mouse Heart Tissue				
ANOVA Contrasts	<u>SHAM SLU915 MASS</u> SHAM VEHICLE MASS	<u>TAC SLU915 MASS</u> SHAM SLU915 MASS	<u>TAC SLU915 MASS</u> TAC VEHICLE MASS	<u>TAC VEHICLE MASS</u> SHAM VEHICLE MASS
Total biochemicals $p \leq 0.05$	241	38	166	261
Biochemicals (↑↓)	46 195	23 15	77 89	76 185
Total biochemicals $0.05 < p < 0.10$	59	47	61	74
Biochemicals (↑↓)	23 36	28 19	33 28	22 52

Statistical Comparisons - Mouse Heart Tissue			
Two-Way ANOVA	SURGERY MAIN EFFECT MASS	TREATMENT MAIN EFFECT MASS	SURGERY:TREATMENT INTERACTION MASS
Total biochemicals $p \leq 0.05$	184	248	117
Total biochemicals $0.05 < p < 0.10$	65	67	71

From a total of **787** named and **68** unnamed biochemicals in
Mouse Heart Tissue

Statistical Summary (Skeletal Muscle)



Statistical Comparisons - Mouse Quadricep Tissue	
Welch's Two-Sample t -Test	<u>SLU-PP-332</u> VEHICLE
Total biochemicals $p \leq 0.05$	98
Biochemicals (↑↓)	96 2
Total biochemicals $0.05 < p < 0.10$	46
Biochemicals (↑↓)	40 6

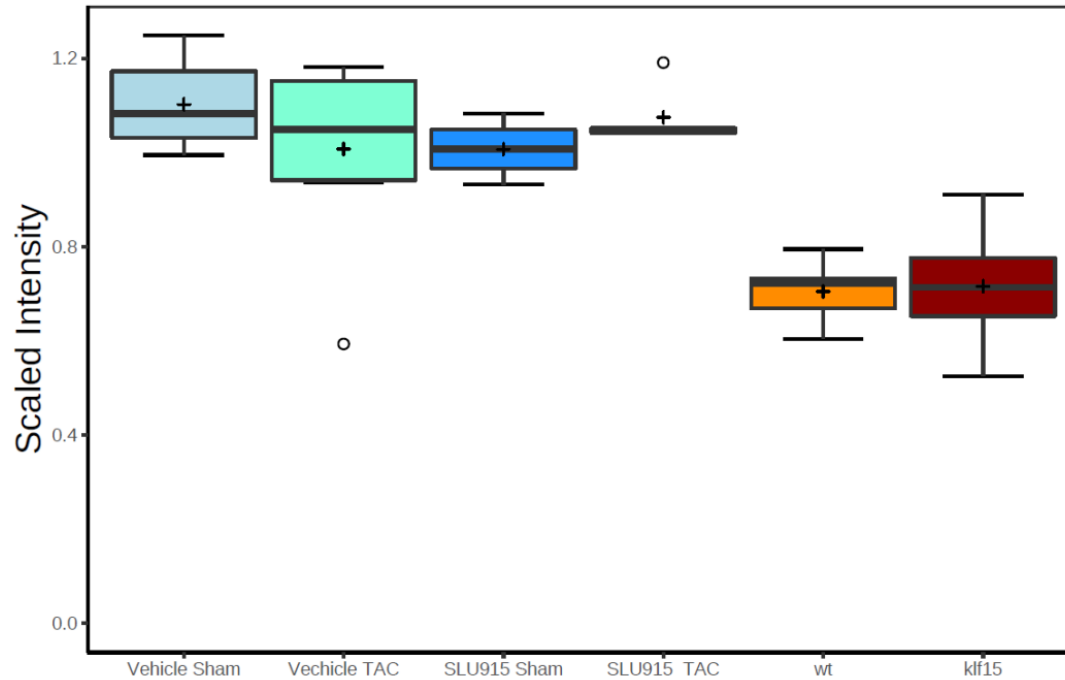
From a total of **663** named and **48** unnamed biochemicals in
Mouse Quadricep Tissue

Data Display



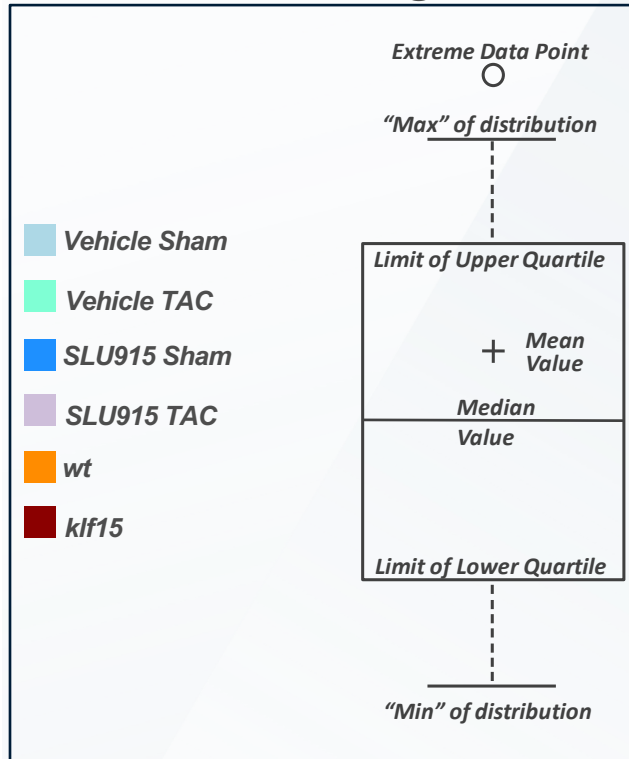
Heart

Metabolite Name

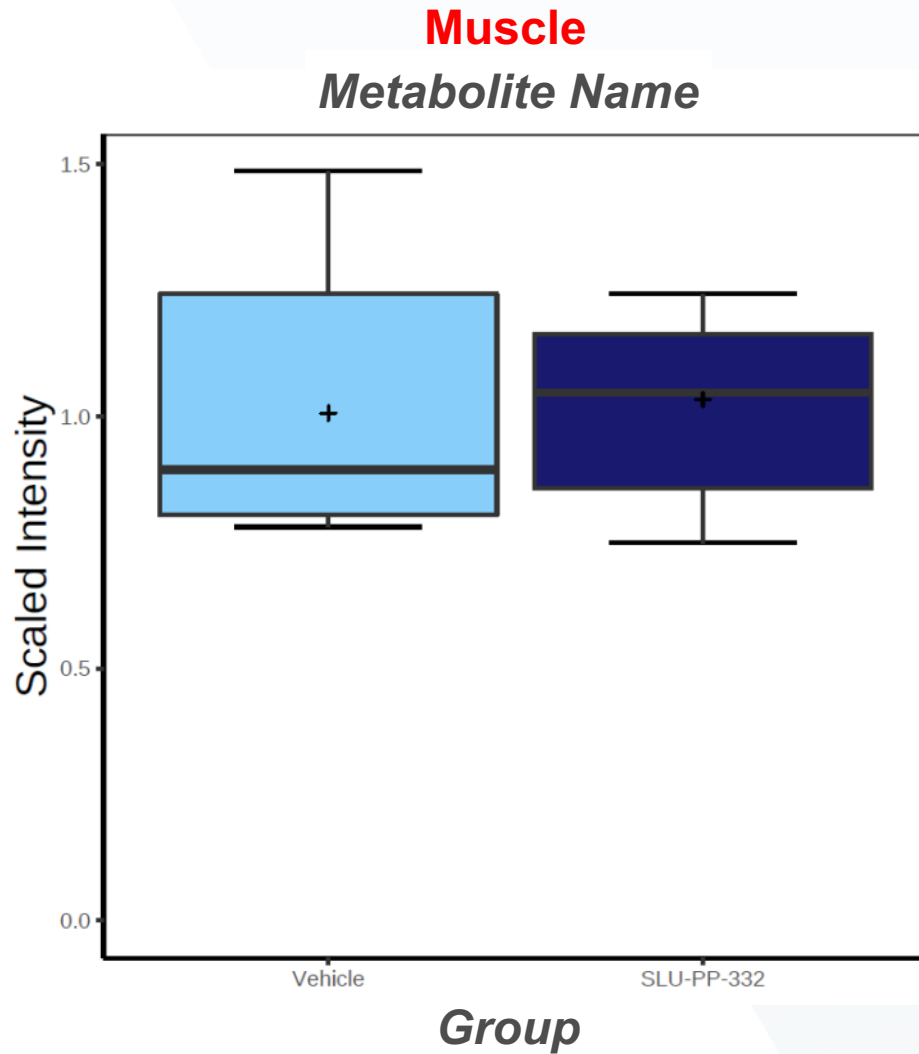


Group

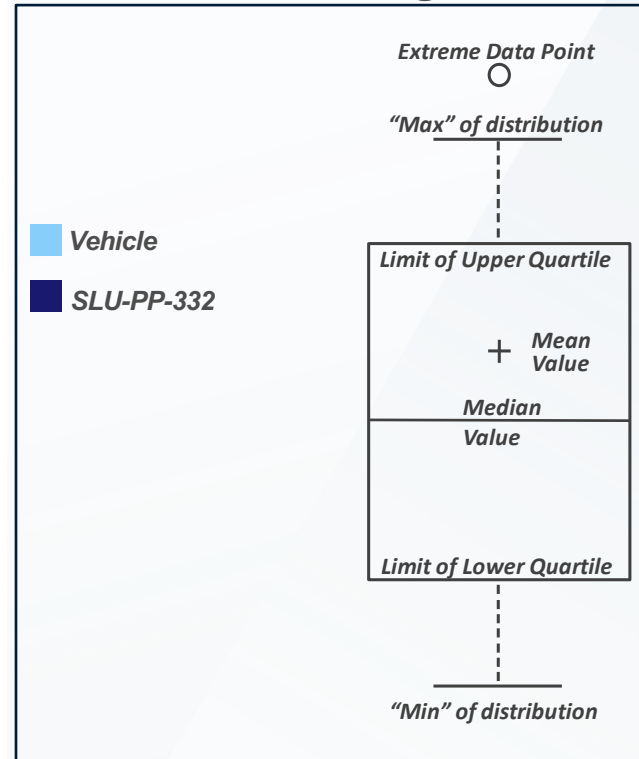
Box Plot Legend



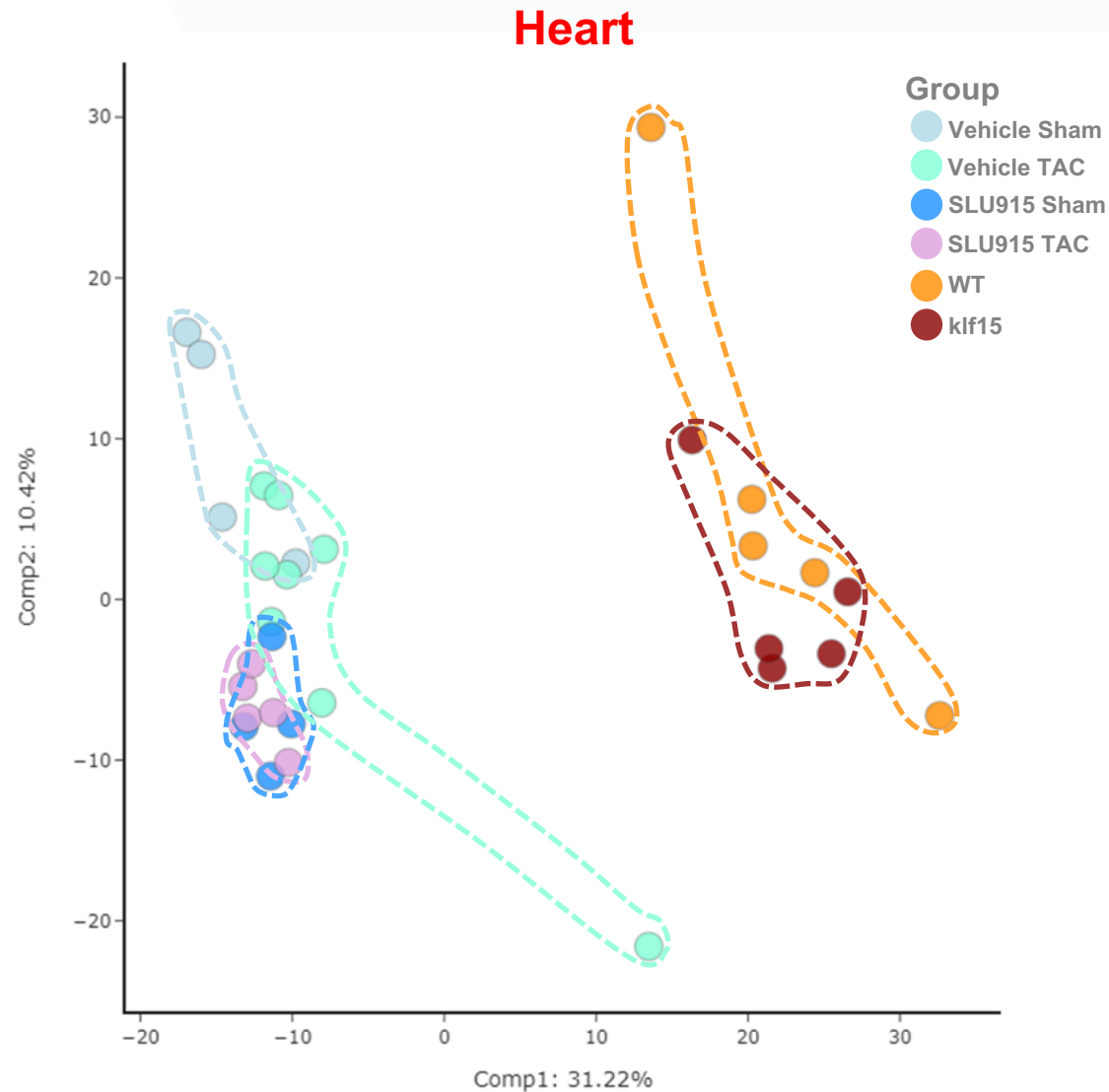
Data Display



Box Plot Legend



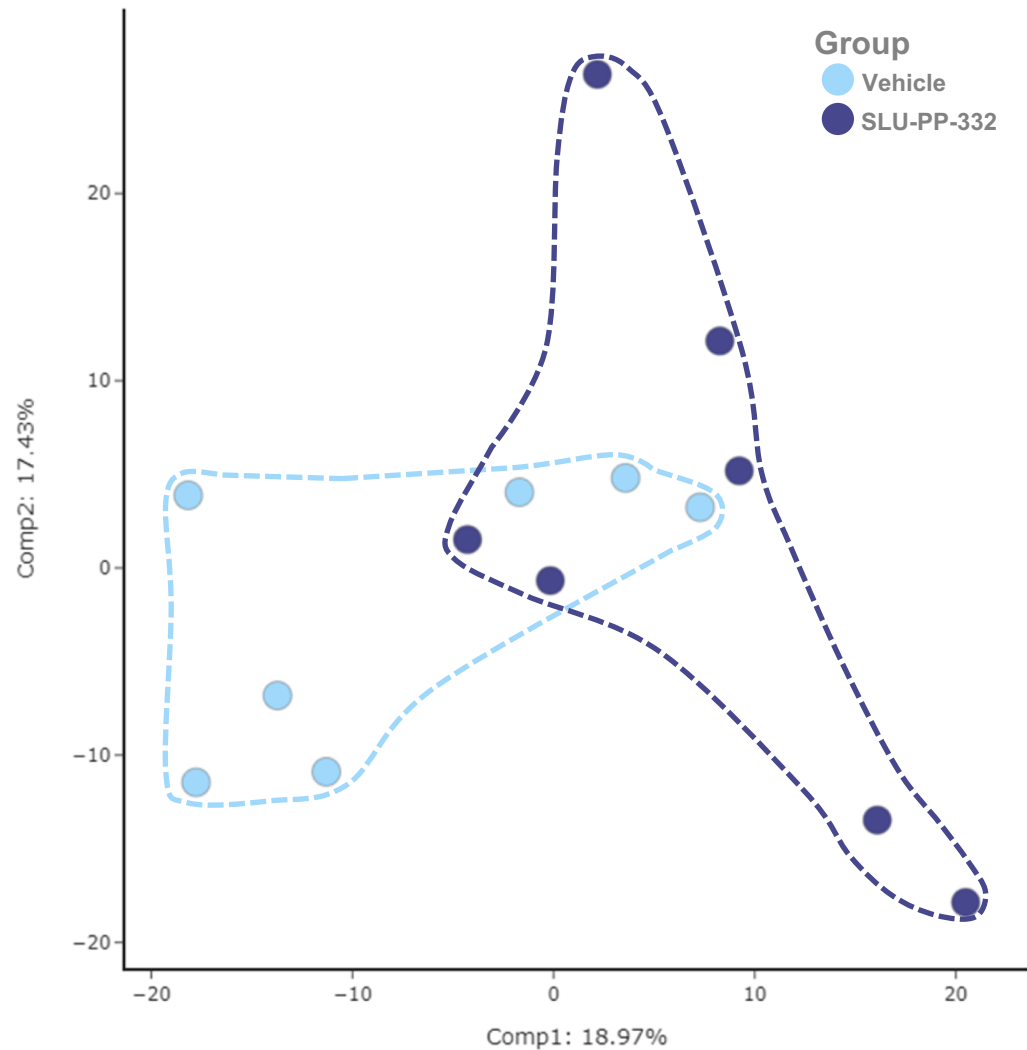
Principal Component Analysis



Principal Component Analysis



Muscle

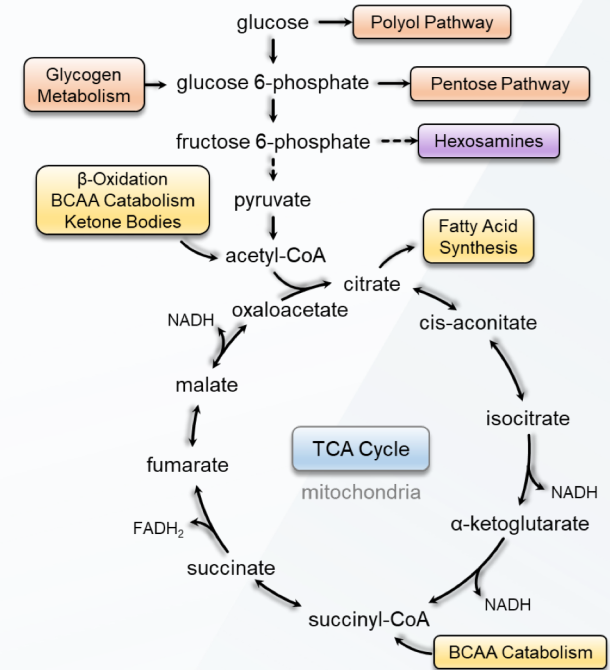


Differences in Carbohydrates and Energy Metabolites



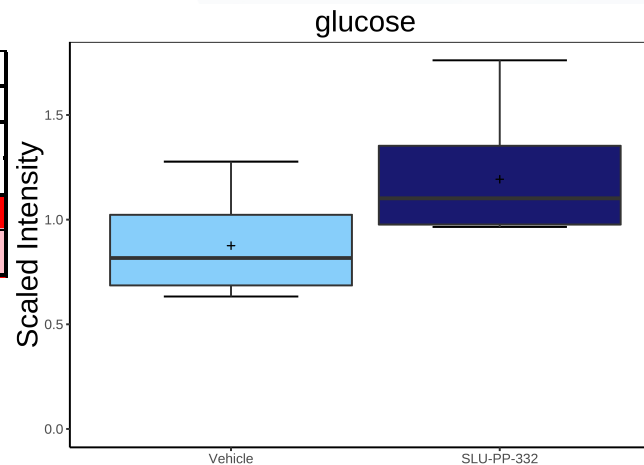
Heart

Sub Pathway	Biochemical Name	Fold of Change				
		Mass Normalized				
		Two Way ANOVA				Welch's t-Test
		(SHAM_SLU915) (SHAM_VEHICLE)	(TAC_SLU915) (SHAM_SLU915)	(TAC_SLU915) (TAC_VEHICLE)	(TAC_VEHICLE) (SHAM_VEHICLE)	
Glycolysis, Gluconeogenesis, and Pyruvate Metabolism	1,5-anhydroglucitol (1,5-AG)	1.24	0.96	1.13	1.05	1.14
	glucose	1.52	0.93	1.23	1.14	0.66
	glucose 6-phosphate	2.54	1.45	1.47	2.51	0.15
	dihydroxyacetone phosphate (DHAP)	3.55	1.05	1.23	3.05	0.56
	3-phosphoglycerate	1.26	1.22	1.79	0.86	2.54
	phosphoenolpyruvate (PEP)	1.30	1.19	2.01	0.77	0.71
	pyruvate	1.05	0.64	0.63	1.07	0.87
TCA Cycle	citrate	0.41	0.89	0.51	0.71	1.52
	aconitate [cis or trans]	0.44	0.83	0.50	0.73	1.57
	alpha-ketoglutarate	0.63	0.93	0.88	0.67	1.25
	succinylcarnitine (C4-DC)	1.17	0.60	1.31	0.54	0.75
	tricarballoylate	0.73	0.93	0.42	1.60	1.08

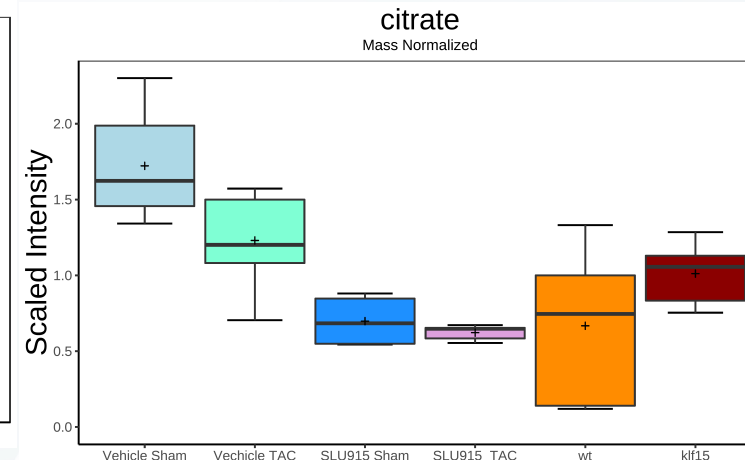


Muscle

Sub Pathway	Biochemical Name	Fold of Change
		Welch's t-Test
		SLU-PP-332 VEHICLE
Glycolysis, Gluconeogenesis, and Pyruvate Metabolism	glucose	1.36
	lactate	1.15



Muscle

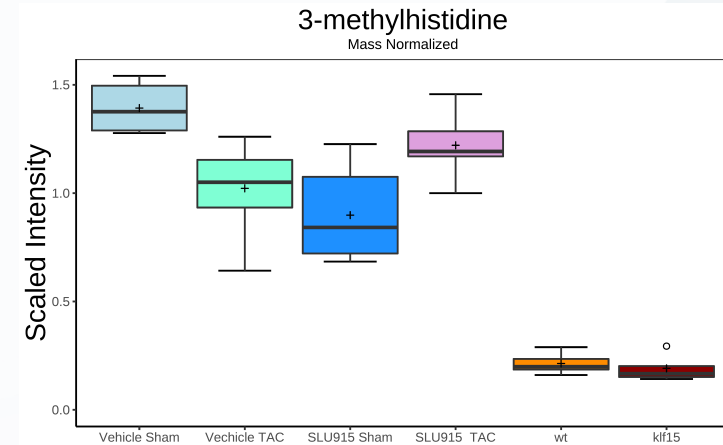


Heart

Differences Histidine and Lysine Metabolism

Heart

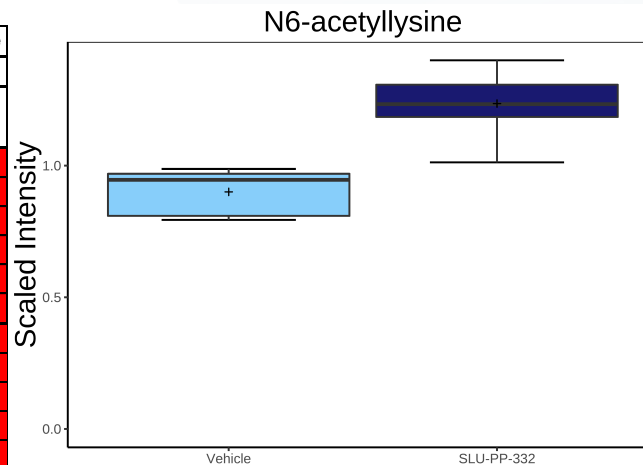
Sub Pathway	Biochemical Name	Fold of Change				
		Mass Normalized				
		Two Way ANOVA				Welch's t-Test
		(SHAM_SLU915) (SHAM_VEHICLE)	(TAC_SLU915) (SHAM_SLU915)	(TAC_SLU915) (TAC_VEHICLE)	(TAC_VEHICLE) (SHAM_VEHICLE)	
Histidine Metabolism	histidine	0.84	1.00	1.16	0.73	0.89
	3-methylhistidine	0.65	1.36	1.19	0.73	0.89
	imidazole propionate	0.82	0.64	0.35	1.49	1.13
	carosine	0.92	0.51	1.12	0.42	1.03
	anserine	0.90	0.46	1.08	0.39	0.99
	1-methylhistamine	1.24	0.63	1.36	0.58	1.24
	1-methyl-4-imidazoleacetate	1.27	0.61	2.07	0.38	0.91
	1-methyl-5-imidazoleacetate	0.46	1.31	0.61	0.99	0.70
	4-imidazoleacetate	0.94	0.79	1.28	0.58	0.50
	histidine methyl ester	1.61	1.05	1.16	1.46	1.24
Lysine Metabolism	lysine	1.23	1.06	1.24	1.05	1.08
	5-hydroxylysine	1.55	1.29	0.96	2.07	1.13
	5-(galactosylhydroxy)-L-lysine	0.94	1.65	0.79	1.97	1.02
	pipecolate	1.16	1.41	0.74	2.20	0.77
	N,N,N-trimethyl-5-aminovalerate	0.40	1.08	0.53	0.82	0.86



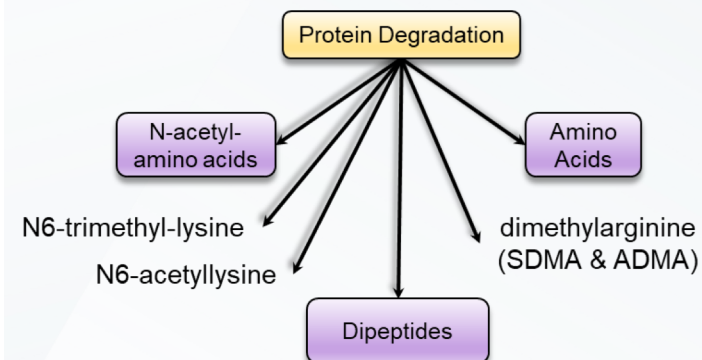
Heart

Muscle

Sub Pathway	Biochemical Name	Fold of Change
		Welch's t-Test
		SLU-PP-332 VEHICLE
Histidine Metabolism	histidine	1.11
	1-methylhistidine	1.36
	3-methylhistidine	1.33
	anserine	1.07
	histamine	1.32
Lysine Metabolism	1-methyl-4-imidazoleacetate	1.70
	lysine	1.32
	N6-acetyllysine	1.37
	N6-methyllysine	1.61
	N6,N6,N6-trimethyllysine	1.36
	5-hydroxylysine	1.49
	fructosyllysine	1.17
	2-aminoadipate	1.29
	N,N,N-trimethyl-5-aminovalerate	1.34



Muscle

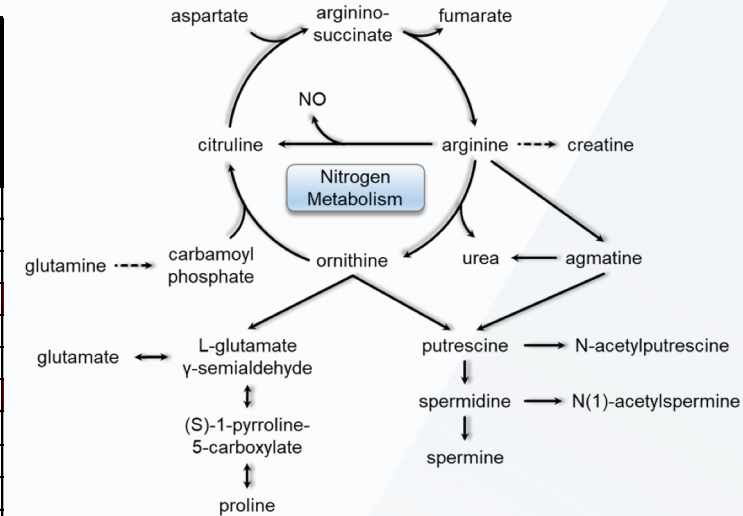


Differences in Arginine & Polyamine Metabolites



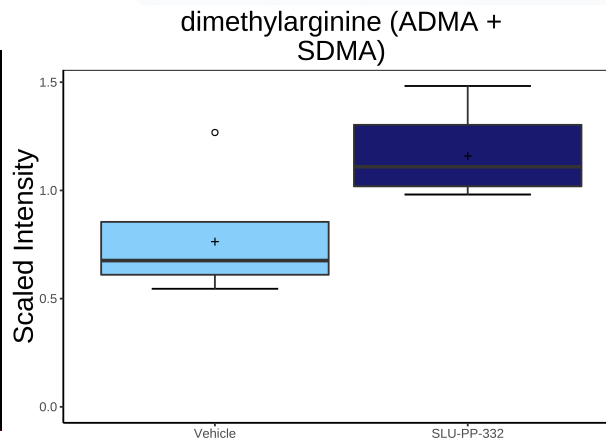
Heart

Sub Pathway	Biochemical Name	Fold of Change				
		Mass Normalized				
		Two Way ANOVA				Welch's t-Test
		(SHAM SLU915) (SHAM_VEHICLE)	(TAC SLU915) (SHAM_SLU915)	(TAC SLU915) (TAC_VEHICLE)	(TAC VEHICLE) (SHAM_VEHICLE)	
Urea cycle; Arginine and Proline Metabolism	arginine	1.06	1.01	1.06	1.02	1.02
	argininosuccinate	1.03	0.73	0.65	1.17	0.92
	N-acetylarginine	1.31	1.17	0.90	1.71	3.09
	N-(ADP-ribosyl)-arginine (1)	1.46	1.21	1.99	0.89	1.04
	N-(ADP-ribosyl)-arginine (2)	1.60	1.48	2.33	1.02	0.85
	trans-4-hydroxyproline	0.93	1.20	0.85	1.31	0.92
	pro-hydroxy-pro	2.77	1.29	0.70	5.09	1.10
	N-monomethylarginine	0.98	0.92	1.24	0.73	0.86
Polyamine Metabolism	putrescine	1.20	1.79	1.02	2.10	1.02
	N-acetylputrescine	1.03	1.50	0.97	1.58	0.68
	spermidine	1.26	1.62	0.99	2.06	0.82
	(N(1) + N(8))-acetylspermidine	1.24	1.30	0.94	1.72	0.97
	spermine	1.36	1.04	1.02	1.38	0.99



Muscle

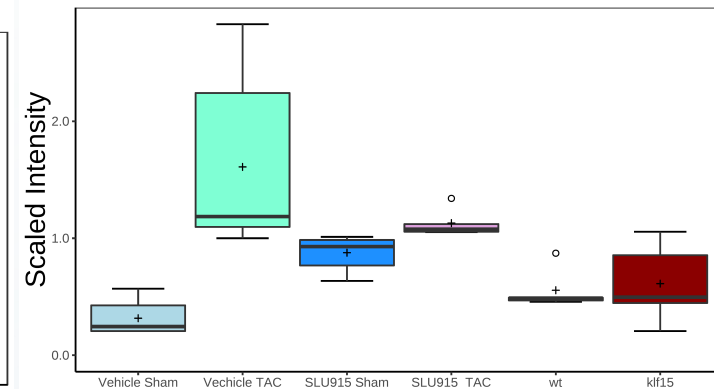
Sub Pathway	Biochemical Name	Fold of Change
		Welch's t-Test
		SLU-PP-332 VEHICLE
Urea cycle; Arginine and Proline Metabolism	homoarginine	2.07
	homocitrulline	1.29
	dimethylarginine (SDMA + ADMA)	1.52
	N-acetylarginine	1.19
	N-delta-acetylornithine	1.15
	trans-4-hydroxyproline	1.33
	N,N,N-trimethyl-alanylproline betaine (TMAP)	1.24
	argininate*	1.54
Polyamine Metabolism	5-methylthioadenosine (MTA)	1.31



Muscle

prolylhydroxyproline

Mass Normalized

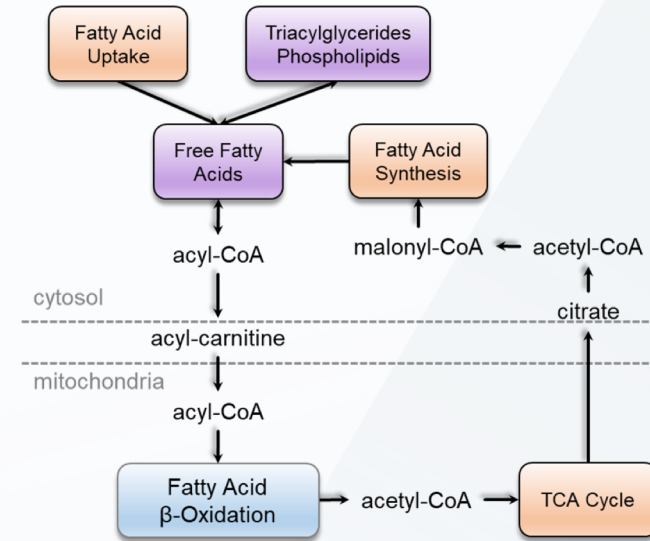


Heart

Differences in Lipid Metabolism

Heart

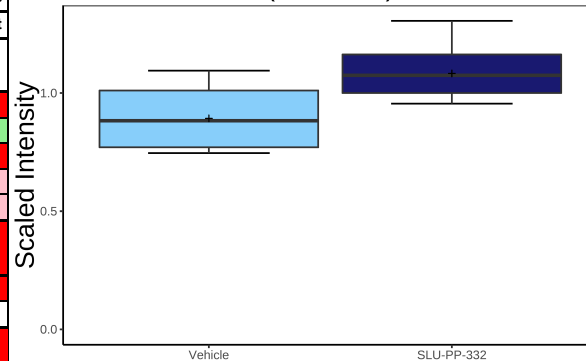
Sub Pathway	Biochemical Name	Fold of Change				
		Mass Normalized				
		Two Way ANOVA				Welch's t-Test
		(SHAM SLU915) (SHAM_VEHICLE)	(TAC SLU915) (SHAM_SLU915)	(TAC SLU915) (TAC_VEHICLE)	(TAC VEHICLE) (SHAM_VEHICLE)	
Phosphatidylcholine (PC)	1-myristoyl-2-palmitoyl-GPC (14:0/16:0)	0.77	0.90	0.94	0.73	1.15
	1,2-dipalmitoyl-GPC (16:0/16:0)	0.81	0.91	0.99	0.74	1.10
	1-palmitoyl-2-palmitoleyl-GPC (16:0/16:1)*	0.83	1.04	1.06	0.81	1.21
	1-palmitoyl-2-stearoyl-GPC (16:0/18:0)	0.73	0.94	1.05	0.65	1.27
	1-palmitoyl-2-oleoyl-GPC (16:0/18:1)	0.81	1.02	1.04	0.80	0.95
	1-palmitoyl-2-linoleoyl-GPC (16:0/18:2)	0.79	1.04	0.96	0.85	0.86
	1-palmitoyl-2-arachidonoyl-GPC (16:0/20:4n6)	0.80	1.00	1.10	0.73	0.89
	1-palmitoyl-2-docosahexaenoyl-GPC (16:0/22:6)	0.79	0.90	1.01	0.70	0.88
	1-stearoyl-2-oleoyl-GPC (18:0/18:1)	0.76	1.13	1.07	0.80	0.88
	1-stearoyl-2-linoleoyl-GPC (18:0/18:2)*	0.78	1.10	1.02	0.84	0.79
	1-stearoyl-2-arachidonoyl-GPC (18:0/20:4)	0.78	1.03	1.11	0.73	0.85
	1-stearoyl-2-docosahexaenoyl-GPC (18:0/22:6)	0.77	0.90	1.00	0.70	0.87
Phosphatidylethanolamine (PE)	1,2-dipalmitoyl-GPE (16:0/16:0)*	0.78	0.97	0.97	0.78	1.01
	1-palmitoyl-2-stearoyl-GPE (16:0/18:0)*	0.66	0.98	1.16	0.56	1.01
	1-palmitoyl-2-linoleoyl-GPE (16:0/18:2)	0.72	1.26	0.84	1.09	0.76
	1-palmitoyl-2-arachidonoyl-GPE (16:0/20:4)*	0.74	1.36	1.07	0.95	0.85
	1-palmitoyl-2-docosahexaenoyl-GPE (16:0/22:6)*	0.72	0.99	0.96	0.74	0.82
	1-stearoyl-2-oleoyl-GPE (18:0/18:1)	0.69	1.18	0.98	0.84	0.89
	1-stearoyl-2-linoleoyl-GPE (18:0/18:2)*	0.67	1.31	0.92	0.95	0.76
	1-stearoyl-2-arachidonoyl-GPE (18:0/20:4)	0.73	1.15	1.07	0.78	0.80
	1-stearoyl-2-docosahexaenoyl-GPE (18:0/22:6)*	0.69	0.95	0.86	0.76	0.79



Muscle

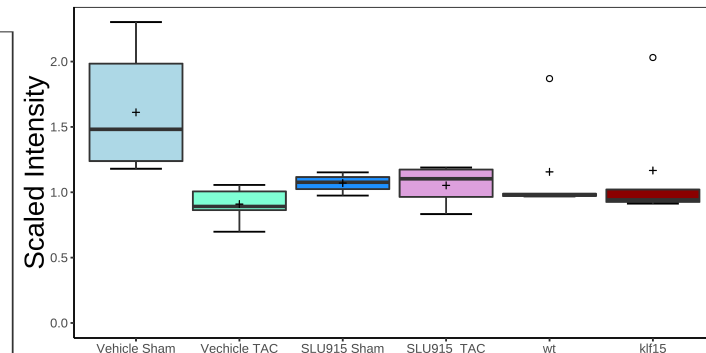
Sub Pathway	Biochemical Name	Fold of Change
		Welch's t-Test
		SLU-PP-332 VEHICLE
Phospholipid Metabolism	choline	1.35
	choline phosphate	0.82
	glycerophosphorylcholine (GPC)	1.29
	phosphoethanolamine	1.20
	glycerophosphoethanolamine	1.29
Phosphatidylcholine (PC)	1-palmitoyl-2-stearoyl-GPC (16:0/18:0)	1.21
Sphingolipid Synthesis	sphinganine	1.33
	sphingadienine	1.30
Mevalonate Metabolism	3-hydroxy-3-methylglutarate	1.30
Sterol	cholesterol	1.19
	7-alpha-hydroxy-3-oxo-4-cholestenate (7-Hcca)	1.45
	4-cholesten-3-one	1.70

1-palmitoyl-2-stearoyl-GPC (16:0/18:0)



Muscle

1-palmitoyl-2-stearoyl-GPE (16:0/18:0)*
Mass Normalized

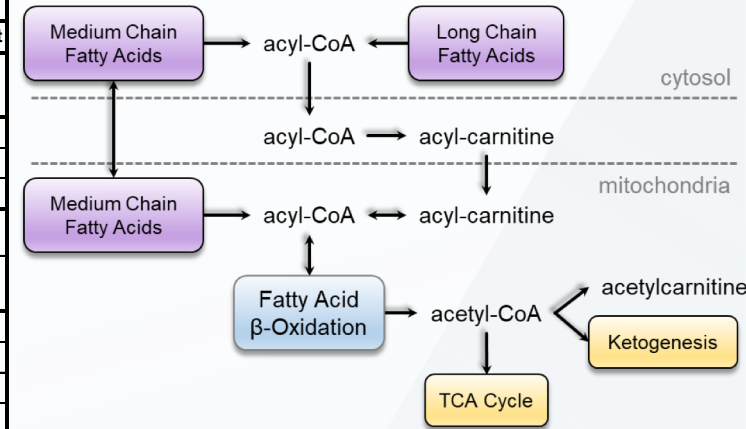


Heart

Differences in Fatty Acid Metabolism

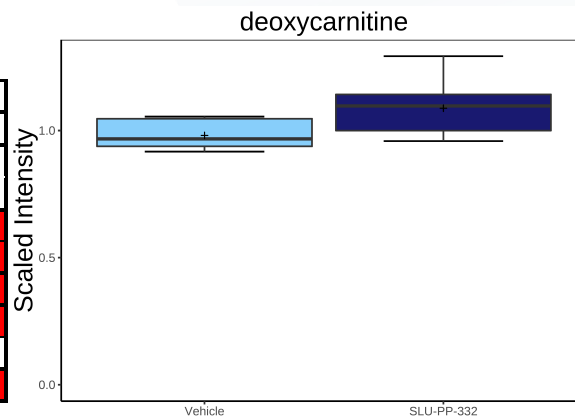
Heart

Sub Pathway	Biochemical Name	Fold of Change				
		Mass Normalized				
		Two Way ANOVA				Welch's t-Test
		(SHAM SLU915) (SHAM_VEHICLE)	(TAC SLU915) (SHAM_SLU915)	(TAC SLU915) (TAC_VEHICLE)	(TAC_VEHICLE) (SHAM_VEHICLE)	
Medium Chain Fatty Acid	caprate (10:0)	0.53	0.80	0.75	0.57	0.80
	(2 or 3)-decanoate (10:1n7 or n8)	0.27	0.96	0.41	0.64	0.79
	5-dodecanoate (12:1n7)	0.33	1.29	0.73	0.59	1.11
Long Chain Polyunsaturated Fatty Acid (n3 and n6)	tetradecadienoate (14:2)*	0.52	1.14	0.86	0.69	0.86
	hexadecatrienoate (16:3n3)	0.32	1.09	0.71	0.50	0.76
Fatty Acid Metabolism (Acyl Carnitine, Medium Chain)	hexanoylcarnitine (C6)	0.29	1.30	0.84	0.44	1.08
	octanoylcarnitine (C8)	0.25	1.36	0.67	0.52	0.80
	nonanoylcarnitine (C9)	0.28	1.58	0.72	0.62	1.00
	decanoylcarnitine (C10)	0.26	1.42	0.77	0.48	1.30
	laurylcarnitine (C12)	0.21	1.36	0.71	0.41	1.25
Fatty Acid Metabolism (Acyl Carnitine, Long Chain Saturated)	myristoylcarnitine (C14)	0.15	1.49	0.65	0.35	1.73
	pentadecanoylcarnitine (C15)*	0.24	1.81	1.15	0.37	1.35
	palmitoylcarnitine (C16)	0.18	1.92	0.97	0.35	1.70
	margaroylcarnitine (C17)*	0.30	1.53	1.02	0.45	1.26
	stearoylcarnitine (C18)	0.54	1.13	1.28	0.48	1.23
	arachidoylcarnitine (C20)*	0.34	1.36	1.17	0.40	1.63



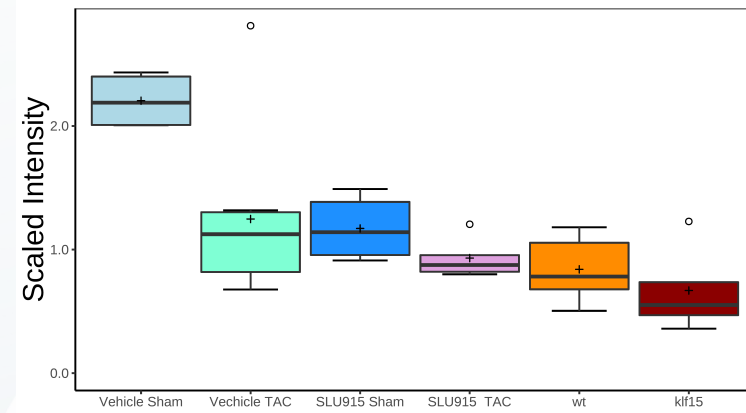
Muscle

Sub Pathway	Biochemical Name	Fold of Change
		Welch's t-Test
		SLU-PP-332 VEHICLE
Fatty Acid, Dicarboxylate	2-hydroxyadipate	1.41
	sebacate (C10-DC)	1.41
Carnitine Metabolism	deoxycarnitine	1.11
Fatty Acid Metabolism (Acyl Choline)	palmitoylcholine	1.43
	oleoylcholine	1.36
Fatty Acid, Monohydroxy	4-hydroxybutyrate (GHB)	1.29



Muscle

caprate (10:0)
Mass Normalized



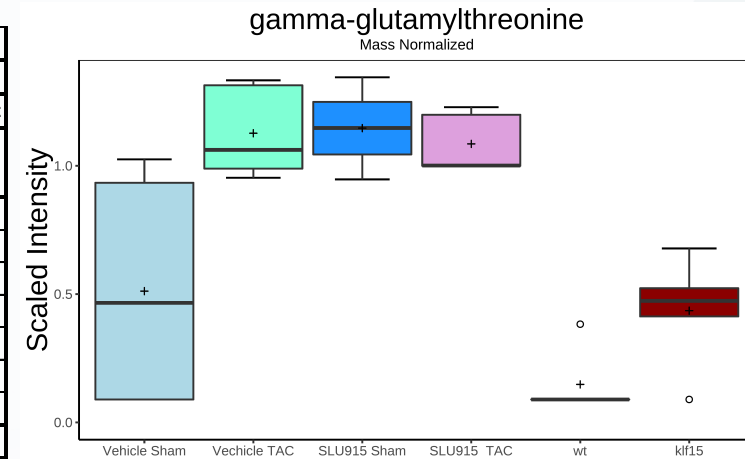
Heart

Differences in Oxidative Stress Metabolites

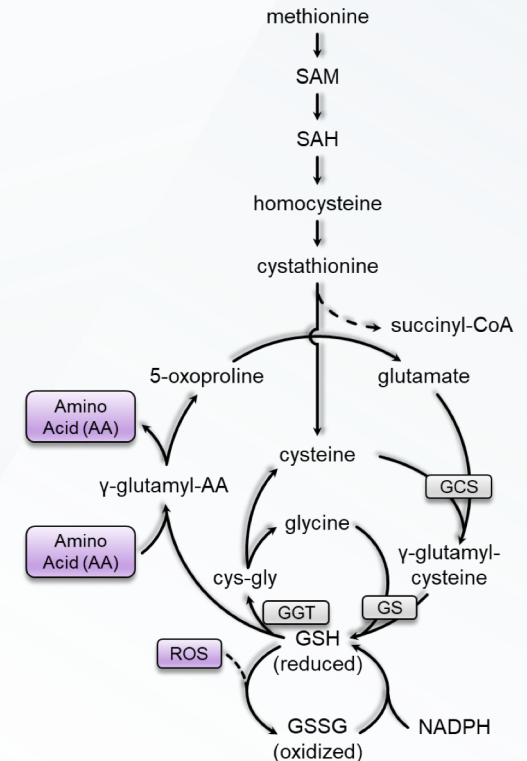


Heart

Sub Pathway	Biochemical Name	Fold of Change				
		Mass Normalized				
		Two Way ANOVA				Welch's t-Test
		(SHAM SLU915) (SHAM_VEHICLE)	(TAC SLU915) (SHAM_SLU915)	(TAC SLU915) (TAC_VEHICLE)	(TAC VEHICLE) (SHAM_VEHICLE)	(KLF15) (WT)
Methionine, Cysteine, SAM and Taurine Metabolism	N-formylmethionine	1.07	1.14	0.97	1.25	1.11
	S-adenosylhomocysteine (S	0.96	0.78	1.09	0.69	1.08
	cysteine	1.24	1.04	1.09	1.17	1.18
	hypotaurine	0.74	0.93	1.12	0.61	1.16
	taurine	0.85	1.05	1.01	0.88	0.93
	succinoyltaurine	1.02	1.20	1.32	0.93	0.81
	taurocyamine	0.63	1.31	0.63	1.31	1.03
Glutathione Metabolism	glutathione, reduced (GSH)	1.43	0.85	1.47	0.83	0.95
	cysteine-glutathione disulfid	1.58	1.04	0.59	2.77	1.69
	S-methylglutathione	0.88	1.02	1.05	0.85	1.32
	S-lactoylglutathione	1.92	0.80	1.53	1.00	0.92
	cysteinyglycine	2.09	0.80	1.39	1.20	1.30
	ophthalmate	1.31	0.86	1.14	0.99	1.71
Gamma-glutamyl Amino Acid	gamma-glutamylleucine	1.30	1.04	1.19	1.14	1.40
	gamma-glutamyl-alpha-lysin	2.02	1.04	1.19	1.76	3.06
	gamma-glutamylthreonine	2.24	0.95	0.96	2.20	2.94
	gamma-glutamylvaline	2.20	0.98	1.13	1.91	1.00

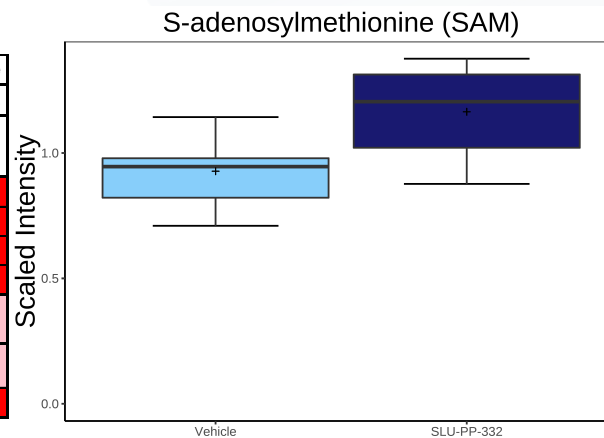


Heart



Muscle

Sub Pathway	Biochemical Name	Fold of Change
		Welch's t-Test
		SLU-PP-332 VEHICLE
Methionine, Cysteine, SAM and Taurine Metabolism	S-methylmethionine	3.23
	methionine sulfone	1.58
	S-adenosylmethionine (SAM)	1.26
	N-acetyltaurine	1.16
Glutathione Metabolism	5-oxoproline	1.14
Gamma-glutamyl Amino Acid	gamma-glutamylleucine	1.26
	gamma-glutamylvaline	1.30



Muscle



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