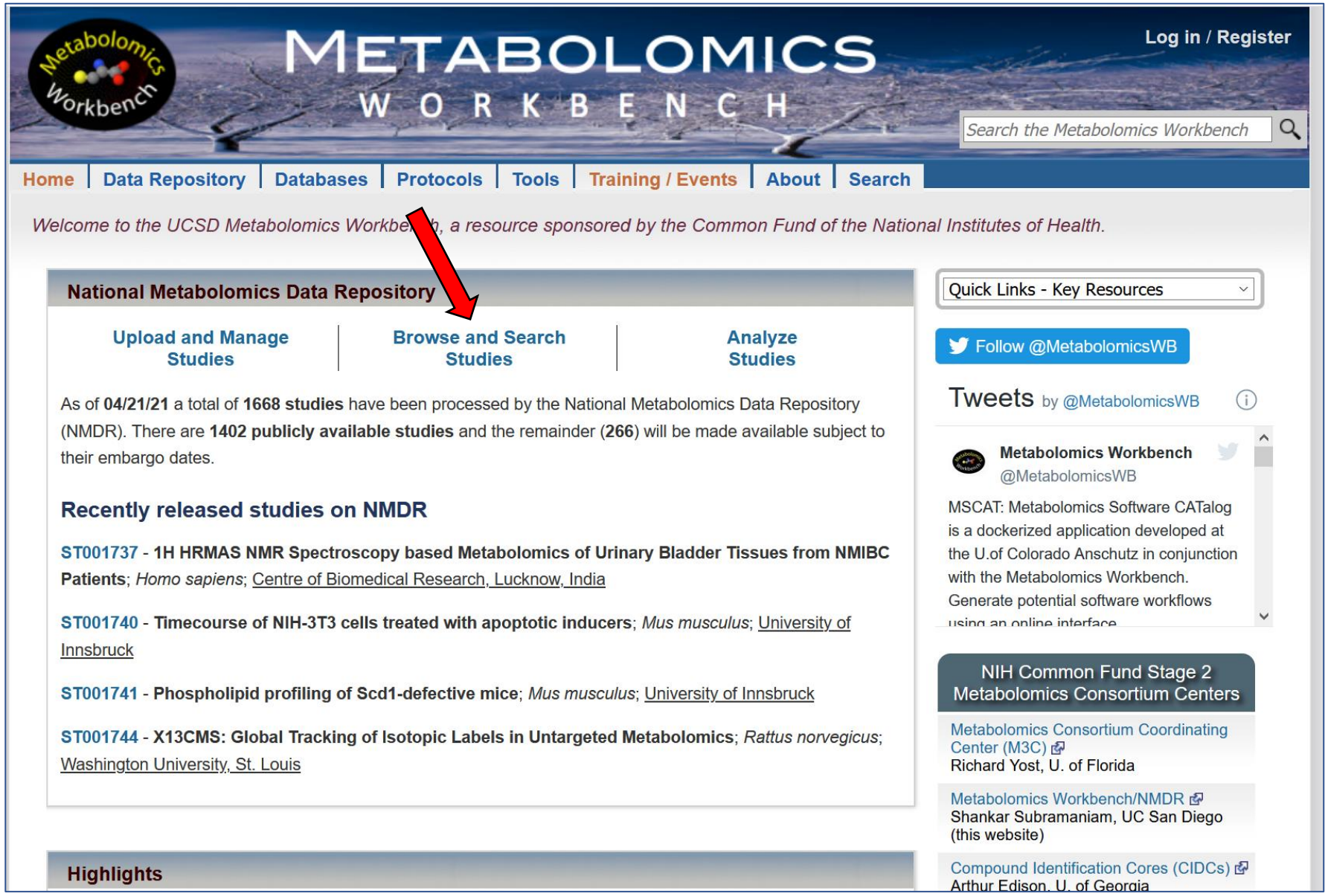
Using MetStat to view typical concentration ranges for a metabolite of interest



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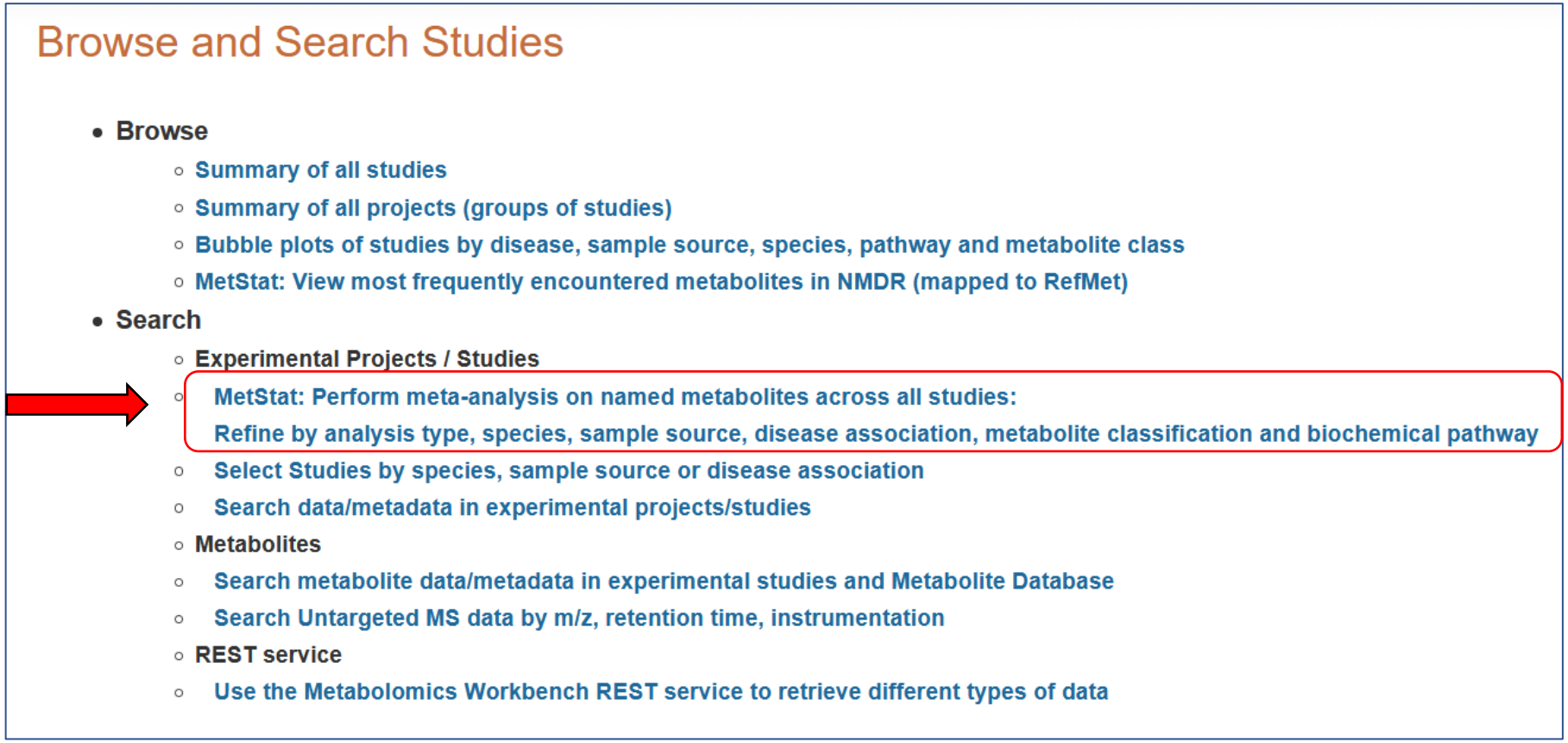


MetStat query buider: Select criteria, e.g. species, sample source, analysis type, ion mode, disease association, metabolite class, etc.

MetStat: Generate Metabolite report for studies on the Metabolomics Workbench

Tables of metabolites (identified by RefMet name) show the **number of unique studies containing that metabolite** along with the median value of the **relative standard deviation (RSD)** across all those studies. (RSD=100*Std.Deviation/mean). RSD is first calculated for each experimental condition within each analysis to assess the variance across sample replicates.
The RefMet metabolite names are mapped to the **MW classification system** and displayed as "Main class" and "Sub class". Rows are also color-coded based on 11 top-level classification groups: Amino acids/peptides, Glycerolipids, Fatty acyls, Terpenoids, Sugars, Phospholipids, Sterols, Sphingolipids, Nucleic acids, Flavonoids and "Others".
ANOVA p-values and FDR-corrected values are calculated for each metabolite and each distinct experimental condition in every analysis.
RefMet metabolite names are hyperlinked to the molecular structures in the MW database and to the relevant **biochemical pathways** in HMDB and KEGG (where applicable)

Analysis Type:		**MS Ion Mode:**	
Chromatography Type:			
Disease:			
Sample source:	Blood (183)		
Species:	Human (183)	**Sp. class:**	
RefMet name:	Contains	(case insensitive)	
Metabolite superclass:	All		
Human pathway:			
Records to display:	200	Generate	Reset

1 Amino acid/peptides
2 Glycerolipids
3 Fatty acyls
4 Terpenoids
5 Sugars
6 Phospholipids
7 Sterols
8 Sphingolipids
9 Nucleic acids
10 Flavonoids
11 Others

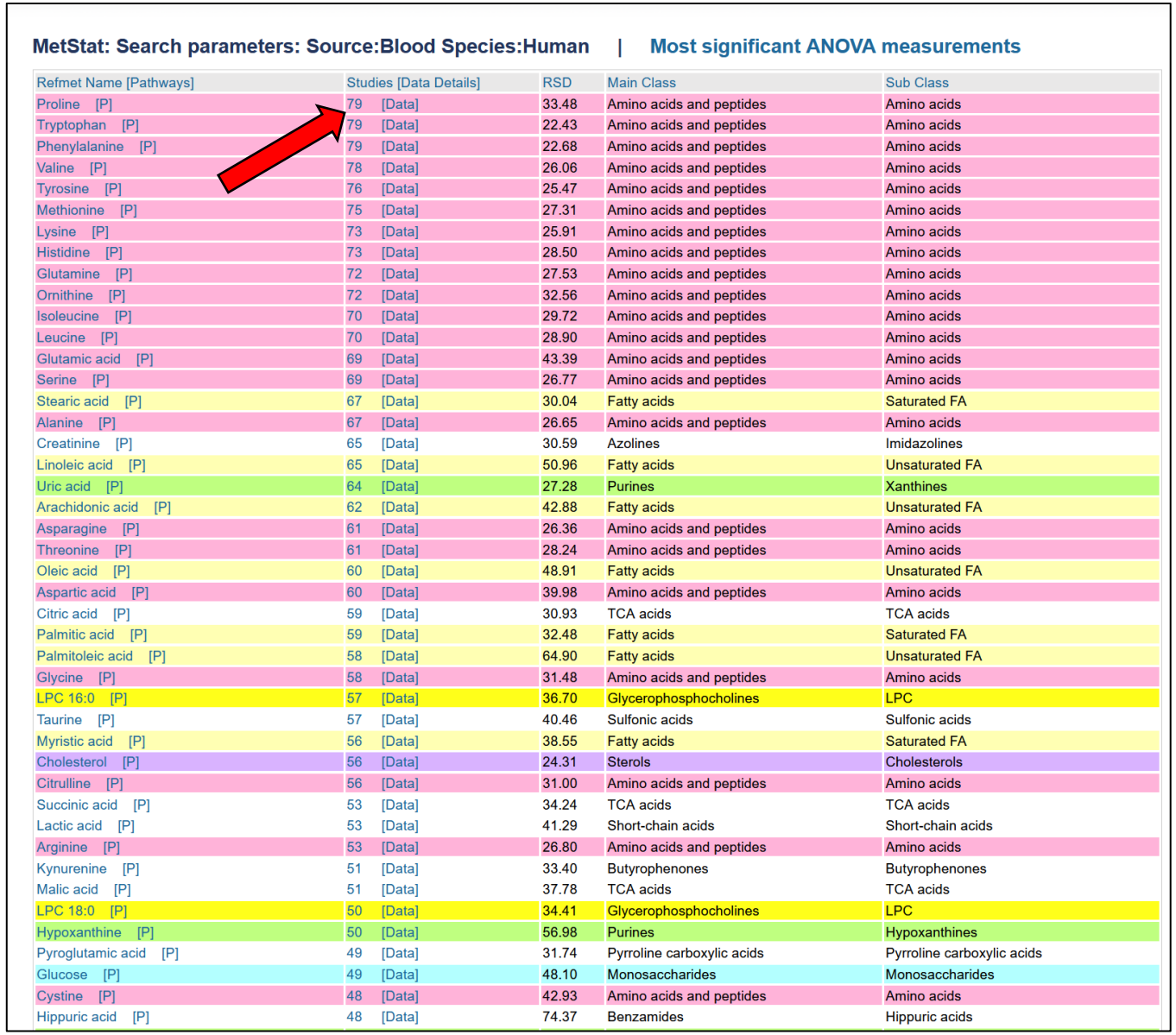
In this example, all human studies with blood* as the sample source are selected

*** "Blood" may refer to whole blood, serum or plasma-see individual study metadata for details**

MetStat summary table of human metabolites detected in blood

Sorted by number of studies in which that metabolite is reported

Click on “Studies” link for a metabolite of interest



MetStat: Search parameters: Source:Blood Species:Human | Most significant ANOVA measurements

Refmet Name [Pathways]	Studies [Data Details]	RSD	Main Class	Sub Class
Proline [P]	79 [Data]	33.48	Amino acids and peptides	Amino acids
Tryptophan [P]	79 [Data]	22.43	Amino acids and peptides	Amino acids
Phenylalanine [P]	79 [Data]	22.68	Amino acids and peptides	Amino acids
Valine [P]	78 [Data]	26.06	Amino acids and peptides	Amino acids
Tyrosine [P]	76 [Data]	25.47	Amino acids and peptides	Amino acids
Methionine [P]	75 [Data]	27.31	Amino acids and peptides	Amino acids
Lysine [P]	73 [Data]	25.91	Amino acids and peptides	Amino acids
Histidine [P]	73 [Data]	28.50	Amino acids and peptides	Amino acids
Glutamine [P]	72 [Data]	27.53	Amino acids and peptides	Amino acids
Ornithine [P]	72 [Data]	32.56	Amino acids and peptides	Amino acids
Isoleucine [P]	70 [Data]	29.72	Amino acids and peptides	Amino acids
Leucine [P]	70 [Data]	28.90	Amino acids and peptides	Amino acids
Glutamic acid [P]	69 [Data]	43.39	Amino acids and peptides	Amino acids
Serine [P]	69 [Data]	26.77	Amino acids and peptides	Amino acids
Stearic acid [P]	67 [Data]	30.04	Fatty acids	Saturated FA
Alanine [P]	67 [Data]	26.65	Amino acids and peptides	Amino acids
Creatinine [P]	65 [Data]	30.59	Azolines	Imidazolines
Linoleic acid [P]	65 [Data]	50.96	Fatty acids	Unsaturated FA
Uric acid [P]	64 [Data]	27.28	Purines	Xanthines
Arachidonic acid [P]	62 [Data]	42.88	Fatty acids	Unsaturated FA
Asparagine [P]	61 [Data]	26.36	Amino acids and peptides	Amino acids
Threonine [P]	61 [Data]	28.24	Amino acids and peptides	Amino acids
Oleic acid [P]	60 [Data]	48.91	Fatty acids	Unsaturated FA
Aspartic acid [P]	60 [Data]	39.98	Amino acids and peptides	Amino acids
Citric acid [P]	59 [Data]	30.93	TCA acids	TCA acids
Palmitic acid [P]	59 [Data]	32.48	Fatty acids	Saturated FA
Palmitoleic acid [P]	58 [Data]	64.90	Fatty acids	Unsaturated FA
Glycine [P]	58 [Data]	31.48	Amino acids and peptides	Amino acids
LPC 16:0 [P]	57 [Data]	36.70	Glycerophosphocholines	LPC
Taurine [P]	57 [Data]	40.46	Sulfonic acids	Sulfonic acids
Myristic acid [P]	56 [Data]	38.55	Fatty acids	Saturated FA
Cholesterol [P]	56 [Data]	24.31	Sterols	Cholesterols
Citrulline [P]	56 [Data]	31.00	Amino acids and peptides	Amino acids
Succinic acid [P]	53 [Data]	34.24	TCA acids	TCA acids
Lactic acid [P]	53 [Data]	41.29	Short-chain acids	Short-chain acids
Arginine [P]	53 [Data]	26.80	Amino acids and peptides	Amino acids
Kynurenine [P]	51 [Data]	33.40	Butyrophenones	Butyrophenones
Malic acid [P]	51 [Data]	37.78	TCA acids	TCA acids
LPC 18:0 [P]	50 [Data]	34.41	Glycerophosphocholines	LPC
Hypoxanthine [P]	50 [Data]	56.98	Purines	Hypoxanthines
Pyroglutamic acid [P]	49 [Data]	31.74	Pyrroline carboxylic acids	Pyrroline carboxylic acids
Glucose [P]	49 [Data]	48.10	Monosaccharides	Monosaccharides
Cystine [P]	48 [Data]	42.93	Amino acids and peptides	Amino acids
Hippuric acid [P]	48 [Data]	74.37	Benzamides	Hippuric acids

List of human studies on blood that report Proline

List of Studies (Metabolite:Proline Source:Blood Species:Human)

Study_id	Analysis_id	Study_title	Source	Species	Disease	Institute	Units(range)
ST001037	AN001698	High Resolution GC-MS and FID Metabolomics of Human Serum	Blood	Human		Wake Forest Baptist Medical Center	Abundance
ST000450	AN000705	Metabolic features of chronic fatigue syndrome	Blood	Human	Chronic fatigue syndrome	University of California, San Diego	Area under curve
ST000617	AN000947	Validation of the application of targeted metabolomic appraoch in the diagnosis of CFS	Blood	Human	Chronic fatigue syndrome	University of California, San Diego	Area under curve
ST000041	AN000062	High PUFA diet in humans	Blood	Human		University of Michigan	Counts
ST000041	AN000063	High PUFA diet in humans	Blood	Human		University of Michigan	Counts
ST000105	AN000173	SCOR Metabolomics	Blood	Human		University of Chicago	Counts
ST000105	AN000174	SCOR Metabolomics	Blood	Human		University of Chicago	Counts
ST000106	AN000175	IWMS Study 1:Weight comparison of obese and lean patients	Blood	Human	Obesity	University of Michigan	Counts
ST000106	AN000176	IWMS Study 1:Weight comparison of obese and lean patients	Blood	Human	Obesity	University of Michigan	Counts
ST000368	AN000602	Investigation of metabolomic blood biomarkers for detection of adenocarcinoma lung cancer	Blood	Human	Cancer	University of California, Davis	Counts

...

ST001515	AN002511	A Metabolomic Signature of Glucagon Action in Healthy Individuals with Overweight/Obesity Humans	Blood	Human	Obesity	Translational Research Institute-AdventHealth Orlando	scaled units
ST000091	AN000145	Quantitative Metabolomics by 1H-NMR and LC-MS/MS Confirms Altered Metabolic Pathways in Diabetes	Blood	Human	Diabetes	Mayo Clinic	uM
ST000137	AN000219	Metabolomics in sarcoidosis	Blood	Human	Sarcoidosis	Wayne State University	uM
ST000168	AN000262	Effect of Insulin Sensitizer Therapy on Amino Acids and Their Metabolites	Blood	Human	Diabetes	Mayo Clinic	uM
ST000435	AN000685	Quantitative measurements of amino acids in T1D poor control, good control, and controls.	Blood	Human	Diabetes	Mayo Clinic	uM
ST000483	AN000749	Amino Acid Quantifcation of obese patients on a 16 week caloric restriction from Plasma	Blood	Human	Obesity	Mayo Clinic	uM
ST000491	AN000757	Sleep apnea and cardiovascular samples amino acid metabolites	Blood	Human	Sleep apnea	Mayo Clinic	uM
ST000524	AN000802	Effects of Curcumin Supplementation on the Amino Acid Concentration of Older Adults: Relation to Vascular Function	Blood	Human	Heart disease	Mayo Clinic	uM
ST000605	AN000926	Whole blood reveals more metabolic detail of the human metabolome than serum as measured by 1H-NMR spectroscopy: Implications for sepsis metabolomics	Blood	Human		University of Michigan	uM
ST000641	AN000973	Targeted Amino Acids in American Indian Adolescents (part II)	Blood	Human	Diabetes	Mayo Clinic	uM
ST000783	AN001239	Absolute Quantification of 180 metabolites in serum from african american and european american in prostate cancer and case control samples	Blood	Human	Cancer	Baylor College of Medicine	uM
ST000785	AN001244	Pharmacometabolomics of L-Carnitine Treatment Response Phenotypes in Patients with Septic Shock	Blood	Human	Sepsis	University of Michigan	uM
ST000825	AN001311	CHEAR Christiani Biocrates	Blood	Human		RTI International	uM
ST000826	AN001414	CHEAR Christiani NMR	Blood	Human		RTI International	uM
ST000876	AN001413	Human serum for a patient with neuropathy being treated with L-serine.	Blood	Human	Neuropathy	University of Helsinki	uM
ST000944	AN001549	Amino Acids, Acylcarnitine, & Insulin for P20 Participants	Blood	Human		University of Michigan	uM
ST000995	AN001624	Amino Acid Concentrations of Primary Sclerosing Cholangitis (part I)	Blood	Human		Mayo Clinic	uM
ST001012	AN001654	Amino Acid Concentrations in Serum for Muscle Wasting in Cancer Cachexia (part-VII)	Blood	Human	Cachexia	Mayo Clinic	uM
ST001097	AN001785	Metabolomics of Metabolic Risk in Patients Taking Atypical Antipsychotics	Blood	Human	Schizophrenia	University of Michigan	uM
ST001176	AN001952	Metabolite changes in human plasma before and after YF17D vaccination in symptomatic and asymptomatic subjects	Blood	Human	Yellow fever	Duke-NUS Medical School	uM
ST001295	AN002156	Estimating Platelet Mitochondrial Function in Patients with Sepsis - WB NMRs (part-II)	Blood	Human	Sepsis	University of Michigan, University of Mississippi, University of Minnesota	uM
ST001319	AN002195	Pre-treatment L-Carnitine Pharmacometabolomics in Sepsis (CaPS) Patients	Blood	Human	Sepsis	University of Michigan	uM
ST001354	AN002253	48 hours post-treatment L-Carnitine Pharmacometabolomics in Sepsis (CaPS) Patients	Blood	Human	Sepsis	University of Michigan	uM
ST001521	AN002533	Plasma metabolites of known identity profiled using hybrid nontargeted methods (part-III)	Blood	Human		Broad Institute of MIT and Harvard	unitless peak areas

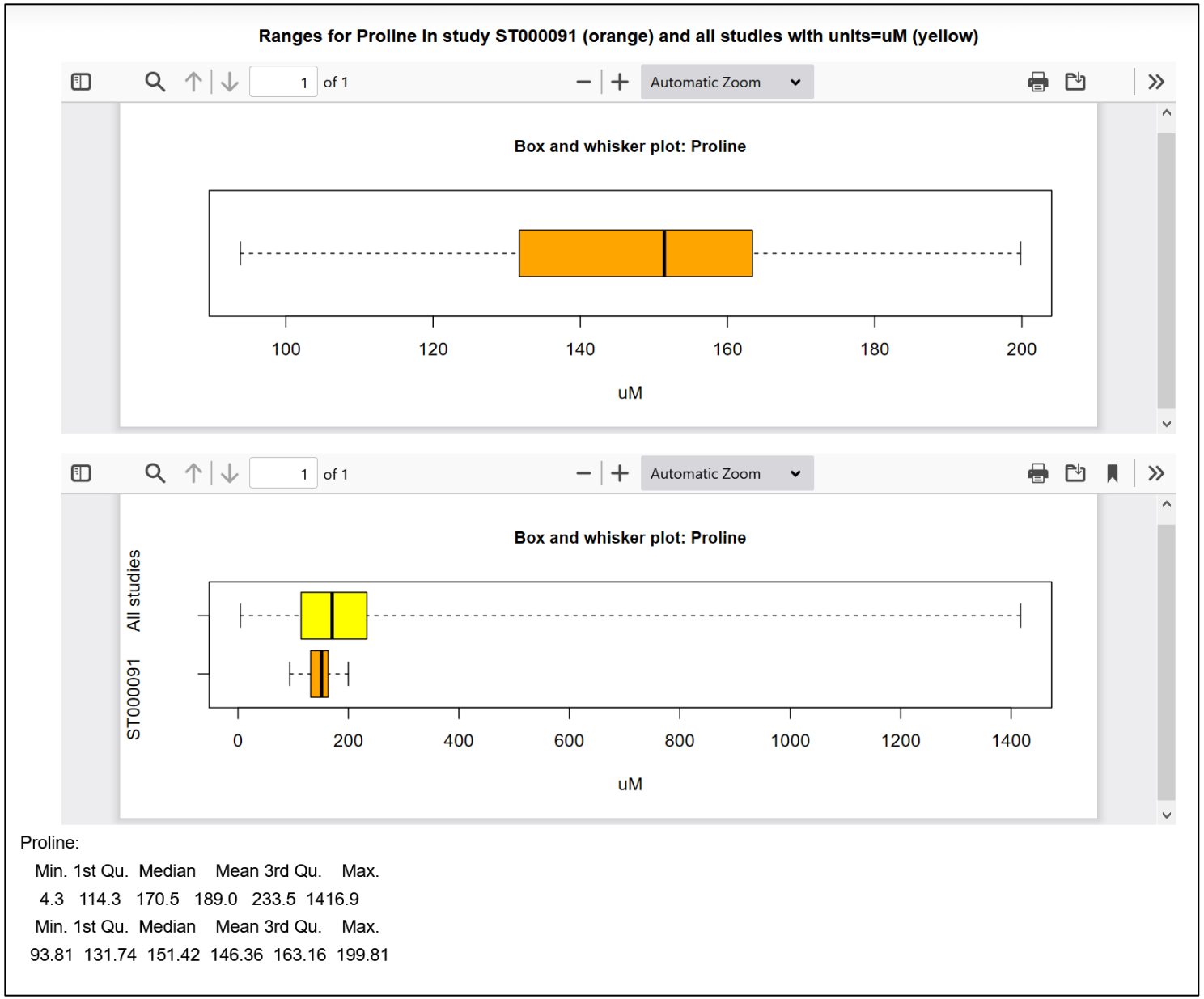
Click on a study link in the “Units(range) column

Focus on the targeted assays that report quantitative results (untargeted assays that report peak intensity, area, etc. are no good)

Boxplot for Proline in human blood

Study ST000091

Comparison with all studies (yellow) that report proline in human blood.
Notice the outlier(s) since 22 different studies are involved. However the median is not significantly affected



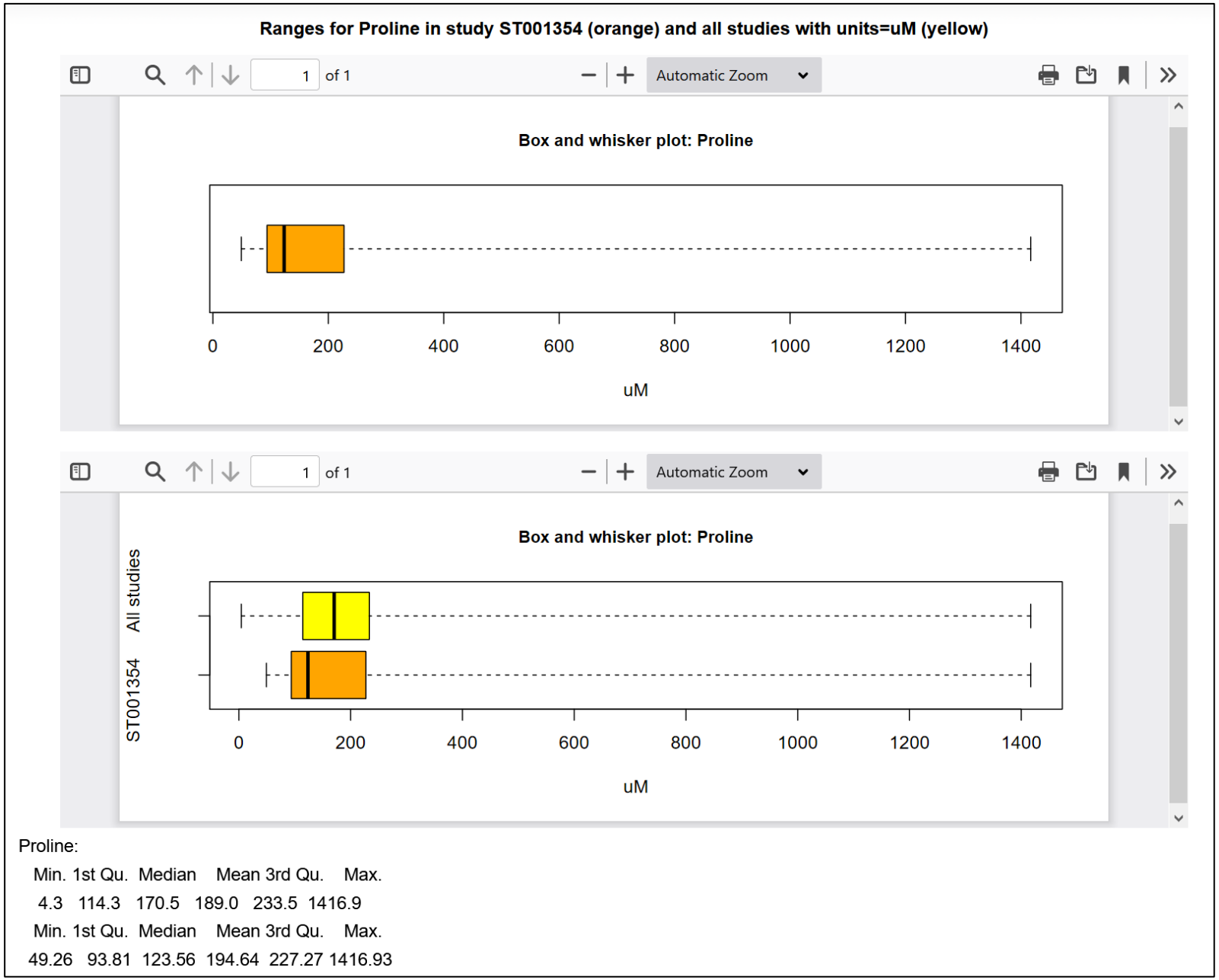
Proline:

Min.	1st Qu.	Median	Mean	3rd Qu.	Max.
4.3	114.3	170.5	189.0	233.5	1416.9

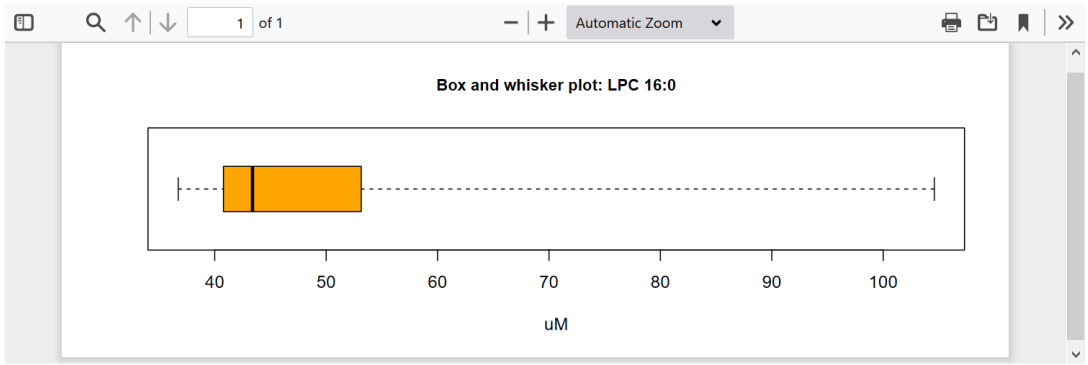
Min.	1st Qu.	Median	Mean	3rd Qu.	Max.
93.81	131.74	151.42	146.36	163.16	199.81

Boxplot for Proline in human blood

In this case Study ST001354 is the study containing the proline outlier



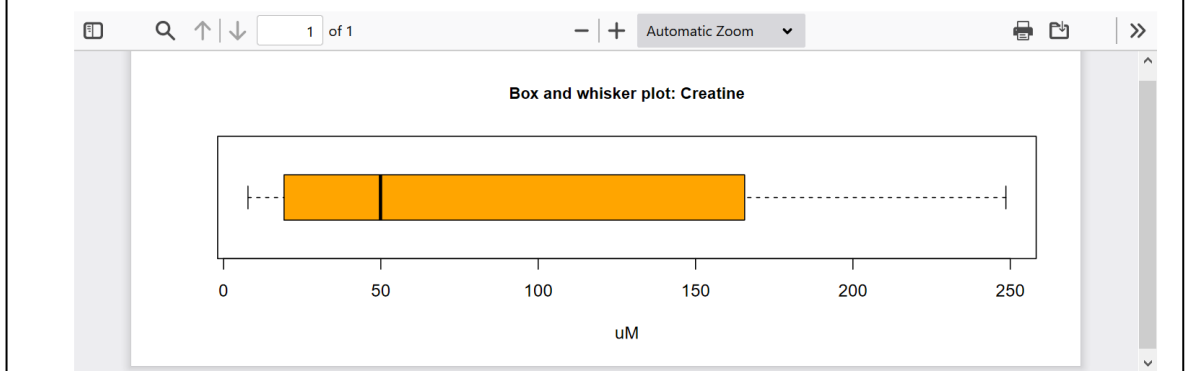
Boxplot for LPC 16:0 and Creatine in human blood



LPC 16:0:

Min.	1st Qu.	Median	Mean	3rd Qu.	Max.
0.01	53.90	78.80	80.14	110.00	279.00

Min.	1st Qu.	Median	Mean	3rd Qu.	Max.
36.72	41.83	43.39	50.16	52.20	104.59

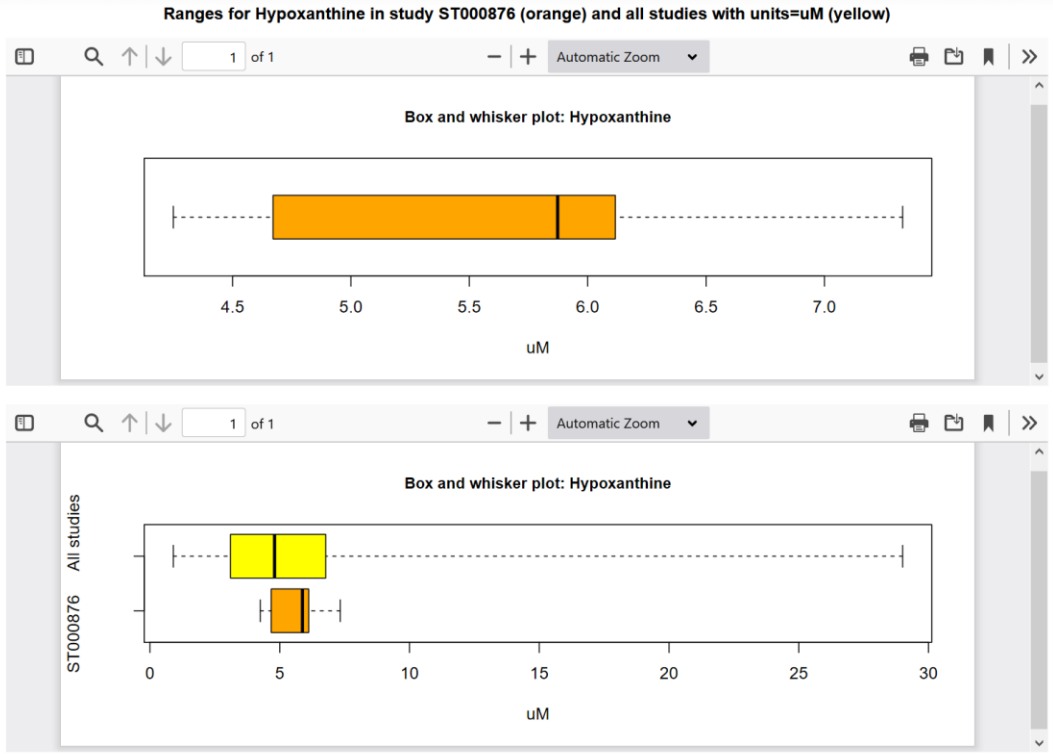


Creatine:

Min.	1st Qu.	Median	Mean	3rd Qu.	Max.
1.30	19.30	44.80	83.82	100.00	1420.41

Min.	1st Qu.	Median	Mean	3rd Qu.	Max.
7.80	19.25	49.90	90.42	165.60	248.60

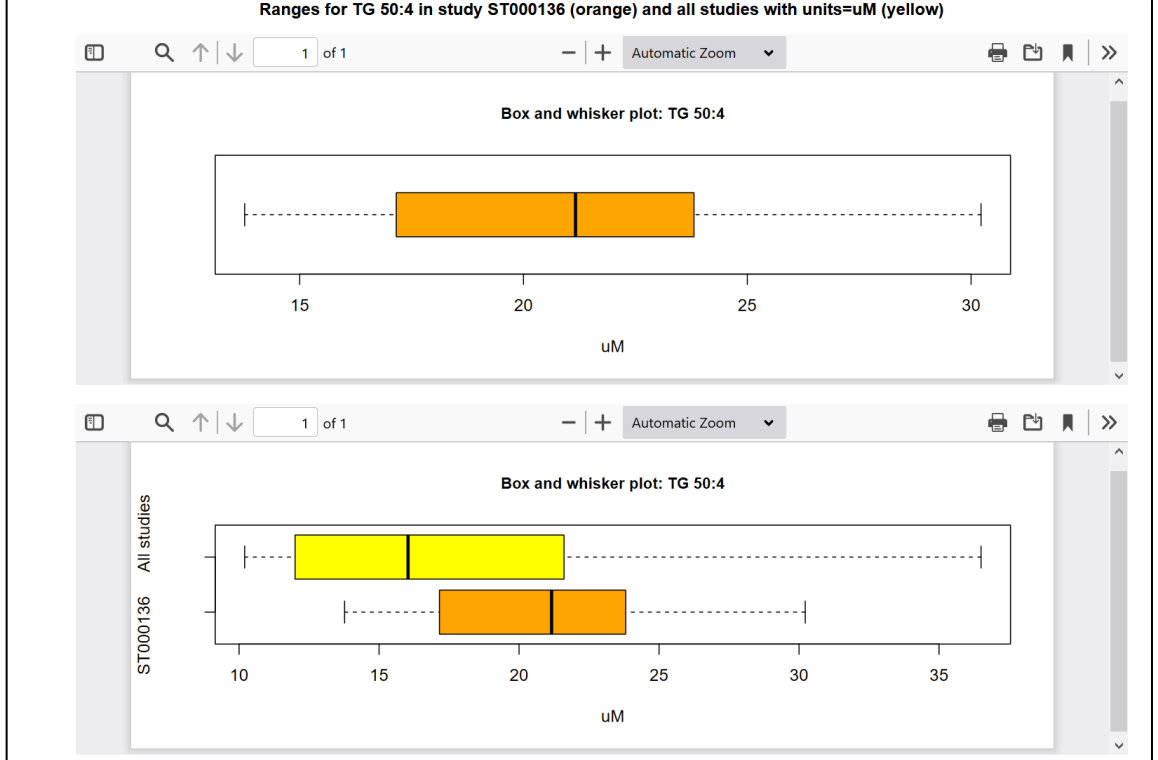
Boxplot for Hypoxanthine and TG 50:4 in human blood



Hypoxanthine:

Min.	1st Qu.	Median	Mean	3rd Qu.	Max.
0.900	3.100	4.800	6.223	6.775	29.000

Min.	1st Qu.	Median	Mean	3rd Qu.	Max.
4.250	4.671	5.873	5.689	6.117	7.330



TG 50:4:

Min.	1st Qu.	Median	Mean	3rd Qu.	Max.
10.20	12.03	16.04	17.88	21.38	36.50

Min.	1st Qu.	Median	Mean	3rd Qu.	Max.
13.77	18.00	21.16	20.72	23.32	30.22

Summary: Determining typical metabolite concentration ranges via MetStat in NMDR

The Metabolomics Workbench NMDR containing >1600 studies is a key resource for determining the typical concentration range for a metabolite of interest, based on species, sample source, analytical method, etc.

Focus on the (targeted) studies where quantitative methods were used (units in uM, uM/mg protein, etc) as opposed to untargeted studies (units in counts, peak intensity , peak area, etc)

Be aware that sample source is a “coarse-grained” designation, e.g “blood” could be either whole blood, serum or plasma- see individual study metadata for details

Be aware that these values represent ALL samples in a particular study, e.g. treated/untreated, controls/disease state- see individual study metadata for details

Median values and “box” ranges (middle 2 quartiles) are not heavily affected by extreme outliers and will improve in statistical reliability as more studies are added to NMDR