GBS 724
2-10-16

Pathway software and databases

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Synopsis

- Public and proprietary metabolite databases
  - Instrument manufacturers provide software and search tools for their proprietary databases
  - Usually a single copy of the software is provided
  - Sciex and Waters provide additional copies at >$35,000 for each
  - Metabolomics service companies have proprietary databases and do not allow investigators submitting samples to have access to them
    - This discourages deeper research to be performed on metabolomics data

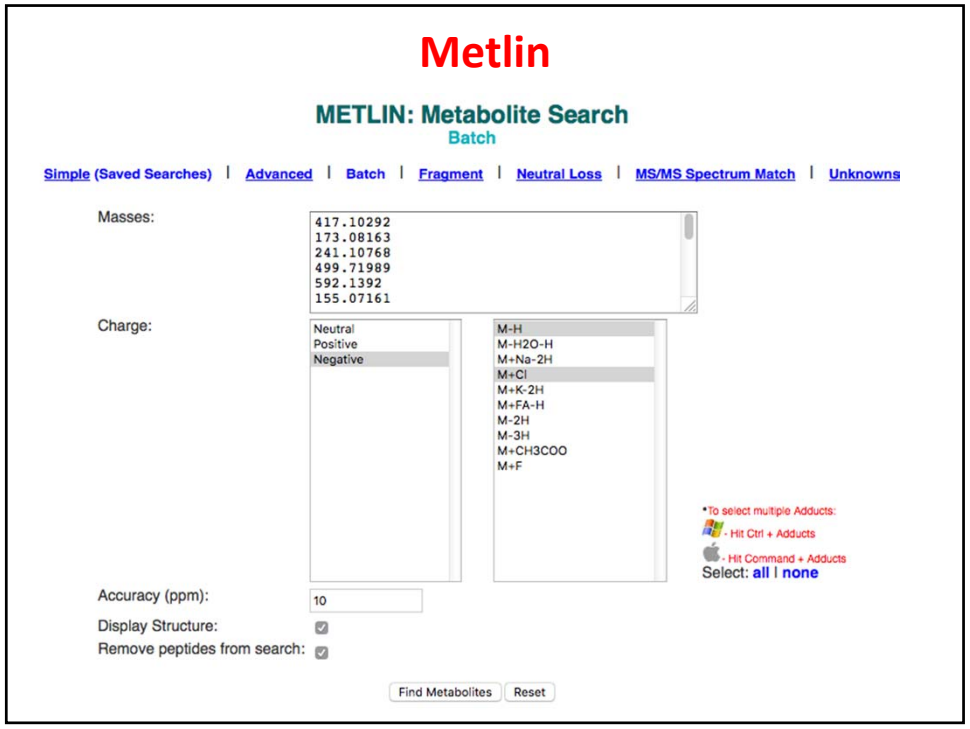
Public databases

- North America
  - Metlin (https://metlin.scripps.edu/index.php)
  - Human metabolomics database http://www.hmdb.ca/
  - PubChem http://pubchem.ncbi.nlm.nih.gov/
- Europe
  - ChemSpider (http://www.chemspider.com/)
- Asia
  - Kyoto Encyclopedia of Genes and Genomes (KEGG) (http://www.genome.jp/kegg/)

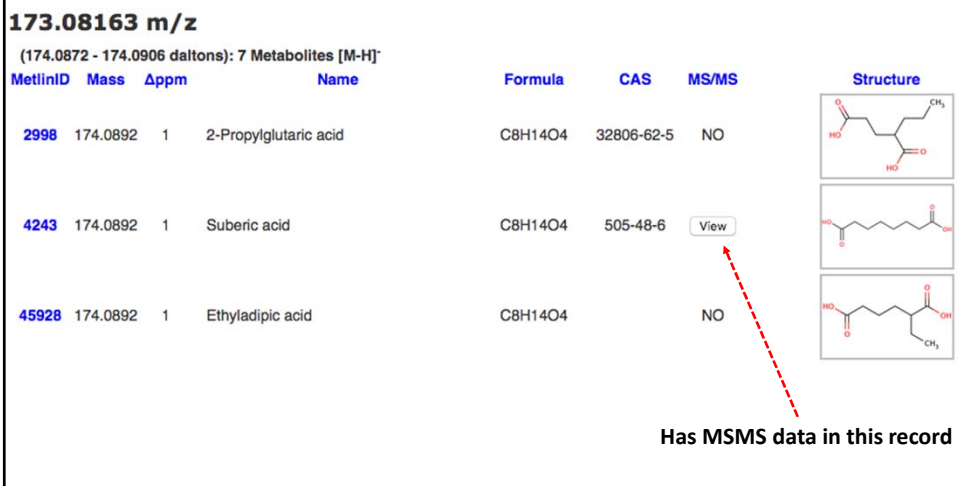
Choosing the ions to search

- Go to the Download file from Metaboanalyst and open the file "peak_normalized_rt_mz.csv"
- Use Excel to calculate the p-values for all the metabolites (they're ordered by m/z in the file)
- Now sort the entire file by the p-values
- Choose the ions with p-values <0.001 (there should be 80) and copy them into a Word file and save the file
  - We'll search these in multiple databases

Metlin



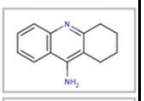
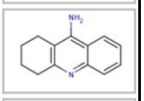
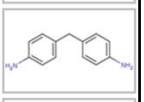
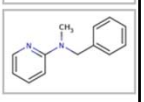
Metlin output-1



Metlin output-2

197.11032 m/z

(198.1156 - 198.1196 daltons): 4 Metabolites [M-H]⁻

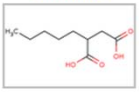
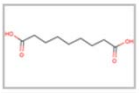
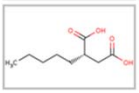
MetlinID	Mass	Δppm	Name	Formula	CAS	MS/MS	Structure
44521	198.1157	9	9-AMINO-1,2,3,4-TETRAHYDROACRIDINE	C13H14N2	NA	View	
2616	198.1157	9	Tacrine	C13H14N2	321-64-2	View	
69942	198.1157	9	4,4'-Methylenedianiline	C13H14N2	101-77-9	NO	
70631	198.1157	9	N-(Phenylmethyl)-N-methyl-2-pyridinamine	C13H14N2		NO	

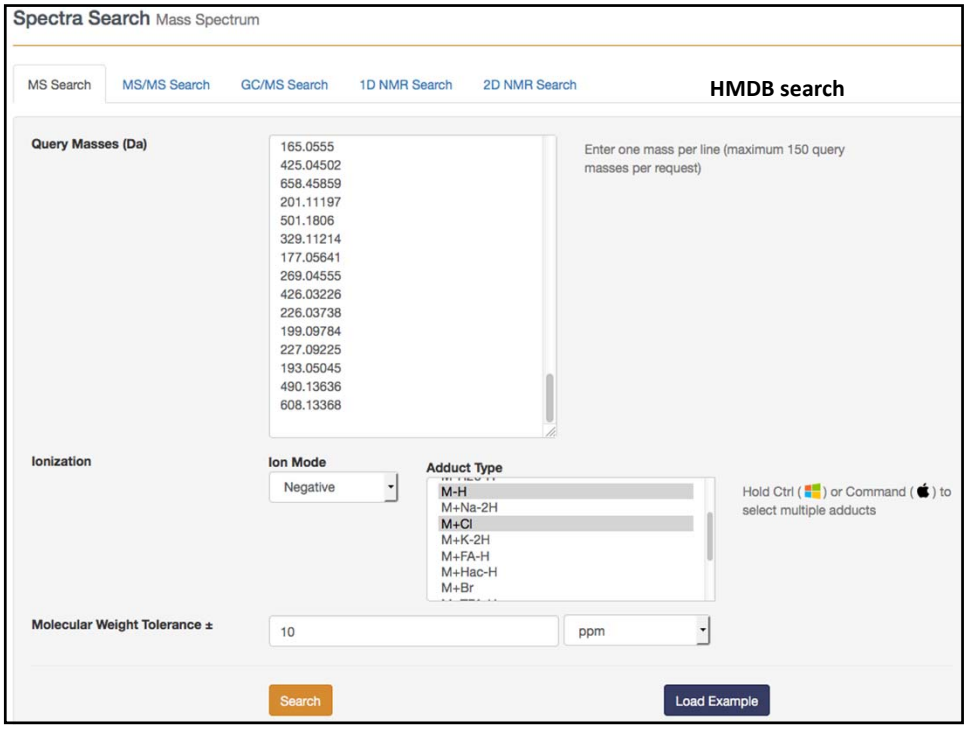
Unlikely fits – high Δ ppm

Metlin output-3

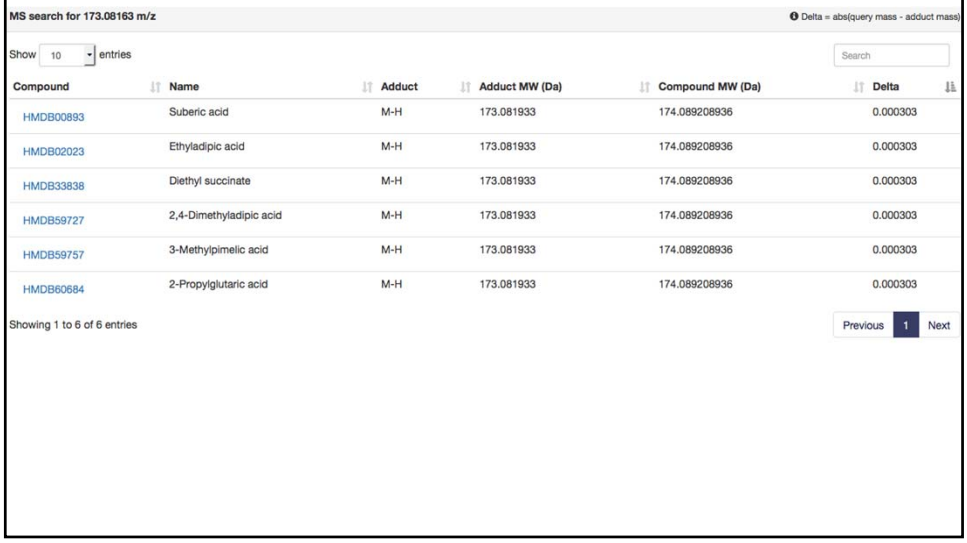
187.09745 m/z

(188.1029 - 188.1066 daltons): 8 Metabolites [M-H]⁻

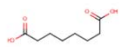
MetlinID	Mass	Δppm	Name	Formula	CAS	MS/MS	Structure
44183	188.1049	0	NONIC ACID	C9H16O4		View	
5750	188.1049	0	Nonanedioic acid	C9H16O4		View	
62450	188.1049	0	Nonate	C9H16O4		NO	

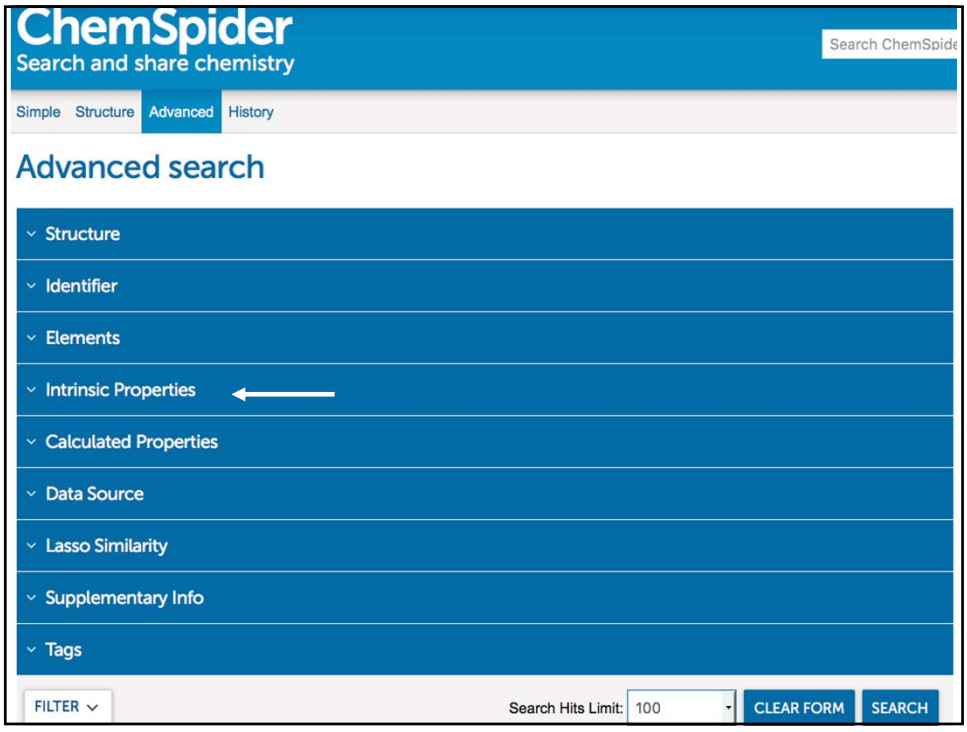


HMDB search output-1

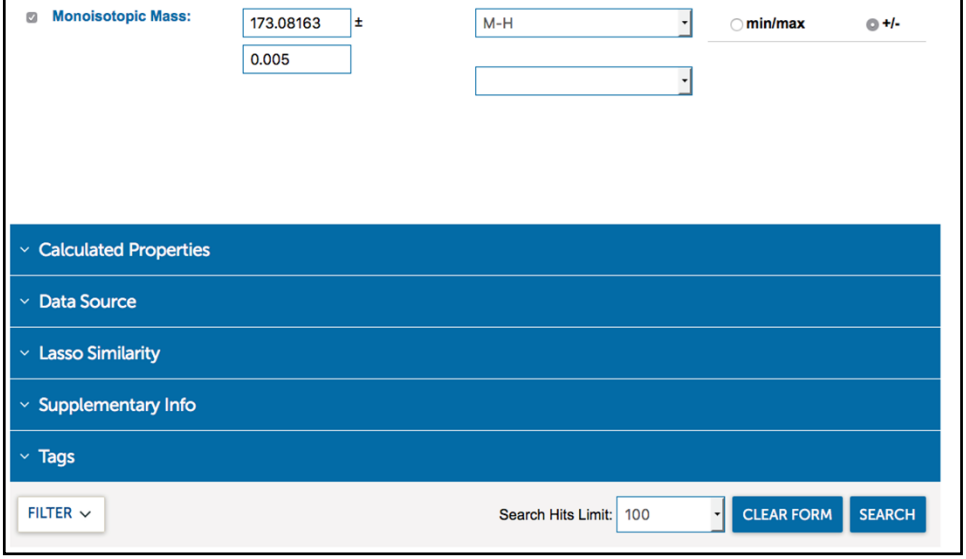


Click on HMDB record

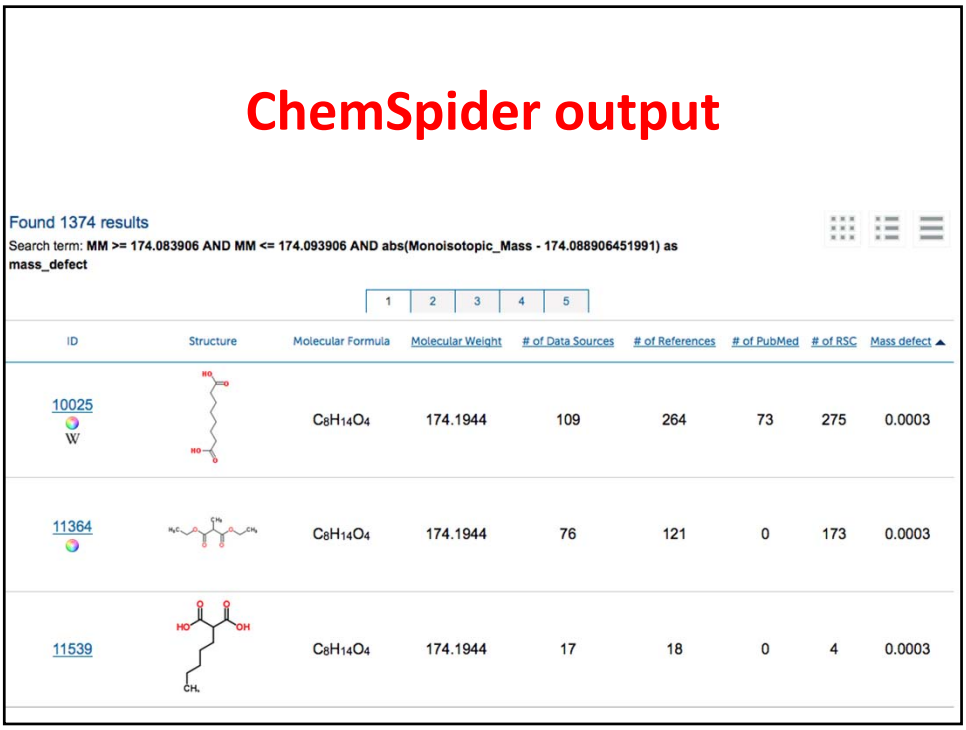
Record Information	
Version	3.6
Creation Date	2005-11-16 15:48:42 UTC
Update Date	2015-12-02 05:10:07 UTC
HMDB ID	HMDB00893
Secondary Accession Numbers	• HMDB00837
Metabolite Identification	
Common Name	**Suberic acid**
Description	Suberic acid, also octanedioic acid, is a dicarboxylic acid, with formula C6H12(COOH)2. It is present in the urine of patients with Fatty Acid Oxidation Disorders (PMID 10404733). A metabolic breakdown product derived from oleic acid. Elevated levels of this unstaruated dicarboxylic acid are found in individuals with dicarboxylic acid and medium-chain acyl-CoA dehydrogenase deficiency (MCAD).
Structure	 MOL SDF PDB SMILES InChI
Synonyms	1. 1,6-Dicarboxyhexane 2. 1,6-Hexanedicarboxylate 3. 1,6-Hexanedicarboxylic acid 4. 1,8-Octanedioate 5. 1,8-Octanedioic acid 6. Cork acid



Searching in ChemSpider



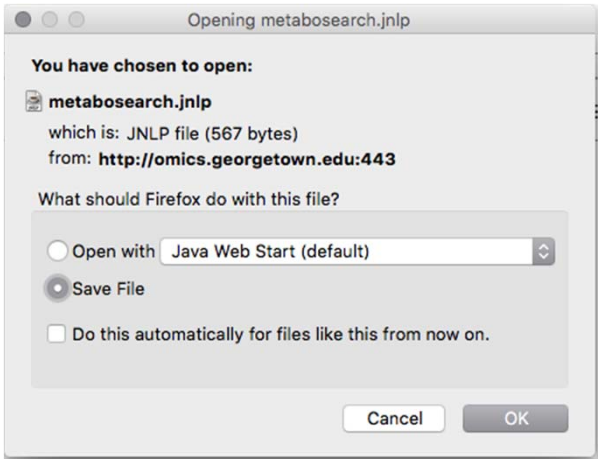
ChemSpider output



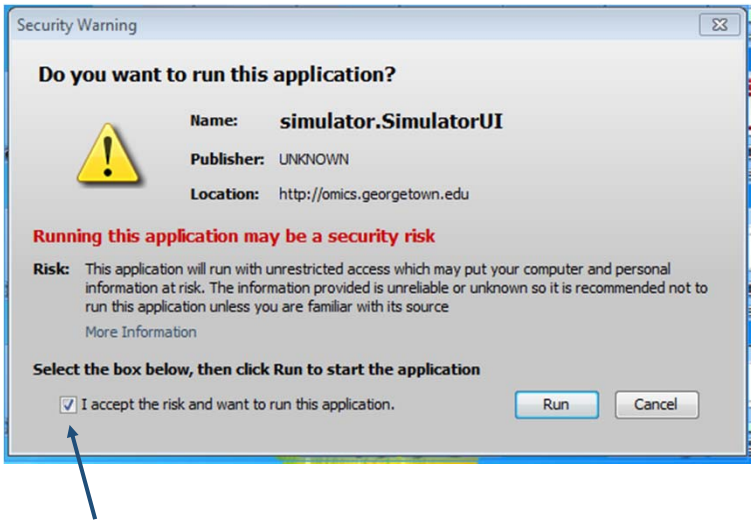
MetaboSearch

- **Find MetaboSearch using your browser**
  - **it's at http://omics.georgetown.edu/metabosearch.html**

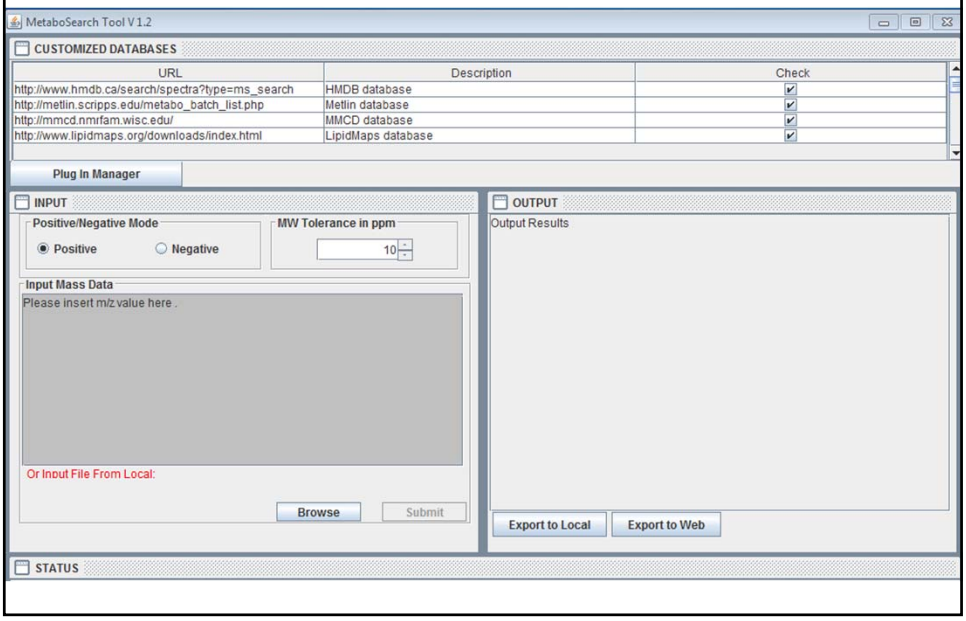
Download at Ressom lab



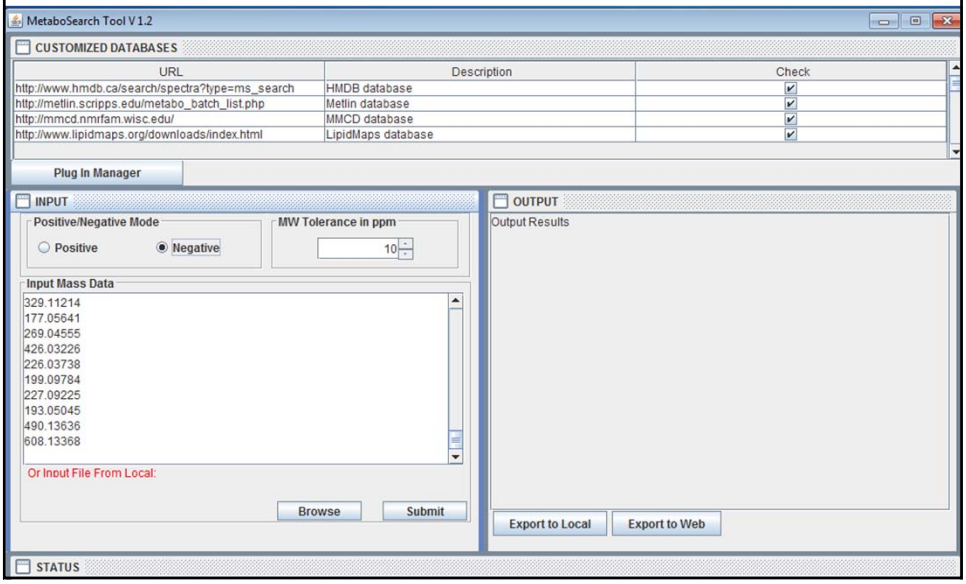
Opening MetaboSearch gives you this



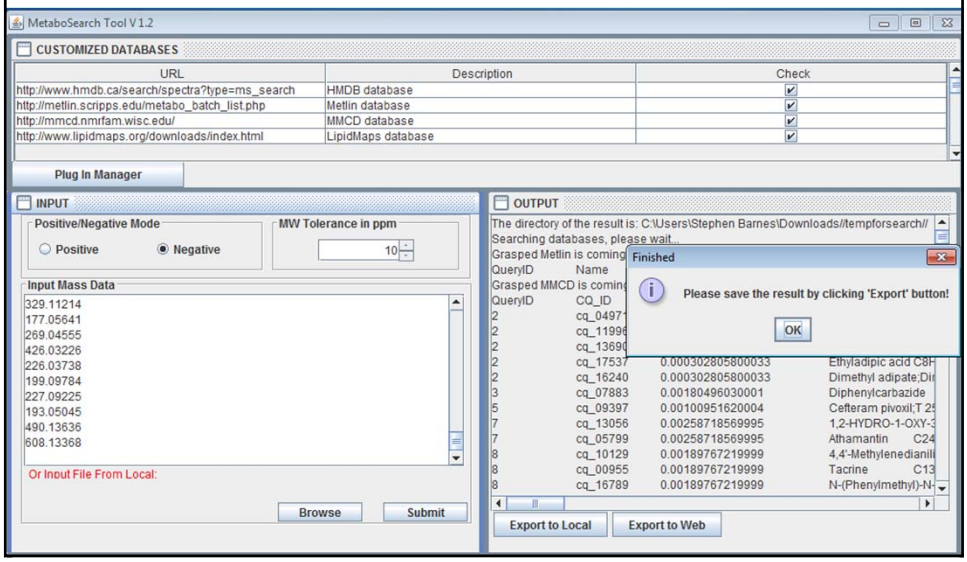
MetaboSearch set up page



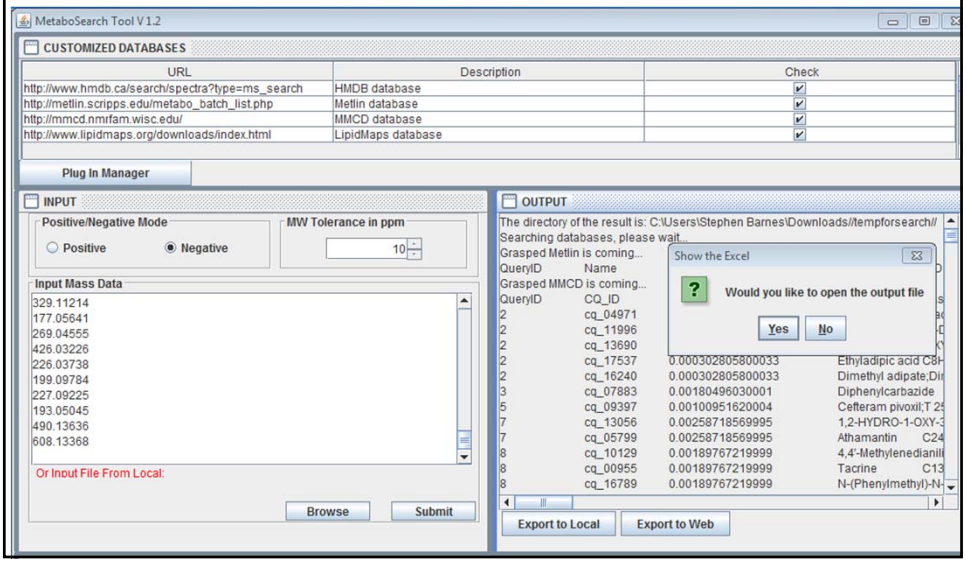
Data loaded – note negative ions



MetaboSearch completed



Opening Metabosearch file



MetaboSearch output

A	B	C	D	E	F	G	H	I	J	K	L	M
Query_ID	Query_m/	Input_RT	Name	Formula	Exact_Ma	KEGG ID	PubChem	PubChem	HMDB ID	Databases	dppm	Delta
1	417.1029	-	-	-	-	-	-	-	-	-	-	-
2	173.0816	-	[O4]-ACETOXY-2,3-DIDEOXYFI	C8H14O4	174.0892	-	-	-	-	MMCD	1.665336	2.90E-04
2	173.0816	-	2-(ALPHA-HYDROXYISOVALER	C8H14O4	174.0892	-	-	-	-	MMCD	1.665336	2.90E-04
2	173.0816	-	Ethyladipic acid	C8H14O4	174.0892	-	-	152459	HMDB020	MMCD	1.665336	2.90E-04
2	173.0816	-	Dimethyl adipate;Dimethyl h	C8H14O4	174.0892	C14570	-	-	-	MMCD	1.665336	2.90E-04
2	173.0816	-	Suberic acid	C8H14O4	174.0892	C08278	10457;-	10457	HMDB008	LIPIDMaps	1.665336	2.90E-04
2	173.0816	-	Ethyladipic acid	C8H14O4	174.0892	-	152459;-	152459	HMDB020	LIPIDMaps	1.665336	2.90E-04
2	173.0816	-	Diethyl succinate	C8H14O4	174.0892	-	-	31249	HMDB338	HMDB	1.665336	2.90E-04
2	173.0816	-	Suberic acid;Cork acid;1,8-Oct	C8H14O4	174.0892	C08278	153742	10457	HMDB008	MMCD	1.665336	2.90E-04
3	241.1077	-	Diphenylcarbazide	C13H14N4	242.1168	C11232	151941	-	-	MMCD	7.436648	0.001801
4	499.7199	-	-	-	-	-	-	-	-	-	-	-
5	592.1392	-	Cefteram pivoxil;T 2588	C22H27N9	593.1475	C13147	192387	54885	-	MMCD	1.646408	9.77E-04
6	155.0716	-	-	C8H12O3	156.0786	-	5312943	-	-	LIPIDMaps	1.857506	2.90E-04
6	155.0716	-	8-Hydroxy-5,6-octadienoic ac	C8H12O3	156.0786	-	-	-	HMDB311	HMDB	1.564215	2.44E-04
6	155.0716	-	2,5-Dimethyl-4-ethoxy-3(2H)-	C8H12O3	156.0786	-	-	3017596	HMDB322	HMDB	1.564215	2.44E-04
7	429.1893	-	Mammea E/BA	C24H30O7	430.1992	-	-	11517592	HMDB308	HMDB	6.029752	0.002594
7	429.1893	-	Armillarilin	C24H30O7	430.1992	-	-	21126389	HMDB316	HMDB	6.029752	0.002594
7	429.1893	-	Athamantin	C24H30O7	430.1992	C09123	11315	442051	-	MMCD	6.029752	0.002594
7	429.1893	-	1,2-HYDRO-1-OXY-3,4-HYDRO	C24H30O7	430.1992	-	-	-	-	MMCD	6.029752	0.002594