GNPS Hands-on – Exploring Chemical Diversity with Molecular Networks

Pieter C. Dorrestein and Mingxun Wang

Download URL: https://tinyurl.com/2z8n5k93

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Samples Background

MassIVE MSV000088828 Partial Public

GNPS - Nicotinamide Adenine Dinucleotide Biosynthetic Impairment and Urinary Metabolomic Alterations Observed in Hospitalized Adults With COVID-19

Subscribe | Comment | Convert Spectra | Reanalyze Spectra | Add Reanalysis

Description

Nicotinamide Adenine Dinucleotide Biosynthetic Impairment and Urinary Metabolomic Alterations Observed in Hospitalized Adults With COVID-19 Nicotinamide Adenine Dinucleotide Biosynthetic Impairment and Urinary Metabolomic Alterations Observed in Hospitalized Adults With COVID-19 Nicotinamide Adenine Dinucleotide Biosynthetic Impairment and Urinary Metabolomic Alterations Observed in Hospitalized Adults With COVID-19 [doi:10.25345/C53P23] [dataset license: CC0 1.0 Universal (CC0 1.0)]

Keywords: Metabolomics

Contact

Principal Investigators: (in alphabetical order) Stephen Barnes, University of Alabama, USA

Submitting User: mwang87

Number of Files: 60
Total Size: 15.40 GB
Subscribers: 1

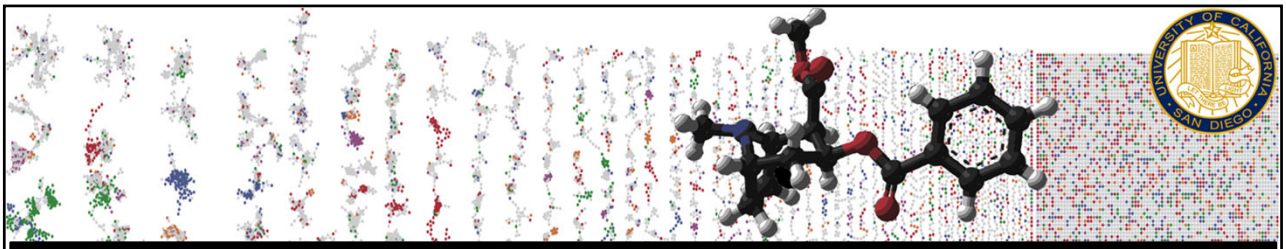
		Owner Reanalyses
Identification Results		
Proteins (Reported):	N/A	N/A
Peptides:	N/A	N/A
Variant Peptides:	N/A	N/A
PSMs:	N/A	N/A

Browse Dataset Files

Browse Metadata

Raines et al. 2021

2



GNPS Classic Molecular Networking Job Submission
HANDS ON

Ming Wang, Pieter Dorrestein, University of California San Diego

@Pdorrestein1
https://dorresteinlab.ucsd.edu/

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Outline for today

- Submit a molecular networking job (Hands-on, Pieter).
- Explanation of what was just submitted (Pieter).
- Exploring the molecular network (Ming).
- GNPS dashboard for inspecting the data (Ming).
- MASST (If we have time, Pieter)

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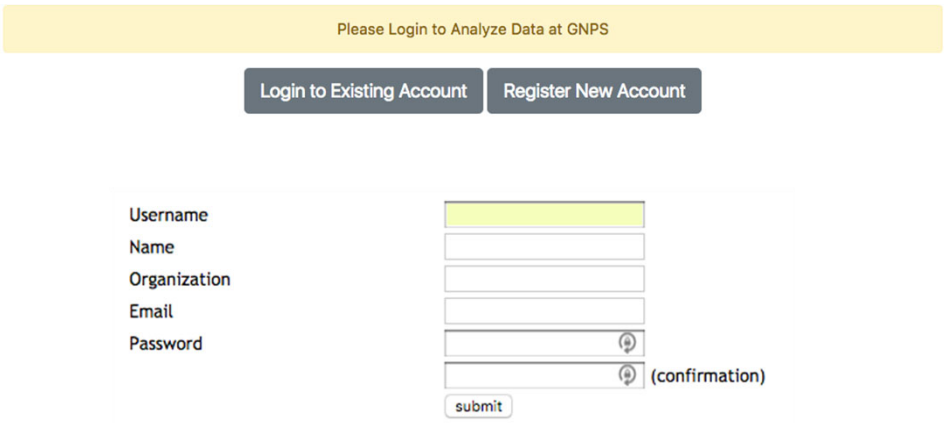
5

Go to GNPS (gnps.ucsd.edu)

6

Create an Account
(If you don't have one already)



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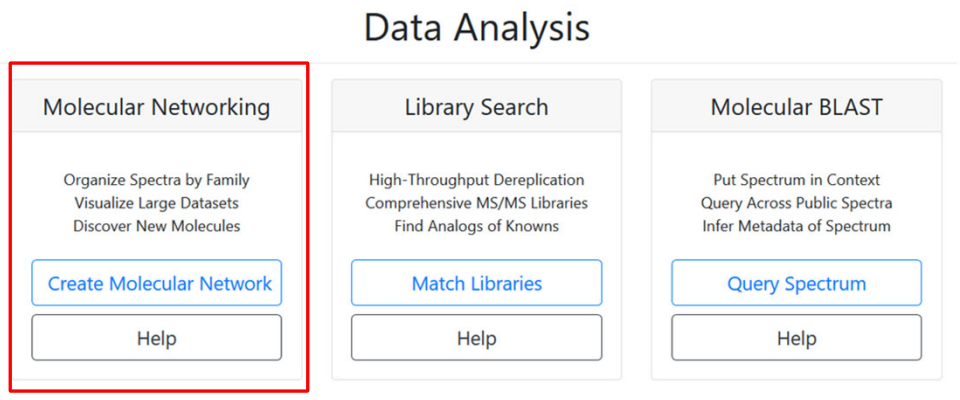

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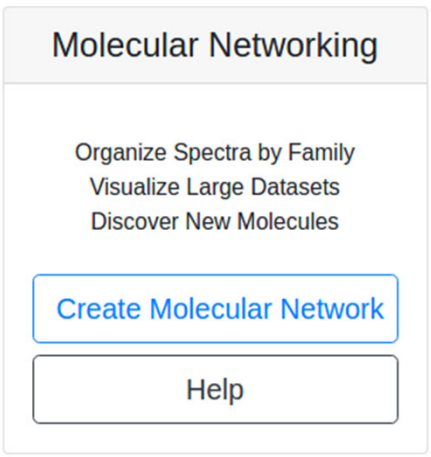

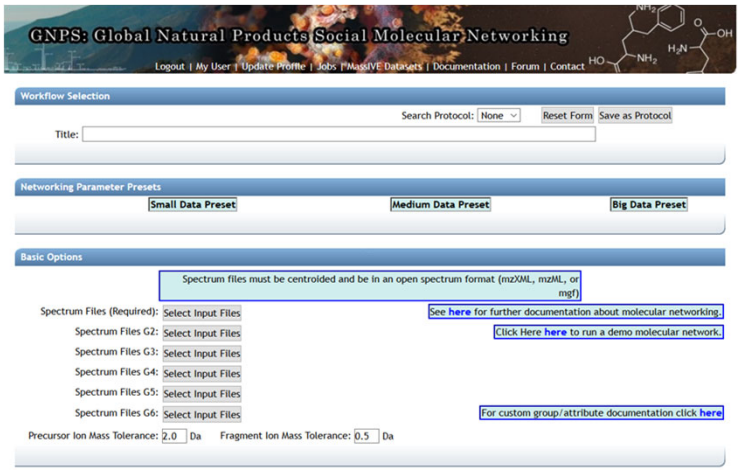

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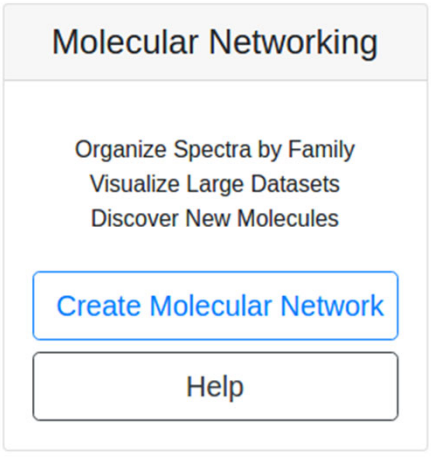

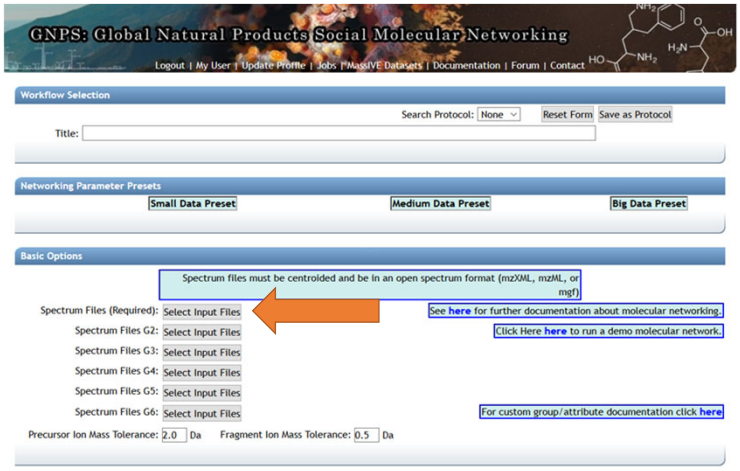

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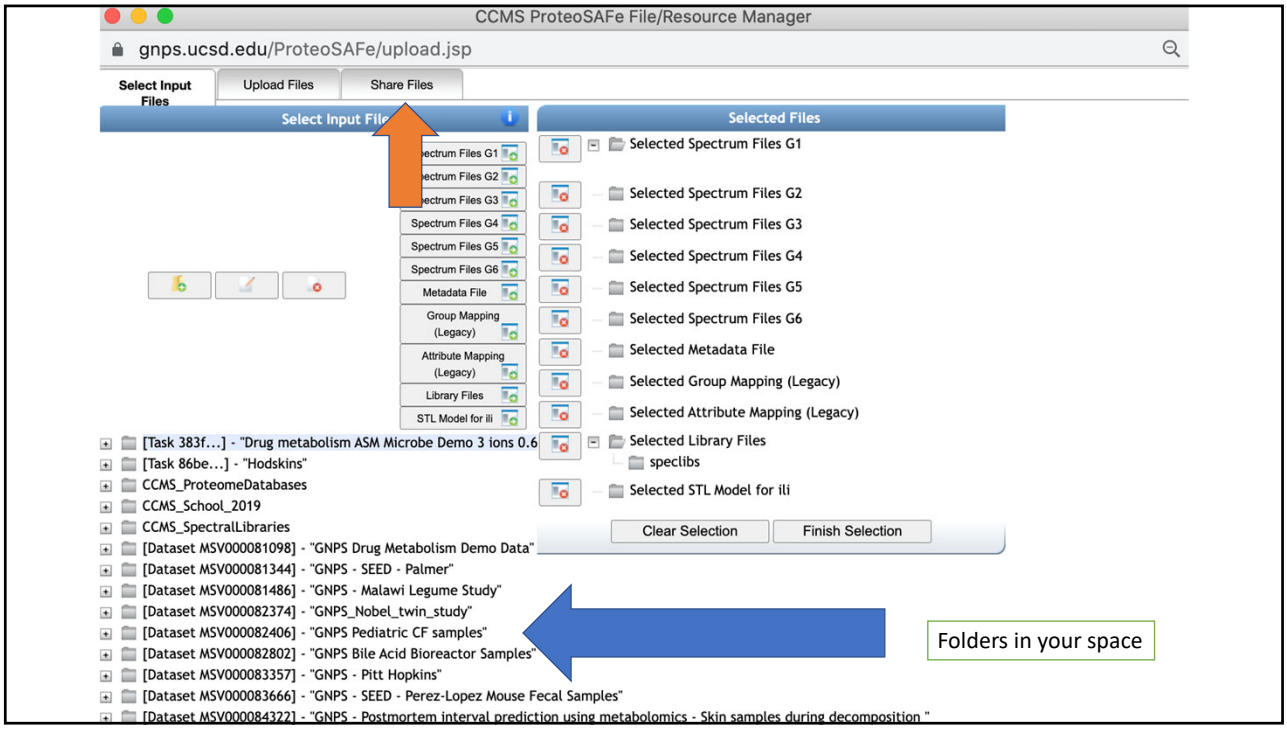
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Upload Files
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Spectrum Files G1
Spectrum Files G2
Spectrum Files G3
Spectrum Files G4
Spectrum Files G5
Spectrum Files G6
Metadata File
Group Mapping (Legacy)
Attribute Mapping (Legacy)
Library Files
STL Model for ili
Selected Files
Selected Spectrum Files G1
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Selected Spectrum Files G4
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Selected Attribute Mapping (Legacy)
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Finish Selection
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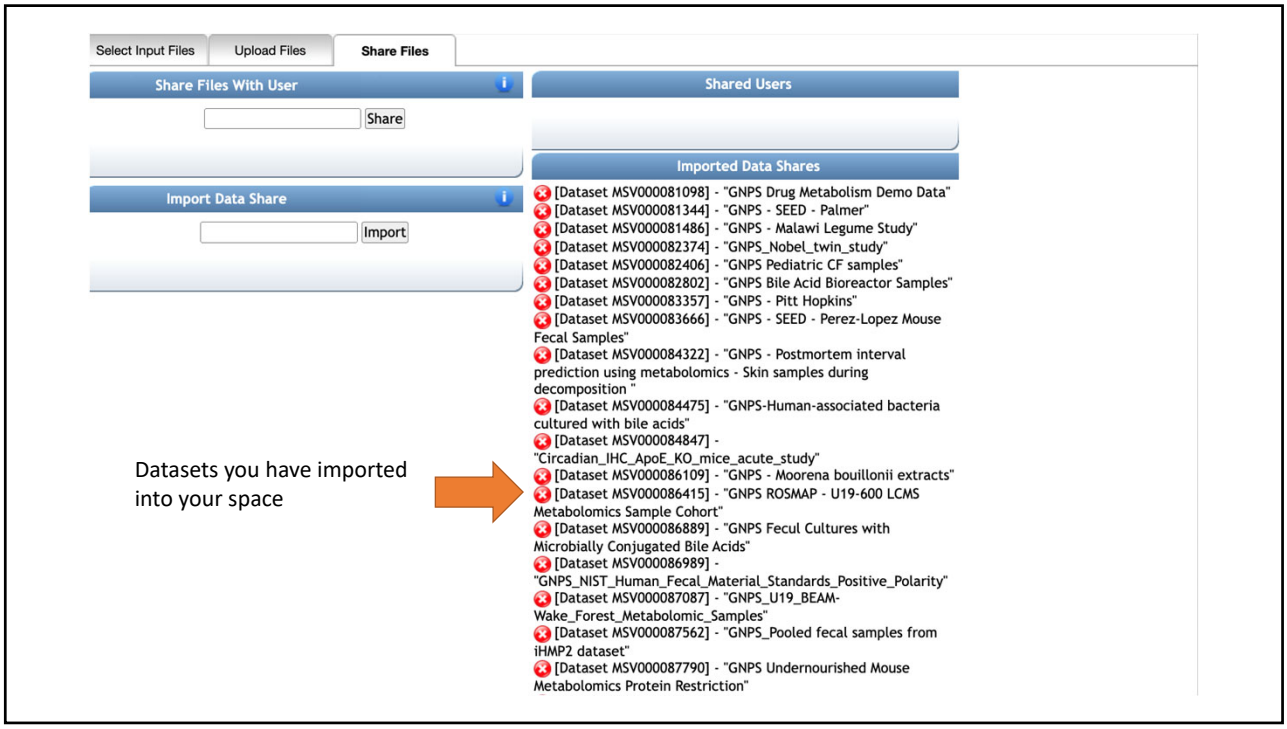
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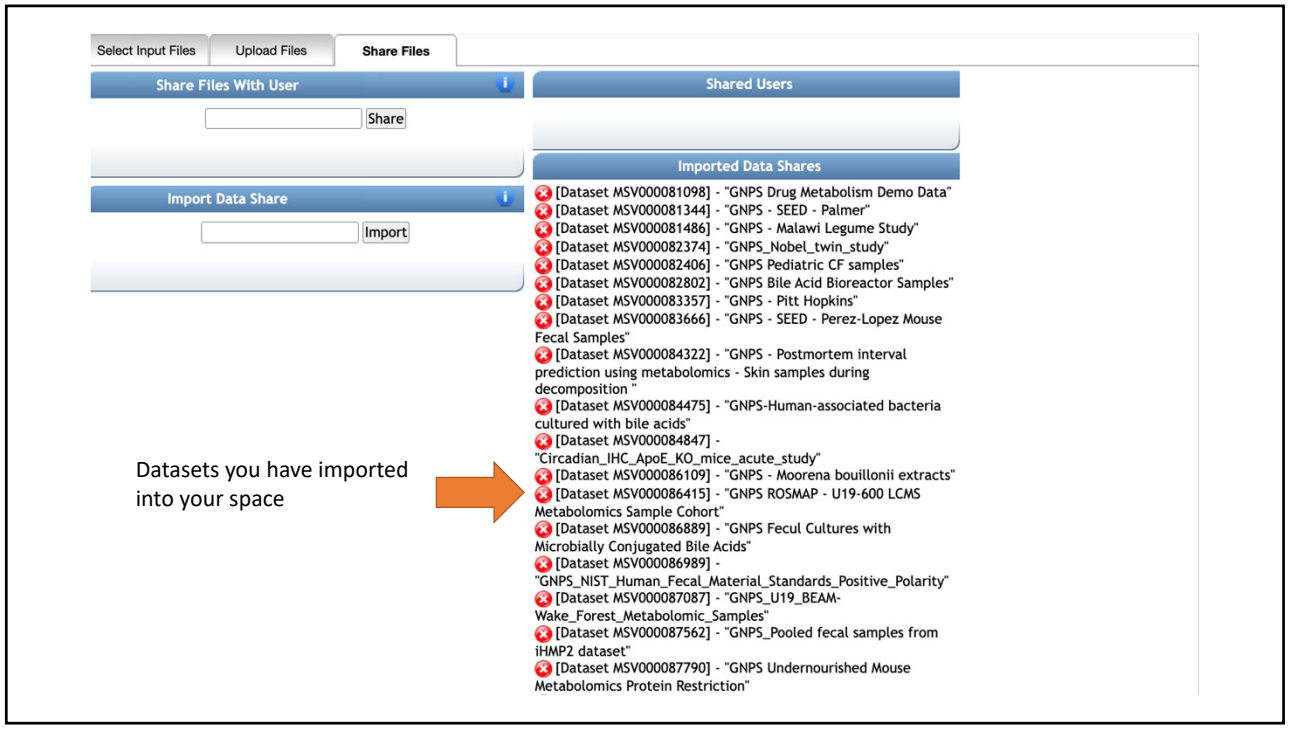
Datasets you have imported into your space

12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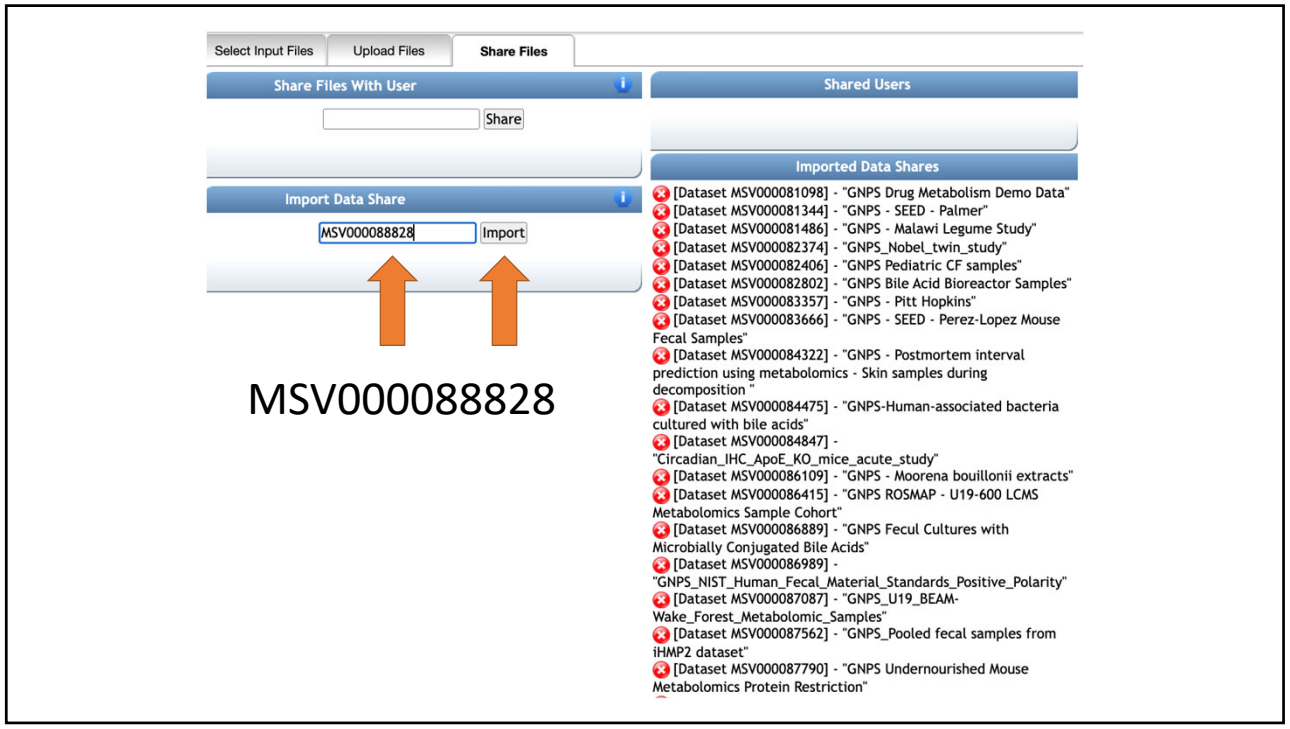
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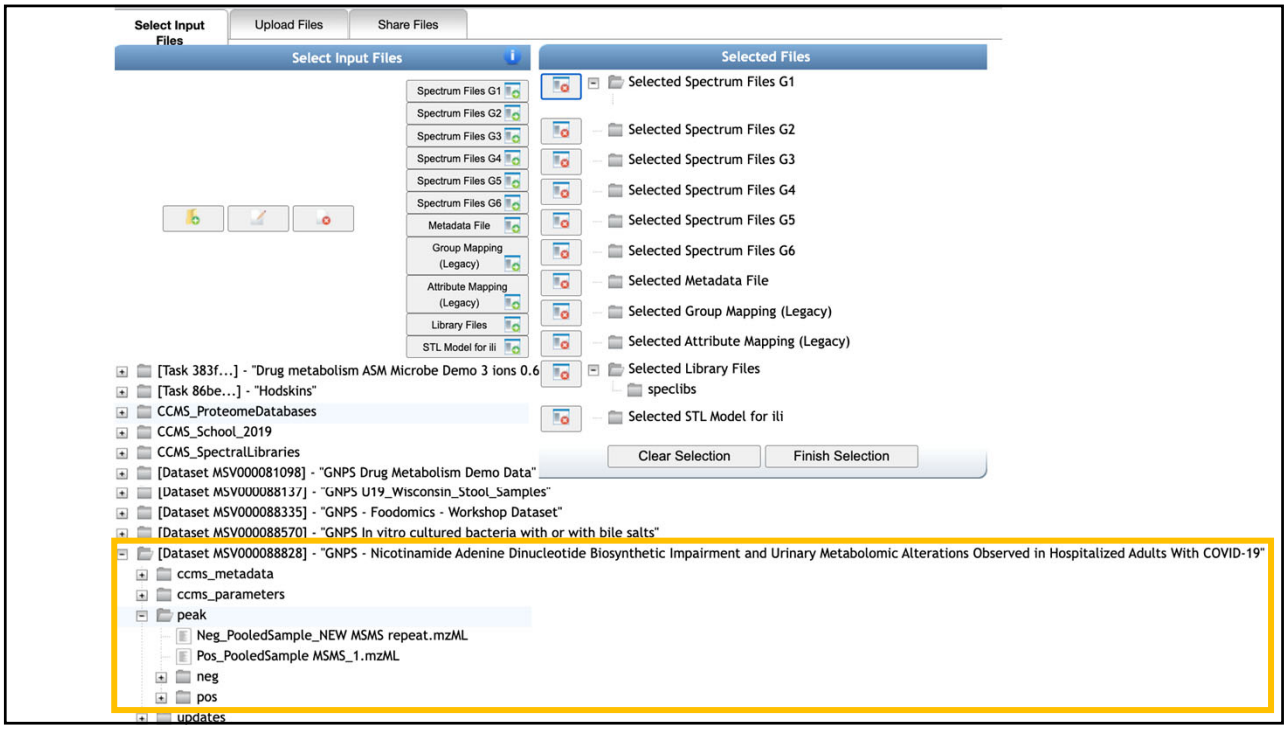
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Spectrum Files G3
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Metadata File
Group Mapping (Legacy)
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Pos_PooledSample MSMS_1.mzML
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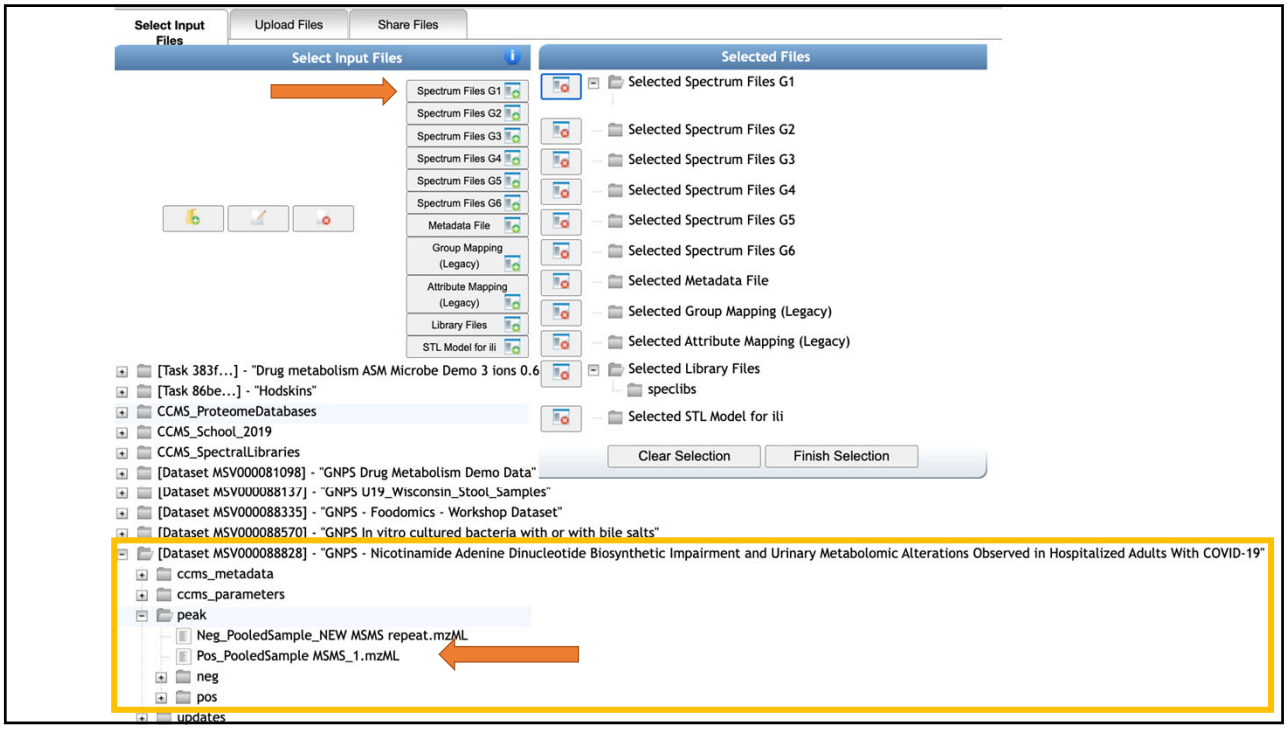
15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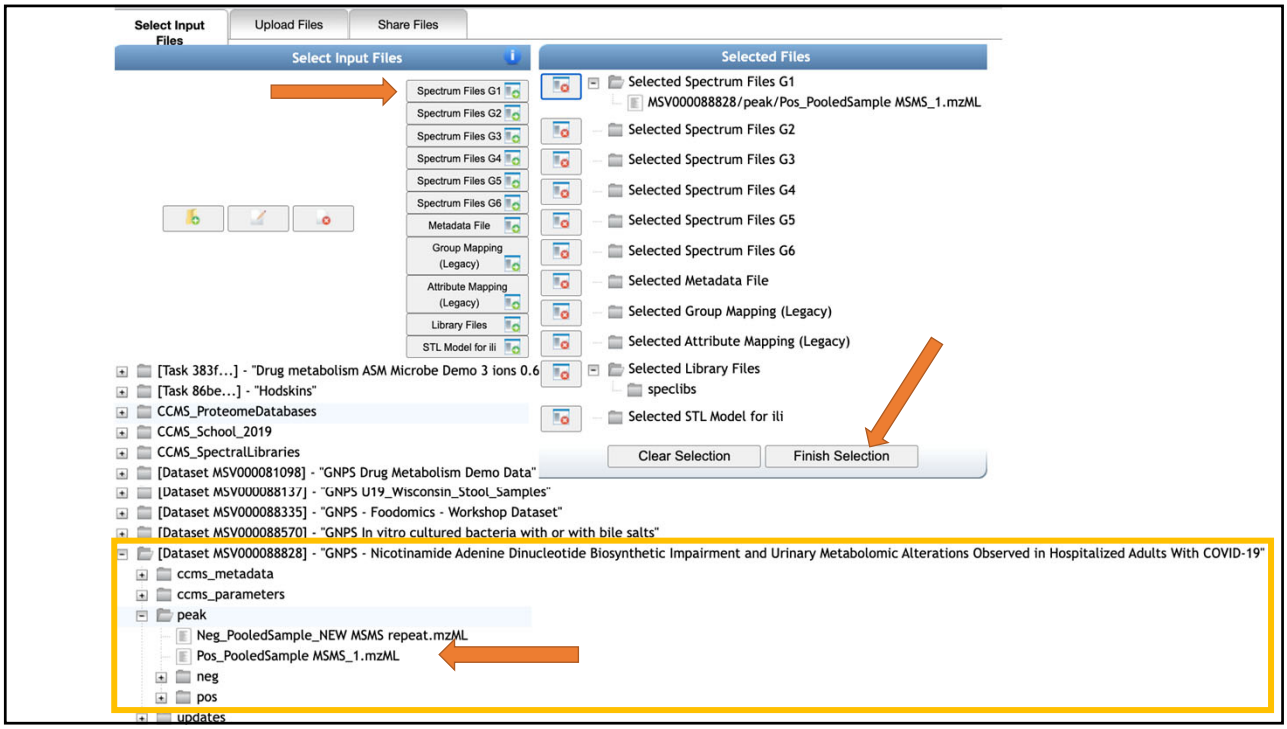
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Pos_PooledSample MSMS_1.mzML
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updates

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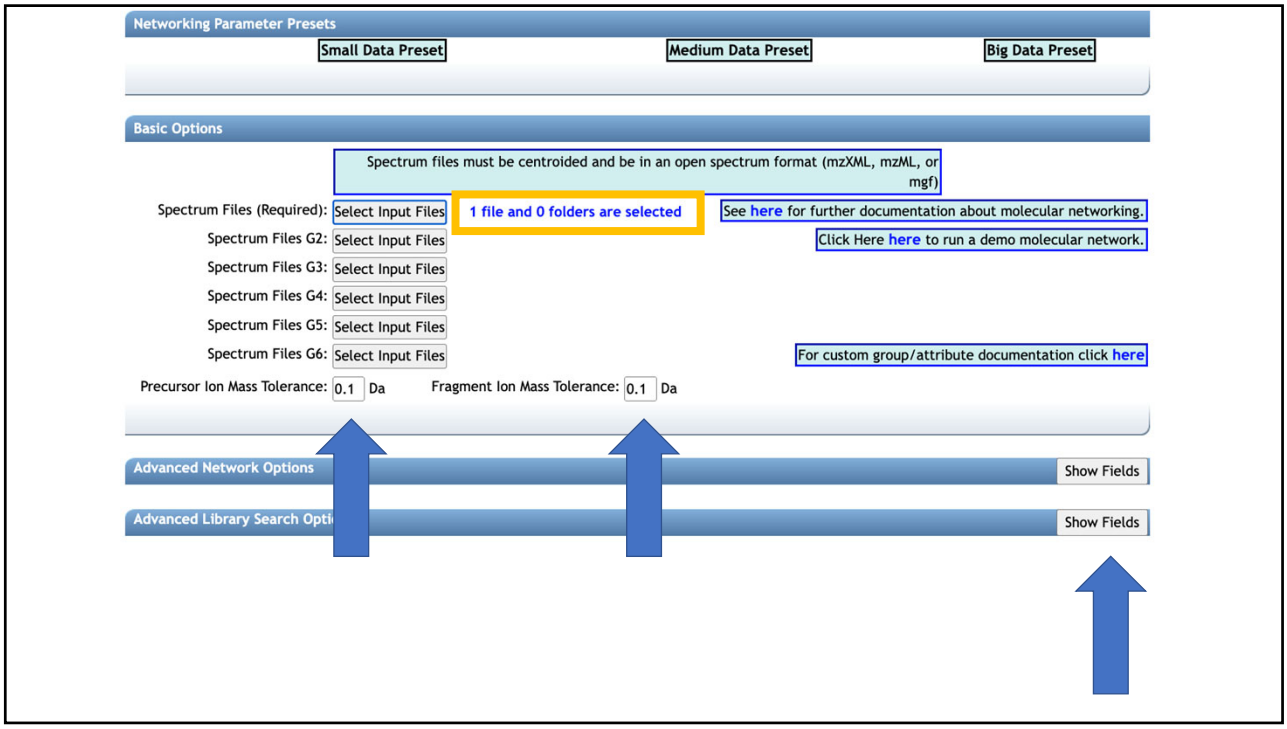
Networking Parameter Presets
Small Data Preset
Medium Data Preset
Big Data Preset
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1 file and 0 folders are selected
See here for further documentation about molecular networking.
Spectrum Files G2: Select Input Files
Click Here here to run a demo molecular network.
Spectrum Files G3: Select Input Files
Spectrum Files G4: Select Input Files
Spectrum Files G5: Select Input Files
Spectrum Files G6: Select Input Files
For custom group/attribute documentation click here
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Fragment Ion Mass Tolerance: 0.1 Da
Advanced Network Options
Show Fields
Advanced Library Search Opti
Show Fields

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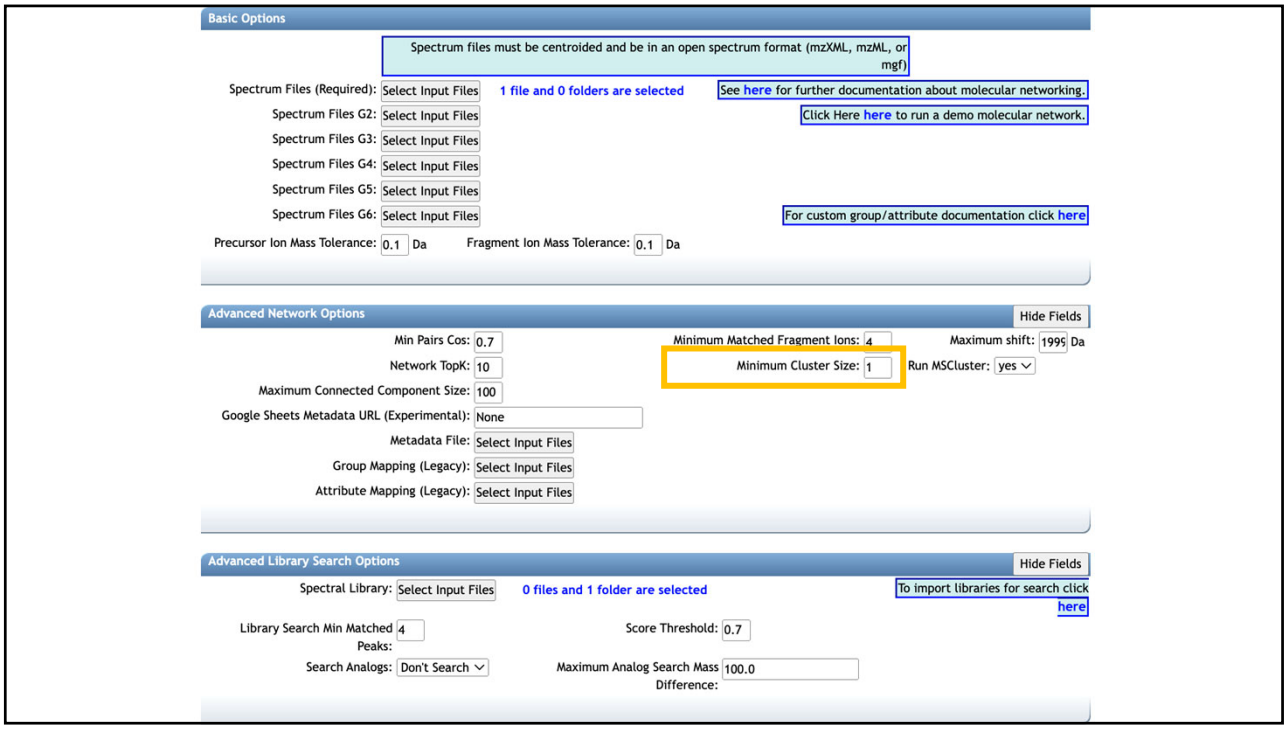
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Fragment Ion Mass Tolerance: 0.1 Da
Advanced Network Options
Hide Fields
Min Pairs Cos: 0.7
Minimum Matched Fragment Ions: 4
Maximum shift: 1995 Da
Network TopK: 10
Minimum Cluster Size: 1
Run MSCluster: yes
Maximum Connected Component Size: 100
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Group Mapping (Legacy): Select Input Files
Attribute Mapping (Legacy): Select Input Files
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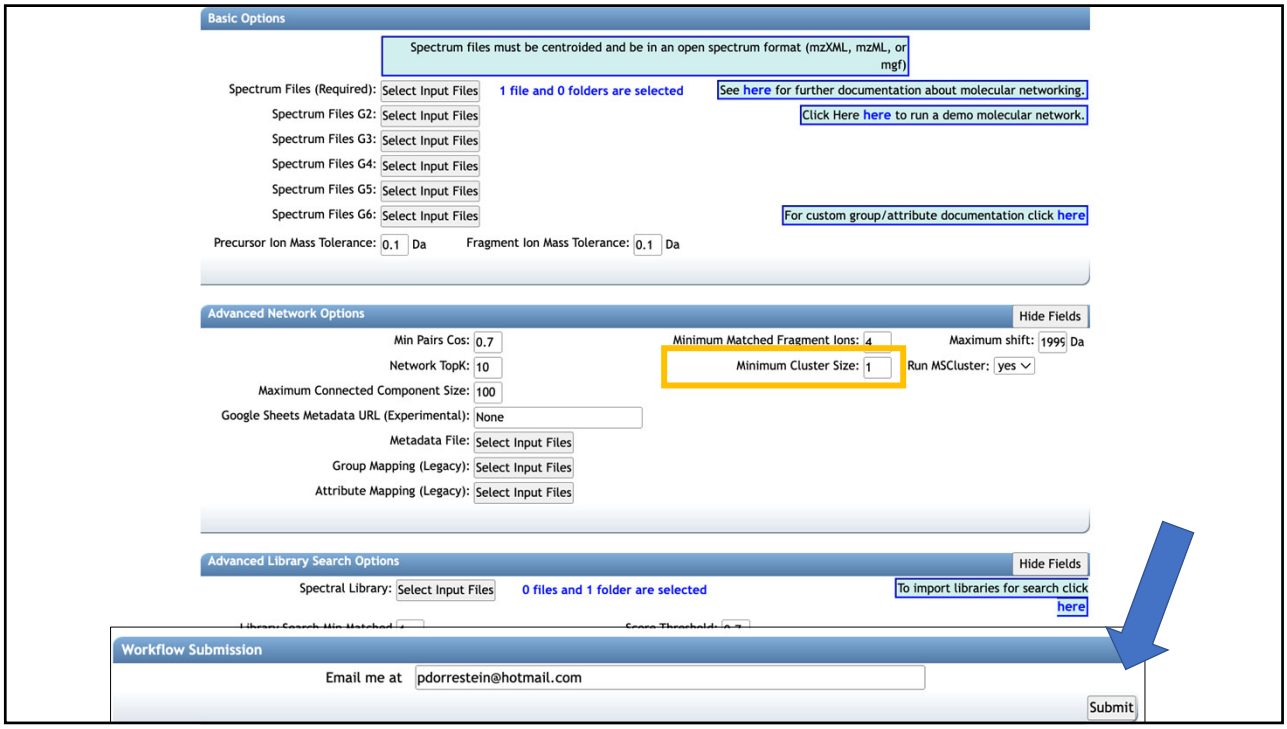
Search Analogs: Don't Search
Maximum Analog Search Mass Difference: 100.0

19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Fragment Ion Mass Tolerance: 0.1 Da
Advanced Network Options
Hide Fields
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Minimum Matched Fragment Ions: 4
Maximum shift: 1995 Da
Network TopK: 10
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Metadata File: Select Input Files
Group Mapping (Legacy): Select Input Files
Attribute Mapping (Legacy): Select Input Files
Advanced Library Search Options
Hide Fields
Spectral Library: Select Input Files
0 files and 1 folder are selected
To import libraries for search click here
Workflow Submission
Email me at pdorrestein@hotmail.com
Submit

20

Outline for today

- **Submit a molecular networking job (Hands-on, Pieter).**
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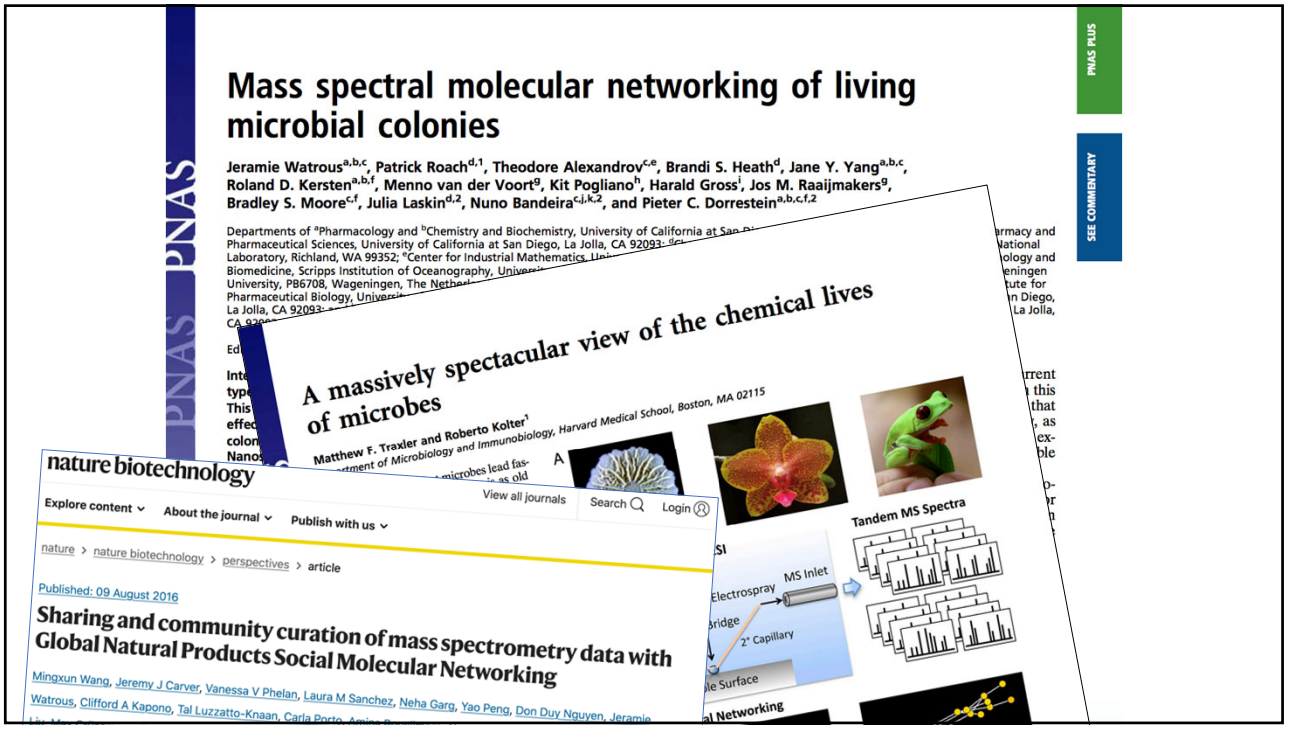

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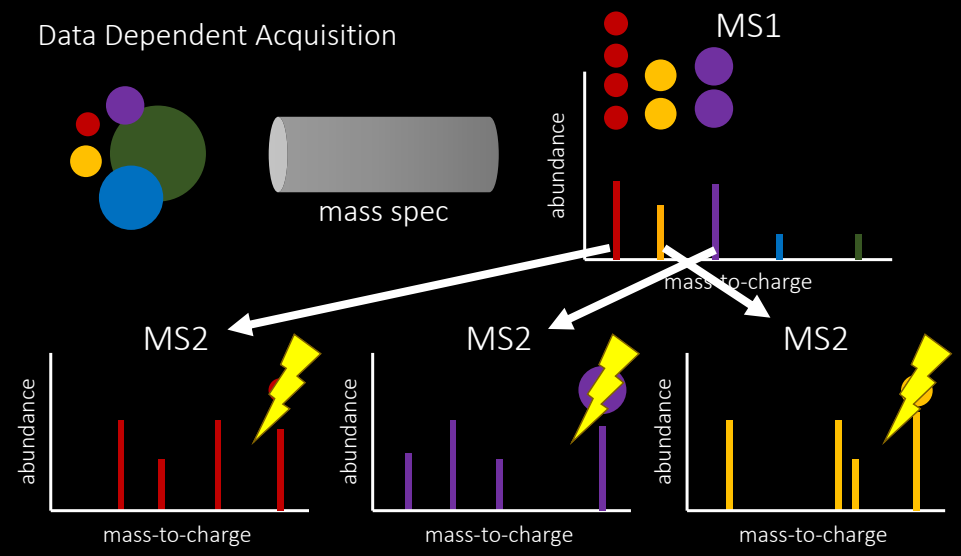
Untargeted Mass Spectrometry



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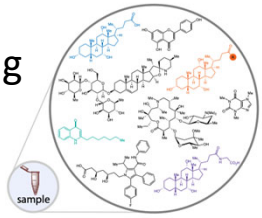
Molecular Networking



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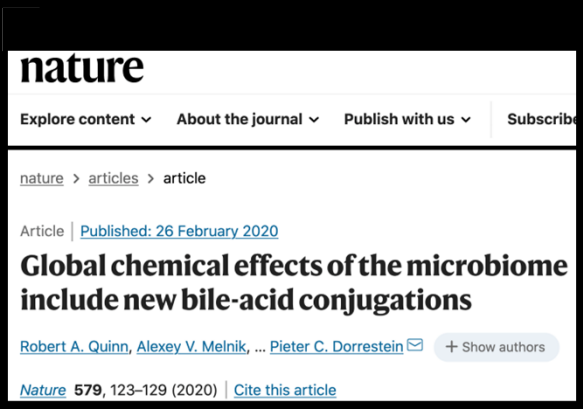
Molecular Networking

Robert Quinn



How much does the microbiome impact the chemistry of the host?

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Molecular Networking

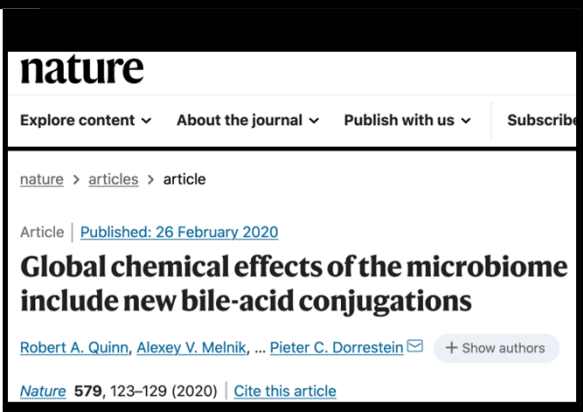
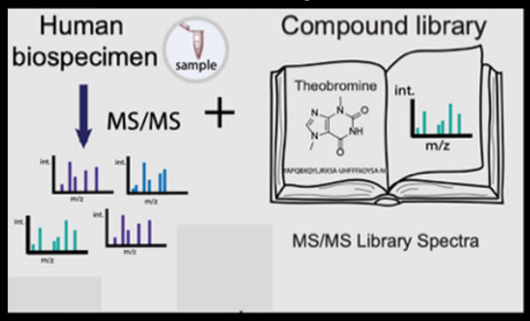


Figure from Aron, Gentry Nature Protocols 2020

26

Growing public reference libraries (>620,000 public ref spectra) can be used to hypothesize the structure.



5% Annotated
(10% human)

Julia Gauglitz and Kiana West Wang et al Nature Biotech. 2016, Bauemeister et al, Microbiome Metabolomics Nature Micro. Reviews, 2021

27

Molecular Networking

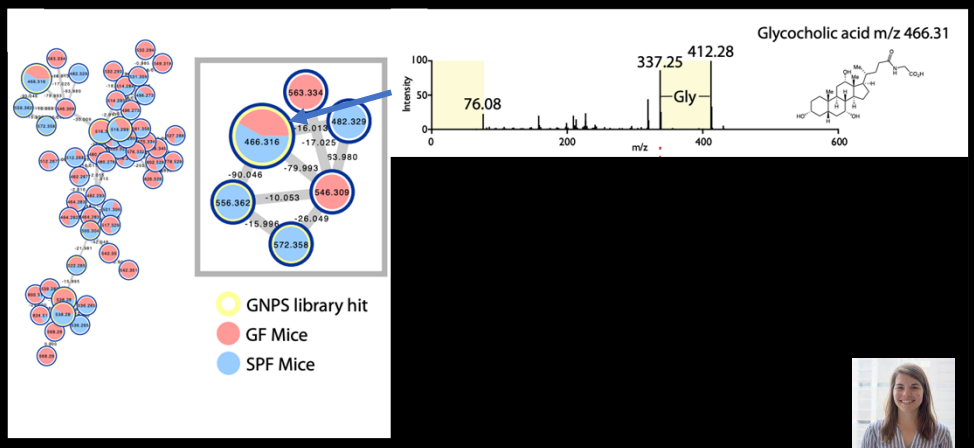


Figure by Emily Gentry

Figure from Aron, Gentry Nature Protocols 2020

28

Molecular Networking

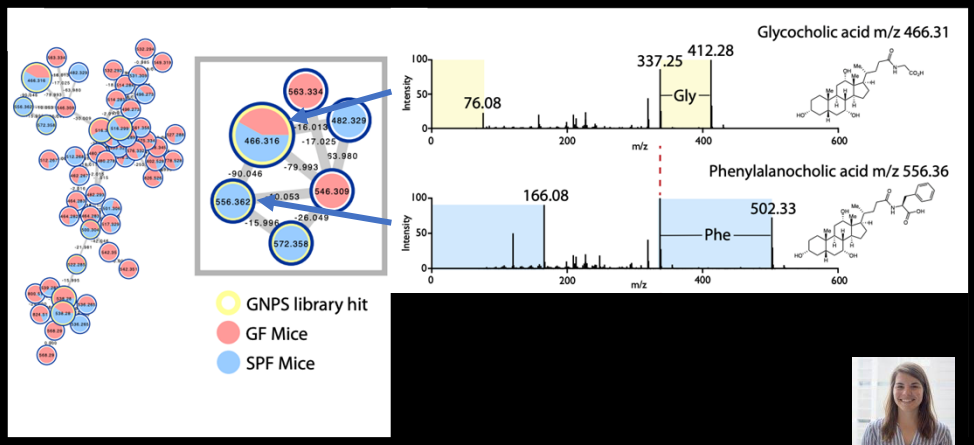
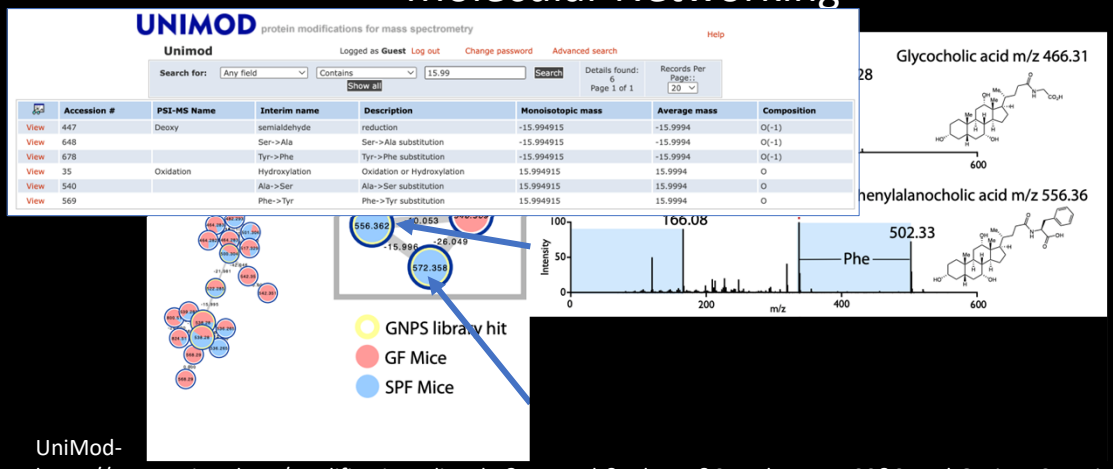


Figure by Emily Gentry

Figure from Aron, Gentry Nature Protocols 2020

29

Molecular Networking



UniMod-
https://www.unimod.org/modifications_list.php?a=search&value=1&SearchFor=15.99&SearchOption=Contains&SearchField=

Curated list of delta masses (we don't vouch for accuracy so use your thinking caps).
https://docs.google.com/spreadsheets/d/1RbhwM8KPUUBTrppcYrKp5hs8B_ZPJKxO-WcyHDoU074/edit#gid=566878567

Figure from Aron, Gentry Nature Protocols 2020

30

Molecular Networking

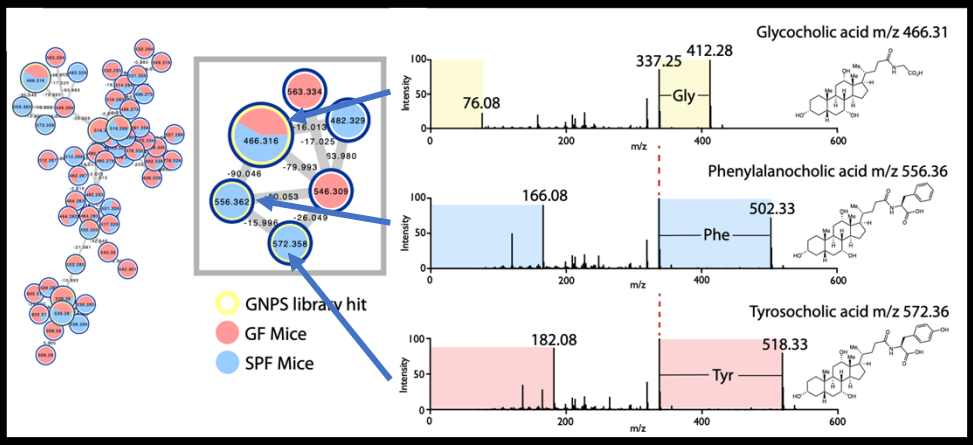


Figure from Aron, Gentry Nature Protocols 2020

31

From untargeted data to chemicals

1,894,519 MS^2 spectra

6 product ions

≥5 identical MS^2 spectra

26,956 Consensus MS^2 spectra

Wang, M., et al. *Nature Biotechnology* 34.8 (2016): 828-837.

32

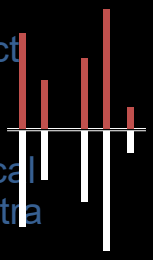
From untargeted data to chemicals

1,894,519 MS^2 spectra

6 product ions

Spectral Library Match

≥5 identical MS^2 spectra



26,956 Unique chemicals

Consensus MS^2 spectra annotated

Wang, M., et al. *Nature Biotechnology* 34.8 (2016): 828-837.

33

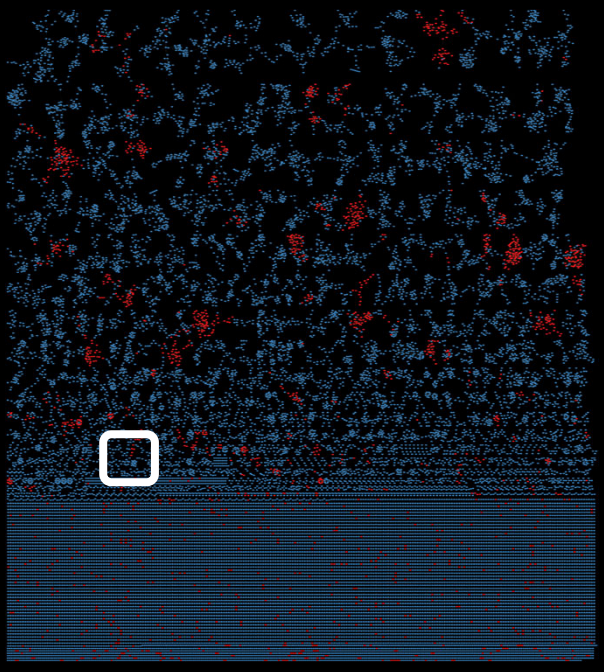
AGP - molecular network

Every dot is a MS/MS spectrum

~5% annotated

annotated

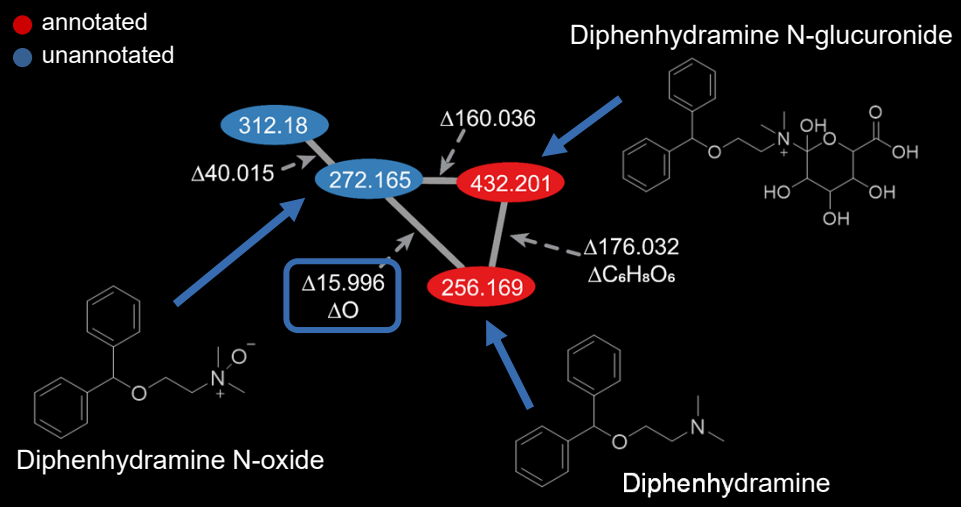
unannotated



unpublished

34

Identifying unknowns using molecular networking



35

5 min break
Before we analyze the submitted job!

36

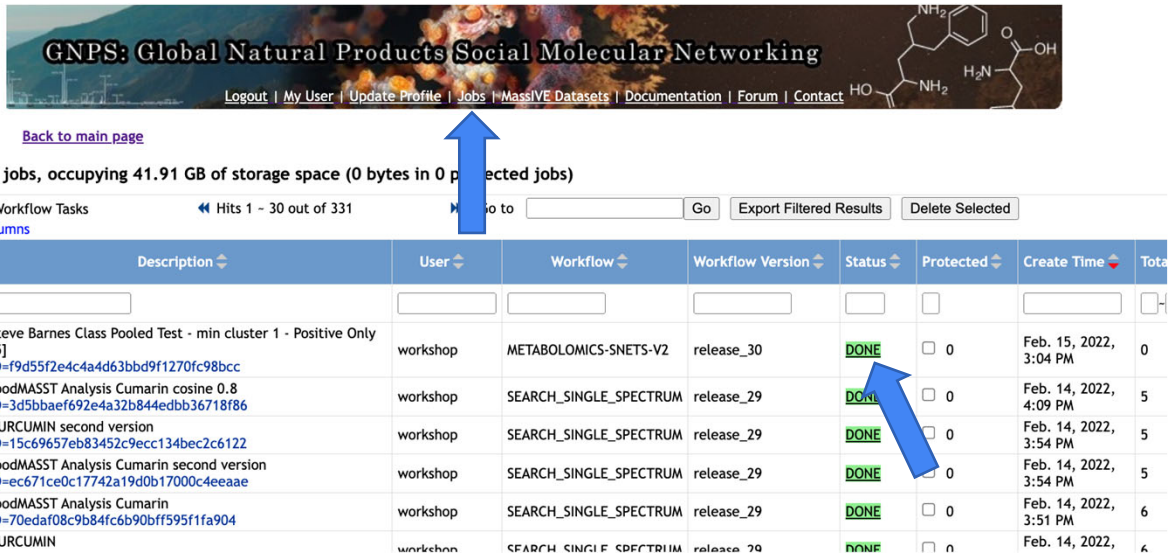
Outline for today

- **Submit a molecular networking job (Hands-on, Pieter).**
- **Explanation of what was just submitted (Pieter).**
- **Exploring the molecular network (Ming).**
- GNPS dashboard for inspecting the data (Ming).
- MASST (If we have time, Pieter)

Catch up Link - In case the MN failed for anyone.

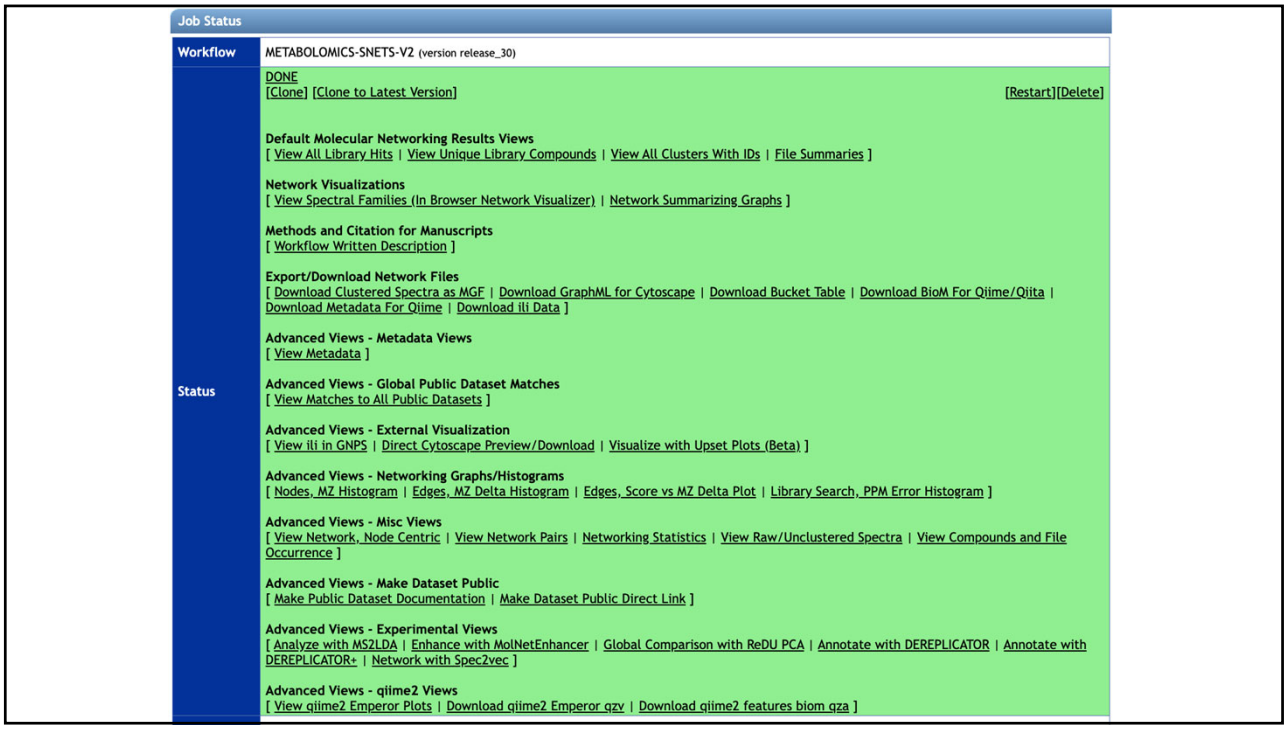
37

Ming will carry you through the analysis.



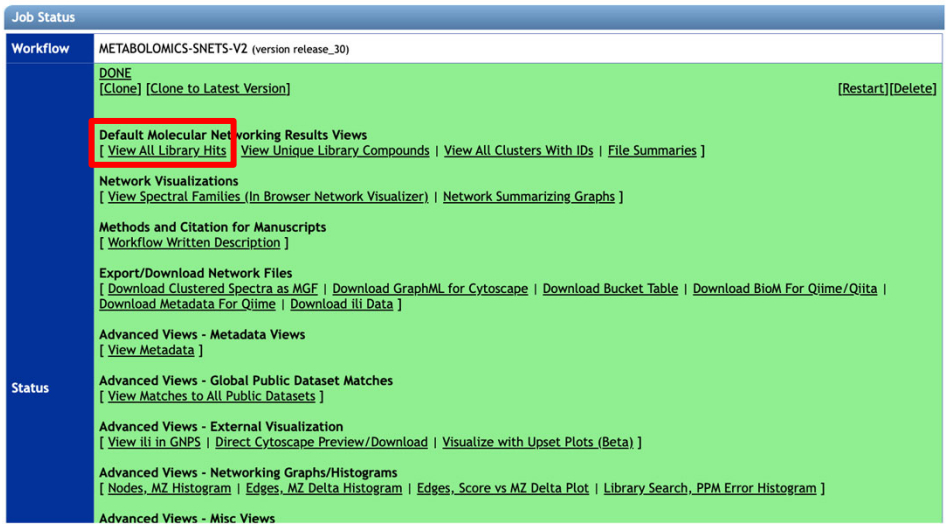
Catch up Link - In case the MN failed for anyone.

38



39

Let's Explore What Molecules are in these Urine Sample



40

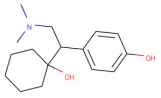
Let's see if any drugs are being detected

Steve Barnes Class Pooled Test - min cluster 1 - Positive Only [5] Hits 1 ~ 1 out of 1 Go to Go

Select columns

Apply Filters	ViewLib	Explore	Compound_Name	ClusterIdx	View All Spectra	Library Class
Filter By:			desv	~		
View Mirror Match USI Links 1	ViewLib	Explore Molecule in 0 Files and 0 Datasets	Massbank:EA105309 O-desmethylvenlafaxine|Desvenlafaxine|4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]phenol	483	View Raw Spectra	Bronze

desv



Desmethylvenlafaxine is an antidepressant

41

Let's compare this to GNPS MS/MS Reference Spectrum

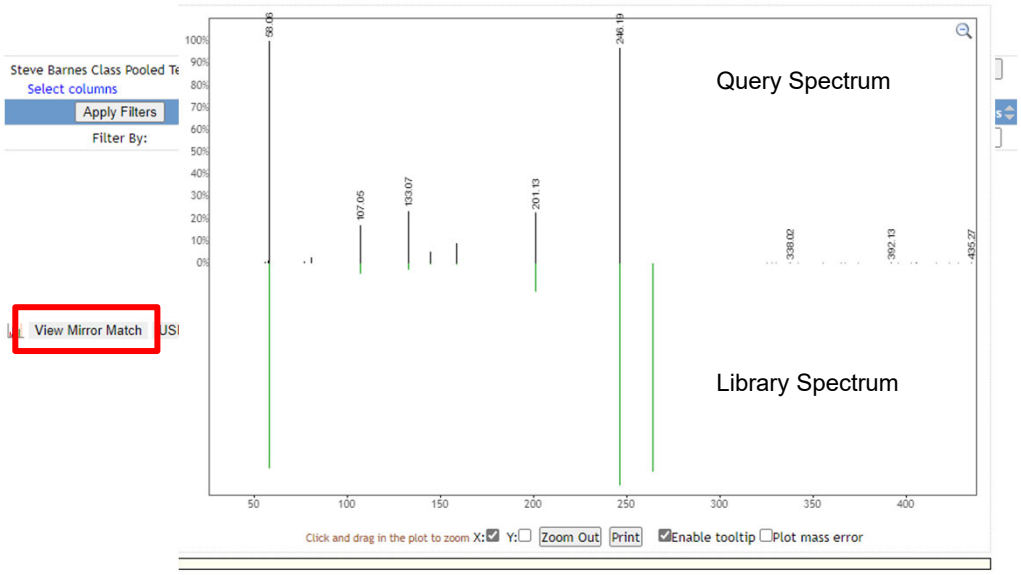
Steve Barnes Class Pooled Test - min cluster 1 - Positive Only [5] Hits 1 ~ 1 out of 1 Go to Go

Select columns

Apply Filters	ViewLib	Explore	Compound_Name	ClusterIdx	View All Spectra	Library Class
Filter By:			desv	~		
View Mirror Match USI Links 1	ViewLib	Explore Molecule in 0 Files and 0 Datasets	Massbank:EA105309 O-desmethylvenlafaxine|Desvenlafaxine|4-[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]phenol	483	View Raw Spectra	Bronze

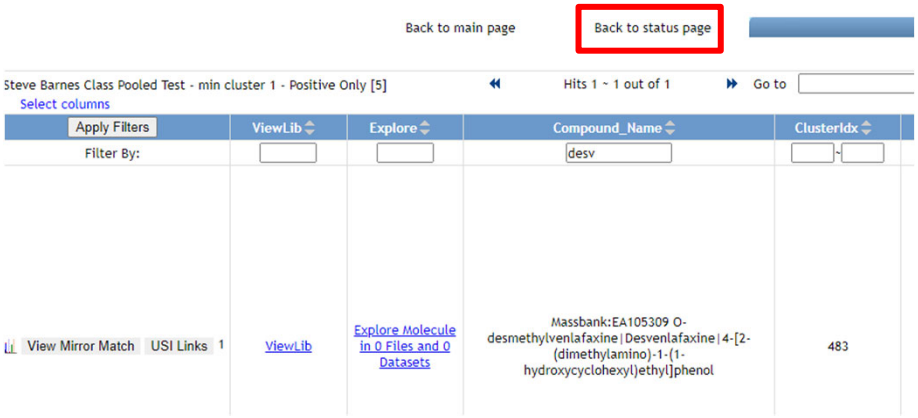
42

Let's compare this to GNPS MS/MS Reference Spectrum



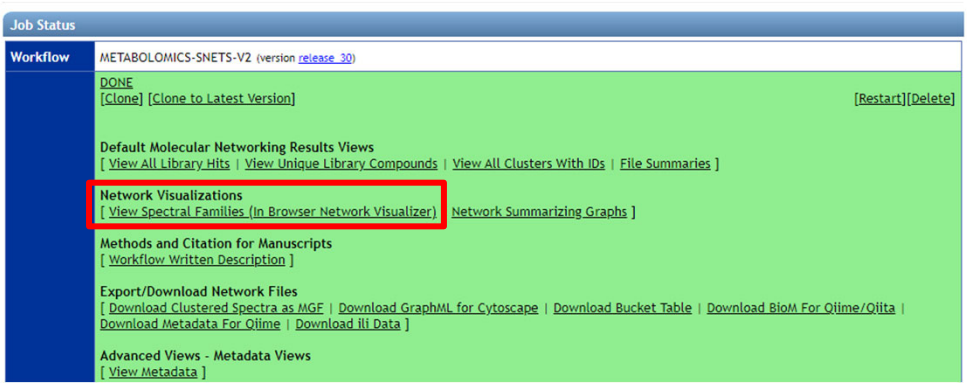
43

Let's explore potential analogs of Desmethylvenlafaxine



44

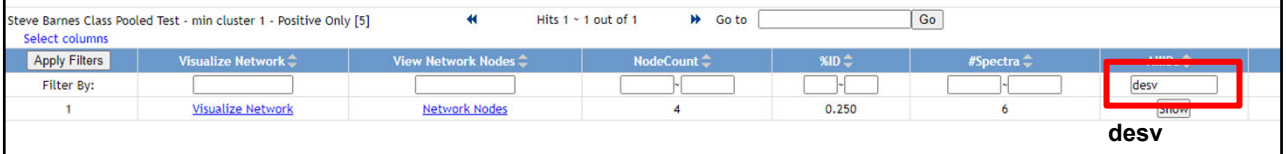
Let's explore potential analogs of Desmethylvenlafaxine



https://gnps.ucsd.edu/ProteoSAFe/status.jsp?task=f9d55f2e4c4a4d63bbd9f1270fc98bcc

45

Let's explore potential analogs of Desmethylvenlafaxine



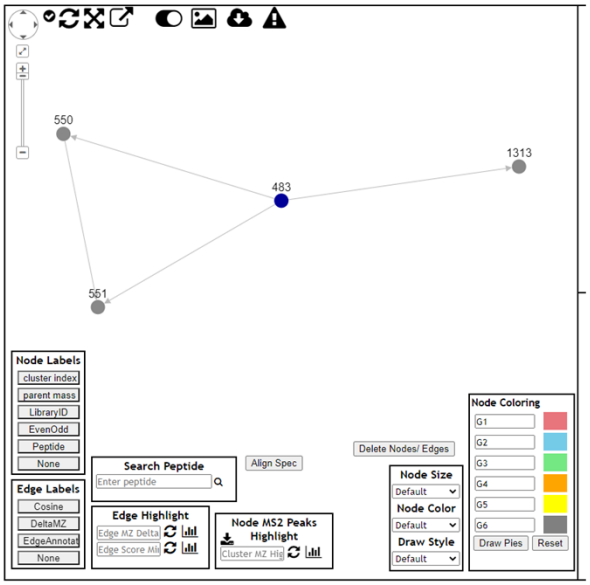
desv

Catch up Link

46

Let's explore potential analogs of Desmethylvenlafaxine

- Each Circle (node) is a molecule in data
- Blue nodes are identified to known compounds
- Connected nodes mean similar MS/MS fragmentation



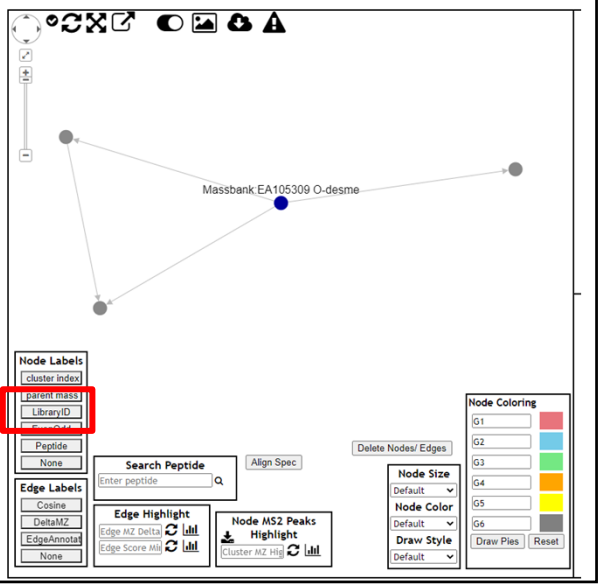
Catch up Link

47

Let's explore potential analogs of Desmethylvenlafaxine

Show the Library ID for the network

We can see it is Desvenlafaxine



Catch up Link

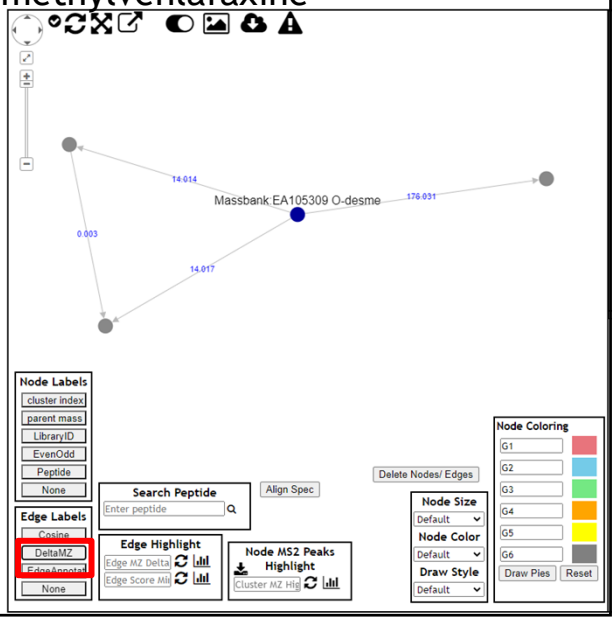
48

Let's explore potential analogs of Desmethylvenlafaxine

Show the mass deltas to putative analogs

Can you explain what these mass deltas could mean?

Catch up Link



49

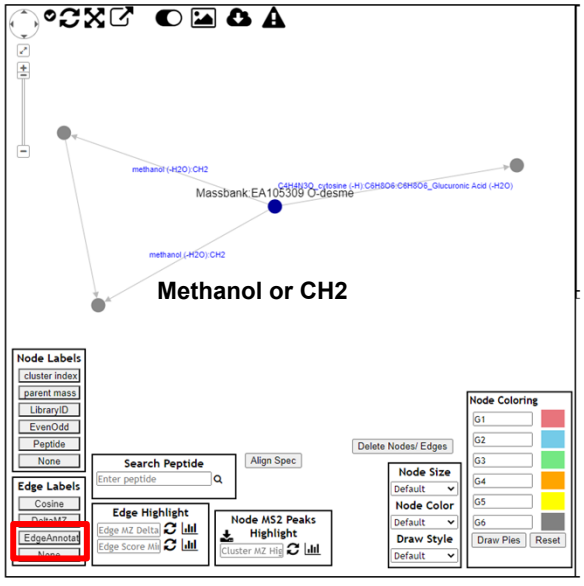
Let's explore potential analogs of Desmethylvenlafaxine

Show the mass deltas to putative analogs

Can you explain what these mass deltas could mean?

We try to help with that by curating a common but not exhaustive list of potential modifications. Could also be multiple options for you to decide what makes sense biologically and chemically.

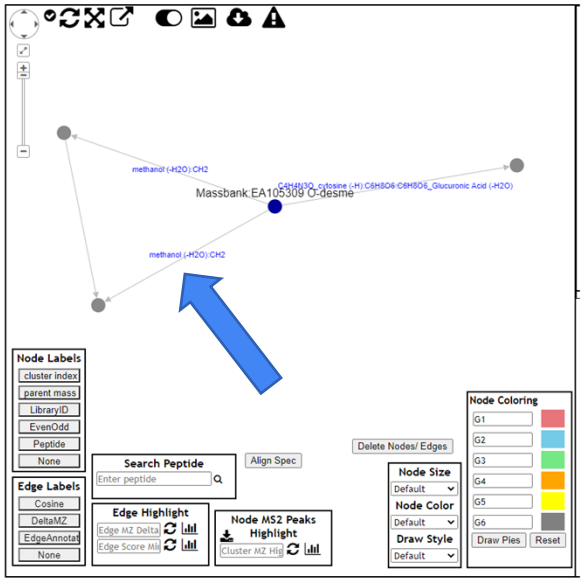
Catch up Link



50

Let's explore potential analogs of Desmethylvenlafaxine

Let's inspect the MS/MS spectra!

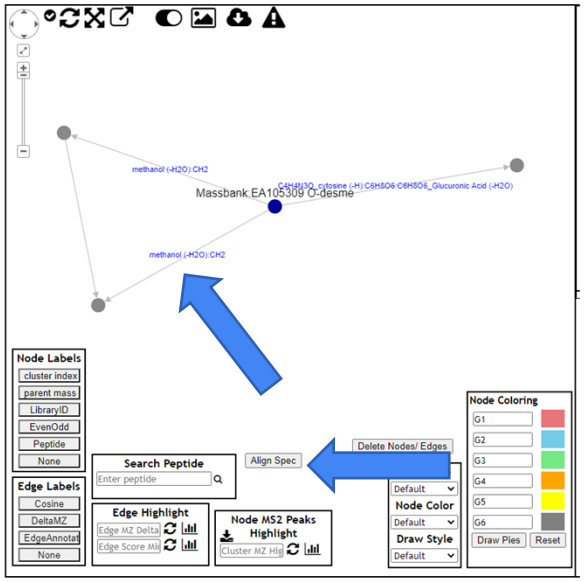


Catch up Link

51

Let's explore potential analogs of Desmethylvenlafaxine

Let's inspect the MS/MS spectra!

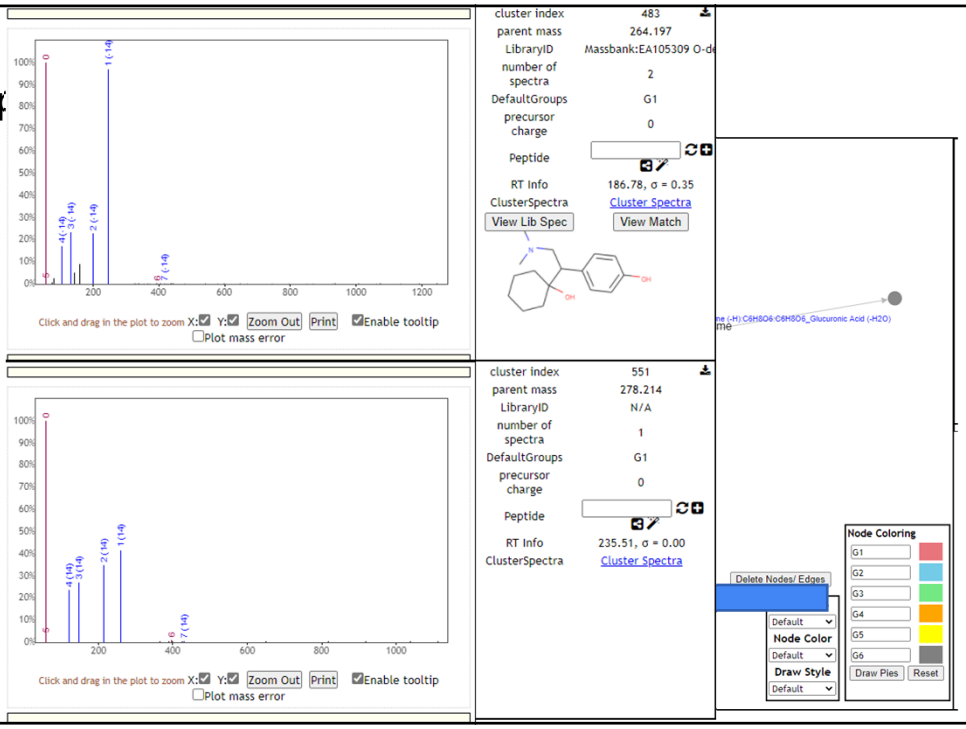


Catch up Link

52

Let's explore p

Blue peaks shifted
Red peaks same



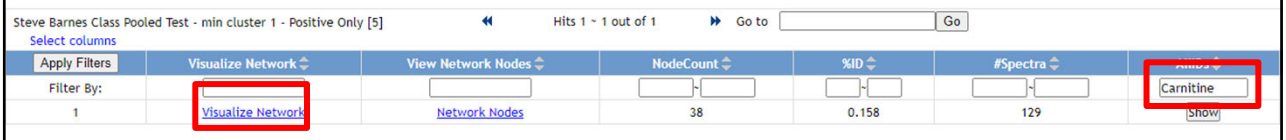
53

Explore endogenous molecule - Carnitines

Catch up Link

54

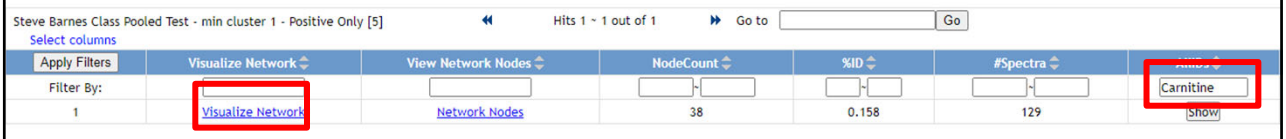
Explore endogenous molecule - Carnitines



Catch up LInk

55

Explore endogenous molecule - Carnitines

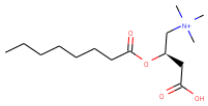


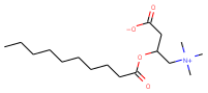
Catch up Link

56

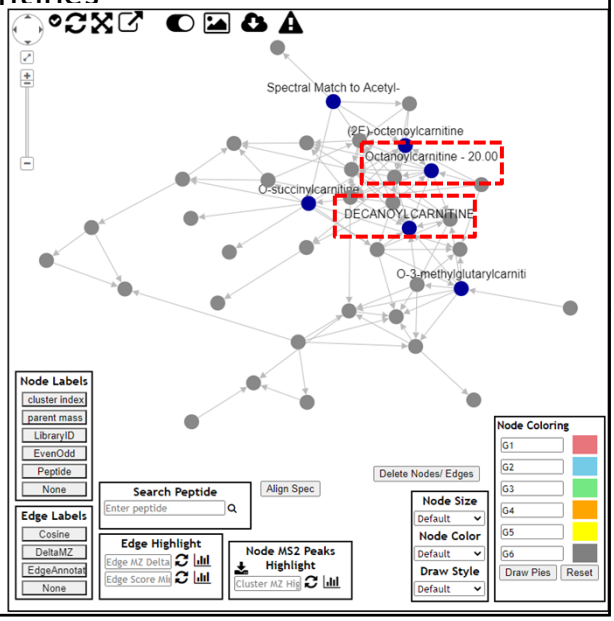
Let's explore potential analogs of Carntines

- Octanoylcarnitine related to Decanoylcarnitine





Catch up Link

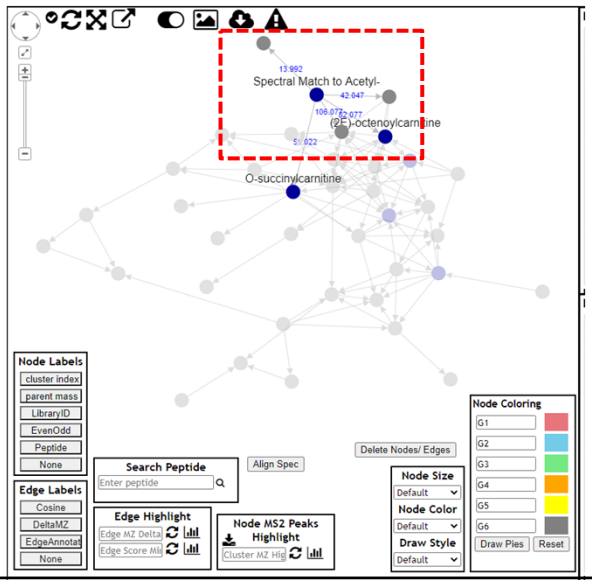


57

Let's explore potential analogs of Carntines

- Activity: Can you find new putative analog of Acetyl-DL-carnitine?

Catch up Link



58

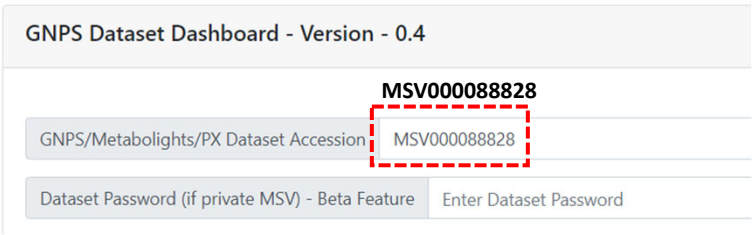
Outline for today

- **Submit a molecular networking job (Hands-on, Pieter).**
- **Explanation of what was just submitted (Pieter).**
- **Exploring the molecular network (Ming).**
- **GNPS dashboard for inspecting the data (Ming).**
- MASST (If we have time, Pieter)

59

Connecting Networks Back to Raw Data - Visualizing Data GNPS Dashboard

- Let's use GNPS Explorer to Select Data to Visualize https://gnps-explorer.ucsd.edu/
- COVID-19 Urine Samples



Link

60

Visualizing Data GNPS Dashboard

- Select Metadata to Use

61

Visualizing Data GNPS Dashboard

- Select Positive AKI (Acute Kidney Injury Samples)

Export

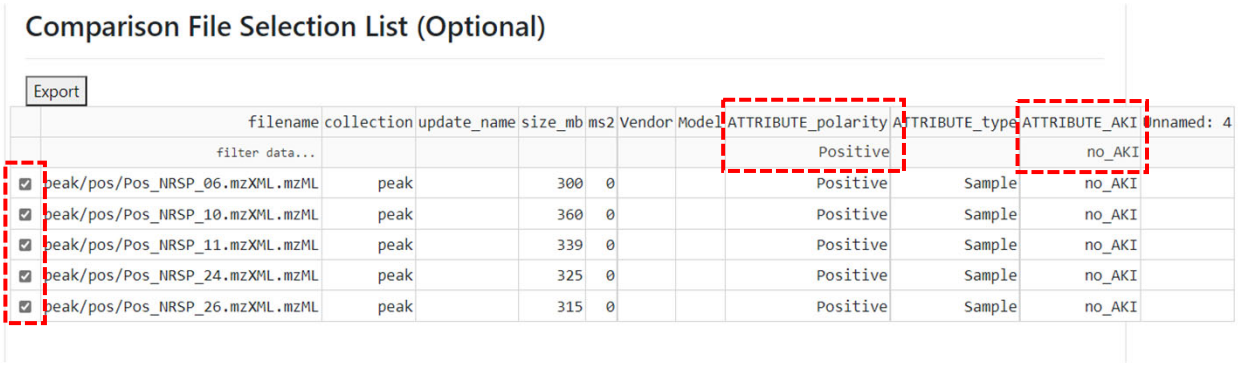
	filename	collection	update_name	size_mb	ms2	Vendor	Model	ATTRIBUTE_polarity	ATTRIBUTE_type	ATTRIBUTE_AKI	Unnamed: 4
	filter data...							Positive		AKI	
☑	peak/pos/Pos_NRSP_04.mzXML.mzML	peak		316	0			Positive	Sample	AKI	
☑	peak/pos/Pos_NRSP_05.mzXML.mzML	peak		321	0			Positive	Sample	AKI	
☐	peak/pos/Pos_NRSP_06.mzXML.mzML	peak		300	0			Positive	Sample	no_AKI	
☑	peak/pos/Pos_NRSP_07.mzXML.mzML	peak		301	0			Positive	Sample	AKI	
☑	peak/pos/Pos_NRSP_08.mzXML.mzML	peak		318	0			Positive	Sample	AKI	
☐	peak/pos/Pos_NRSP_10.mzXML.mzML	peak		360	0			Positive	Sample	no_AKI	
☐	peak/pos/Pos_NRSP_11.mzXML.mzML	peak		339	0			Positive	Sample	no_AKI	
☑	peak/pos/Pos_NRSP_12.mzXML.mzML	peak		299	0			Positive	Sample	AKI	
☑	peak/pos/Pos_NRSP_13.mzXML.mzML	peak		344	0			Positive	Sample	AKI	
☐	peak/pos/Pos_NRSP_24.mzXML.mzML	peak		325	0			Positive	Sample	no_AKI	

« < 1 / 2 > »

62

Visualizing Data GNPS Dashboard

- Select Positive no_AKI (Acute Kidney Injury Samples) in Comparison Selector Below



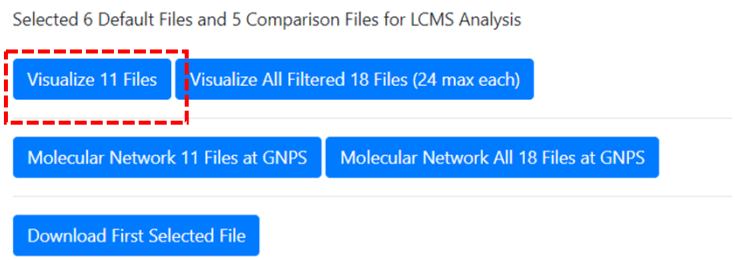
Comparison File Selection List (Optional)

Export

	filename	collection	update_name	size_mb	ms2	Vendor	Model	ATTRIBUTE_polarity	ATTRIBUTE_type	ATTRIBUTE_AKI	Unnamed: 4
	filter data...							Positive		no_AKI	
☑	peak/pos/Pos_NRSP_06.mzXML.mzML	peak		300	0			Positive	Sample	no_AKI	
☑	peak/pos/Pos_NRSP_10.mzXML.mzML	peak		360	0			Positive	Sample	no_AKI	
☑	peak/pos/Pos_NRSP_11.mzXML.mzML	peak		339	0			Positive	Sample	no_AKI	
☑	peak/pos/Pos_NRSP_24.mzXML.mzML	peak		325	0			Positive	Sample	no_AKI	
☑	peak/pos/Pos_NRSP_26.mzXML.mzML	peak		315	0			Positive	Sample	no_AKI	

63

Visualizing Data GNPS Dashboard



Selected 6 Default Files and 5 Comparison Files for LCMS Analysis

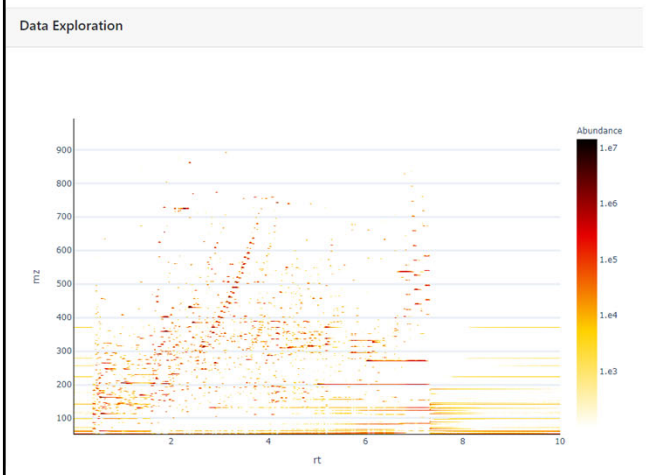
Visualize 11 Files | Visualize All Filtered 18 Files (24 max each)

Molecular Network 11 Files at GNPS | Molecular Network All 18 Files at GNPS

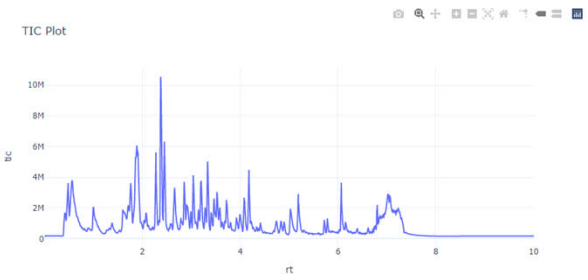
Download First Selected File

64

The GNPS Dashboard – Visualizing Raw MS Data in the Browser



- No Software Install
- Interactive
- Shareable
- Collaborative



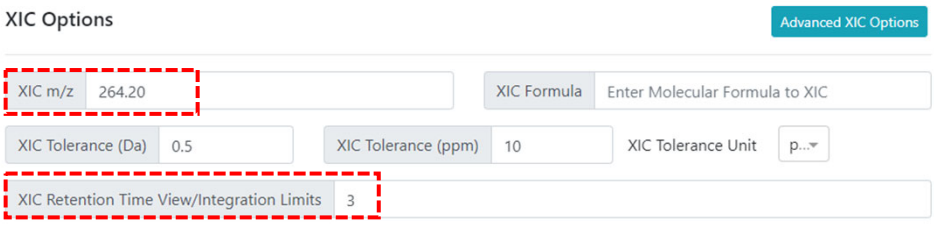
Catch up LInk

Petras et al. Nature Methods 2021

65

Connecting to Raw Data – which samples have drugs?

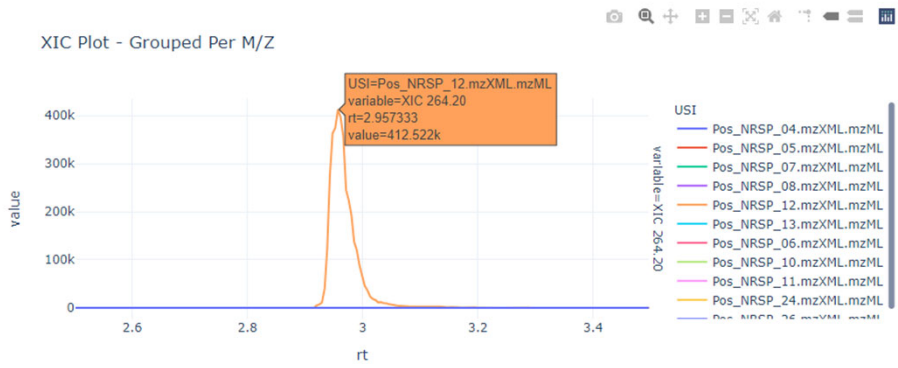
- Extracted Ion Chromatogram Desmethylvenlafaxine
- **264.20 m/z**
- **3 min Retention Time**



66

Connecting to Raw Data – which samples have drugs?

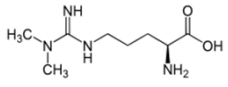
- Extracted Ion Chromatogram – Desmethylvenlafaxine
- A single AKI Sample – what might this mean?



67

Validating Differentially Expressed Metabolites in Publication

Metabolites	Metabolic pathways involved	Boston FC	Boston Raw *P*
Decreased			
Xanthine (+)	Purine, caffeine	0.26	4.00e−6
N,N-dimethylarginine (+)	Arginine, urea	0.36	5.45e−6
Cyclic AMP (−)	Purine, cellular signaling	0.42	5.80e−6



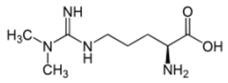
Observed in Positive Mode
203.150 m/z @ 0.6 min retention time

Raines et al. 2021

68

Validating Differentially Expressed Metabolites in Publication

Metabolites	Metabolic pathways involved	Boston FC	Boston Raw *P*
Decreased			
Xanthine (+)	Purine, caffeine	0.26	4.00e−6
N,N-dimethylarginine (+)	Arginine, urea	0.36	5.45e−6
Cyclic AMP (−)	Purine, cellular signaling	0.42	5.80e−6

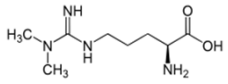


Observed in Positive Mode
203.150 m/z @ 0.6 min retention time

69

Validating Differentially Expressed Metabolites in Publication

Metabolites	Metabolic pathways involved	Boston FC	Boston Raw *P*
Decreased			
Xanthine (+)	Purine, caffeine	0.26	4.00e−6
N,N-dimethylarginine (+)	Arginine, urea	0.36	5.45e−6
Cyclic AMP (−)	Purine, cellular signaling	0.42	5.80e−6



Observed in Positive Mode
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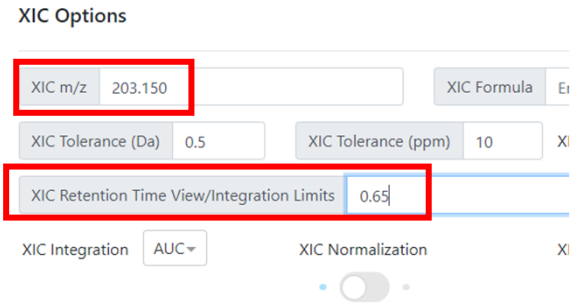
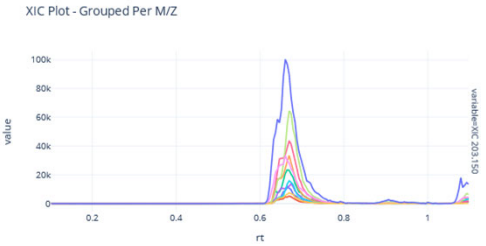
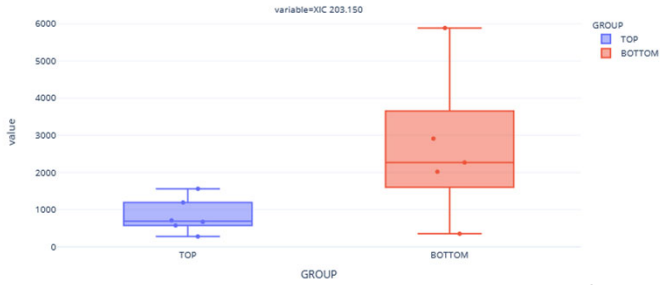


70

Validating Differentially Expressed Metabolites in Publication

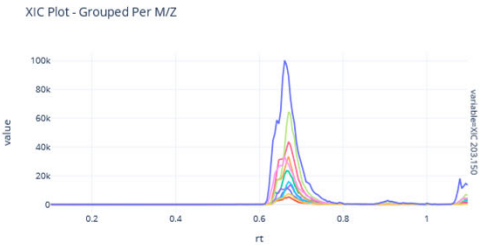


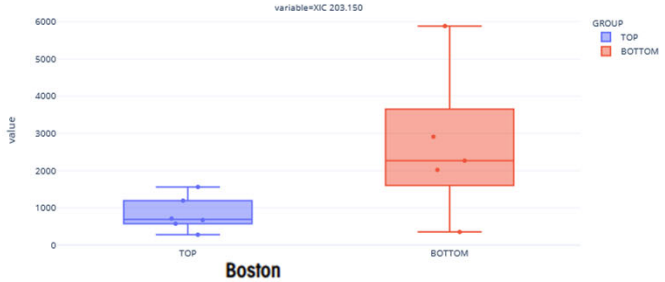


Top: **Acute Kidney Injury**
Bottom: **No Acute Kidney Injury**

71

Validating Differentially Expressed Metabolites in Publication





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Top: **Acute Kidney Injury**
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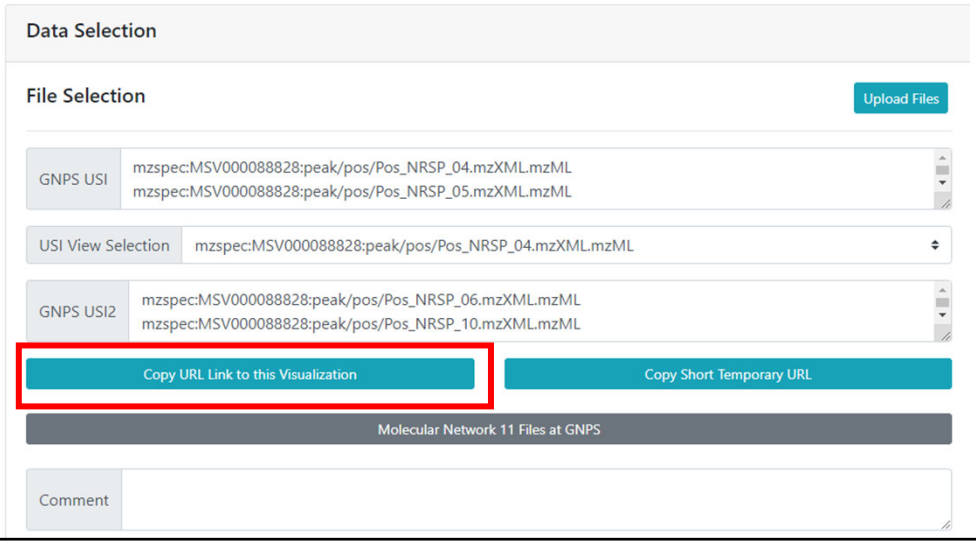
72

Sharing Visualization – Share exactly what you see with others



73

Outline for today

- **Submit a molecular networking job (Hands-on, Pieter).**
- **Explanation of what was just submitted (Pieter).**
- **Exploring the molecular network (Ming).**
- **GNPS dashboard for inspecting the data (Ming).**
- **MASST (If we have time, Pieter)**

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Growing repositories

Leveraging repository scale information to annotate unknowns

MASST

masst.ucsd.edu

= BLAST for molecules

Ming Wang

Wang Et al Nature Biotechnology 2020

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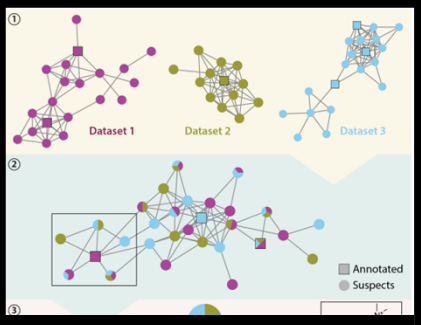
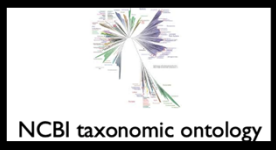
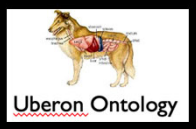


Global Molecular Network



Age

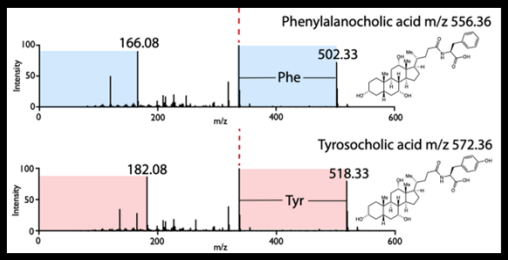


Sex

Wang Et al Nature Biotechnology 2020

76

Question:
Is the work in an animal model translational to humans?



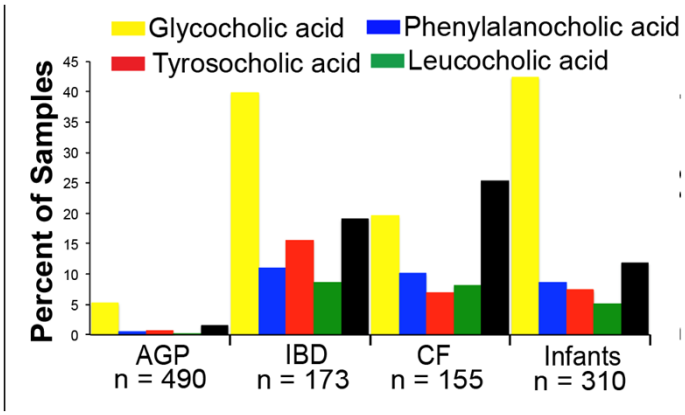
MASST

Wang Et al Nature Biotechnology 2020

Quinn et al Nature 2020

77

Now we know these bile acids are found in humans and that the work is translational.



+27 other public projects from human samples.

78

Topic/domain specific MASST's


Kiana West

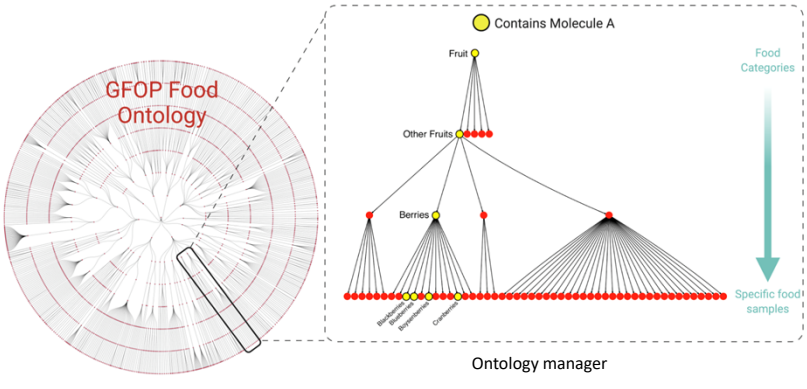

Robin Schmid


Ming Wang

PhyloMASST, DiseaseMASST, MicrobeMASST, ExposureMASST etc will be available in the future

79

Connect molecules to food ontologies.



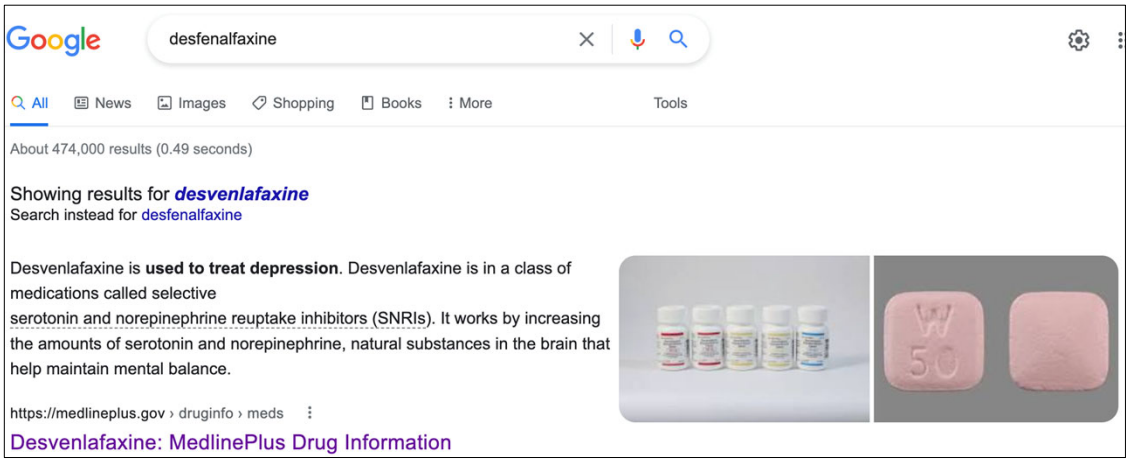
Ontology manager


Kiana West

80

80

Is this drug often observed?
What sample types is this drug found in?
Is there evidence it is found in the environment?

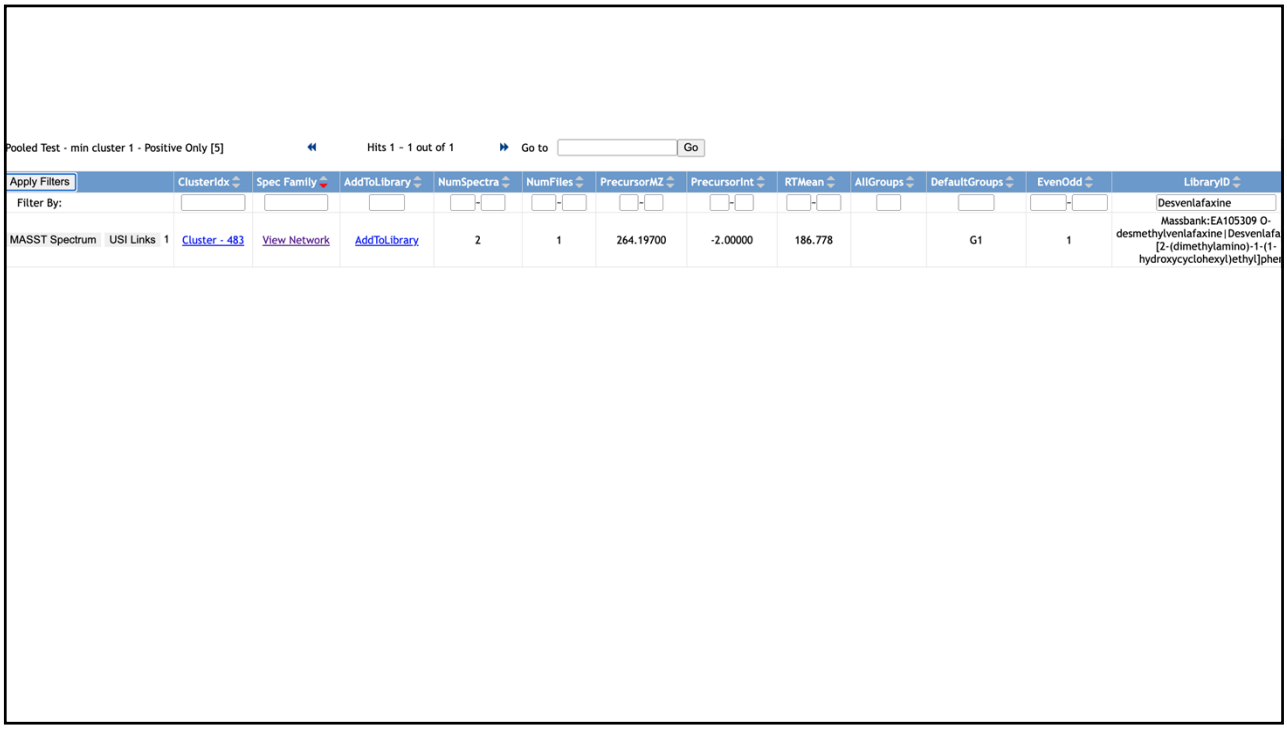


81

Or

masst.ucsd.edu

82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Go
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Spec Family
AddToLibrary
NumSpectra
NumFiles
PrecursorMZ
PrecursorInt
RTMean
AllGroups
DefaultGroups
EvenOdd
LibraryID
Filter By:
Desvenlafaxine
MASST Spectrum
USI Links
1
Cluster - 483
View Network
AddToLibrary
2
1
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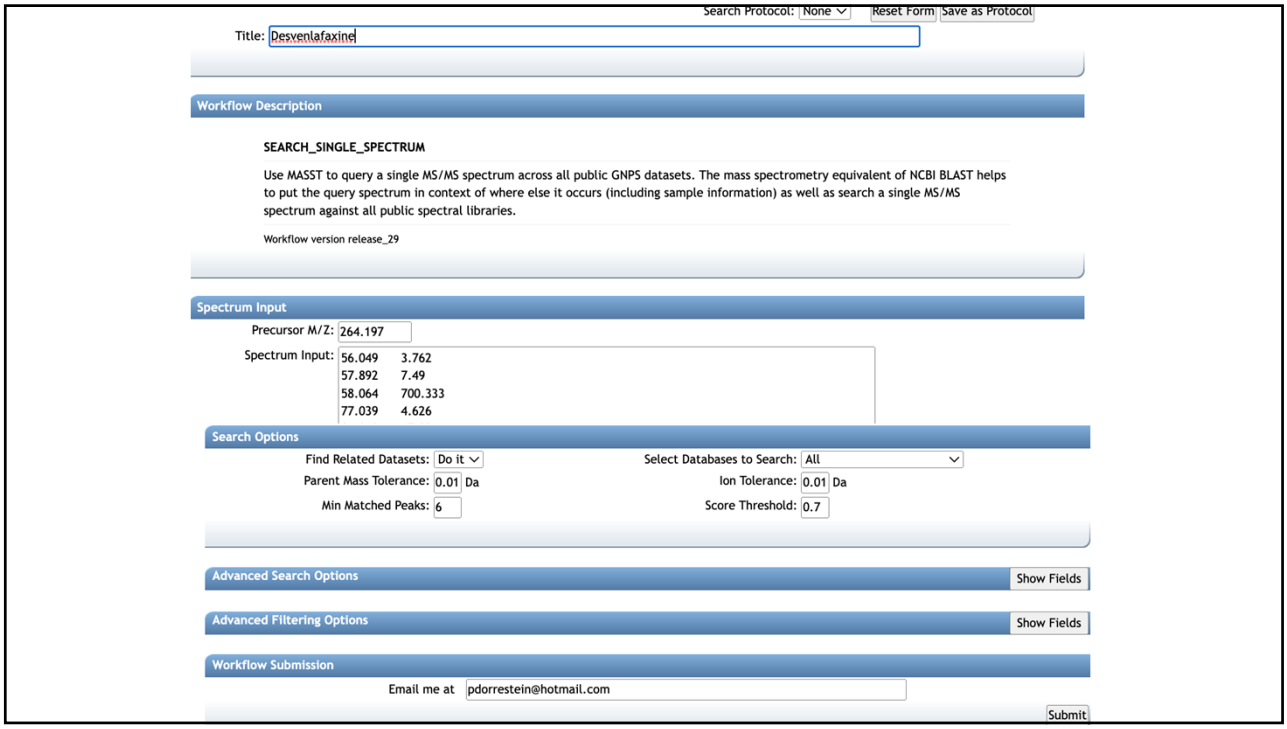
[2-(dimethylamino)-1-(1-hydroxycyclohexyl)ethyl]phe

83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Reset Form
Save as Protocol
Title:
Desvenlafaxine
Workflow Description
SEARCH_SINGLE_SPECTRUM
Use MASST to query a single MS/MS spectrum across all public GNPS datasets. The mass spectrometry equivalent of NCBI BLAST helps to put the query spectrum in context of where else it occurs (including sample information) as well as search a single MS/MS spectrum against all public spectral libraries.
Workflow version release_29
Spectrum Input
Precursor M/Z:
264.197
Spectrum Input:
56.049 3.762
57.892 7.49
58.064 700.333
77.039 4.626
Search Options
Find Related Datasets:
Do it
Select Databases to Search:
All
Parent Mass Tolerance:
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Da
Ion Tolerance:
0.01
Da
Min Matched Peaks:
6
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Advanced Search Options
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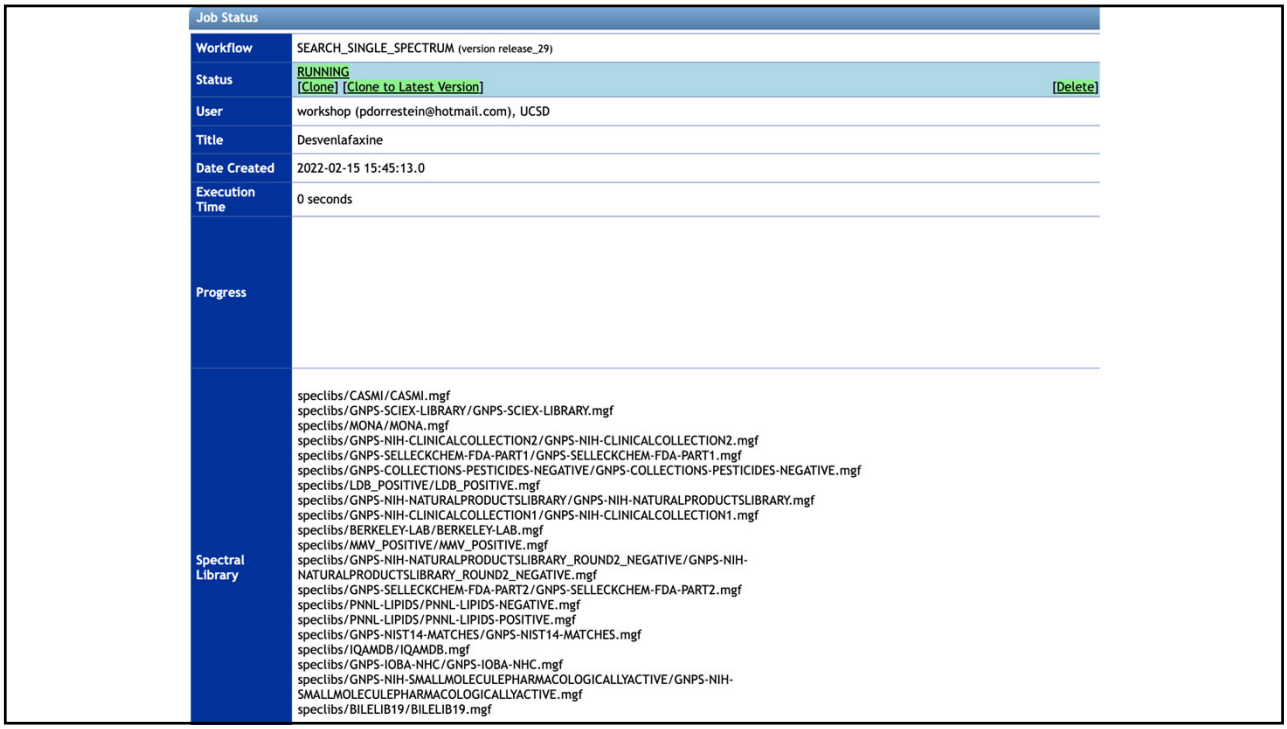
Show Fields
Workflow Submission
Email me at
pdorrestein@hotmail.com
Submit

84



Job Status

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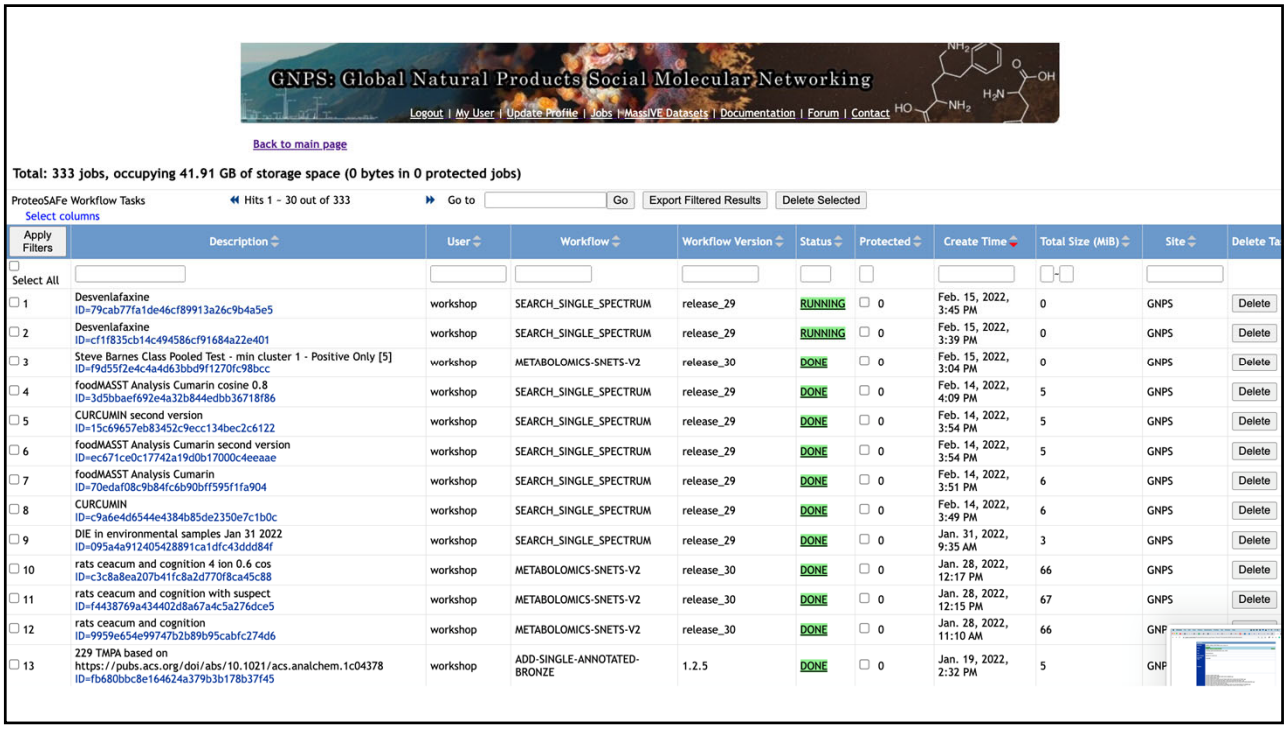
Date Created	2022-02-15 15:45:13.0
Execution Time	0 seconds
Progress	
Spectral Library	specLibs/CASMI/CASMI.mgf specLibs/GNPS-SCIEX-LIBRARY/GNPS-SCIEX-LIBRARY.mgf specLibs/MONA/MONA.mgf specLibs/GNPS-NIH-CLINICALCOLLECTION2/GNPS-NIH-CLINICALCOLLECTION2.mgf specLibs/GNPS-SELLECKCHEM-FDA-PART1/GNPS-SELLECKCHEM-FDA-PART1.mgf specLibs/GNPS-COLLECTIONS-PESTICIDES-NEGATIVE/GNPS-COLLECTIONS-PESTICIDES-NEGATIVE.mgf specLibs/LDB_POSITIVE/LDB_POSITIVE.mgf specLibs/GNPS-NIH-NATURALPRODUCTSLIBRARY/GNPS-NIH-NATURALPRODUCTSLIBRARY.mgf specLibs/GNPS-NIH-CLINICALCOLLECTION1/GNPS-NIH-CLINICALCOLLECTION1.mgf specLibs/BERKELEY-LAB/BERKELEY-LAB.mgf specLibs/MMV_POSITIVE/MMV_POSITIVE.mgf specLibs/GNPS-NIH-NATURALPRODUCTSLIBRARY_ROUND2_NEGATIVE/GNPS-NIH-NATURALPRODUCTSLIBRARY_ROUND2_NEGATIVE.mgf specLibs/GNPS-SELLECKCHEM-FDA-PART2/GNPS-SELLECKCHEM-FDA-PART2.mgf specLibs/PNNL-LIPIDS/PNNL-LIPIDS-NEGATIVE.mgf specLibs/PNNL-LIPIDS/PNNL-LIPIDS-POSITIVE.mgf specLibs/GNPS-NIST14-MATCHES/GNPS-NIST14-MATCHES.mgf specLibs/IQAMDB/IQAMDB.mgf specLibs/GNPS-IOBA-NHC/GNPS-IOBA-NHC.mgf specLibs/GNPS-NIH-SMALLMOLECULEPHARMACOLOGICALLYACTIVE/GNPS-NIH-SMALLMOLECULEPHARMACOLOGICALLYACTIVE.mgf specLibs/BILELIB19/BILELIB19.mgf

85



GNPS: Global Natural Products Social Molecular Networking

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Total: 333 jobs, occupying 41.91 GB of storage space (0 bytes in 0 protected jobs)

ProteoSAFe Workflow Tasks Hits 1 - 30 out of 333 Go to Go Export Filtered Results Delete Selected

Select columns

Apply Filters	Description	User	Workflow	Workflow Version	Status	Protected	Create Time	Total Size (MiB)	Site	Delete Ta
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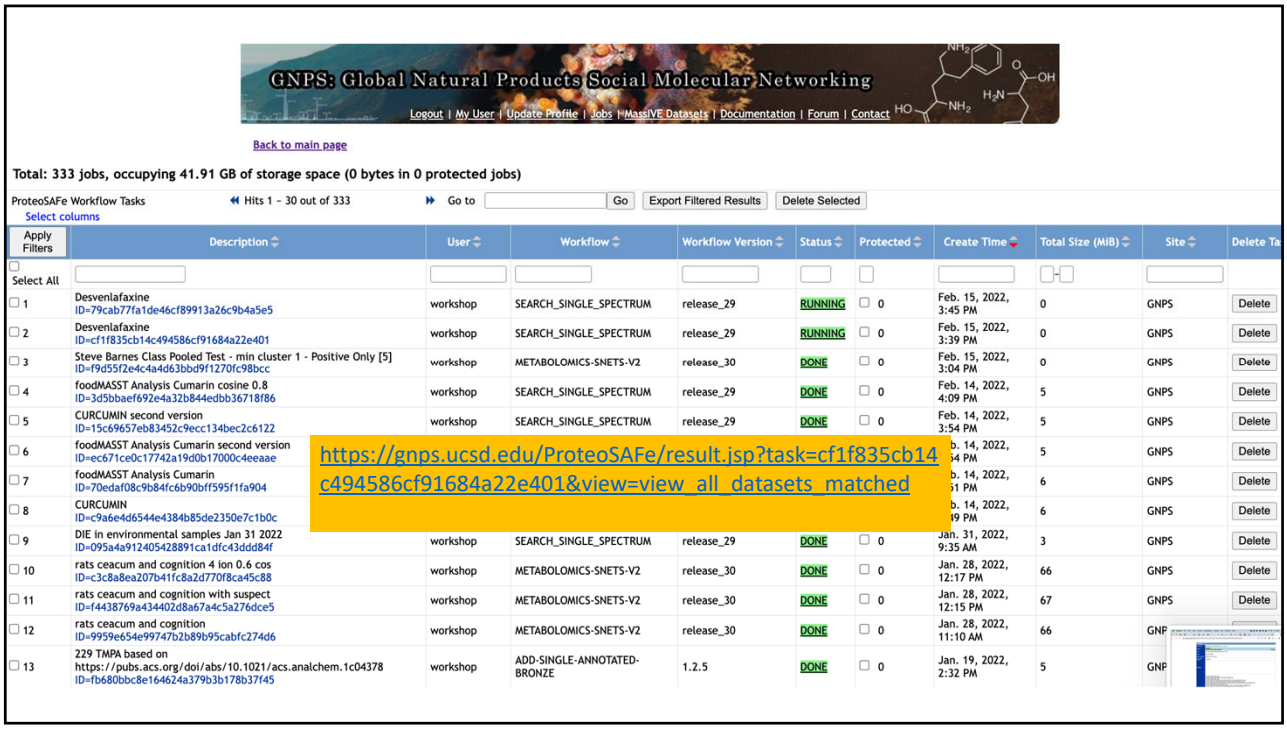
GNPS: Global Natural Products Social Molecular Networking
Logout | My User | Update Profile | Jobs | MassIVE Datasets | Documentation | Forum | Contact
Back to main page
Total: 333 jobs, occupying 41.91 GB of storage space (0 bytes in 0 protected jobs)
ProteoSAFe Workflow Tasks
Hits 1 - 30 out of 333
Go to
Go
Export Filtered Results
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Select columns
Apply Filters
Description
User
Workflow
Workflow Version
Status
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Select All
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