

FlyMet: an online metabolomics atlas and resource for *Drosophila*

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ABSTRACT

Untargeted mass spectrometry-based metabolomics is a powerful technique which attempts to identify all the metabolites in a system (the metabolome). It produces large and complex data sets, creating a need for compact and comprehensible analysis tools. Based on previous work demonstrating the feasibility of metabolomic analysis of whole flies and individual tissues, our lab is now developing FlyMet.org, a comparable atlas of 19 reference tissue metabolomes, obtained by separately microdissecting tissues of adult (male and female) and larval *Drosophila melanogaster*. Our database and web application (FlyMet.org) provide information on peaks, their identification and confidence levels, and relative abundances. Metabolites will be linked to metabolic pathways and gene identifiers where available, and thus to FlyAtlas.org and FlyAtlas2.org. Through the development of FlyMet.org, we will use metabolomics to help characterize putative enzymes as well as to add phenotypic information to uncharacterized genes.

INTRODUCTION

FlyMet provides a detailed tissue-specific map of the metabolites in *Drosophila* for use in the public domain (available at flymet.org).

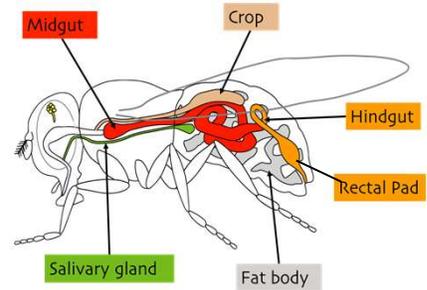
FlyMet aims to:

- Present a user-friendly easily accessible interface to metabolomics data for all users.
- Provide a detailed tissue-specific map of *Drosophila* metabolites with access to parallel large-scale gene expression data (FlyAtlas web applications).
- Give biological insight into metabolic processes and pathways in different *Drosophila* tissues.
- Allow an understanding of the roles of different tissues in the context of the whole fly.

TISSUES COLLECTION

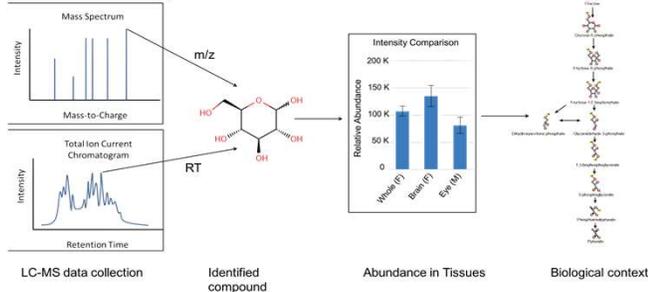
Nineteen separate reference tissues samples are painstakingly collected, in quadruplicate, by delicate microdissections of adult (male and female) and third instar larvae *Drosophila*. Samples are pooled as required, extracted in chloroform: methanol: water, then frozen until mass-spec analysis.

The tissue samples include: Accessory glands, Brain, Carcass, Crop, Eye, Fat Body, Head, Heart, Hemolymph, Hindgut, Mated Spermatheca, Midgut, Ovary, Rectal Pads, Salivary gland, Testes, Thoracoabdominal ganglion, Trachea, Tubules and Virgin Spermatheca.



METABOLOMICS

The metabolomics pipeline



In all multicellular organisms, the metabolomes of different tissues are likely to differ significantly, reflecting the different specialized jobs they perform. Studying the composition of tissues in humans is obviously hard to perform, however *Drosophila* has proved itself to be an excellent 'model' for many human processes.

Our pipeline uses liquid chromatography mass-spectrometry – where the mass and retention time are collected to identify possible compounds. This information is then used to look at the relative abundance of the compounds in the different tissues and what this means in a biological context.

FLYMET.ORG

FlyMet.org is a continual work in process. To date, the web application contains the metabolome for twelve different tissue types differentiated into male (M), female (F) and larval (L) *Drosophila*. The data includes whole fly (M, F and L) samples for comparison. Peaks, Metabolites and associated Pathways can be viewed on an individual basis or as a collection through the associated Explorer pages. For example using the Peak Explorer, the abundance of all the annotated mass-spec peaks can be compared across tissue-types along with the fold-change between individual tissues and whole flies. Compound annotations along with a confidence factor can be easily viewed. In addition, identified and annotated metabolites can be searched and changes in metabolic pathways between tissues and whole flies explored.

FlyMet Peak Explorer

Intensities Comparisons Mutants Growth Conditions Peak Explorer

The log₂ fold-change (FC) in peak intensity levels between *Drosophila* tissues and the whole flies

Columns can be dragged to reorganise the data as required.

Peak ID	m/z	RT	Brain (F)	Brain (L)	Brain (M)	Carcass (F)	Carcass (L)	Carcass (M)	Eye (F)	Eye (M)
2376	809479	732.09	2.97	2.81	3.38	2.46	1.76	3.09	4.03	4.69
2540	370.1705	774.93	2.96	-	2.68	-	-	-	-	0.83
2209	780.4806	199.12	2.95	-	2.14	-2.49	-	-0.93	-0.16	-0.65
446	178.0863	422.15	2.88	1.72	3.32	-4.29	-0.78	-2.33	-3.81	-2.48
2711	241.1448	274.74	2.76	-2.11	2.49	-0.64	-0.63	-0.24	0.68	1.17
1504	132.0304	733.56	3.65	-0.02	3.53	-1.68	-1.40	0.34	1.31	0.54
1506	115.0037	682.95	2.55	0.53	2.50	-0.42	1.58	-0.76	1.93	2.01
321	165.0195	711.40	2.54	-0.09	2.70	-0.79	1.64	-0.91	1.56	1.81
530	272.1854	413.51	2.52	1.09	0.57	1.14	1.60	-0.86	2.86	0.94
2384	728.5594	211.62	2.46	-	1.76	-0.62	-	0.07	-1.65	-1.76

Showing 11 to 20 of 3,391 entries 1 row selected

Peak Annotations

Peak 1504

MH+M-H All adducts

- Chlorogenic acid
Ion: MH- Mass: 133.0376
- Malonic acid
Ion: MH- Mass: 133.0376
- D-isopropic acid
Ion: MH- Mass: 133.0376
- Isopropic acid
Ion: MH- Mass: 133.0376

METABOLITE SEARCH

Searching for an individual metabolite reveals the fold change of that metabolite in *Drosophila* tissues compared to that found in the whole fly. By clicking on a tissue the different abundancies of that metabolite in the different sex/life-stage against whole fly can be investigated.

Searching for Xanthurenic Acid

Enzymes Metabolites Pathways Tissues

Search for a metabolite and find out the abundance in *Drosophila* tissues:

Metabolite Search

xanthurenic acid

Search for a metabolite and find out the abundance in *Drosophila* tissues:

Metabolite Search

xanthurenic acid levels in *Drosophila* tissues

Tissue-Type	Adult Female FC	Adult Male FC	Larvae FC
Brain	-4.04	-4.91	-7.54
Carcass	-11.38	-4.68	-6.4
Eye	2.43	3.01	nm
Fat Body	nm	nm	-5.34
Fatbody	72.6	-11.6	nm
Head	1.55	1.2	nm
Hemolymph	-6.74	-6.87	-2.73
Hindgut	nm	nm	-0.79
Midgut	-11.25	-9.98	-7.41

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ACKNOWLEDGEMENTS

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