

Introduction & Update of Metabolomics Core Facility at FSM of NU

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May 2020

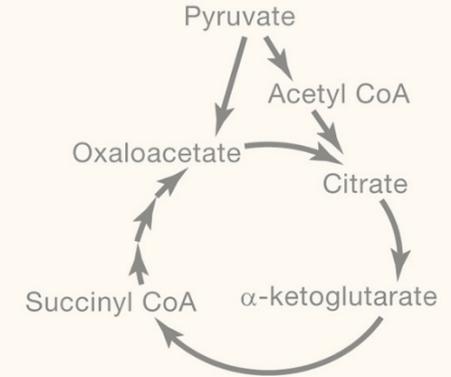
Medicine

Biomarkers
Disease mechanisms
Drug target identification

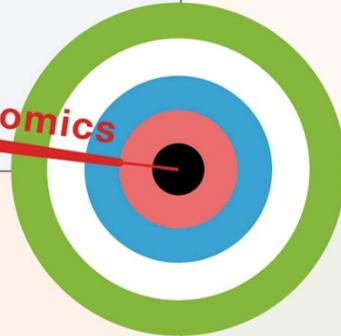


Biochemistry and bioengineering

Pathway mapping
Enzyme regulation
Yield enhancement



Metabolomics



Food and agriculture

Nutrient composition
Crop fitness
Dietary choices



Environment

Microbial communities
Nutrient cycles
Bioremediation



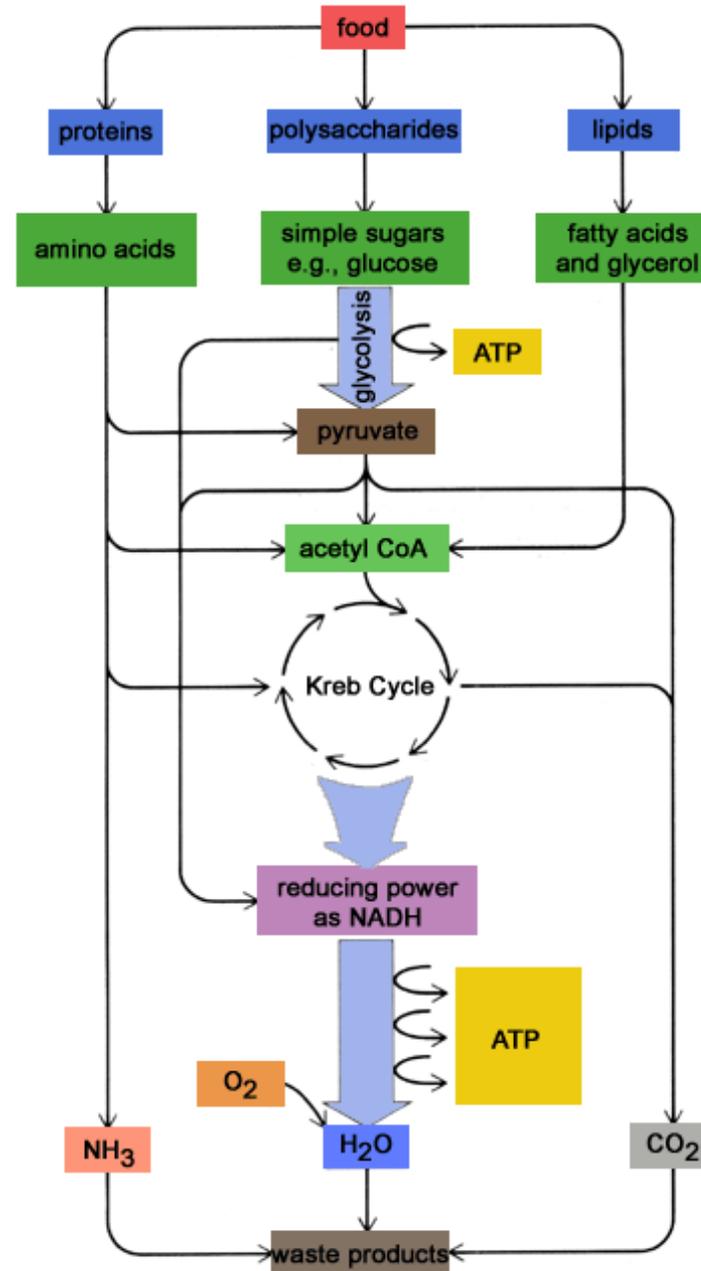
What is Metabolomics

- **Metabolomics** is the study of chemical processes involving metabolites, the small molecule intermediates and products of metabolism. Specifically, metabolomics is the "systematic study of the unique chemical fingerprints that specific cellular processes leave behind", the study of their small-molecule metabolite profiles.
- **Metabolome** represents the complete set of metabolites in a biological cell, tissue, organ or organism, which are the end products of cellular processes.

stage 1:
breakdown of large macro-
molecules to
simple subunits

stage 2:
breakdown of
simple subunits
to acetyl CoA
accompanied by
production of
limited ATP
and NADH

stage 3:
complete oxida-
tion of acetyl
CoA to H₂O and
CO₂ involves
production of
much NADH,
which yields
much ATP via
electron
transport

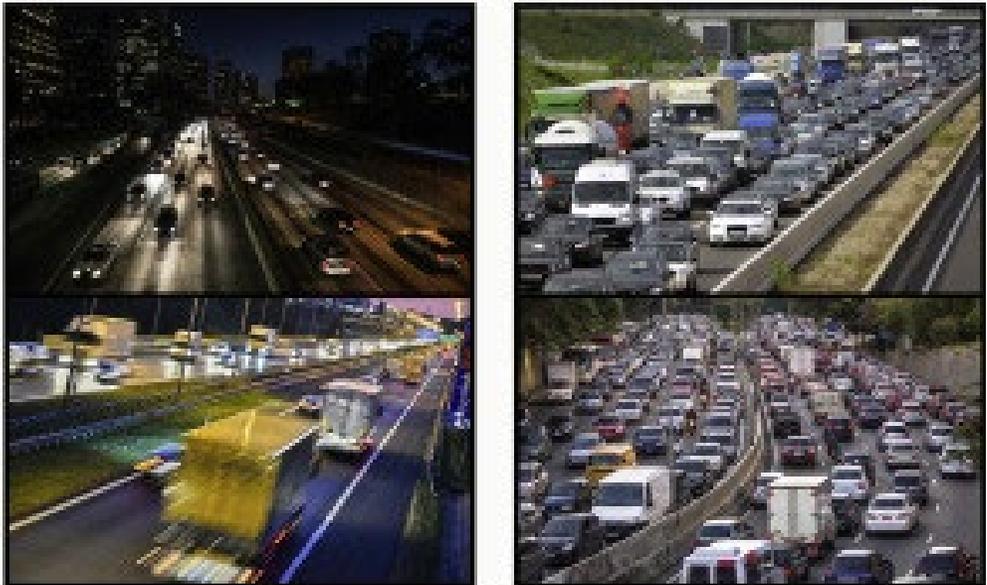


Types of Metabolomics

A

Metabolomics
→ measures concentration

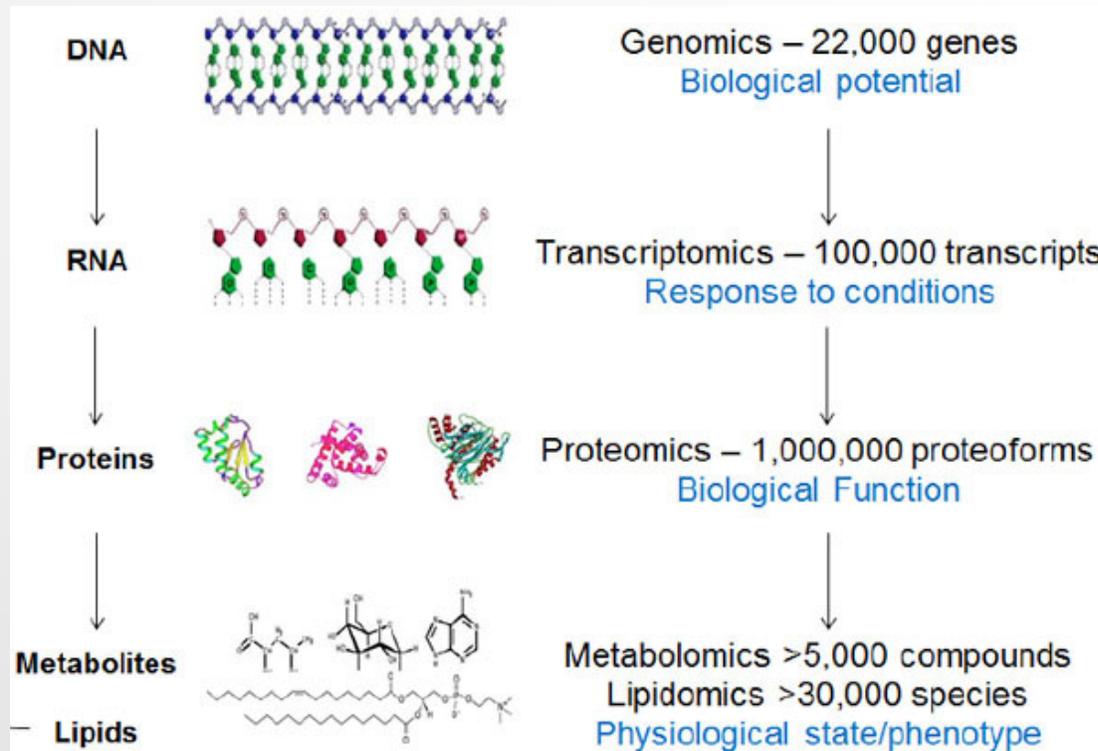
Isotope tracing
→ probes flux



Flux increases with car density (concentration) until traffic slows

Very high car density but low flux

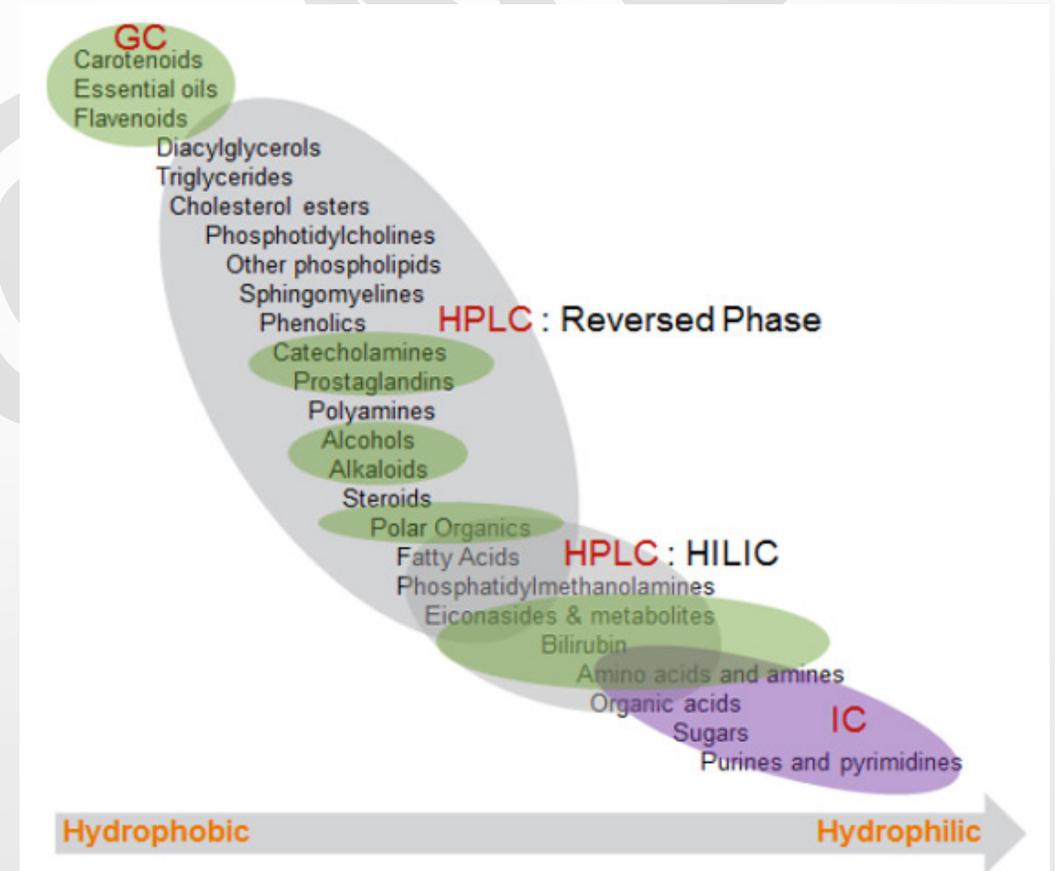
Why Metabolomics



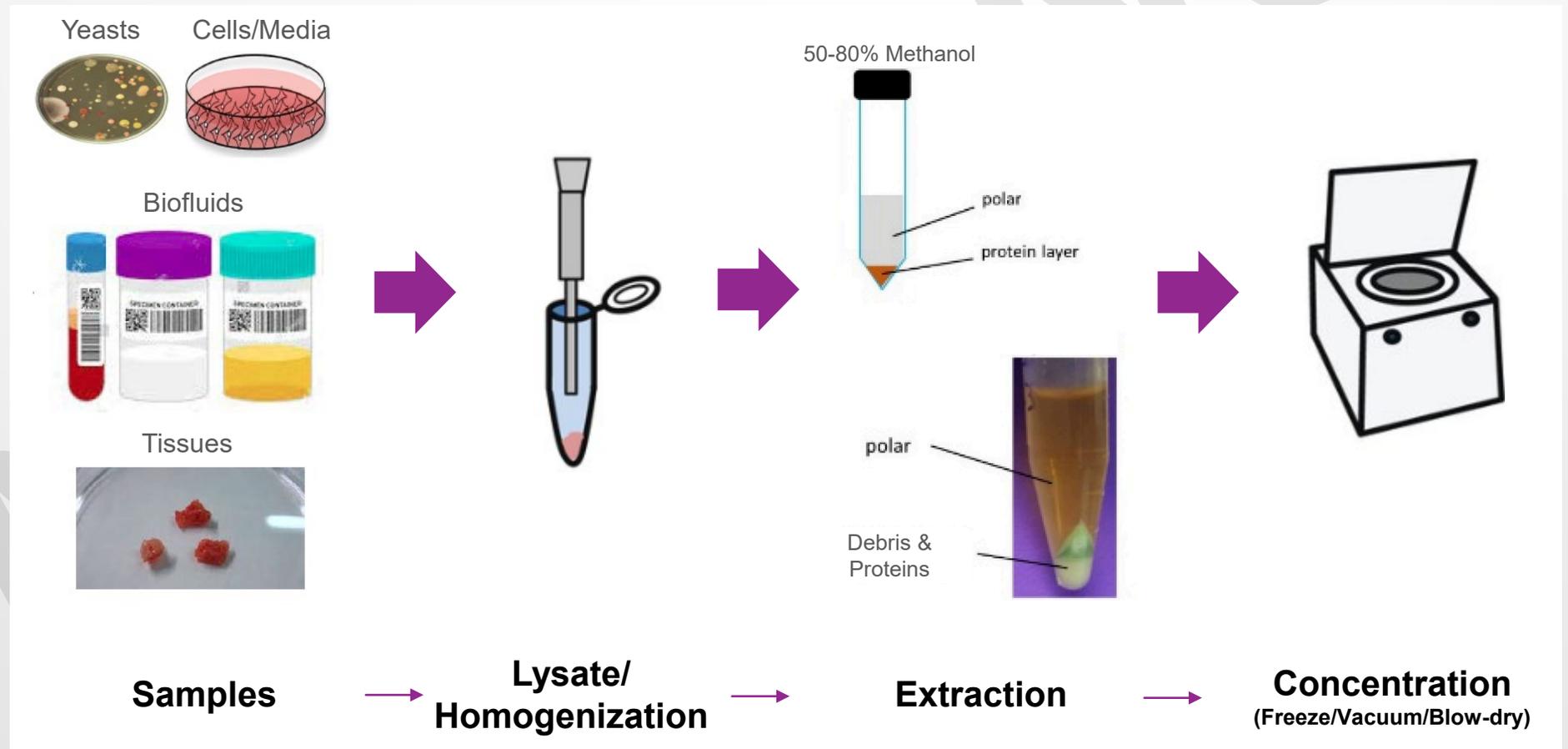
- Metabolomics makes it feasible to uniquely profile the biochemistry of an individual, or model.
- Metabolomics is being used to reveal biomarkers for the early detection and diagnosis of disease, to predict outcomes, monitor therapeutic treatments and interventions, and to provide insights into biological mechanisms.

How to Do Metabolomics

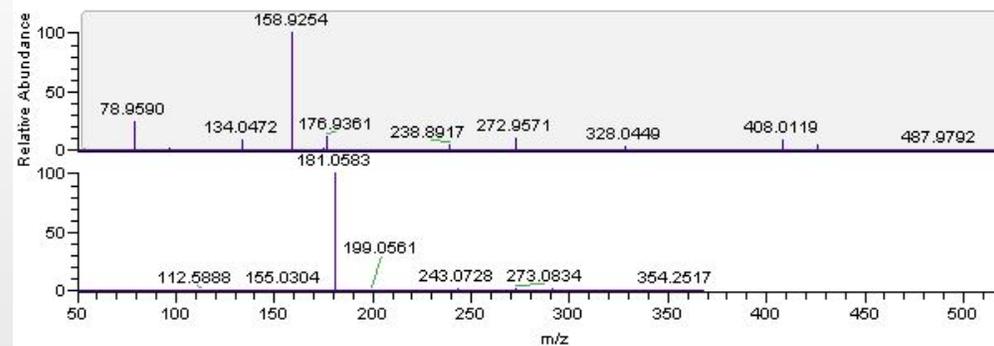
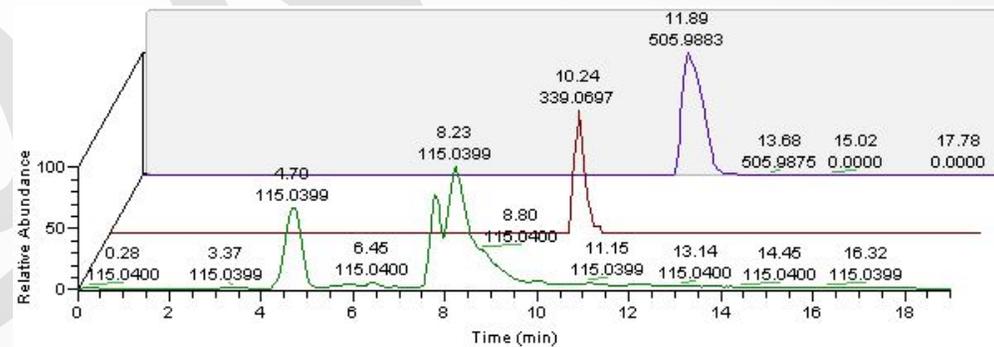
- Metabolomics investigations generally employ MS (Mass Spectrometry) coupled with GC, LC, IC (gas / liquid / ion mobility Chromatography)



Sample Preparation



LC-MS Workflow



Purpose of Metabolomics Core

- To support investigators in their research in the study of metabolism in cancer or other diseases qualitatively or quantitatively
- To assist understanding of the mechanisms of particular cancer states and other diseases, which will ideally lead to earlier detection and better treatments

Model Facilities

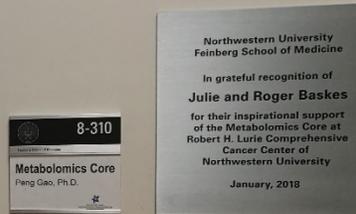
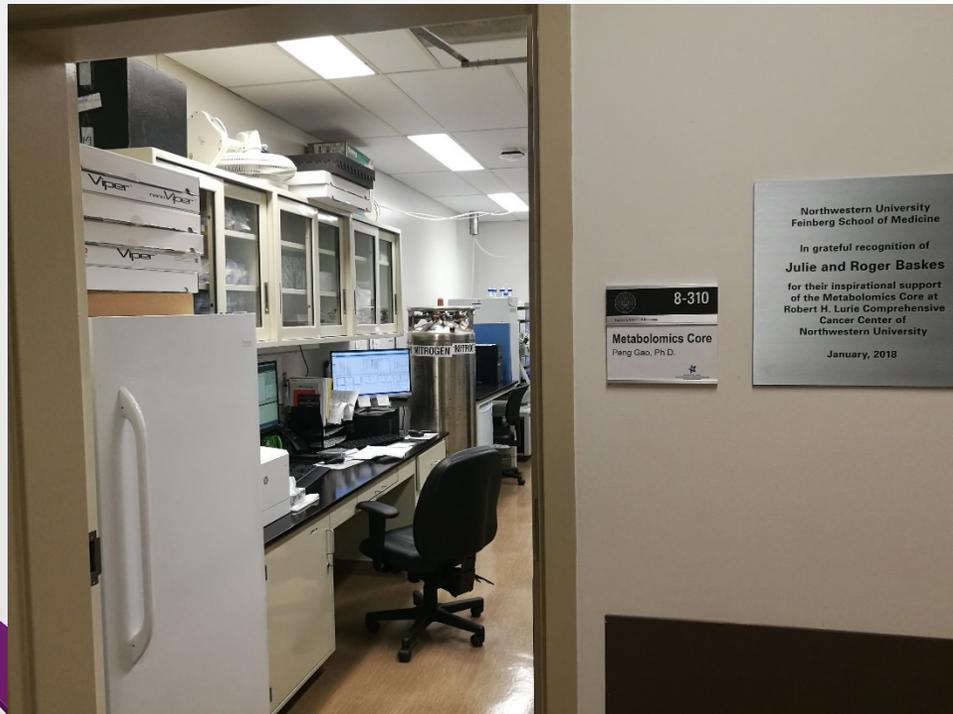
- Research Institution: Metabolites Profiling Core facility at Whitehead MIT
 - Comprehensive metabolomics services provided
 - Efficient and quick turnover time
- Commercial Company: Metabolon, Inc.
 - Well organized, efficiently run
 - Equipped with variety of Mass Spec instruments and related knowledge

Timeline

- Jun 2016 - RHLCCC received funding from Alumni Baskes' Gift
- Oct 2016 - Core lab established
- Dec 2016 - LCMS (UPLC-Q Exactive) installed
- Nov 2017 - Main protocols and methods were optimized
- Jan 2018 - Soft opening for trial samples from RHLCCC members
- Jun 2018 - Grand opening for all NU users
- Sep 2018 - Second set of LCMS (UPLC-QQQ) installed
- Mid 2020 - Seahorse Installation for Shared Resource

Infrastructure – Physical Location

- Lab Location – NU downtown campus, Olson Pavilion, 8th flr, 8-310



Infrastructure – Online Location

<https://www.cancer.northwestern.edu/research/shared-resources/metabolomics.html>

<https://nucore.northwestern.edu/facilities/Metabo>

Robert H. Lurie Comprehensive Cancer Center of Northwestern University

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Home » Research » Shared Resources » Metabolomics Core Facility

Shared Resources

- Center for Advanced Microscopy
- ChemCore
- Developmental Therapeutics Core
- Flow Cytometry Facility
- High Throughput Analysis Laboratory
- Keck Biophysics Facility
- Metabolomics Core Facility**
- Molecular and Translational Imaging Core
- Mouse Histology & Phenotyping Laboratory
- Outcomes Measurement and Survey Core Facility
- Pathology Core Facility
- Proteomics Core Facility
- Quantitative Data Sciences Core

Metabolomics Developing Core Facility

The mission of the developing Metabolomics Core Facility at Robert H. Lurie Comprehensive Cancer Center of Northwestern University is to provide LC-MS based metabolomics service including identification, semi-quantification and quantification of primary and secondary metabolites from biological samples such as cultured cells, tissues and body fluids. The Metabolomics Core supports investigators engaged in basic, preclinical and clinical cancer research, including scientists examining basic mechanisms in of disease, as well as those seeking to identify novel targets for therapy or biomarkers that can be used for early detection, diagnosis, prognosis or response to therapy.

Contact Us

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metabo@northwestern.edu
312-908-8312

Services & Equipment

- Key Services
- Equipment
- Sample Submission Process & More Information
- Highlighted Projects
- Acknowledgement

NUcore

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Home » RHLCCC Metabolomics Core (Metabo)

RHLCCC Metabolomics Core (Metabo)

The mission of the Metabolomics Core Facility at Robert H. Lurie Comprehensive Cancer Center of Northwestern University is to provide LC-MS based metabolomics service including identification, semi-quantification and quantification of primary and secondary metabolites from biological samples such as cultured cells, tissues and body fluids. The Metabolomics Core supports investigators engaged in basic, preclinical and clinical cancer research, including scientists examining basic mechanisms in of disease, as well as those seeking to identify novel targets for therapy or biomarkers that can be used for early detection, diagnosis, prognosis or response to therapy.

INSTRUCTIONS TO PLACE AN ORDER

Please visit [Metabolomics Core Facility webpage](#) before placing any order.

Metabolomics Core Facility uses NUCORE service which requiring all customers to create an order in NUCORE system prior to delivering samples to the Core. Please follow the instructions below to place an order:

- Access and log in (NU NetID and password) NUCORE system Metabolomics Core section <https://nucore.northwestern.edu/facilities/Metabo>. Please contact NUCORE Support nucore@northwestern.edu if you do not have a NUCORE account or if you are unable to log in;
- Select and click the "Request for Service" line from the SERVICES section;
- Click the ADD to CART button;
- Select an appropriate payment source when prompted;
- The CART screen will display. Click the PURCHASE button;
- Click the OK button when prompted to confirm the order;
- Copy the 12-13 digit order # generated by NUCORE, and fill it into the "payment info" section on [Sample Submission Form](#). (Step 1-7 is for NU financial purpose, it does NOT reflect the final bill or scientific request);
- Finish Sample Submission Form with detail-request/study-proposal categorized on [Metabolomics Core Facility webpage](#);
- Bring or email Sample Submission Form to the core metabo@northwestern.edu when samples are delivered.

Please note that samples will NOT enter the queue unless a NUCORE order Number, Sample Submission Form and starting material amount (detailed in [Metabolomics Core Facility webpage](#)) are all provided at the time of sample delivery. If you have any questions or concern, please contact metabo@northwestern.edu.

Thank you.

Metabolomics Core Team

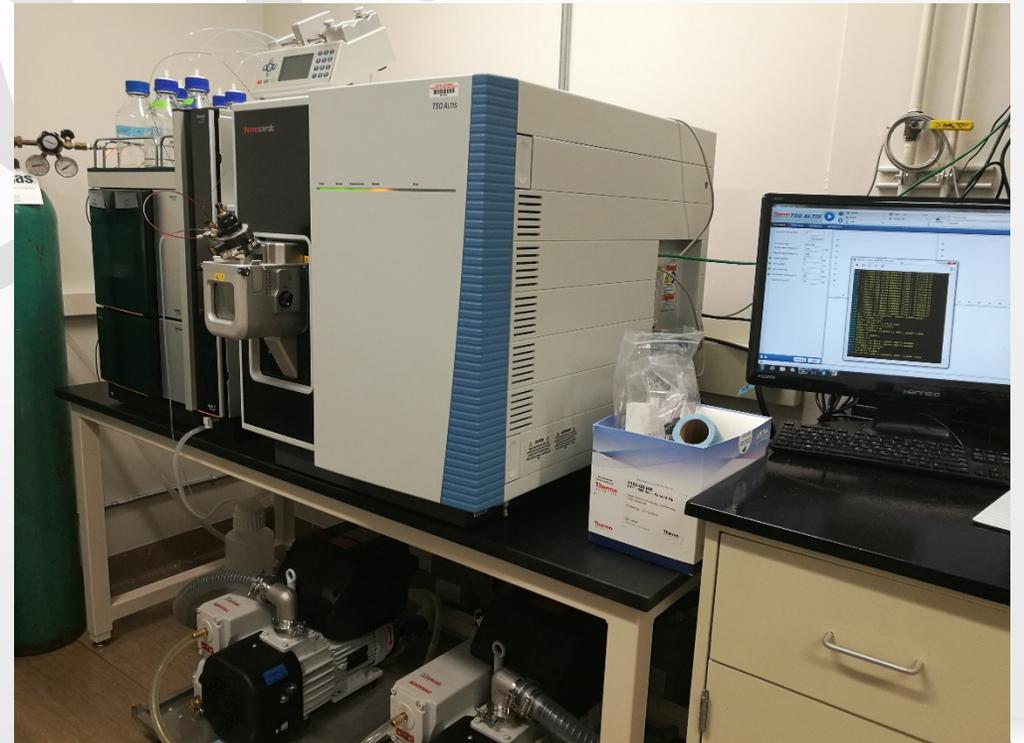
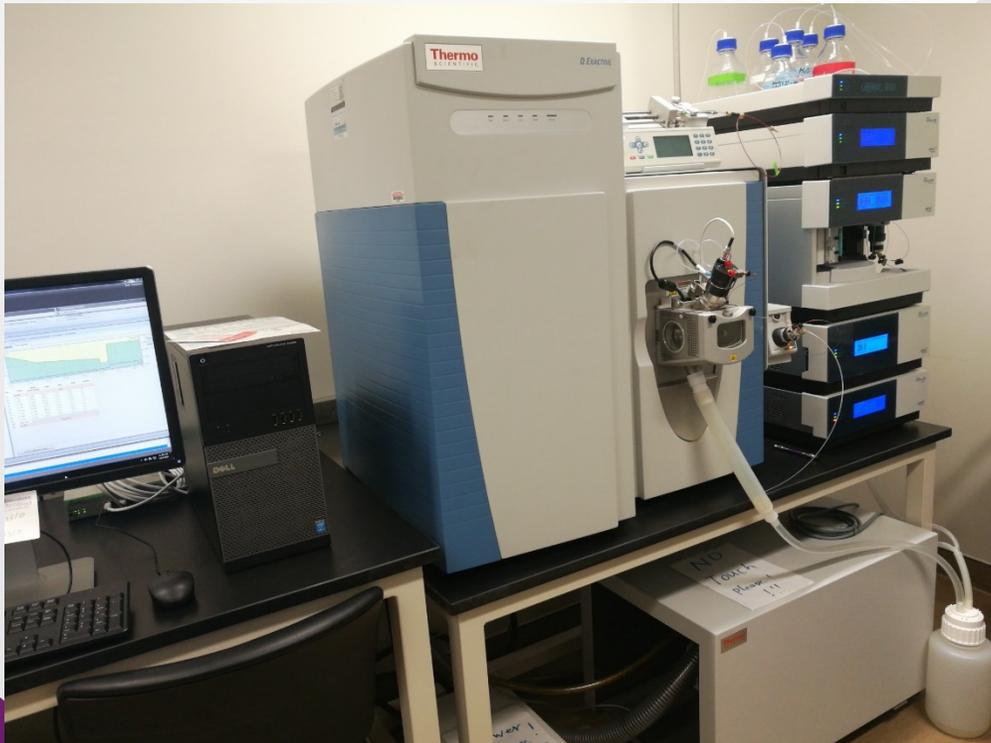
Services

- [Metabolites Profiling - FLUX \(hidden\)](#)
- [Metabolites Profiling - Hydrophilic Panel \(hidden\)](#)
- [Metabolites Profiling - Targeted Species \(hidden\)](#)
- [Metabolites Quantification \(hidden\)](#)
- [Request For Service](#)

Timed Services

Infrastructure – Main Instruments

- Thermo Ultimate3000-Q_Exactive
High Resolution / Accuracy / Sensitivity Orbitrap Mass Spectrometry paired with UHPLC
- Thermo Vanquish-TSQ
High Speed / Sensitivity Triple-Quad Mass Spectrometry paired with UHPLC



Infrastructure – Supplemental Instruments

- High speed centrifuge
- Speed-Vacuum

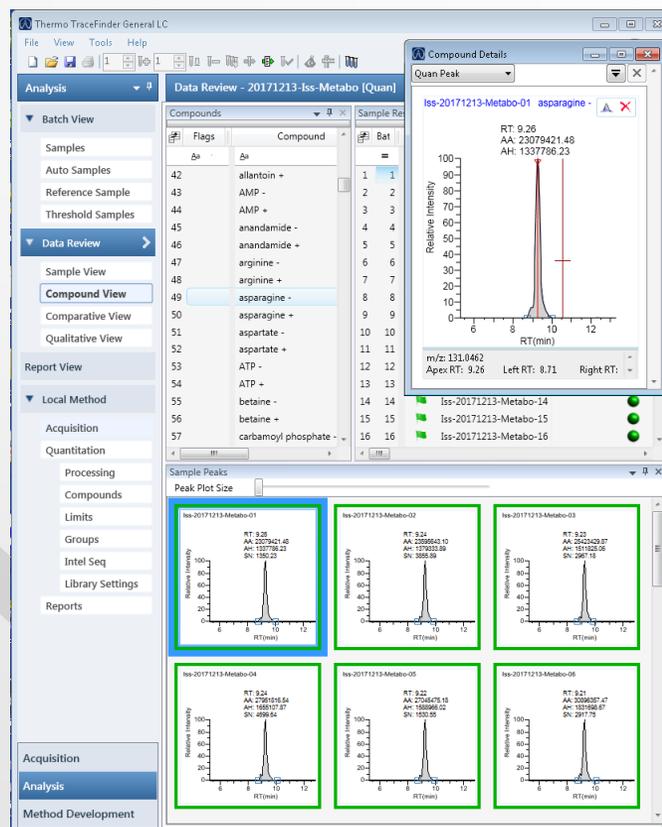


Infrastructure – Data Acquisition / Sharing

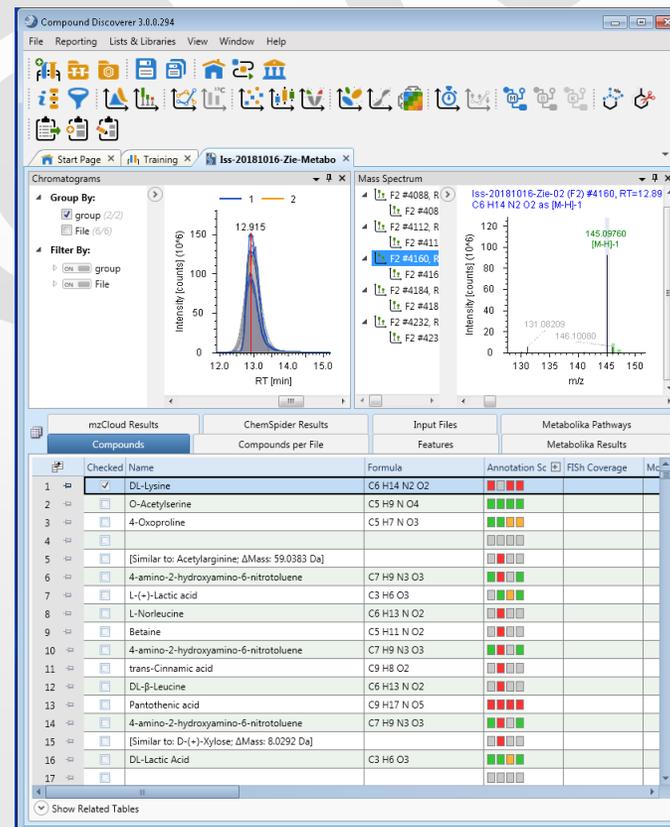
- Data Acquisition
 - X-caliber
 - Trace Finder
- Data Storage and Share
 - Onsite PC and backed-up with NUIT storage
 - NU-Box service for files sharing

Infrastructure – Data Analysis Software

TraceFinder® Targeted Quantification



CompoundDiscoverer® Targeted/Untargeted Metabolomics



Services - Current

- **Metabolites Profiling – Comprehensive Hydrophilic Panel**
Semi-quantification of 150 plus common metabolites including amino acids, nucleotides and nucleobase/nucleosides species, TCA cycle, glycolysis, pyridine and cofactor metabolites, 2-HG, a-KG, pentose phosphate pathway.
- **Metabolites Profiling – Targeted Species**
Measure metabolites on a particular pathway.
- **Metabolites Profiling – Fluxomics**
Use stable isotopes, such as ^{13}C , ^{15}N , ^2H labeled tracer to study metabolic flux in different pathways.
- **Metabolites Quantification**
Quantify metabolites targets from sample extractions, such as D- or L- 2HG, et al.
- **Sample Preparation and Data analysis**
- **Method Development and Consulting**

Services - Future

- **Targeted Metabolomics - Dissect the profiling panel to provide more diverse targets on specific pathways**
 - Amino acids and related metabolites
 - Nucleotides and nucleosides
 - TCA metabolites
 - Glycolysis
 - Pyridine and cofactor metabolites
 - Short chain fatty acids
 - Bile acids
 - More
- **Untargeted Metabolomics**
- **Lipidomics**

Services - Funding Application

- Provide written support for funding application.
- Provide suggestion for experimental design.

Required Sample Amount

	Minimum Amount	Optimal Amount
Cells	1×10^5	1×10^6
Media	2 mL	5 mL
Biofluids	50 μ L	200 μ L
Tissues	10 mg	50 mg

Service Charge

- Fee for service

Price	RHLCCC	NU/CBC	External Academic	Industry
Sample Preparation (hr)	~\$160	~\$200	~\$280	~\$360
Data Acquisition (injection)	~\$60	~\$75	~\$95	~\$125
Data Analysis (hr)	~\$160	~\$200	~\$280	~\$360

- Collaboration and cooperation in funding opportunities (future)

Current Overall Usage

	Number of PI	Number of Projects
Total	>60	>40
Cancer Center	>35	>30
Feinberg School of Medicine	8	8
General NU Groups	5	2
CBC	5	1
External Group	5	1

Publications that Core's Involved

- Hoxhaj G, Ben-Sahra I, Lockwood SE, et al. Direct stimulation of NADP⁺ synthesis through Akt-mediated phosphorylation of NAD kinase. *Science*. 2019;363(6431).
- Zhang Q, Xu H, Liu R, et al. A Novel Strategy for Targeted Lipidomics Based on LC-Tandem-MS Parameters Prediction, Quantification, and Multiple Statistical Data Mining: Evaluation of Lysophosphatidylcholines as Potential Cancer Biomarkers. *Anal Chem*. 2019;91(5).
- Weinberg SE, Singer BD, Steinert EM, et al. Mitochondrial complex III is essential for suppressive function of regulatory T cells. *Nature*. 2019;565(7740).
- Soberanes S, Misharin AV, Jairaman A, et al. Metformin Targets Mitochondrial Electron Transport to Reduce Air-Pollution-Induced Thrombosis. *Cell Metab*. 2019;29(2).
- May JL, Kouri FM, Hurley LA, et al. IDH3 α regulates one-carbon metabolism in glioblastoma. *Sci Adv*. 2019;5(1).

Grant Applications Core Supported

- 3 RO1 applications from NU PIs
- 2 RO1 applications from external PIs.
- 1 R21 application and 1 R15 applications.

Acknowledgment

Alumni Mrs. And Mr. Baskes and NU-RHLCCC.

Metabolomics core committees: Drs. Milan Mrksich, Navdeep Chandel, Joseph Bass, Issam Ben-Sahra and Paul Thomas.

Mrs. Eleni Garbes, Elena Aristide and other administration staffs from RHLCCC and NUcore.

Drs. Neil Kelleher and Young Ah Goo from PCE.

Thank you!