

Challenges and Strategies for FAIRification of Lipidomics Data

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The Reproducibility Crisis



<https://www.digital-science.com/blog/2015/11/coffeetime-science-that-last-experiment-before-leaving-the-lab/>



<https://pixabay.com/photos/computer-scrap-metal-technology-2049019/>

The Reproducibility Crisis

npj Digital Medicine

PERSPECTIVE OPEN

The reproducibility crisis in the age of digital medicine

Aaron Stupple^{1,2}, David Singerman³ and Leo Anthony Celi^{2,4}

npj Digital Medicine (2019)2:2; https://doi.org/10.1038/s41746-019-0079-z

INTRODUCTION

If anyone doubts the explosive growth of interest in digital medicine, consider a recent conference and workshop in Beijing, jointly organized by the People's Liberation Army General Hospital and MIT Critical Data to showcase the opportunities and challenges of applying machine learning to the kind of data routinely collected during the provision of care. In person, 500 attendees heard a keynote and panels and participated in a health data hackathon. Online, however, the event was streamed to more than one million unique viewers.¹

A. Stupple, D. Singerman, and L. A. Celi, "The reproducibility crisis in the age of digital medicine," *npj Digit. Med.*, vol. 2, no. 1, Art. no. 1, Jan. 2019

Reproducibility is a major concern in many fields

- Medicine
- Biology
- Machine Learning
- ...

www.nature.com/npjdigitalmed

Corrected: Author Correction

Opinion

EMBO
reports

Reproducibility crisis in science or unrealistic expectations?

Thiago FA França¹  & José Maria Monserrat² 

Nature survey found that doctors and others in biomedicine are the most concerned of all.⁵

Much of the criticism and comment about reproducibility and solutions to the crisis—both real and perceived—focuses on statistics and methodology. In the past decade, statisticians have shown how statistics may be unintentionally misused or, in some cases, intentionally abused as researchers try to produce results that appeal to professional colleagues and attract potential funders.^{6,7} Commonly proposed solutions include better statistical literacy and behavioral norms, reform of peer reviewed journals,

Science appears to be in a crisis caused by the failure to replicate published results, which is undermining confidence in the scientific literature. This

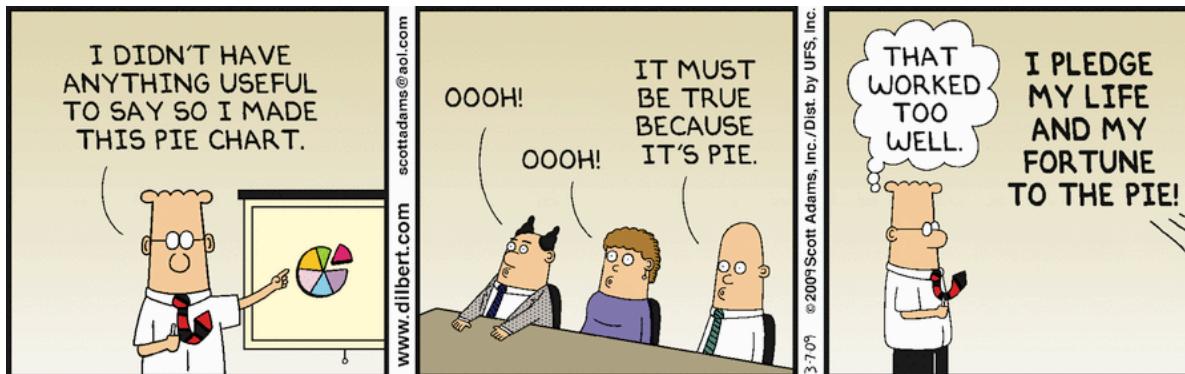
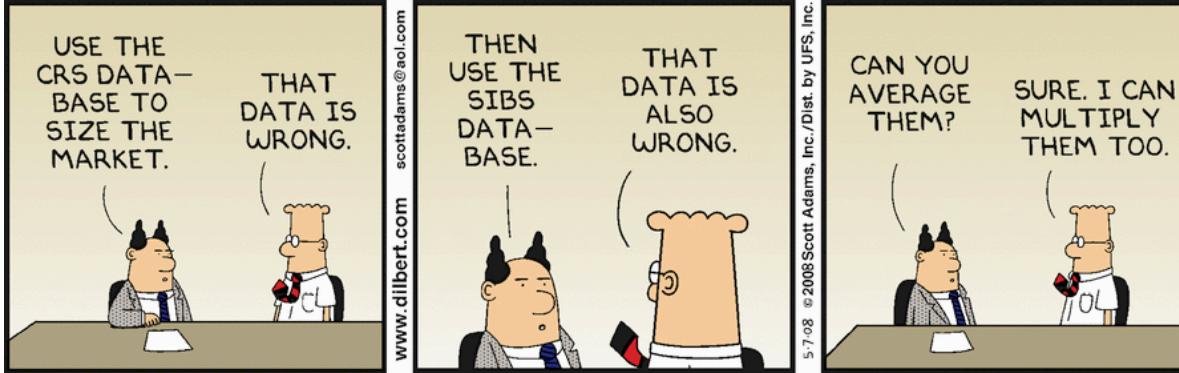
a low sample size led to high variability between samples: In one of their comparisons, the difference between the means of the samples was 1.46 standard deviations,

individual studies. Ethical and practical constraints often impose the necessity to work with relatively small samples sizes; in such cases, failure to replicate should not

T. F. França and J. M. Monserrat, "Reproducibility crisis in science or unrealistic expectations?," *EMBO reports*, vol. 19, no. 6, p. e46008, Jun. 2018

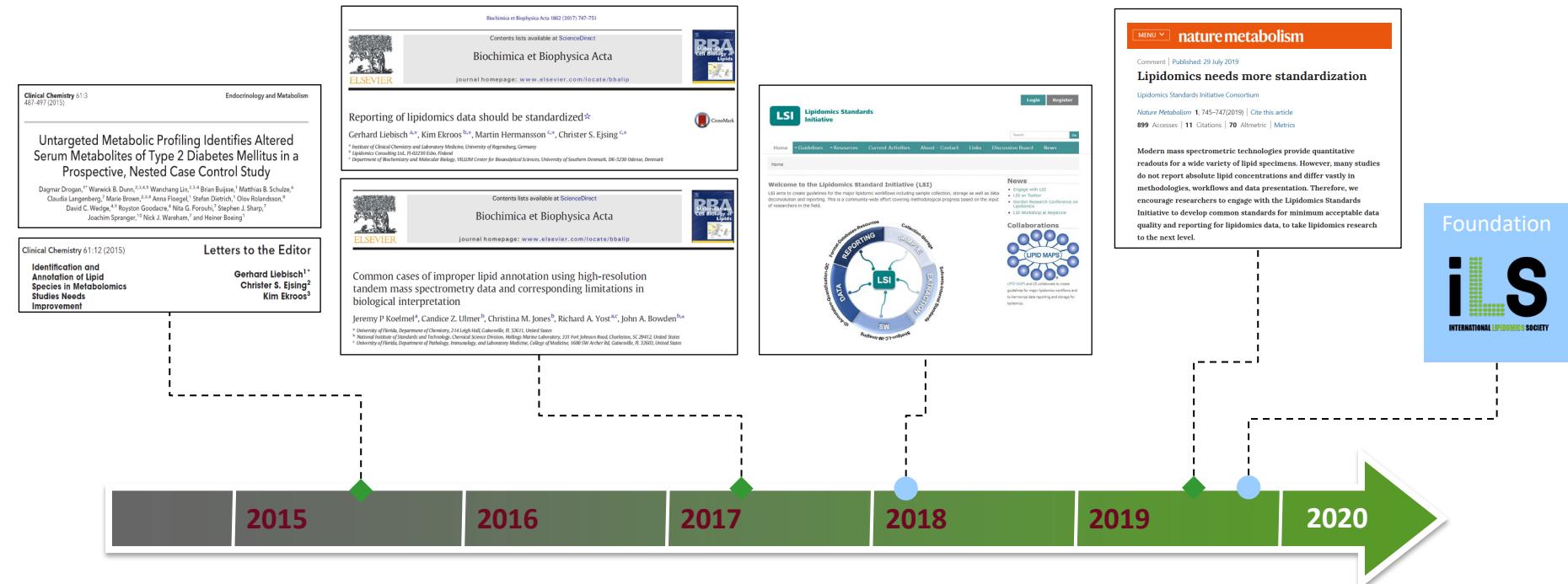
- Why is reproducibility important?
- When is it expendable?

Why Do We Need Good Data?

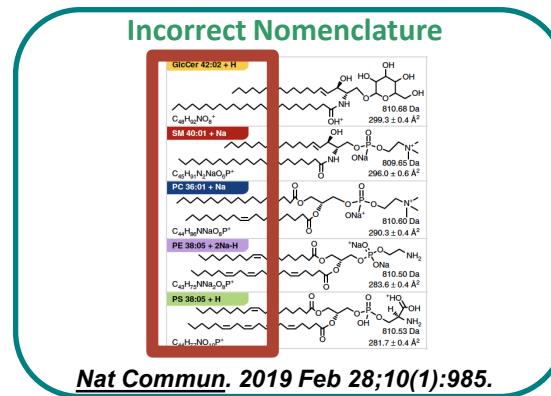
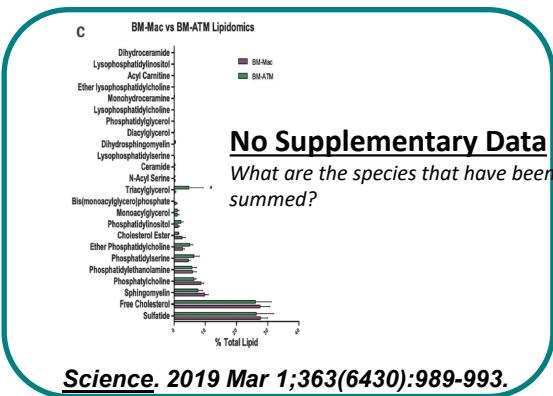


GUIDELINES FOR LIPIDOMICS

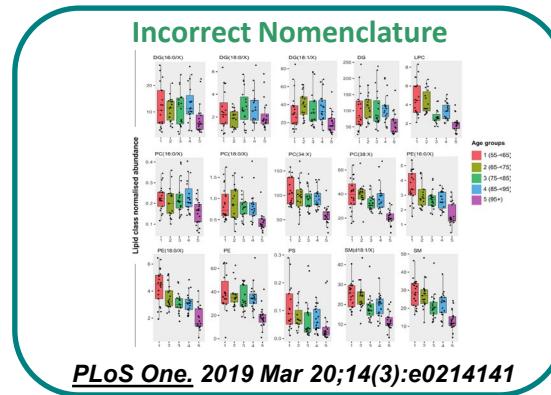
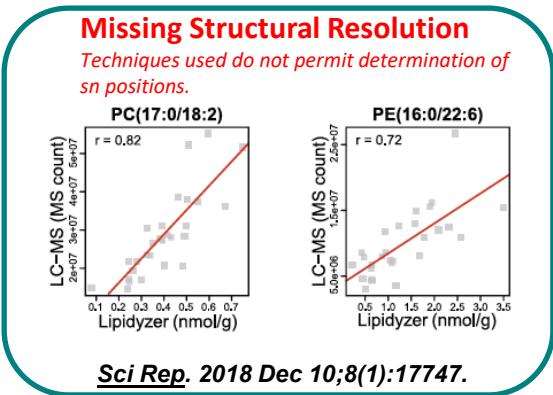
WHY?



ISSUES IN LIPIDOMIC DATA CONTINUE



MISSING STRUCTURAL RESOLUTION – INCORRECT NOMENCLATURE – NO SUPPLEMENTARY DATA



The FAIR Principles For Scientific Data

www.nature.com/scientificdata

SCIENTIFIC DATA



Amended: Addendum

OPEN

SUBJECT CATEGORIES
» Research data
» Publication characteristics

Received: 10 December 2015
Accepted: 12 February 2016
Published: 15 March 2016

Comment: The FAIR Guiding Principles for scientific data management and stewardship

Mark D. Wilkinson *et al.*[#]

There is an urgent need to improve the infrastructure supporting the reuse of scholarly data. A diverse set of stakeholders—representing academia, industry, funding agencies, and scholarly publishers—have come together to design and jointly endorse a concise and measurable set of principles that we refer to as the FAIR Data Principles. The intent is that these may act as a guideline for those wishing to enhance the reusability of their data holdings. Distinct from peer initiatives that focus on the human scholar, the FAIR Principles put specific emphasis on enhancing the ability of machines to automatically find and use the data, in addition to supporting its reuse by individuals. This Comment is the first formal publication of the FAIR Principles, and includes the rationale behind them, and some exemplar implementations in the community.

Supporting discovery through good data management
Good data management is not a goal in itself, but rather is the key conduit leading to knowledge discovery and innovation, and to subsequent data and knowledge integration and reuse by the community after the data publication process. Unfortunately, the existing digital ecosystem surrounding scholarly data publication prevents us from extracting maximum benefit from our research investments in a safe and reliable manner. In response to this concern, funders, publishers, and

- Findable
- Accessible
- Interoperable
- Reusable

→ Mainly geared towards machine usability, but also with humans as benefactors in mind!

The FAIR Principles

To be Findable:

- F1. (meta)data are assigned a globally unique and persistent identifier
- F2. data are described with rich metadata (defined by R1 below)
- F3. metadata clearly and explicitly include the identifier of the data it describes
- F4. (meta)data are registered or indexed in a searchable resource

To be Accessible:

- A1. (meta)data are retrievable by their identifier using a standardized communications protocol
- A1.1 the protocol is open, free, and universally implementable
- A1.2 the protocol allows for an authentication and authorization procedure, where necessary
- A2. metadata are accessible, even when the data are no longer available

To be Interoperable:

- I1. (meta)data use a formal, accessible, shared, and broadly applicable language for knowledge representation.
- I2. (meta)data use vocabularies that follow FAIR principles
- I3. (meta)data include qualified references to other (meta)data

To be Reusable:

- R1. meta(data) are richly described with a plurality of accurate and relevant attributes
- R1.1. (meta)data are released with a clear and accessible data usage license
- R1.2. (meta)data are associated with detailed provenance
- R1.3. (meta)data meet domain-relevant community standards

Good Laboratory Practice – the R in FAIR

Means

- (Electronic) Lab Notebook
- SOPs to ensure reproducible methods
- Documentation of Methods and parameters / settings along instrument output
- Storage and backup of instrument raw files, results and reports
- Documentation of chemicals used and inventory management
- Sample organization (Freezers, different storage conditions,...)
- Documentation of Sample origin and other characteristics

Benefits

- Help ensure that lab results are reproducible or at least comprehensible by others
- Ensures safe and efficient operations
- Ensures traceability and transfer of knowledge
- Ensures that data is available, e.g. for inquiries after publication

INTRODUCING GUIDELINES AND STANDARDS



nature metabolism

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nature > nature metabolism > comment > article

Comment | Published: 08 August 2022

Introducing the Lipidomics Minimal Reporting Checklist

Jeffrey G. McDonald, Christer S. Ejsing, Dominik Kopczynski, Michal Holčapek, Junken Aoki, Makoto Arita, Masanori Arita, Erin S. Baker, Justine Bertrand-Michel, John A. Bowden, Britta Brügger, Shane R. Ellis, Maria Fedorova, William J. Griffiths, Xianlin Han, Jürgen Hartler, Nils Hoffmann, Jeremy P. Koelmel, Harald C. Kófeler, Todd W. Mitchell, Valerie B. O'Donnell, Daisuke Saigusa, Dominik Schwudke, Andrej Shevchenko, ... Kim Ekoos + Show authors

Nature Metabolism 4, 1086–1088 (2022) | Cite this article

3276 Accesses | 76 Altmetric | Metrics

JLR | JOURNAL OF LIPID RESEARCH

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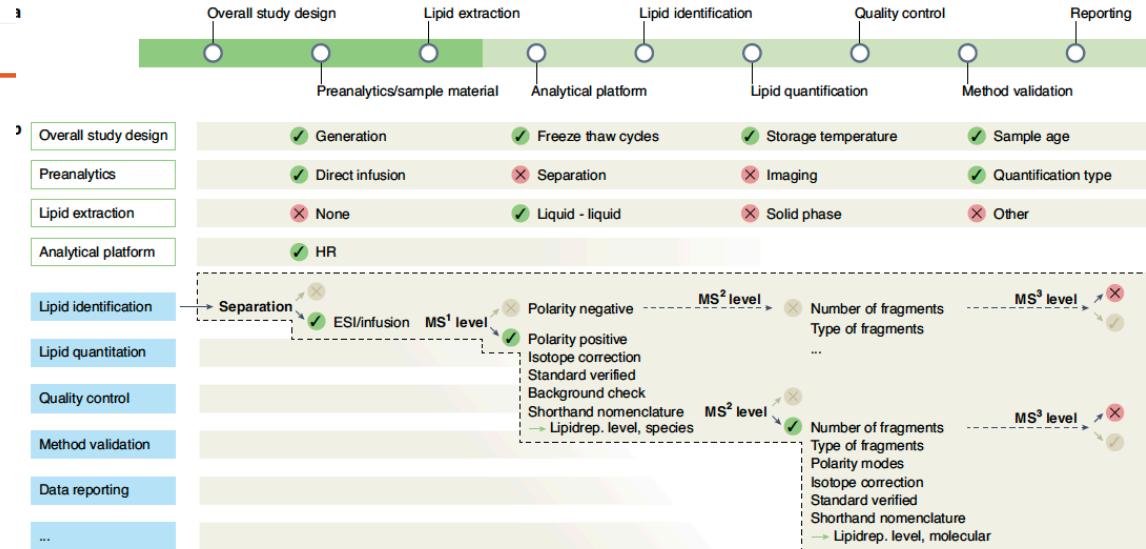
METHODS · Volume 65, Issue 9, 100621, September 2024 · Open Access

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The lipidomics reporting checklist a framework for transparency of lipidomic experiments and repurposing resource data

Dominik Kopczynski^{1,2} Christer S. Ejsing^{3,4,5} Jeffrey G. McDonald⁴ Takeshi Bomba⁵ Erin S. Baker⁶ Justine Bertrand-Michel⁷ Britta Brügger⁸ Cristina Coman¹ Shane R. Ellis⁹ Timothy J. Garrett¹⁰ William J. Griffiths¹¹ Xue Li Guan¹² Xianlin Han¹³ Marcus Höring¹⁴ Michal Holčapek¹⁵ Nils Hoffmann¹⁶ Kevin Huynh^{17,18} Rainer Lehmann¹⁹ Jace W. Jones²⁰ Rima Kaddurah-Daouk^{21,22,23} Harald C. Kófeler²⁴ Peter J. Meikle^{17,18} Valerie B. O'Donnell¹⁶ Daisuke Saigusa²⁷ Dominik Schwudke^{28,29,30} Andrej Shevchenko³¹ Federico Torto^{32,33} Juan Antonio Vizcaíno³⁴ Ruth Welti³⁵ Markus R. Wenk³² Denise Wolrab¹ Yu Xia³⁶ Kim Ekoos³⁷ Robert Ahrends³⁸ Gerhard Liebisch³⁴

Affiliations & Notes ▾ Article Info ▾



<https://lipidomicssociety.org>

- Create your own account
- Fill in the checklist online
- Final report (PDF) created
- Submit with your manuscript

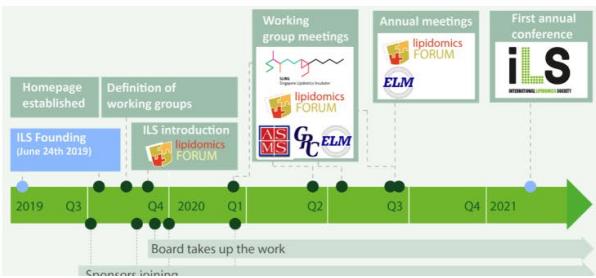


REPORTING CHECKLIST CAN BE FOUND ON THE ILS PAGE

<https://lipidomicssociety.org>

Aims

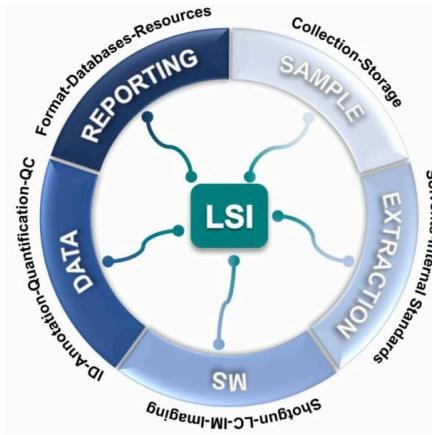
- The International Lipidomics Society (iLS) is a scientific non-profit organization representing and promoting lipidomics through worldwide cooperation.
- iLS aims to foster the development of new technologies, techniques, resources, skills and training through international collaborations.



HOME

Welcome to the Lipidomics Standard Initiative (LSI)

LSI aims to create guidelines for the major lipidomic workflows including sample collection, storage as well as data deconvolution and reporting. This is a community-wide effort covering methodological progress based on the input of researchers in the field.



Checklist

Complete [Lipidomics Minimal Reporting Checklist](#) for your study.

Collaborations



[LIPID MAPS](#) and LSI collaborate to create guidelines for major lipidomics workflows and to harmonize data reporting and storage for lipidomics.

Tweets from @LipidomicsSI

t Lipidomics Standard Initiative (LSI) Retweeted

International Lipido...
@____LS____ · Jan 17

Put in your conference calendar 2023!

8th LIPIDOMICS FORUM
August 27th-30th Vienna
Abstract submission: March 1st-April 30th

[ilsconf.org](#)
#lipidomics #bioinformatics
#clinicalresearch @lipidmaps
@AvantiLipids @EpiLipidNET
@Ahrendts15 @LabShevchenko
@LipidomicsSI



46

t Lipidomics Standard Initiative (LSI) Retweeted

International Lipido...
@____i... · Dec 14, 2022

Do not miss: We Love Lipids! How to validate a lipidomic method? This Friday the 16th of December, 2pm CET, 8 EST

@Ahrendts15 @lipidmaps
@EpiLipidNET @LabShevchenko
@LipidomicsRg @LipidomicsSI
@AvantiLipids #metabolomics



TAKES YOU TO THE LIPIDOMICS STANDARD INITIATIVE (LSI) PAGE

<https://lipidomicstandards.org>



TAKES YOU TO THE LIPIDOMICS STANDARD INITIATIVE (LSI) PAGE

<https://lipidomicstandards.org>



REPORTING CHECKLIST

Lipidomics Minimal Reporting Checklist

This virtual reporting checklist summarises key details of all steps of lipidomic workflows such as how to collect and store samples, extract lipids, perform mass spectrometric analysis, perform data processing and how to report results ([see related commentary](#)). This questionnaire will create a PDF document which may be linked to any study containing lipidomic data. The aim is, to give editors and reviewers an easy overview regarding the quality and completeness of lipidomic data, to further harmonise the field and to improve quality of lipidomic analyses.

How to complete this questionnaire

1. Please [register](#) an account at LSI, unless you already have one
2. [Login](#) with your LSI credentials
3. Start [Reporting Checklist](#)
4. Add a new workflow and start questionnaire or modify an existing workflow
5. Data for samples set may be reused and added to the individual workflow
6. Data for lipid classes (i.e. their identification, quantification) are stored and may either be added, copied or modified.
7. After submission of the questionnaire you will receive the report by email. You may also download a PDF of your report
8. Before submission of your manuscript you should make your final report permanent. Permanent reports will receive a DOI and may neither be modified nor deleted.

FAQs

Q: Is my data secure?

A: Yes, they are only available for the individual user. The final PDF report will be made available under DOI. Of note, the data collected in the checklist contain no detailed methods or experimental data and therefore there is no risk to lose any intellectual property.

Q: Why is registration required?

A: Registration permits saving of lipidomic workflows and sample data that were created by you. This is an easy way to reuse these data for multiple studies.

Q: Is there membership of the International Lipidomics Society (ILS) required?

A: No, this is an independent registration at the LSI homepage and it is not related to an ILS membership.

Q: Can you work together on the same workflow?

A: No, there exist only individual accounts. The only way is to share the login credentials.

Contact/Feedback

For any remarks, questions are welcome to further improve the usability of this checklist.

Please use our [contact form](#).



REPORTING CHECKLIST

New workflow



Disclaimer Impressum

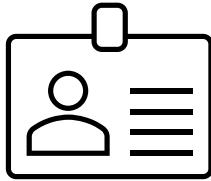
Select your new workflow type

- Direct Infusion
- Separation
- Imaging

Select Cancel



STEP 1 of 8



REPORT

Overall study design - Step 1 of 8

Title of the study *

AOCS rocks

Principle investigator *

Kim Ekoos

Please specify the person / laboratory responsible for the data acquisition.

Institution *

Lipidomics

Please specify the institution where the data was acquired.

Corresponding Email *

kim@lipidomicsconsulting.com

To whom correspondence should be addressed?

Is the workflow targeted or untargeted? *

Targeted

Clinical *

No

Is it clinical lipidomics, i.e. samples were analyzed related to a clinical question using a quantitative, validated method?

Next

Save and Resume



SAMPLE-DESCRIPTION**Sample set name ***

AOCS

Name of the sample set.

Sample origin

Plants

Specify the type of origin of the sample material.

Sample type

Other solid material

Specify the type of the sample material.

Other sample type *

Peanuts

Which other sample type was used?

Provided information

- Time to separate plasma/serum (min)
- Time to freeze (min)
- Storage time (month)
- Freeze-thaw cycles

Which information is provided?

Temperature handling original sample

4-8 °C

Temperature until freezing or extraction.

Instant sample preparation

No

Lipid extraction was performed instantly after sample collection?

Storage temperature

Room temperature

Temperature the samples stored until sample preparation.

Additives

BHT

Were the samples stored with additional preservatives or in buffers/solvents?

Were samples stored under inert gas?

No

Additional preservation methods

No

Were additional preservation methods used?

Biobank samples

No

Were the samples received from a biobank?

Sample homogenization

Yes

Was the sample homogenized prior lipid extraction?

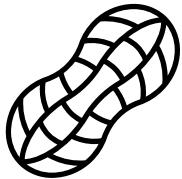
Sample homogenization solvent

Isopropanol

Which solvent was used for sample homogenization?

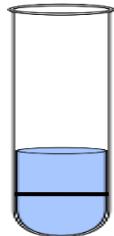
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Skärmbild

STEP 2 of 8



STEP 3 of 8



REPORT

Lipid extraction - Step 3 of 8

Extraction method *

2-phase system

Which type of lipid extraction was applied?

pH adjustment *

None

Was the pH adjusted for extraction? If yes, which buffer, acid/base was added?

2-phase system *

MTBE

Type of 2-phase; for other include reference when available.

Were internal standards added prior extraction? *

Yes

Previous

Next

[Save and Resume](#)





REPORT

Analytical platform - Step 4 of 8



STEP 4 of 8

MS type
QQQ

MS vendor
Shimadzu

Vendor of mass spectrometer.

Ion source
ESI

Which ion source was applied?

Direct type
FIA

Which inlet was used for direct MS?

MS Level *

MS1

MS2

MSn

Which MS level(s) was(were) used for identification?

Mass window for precursor ion isolation (in Da total isolation window) *
0.7

For MS2 and higher - which mass window was applied for precursor selection?

Mass resolution for detected ion at MS2
Low resolution

Which mass resolution was applied for the detected ion?

Resolution in Da at MS2 *
0.7

Specify the total window size in Da.

Additional dimension/techniques

IMS

OzID

UV-PD

Paterno-Büchi

Other

Were additional analytical dimensions applied?



Previous

Next

Save and Resume

LIPID-CLASS-DESCRIPTION

Lipid identification - Step 1 of 2

Lipid class

PE

MS Level *

 MS1 MS2 MSn

Which MS level(s) was(were) used for identification?

Identification level

Species level

Polarity mode

Negative

Which polarity was applied for analysis?

Type of negative (precursor)

[M-H]⁻

How many fragments used for ID *

1 fragment

Number of fragment ions used for identification

Fragment ion 1

PIS m/z 196

Please specify identification principle

Isotope correction at MS2

Type 2

Was Type II overlap corrected?

MS2 verified by standard

Yes

Were standards used to check which product ions are formed for the lipid class?

Background check at MS2

Yes

Was checked whether background ions interfere?

Check isomer overlap

No

Was interference by isomeric lipid classes excluded (see LSI table)?

Lipid identification Software

MS-DIAL

Which software was applied for lipid identification?

Data manipulation

- Smoothing
- Centroiding
- Lock mass correction
- Other

Which kind of data manipulation was applied?

Nomenclature for intact lipid molecule

Yes

Was the latest shorthand notation (doi: 10.1194/jlr.S120001023) used for annotation?

Nomenclature for fragment ions

N/A

Was the recommended annotation of fragment ions (doi: 10.1371/journal.pone.0188394) applied?

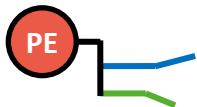
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STEP 5 of 8

MS level

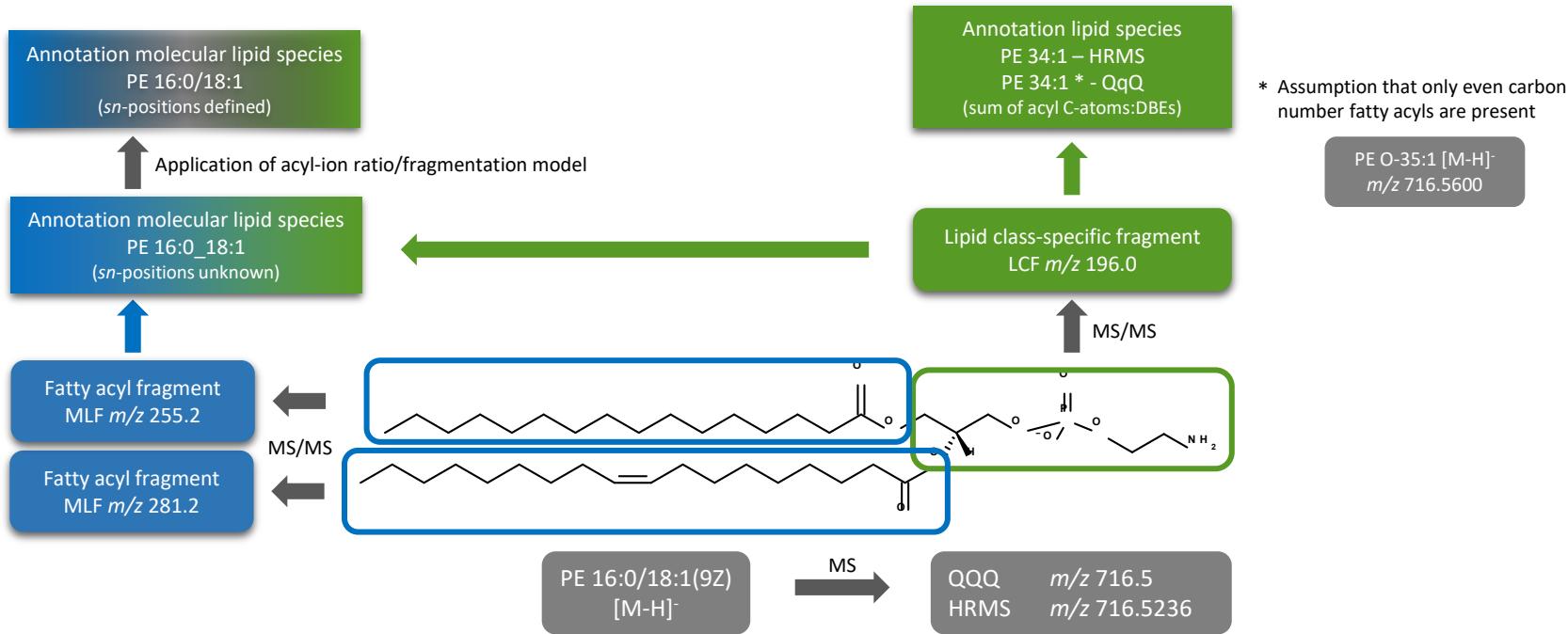
ID level



Isotope correction

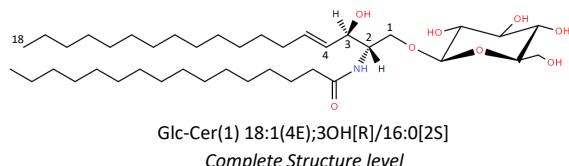
Nomenclature

ANNOTATION HIERARCHY



ANNOTATION OF LIPIDOMIC DATA

Analysis	Annotation
MS1: m/z 700.6 [$M+H$] ⁺ MS2: m/z 538.5 assumption of even hydrocarbon chains	Hex-Cer 34:1;O2 <i>Species level</i>
MS1: m/z 700.5722 [$M+H$] ⁺ MS2: m/z 538.5	Hex-Cer 34:1;O2 <i>Species level</i>
MS1: m/z 700.6 [$M+H$] ⁺ MS2: m/z 264.3, 538.5	Hex-Cer 18:1;O2/16:0 <i>Molecular species level</i>
MS1: m/z 700.6 [$M+H$] ⁺ MS2: m/z 264.3 HILIC-Separation from isomeric Gal-Cer	Glc-Cer 18:1;O2/16:0 <i>Molecular species level</i>
MS1: m/z 700.5722 [$M+H$] ⁺ MS2: m/z 252.3, 264.3, 282.3, 538.5, 682.5 HILIC-Separation from isomeric Gal-Cer Proof of DB position by OzID	Glc-Cer 18:1(4);OH/16:0 <i>Structure defined level</i>



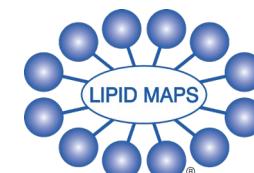
Journal of Lipid Research
Volume 61, Issue 12, December 2020, Pages 1539-1555



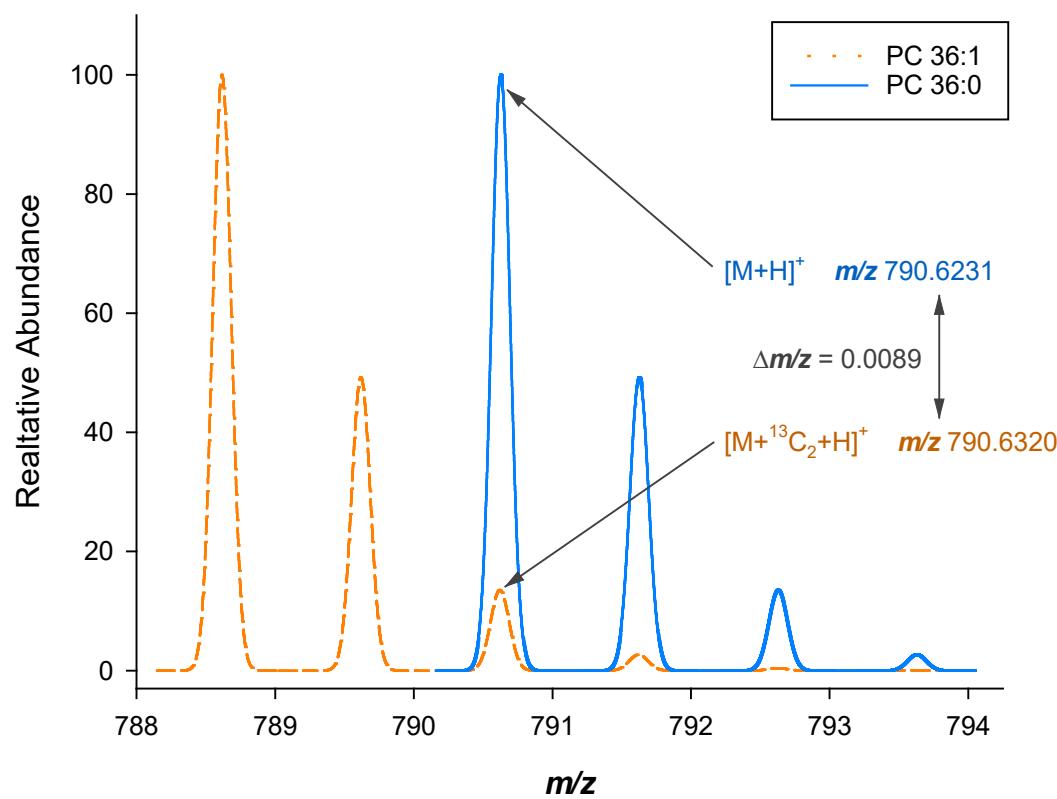
Special Report

Update on LIPID MAPS classification, nomenclature, and shorthand notation for MS-derived lipid structures

Gerhard Liebisch ^{1, †}, Eoin Fahy ^{2, †}, Junken Aoki ³, Edward A. Dennis ⁴, Thierry Durand ⁵, Christer S. Ejising ^{6, 7}, Maria Fedorova ^{8, 9}, Ivo Feussner ¹⁰, William J. Griffiths ¹¹, Harald Köfeler ¹², Merrill, Alfred H. Jr. ¹³, Robert C. Murphy ¹⁴, Valerie B. O'Donnell ¹⁵, Olga Oskolkova ¹⁶, Shankar Subramaniam ¹⁷, Michael J.O. Wakelam ^{18, †}, Friedrich Spener ^{19, 20} ☰ ☱

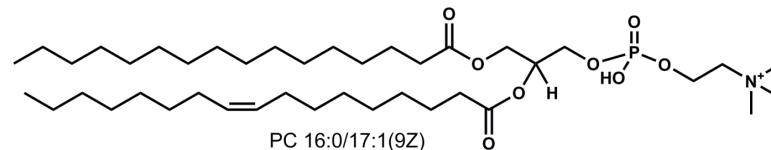


ISOBARS – TYPE II OVERLAP

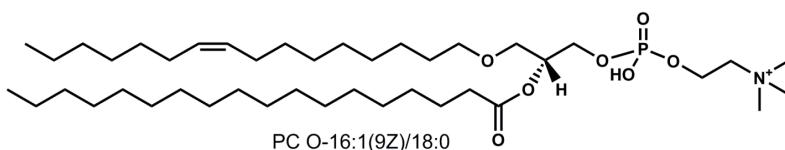


ISOBARIC OVERLAP

Isobars



$[\text{M}+\text{H}]^+$ $m/z = 746.5694$
 $\text{C}_{41}\text{H}_{81}\text{NO}_8\text{P}$



$[\text{M}+\text{H}]^+$ $m/z = 746.6058$
 $\text{C}_{42}\text{H}_{85}\text{NO}_7\text{P}$

$$\Delta m/z = 0.036 \text{ Da}$$

Different sum formula

Same nominal but
different exact m/z

Differentiation by

High resolution MS

ISOBARIC OVERLAP

Positive and negative ion mode

Lipid classes	Type of overlap	$\Delta m/z$	Examples
DB containing classes	$[M+DB+^{13}C_2] \approx [M]^+$ *	0.009	$[PC\ 32:1+H+^{13}C_2]^+ \approx [PC\ 32:0+H]^+$
Glycerolipids	$[M]^+ \approx [M+CH_2+O]$	0.036	$[PC\ 33:1+H]^+ \approx [PC\ 0-34:1+H]^+$
Sphingolipids	$[M]^+ \approx [M+CH_2-DB-OH]$	0.036	$[SM\ t42:2]^+ \approx [SM\ d43:1]^+$
PI - PS	$[PI]^+ \approx [PS+6CH_2+5DB+^{13}C]$	0.002	$[PI\ 34:1-H]^+ \approx [PS\ 40:6-H+^{13}C]^+$
PC - SM	$[PC+^{13}C]^+ \approx [SM-OH_2+4CH_2-DB]$	0.065	$[PC\ 38:3+^{13}C]^+ \approx [SM\ d42:2]^+$

DB = Double bond; O = ether-linkage instead of ester-linkage

Positive ion mode

Lipid classes	Type of overlap	$\Delta m/z$	Examples
DB containing classes	$[M+Na]^+ \approx [M+2CH_2+3DB+H]^+$	0.002	$[PC\ 34:1+Na]^+ \approx [PC\ 36:4+H]^+$
PC - PS	$[PC+H]^+ \approx [PS+DB+H]^+$	0.073	$[PC\ 32:0+H]^+ \approx [PS\ 32:1+H]^+$
DG - CE	$[CE\ X:Y+NH_4]^+ \approx [DG\ X+30:Y+NH_4]^+$	0.015	$[CE\ 18:1+NH_4]^+ \approx [DG\ 38:1+NH_4]^+$

DB = Double bond

ISOMERIC OVERLAP

Positive ion mode

Lipid classes	Type of overlap	Example
PC-PE	$PC = PE + 3CH_2$	$[PC\ 32:0+H]^+ = [PE\ 35:0+H]^+$ $[PC\ 32:0+Na]^+ = [PE\ 35:0+Na]^+$
PC-PA	$[PC+H]^+ = [PA+5CH_2+DB+NH_4]^+$	$[PC\ 32:0+H]^+ = [PA\ 37:1+NH_4]^+$
PE-PA	$[PE+H]^+ = [PA+C_2H_4+DB+NH_4]^+$	$[PE\ 34:1+H]^+ = [PA\ 36:2+NH_4]^+$
PS-PG	$[PS+H]^+ = [PG+2DB+NH_4]^+$	$[PS\ 34:1+H]^+ = [PG\ 34:2+NH_4]^+$
SM - CerPE	$SM = CerPE + 3CH_2$	$[SM\ d34:1+H]^+ = [CerPE\ d37:1+H]^+$

DB = Double bond

Negative ion mode

Lipid classes	Type of overlap	Example
PC-PS*	$[PC+HCOO]^- = [PS+3CH_2-DB-H]^-$	$[PC\ 33:1+HCOO]^- = [PS\ 36:0-H]^-$
PC-PS	$[PC+CH_3CO_2]^- = [PS+4CH_2-DB-H]^-$	$[PC\ 32:1+CH_3COO]^- = [PS\ 36:0-H]^-$
all lipid classes forming acetate/formate adducts*	$[X+CH_2+HCOO]^- = [X+CH_3COO]^-$	$[PC\ 34:1+HCOO]^- = [PC\ 33:1+CH_3COO]^-$ $[Cer\ d35:1+HCOO]^- = [Cer\ d34:1+CH_3COO]^-$

DB = Double bond

*Acetate salts of LC-MS grade can be contaminated with trace amounts of formate, which can lead to false-positive identification. Methanol can be oxidized to formic acid during electrospray ionization.

Identical sum formula

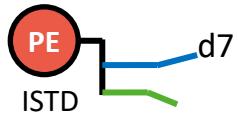
Identical m/z

Differentiation by

Fragmentation MS/MS
Separation LC-MS



STEP 5 of 8



LIPID-CLASS-DESCRIPTION

For additional separation methods/analytical dimension - Step 2 of 2

Quantitative

Yes

Is the lipid quantitatively identified, i.e. concentrations are reported?

Internal lipid standard(s) *

PE 33:1-d7

Which internal standard(s) was(were) used for quantification?

Type of quantification

Internal standard amount

How were the samples quantified?

Response correction

No

Was the analytical response corrected?

Type I isotope correction

No

Was isotopic abundance of individual species corrected (Type I)?

Limit of quantification

No

Was limit of quantification applied?

Normalization to reference

No

Was a normalization applied to a reference?

Lipid Quantification Software

MS-DIAL

Which software was used for quantification?

Batch correction

No

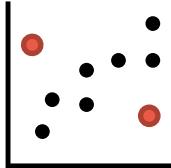
Was a batch correction applied?

Previous

Submit Save and Resume Later



STEP 6 of 8



QC

REPORT

Quality control - Step 6 of 8

Blanks *

Yes

Where blank samples analyzed?

Type of Blanks *

- Extraction blank
- Injection blank

Which types of blank samples were analyzed?

Quality control *

Yes

Were QC samples analyzed?

Type of QC sample *

- Commercial sample
- Sample pool
- Reference material

Which types of QC samples were analyzed?

Previous

Next

Save and Resume



STEP 7 of 8



REPORT

Method qualification and validation - Step 7 of 8

Method validation *

No

Was any method validation performed?

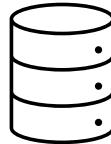
Previous

Next

Save and Resume



STEP 8 of 8



REPORT

Reporting - Step 8 of 8

Are reported raw data uploaded into repository? *

No

Were reported data uploaded into repository or included as supplementary data?

Raw data upload

No

Are raw data, i.e. unprocessed data including peak m/z, intensities/areas, RT (when applicable) available?

Previous

Submit

Save and Resume



STEP 8 of 8



pdf

LSI

Lipidomics Standards
Initiative

Search ...



Home Guidelines ▾ Resources ▾ Reporting Checklist Current Activities Links About Contact

REPORTING CHECKLIST

New workflow

Workflow title	Workflow type	Modification date	Actions
1) AOCS rocks	Direct infusion	Wed, 01 Mar 2023 18:43:53 GMT	

* Status: partial



General Lipidomics Workflow

Overall study design

Title of the study	AOCS rocks		
Principle investigator	Kim Ekoos		
Institution	Lipidomics		
Corresponding Email	kim@lipidomicsconsulting.com		
Document creation date	03/01/2023	Clinical	No
Is the workflow targeted or untargeted?	Targeted		

Lipid extraction

Extraction method	2-phase system	2-phase system	MTBE
pH adjustment	None	Were internal standards added prior extraction?	Yes

Analytical platform

MS type	QQQ	MS Level	MS2
MS vendor	Shimadzu	Mass window for precursor ion isolation (in Da total isolation window)	0.7
Ion source	ESI	Mass resolution for detected ion at MS2	Low resolution
Direct type	FIA	Resolution in Da at MS2	0.7

Quality control

Blanks	Yes	Quality control	Yes
Type of Blanks	Extraction blank, Injection blank	Type of QC sample	Reference material

Method qualification and validation

Method validation	No
-------------------	----

Reporting

Are reported raw data uploaded into repository?	No	Raw data upload	No
---	----	-----------------	----

Sample Descriptions

AOCS / Plants / Peanuts

Temperature handling original sample	4-8 °C	Were samples stored under inert gas?	No
Instant sample preparation	No	Additional preservation methods	No
Storage temperature	Room temperature	Biobank samples	No
Additives	BHT		

Lipid Class Descriptions

Lipid class PE[M-H]- / Lipid identification

Lipid class	PE	Isotope correction at MS2	Type 2
MS Level	MS2	MS2 verified by standard	Yes
Identification level	Species level	Background check at MS2	Yes
Polarity mode	Negative	Check isomer overlap	No
Type of negative (precursor)ion	[M-H]-	Lipid Identification Software	MS-DIAL
How many fragments used for ID	1 fragment	Nomenclature for intact lipid molecule	Yes
Fragment ion 1	PIS m/z 196	Nomenclature for fragment ions	N/A

Lipid class PE[M-H]- / For additional separation methods/analytical dimension

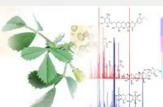
Quantitative	Yes	Limit of quantification	No
Internal lipid standard(s)	PE 33:1-d7	Normalization to reference	No
Type of quantification	Internal standard amount	Lipid Quantification Software	MS-DIAL
Response correction	No	Batch correction	No
Type I isotope correction	No		



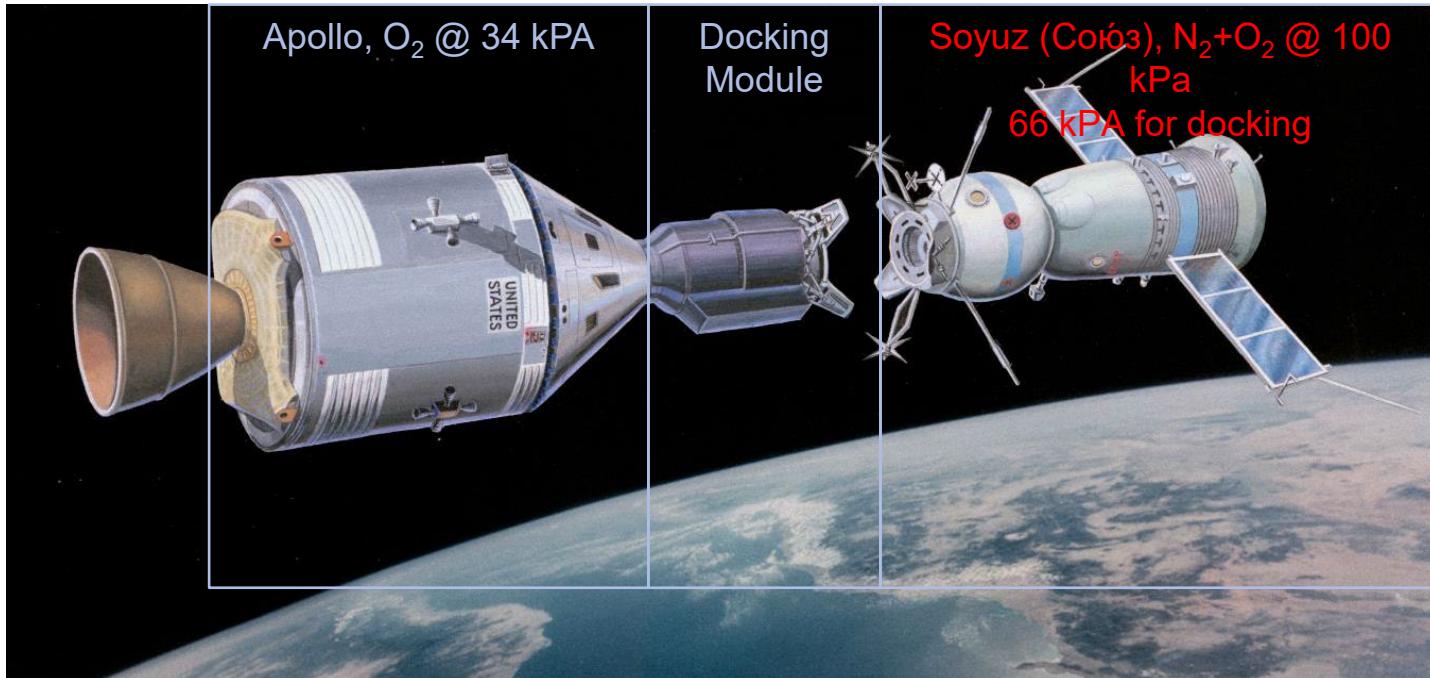
Data standards in the omics

HUPO-PSI Working groups and Outputs

Working Groups	Guidelines	v.	Formats	v.	Controlled Vocabularies	v.
Molecular Interactions	MIMIx	1.1.2	PSI-MI XML	2.5.4	PSI-MI CV	2.5.0
	MIABE	1.0.0	PSI-MI XML	3.0.0		
Group charter	MIAPAR	1.0.0	MITAB	2.7	PAR CV	n/a
	Mass spectrometry (MIAPE-MS)	2.98	mzML	1.1.0		
Mass Spectrometry	Identification (MIAPE-MSI)	1.1	TraML	1.0.0	PSI-MS	4.0.15
	Mass spectrometry Quantification (MIAPE-Quant)	1.0	<i>mzData</i> (<i>deprecated</i>)	1.05		
Proteomics Informatics			mzIdentML	1.2.0	XLMOD	1.1.0
			mzQuantML	1.0.1		
Group charter			mzTab	1.0.0		
			proBed	1.0.0		
Quality Control			proBAM	1.0.0		
			PEFF (under review)			
Group charter			qcML			
			(PSI spec. under construction)			
Protein separations (Inactive)	Gel electrophoresis (MIAPE-GE)	1.4	GelML	1.1.0	sepCV	1.0.0
	Gel informatics (MIAPE-GI)	1.0				
	Column chromatography (MIAPE-CC)	1.1				
	Capillary electrophoresis (MIAPE-CE)	0.9.3	spML	1.0.0		
	Phosphoproteomics (MIASSPE)	0.9.				

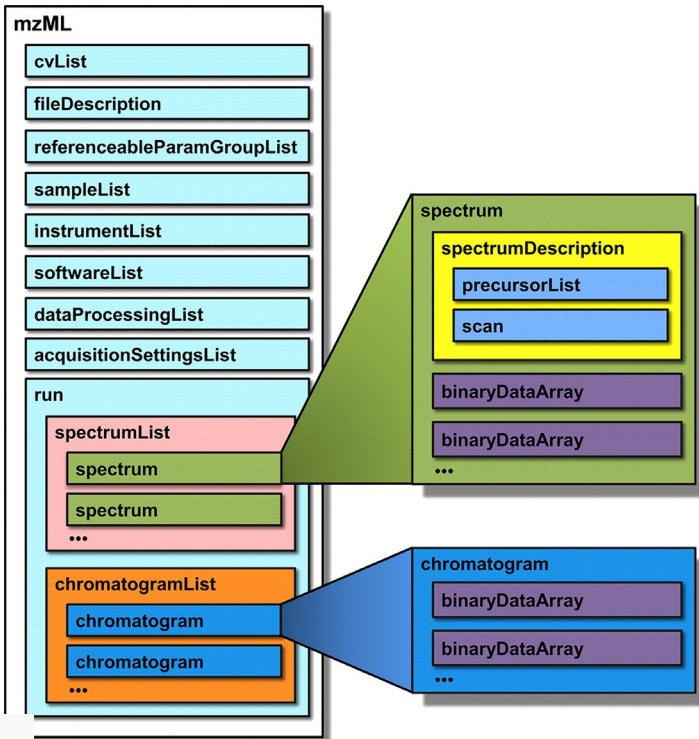


Data Processing & standards – the big picture



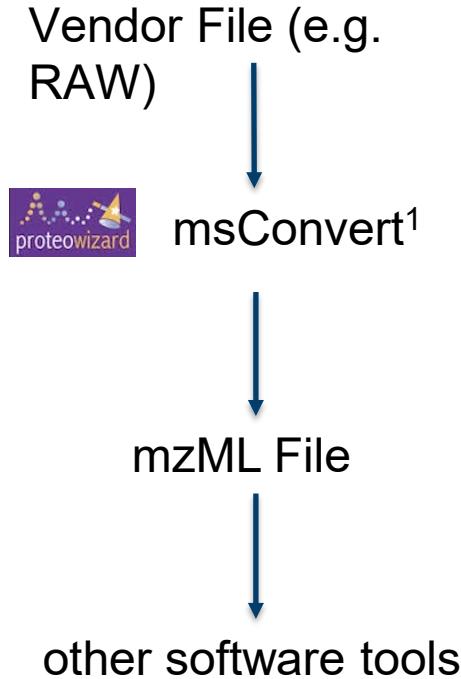
→ Ensure compatibility & interoperability!

mzML



- Open file format
- Developed to unify mzXML and mzData
- Based on eXtensible Markup Language (XML)
- Extensible through addition of Controlled Vocabulary (CV)-Terms with values to element definition
 - E.g. Collisional Cross Section (CCS) for Ion Mobility MS was not yet used when the format was defined, but can be added to spectrum information

mzML - Conversion



- Conversion into open formats enables tools to easily read and process the data
- Vendor formats are often not well described or not disclosed at all without an NDA, some vendors are more open
- Conversion may result in loss of vendor-specific information
 - May sometimes be a problem
- Many vendors have supported development of msConvert to improve conversion and export for the scientific community



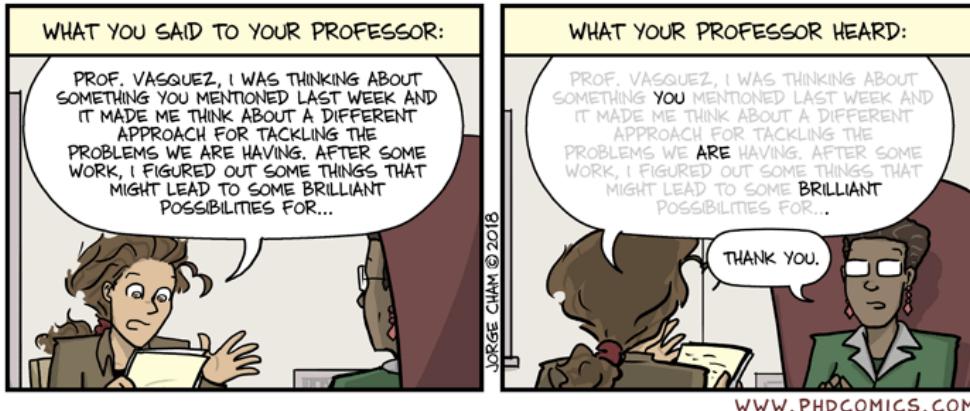
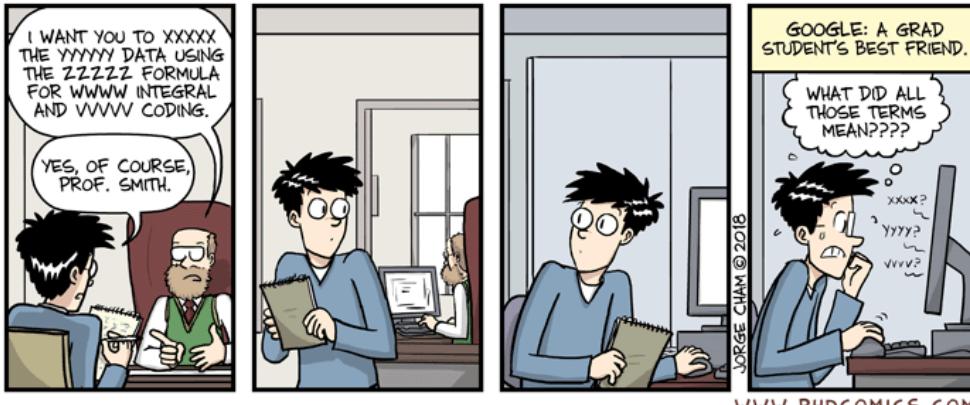
¹M. C. Chambers et al., "A cross-platform toolkit for mass spectrometry and proteomics," Nat Biotechnol, vol. 30, no. 10, Art. no. 10, Oct. 2012

Data Analysis – A Typical Starting Point

Lipid mediators	Docosanoid	10-HDoHE	10-HDoHE	Human	0.01Thr	pmol/mg Protein	35.45294999	1.414411459
Lipid mediators	Docosanoid	10-HDoHE	10-HDoHE	Human	1CRP	pmol/mg Protein	4.024524165	0.482469075
Lipid mediators	Docosanoid	10-HDoHE	10-HDoHE	Human	1Thr	pmol/mg Protein	1.139725223	0.093347863
Lipid mediators	Docosanoid	10-HDoHE	10-HDoHE	Human	1Thr+5CRP	pmol/mg Protein	4.841154264	0.305121574
Lipid mediators	Docosanoid	10-HDoHE	10-HDoHE	Human	5CRP	pmol/mg Protein	6.348954426	0.253939564
Lipid mediators	Docosanoid	10-HDoHE	10-HDoHE	Human	0.01Thr	pmol/mg Protein	24.70348526	1.415245775
Lipid mediators	Docosanoid	10-HDoHE	10-HDoHE	Human	1CRP	pmol/mg Protein	13.40496789	0.257440215
Lipid mediators	Docosanoid	10-HDoHE	10-HDoHE	Human	1Thr	pmol/mg Protein	4.182550807	0.34818124
Lipid mediators	Docosanoid	10-HDoHE	10-HDoHE	Human	1Thr+5CRP	pmol/mg Protein	7.235553509	0.289660945
Lipid mediators	Docosanoid	10-HDoHE	10-HDoHE	Human	5CRP	pmol/mg Protein	26.58278531	1.934955704
Lipid mediators	Docosanoid	10-HDoHE	10-HDoHE	Human	0.01Thr	pmol/mg Protein	10.75216038	0.538137179
Lipid mediators	Docosanoid	10-HDoHE	10-HDoHE	Human	1CRP	pmol/mg Protein	9.969665102	0.448747812
Lipid mediators	Docosanoid	10-HDoHE	10-HDoHE	Human	1Thr	pmol/mg Protein	4.844212811	0.278353983
Lipid mediators	Docosanoid	10-HDoHE	10-HDoHE	Human	1Thr+5CRP	pmol/mg Protein	11.24022274	0.507842294
Lipid mediators	Docosanoid	10-HDoHE	10-HDoHE	Human	5CRP	pmol/mg Protein	24.19398446	0.752801756
Lipid mediators	Docosanoid	10-HDoHE	10-HDoHE	Human	0.01Thr	pmol/mg Protein	34.18168036	0.84291498
Lipid mediators	Docosanoid	10-HDoHE	10-HDoHE	Human	1CRP	pmol/mg Protein	23.49850162	0.823543953
Lipid mediators	Docosanoid	10-HDoHE	10-HDoHE	Human	1Thr	pmol/mg Protein	4.100968977	0.293007541
Lipid mediators	Docosanoid	10-HDoHE	10-HDoHE	Human	1Thr+5CRP	pmol/mg Protein	8.109116225	0.053419681
Lipid mediators	Docosanoid	10-HDoHE	10-HDoHE	Human	5CRP	pmol/mg Protein	61.17187925	1.89422414
Lipid mediators	Docosanoid	10-HDoHE	10-HDoHE	Human	0.01Thr	pmol/mg Protein	23.95756946	0.778102384
Lipid mediators	Docosanoid	10-HDoHE	10-HDoHE	Human	1CRP	pmol/mg Protein	25.65598892	0.543642918
Lipid mediators	Docosanoid	10-HDoHE	10-HDoHE	Human	1Thr	pmol/mg Protein	7.419812494	0.150350617
Lipid mediators	Docosanoid	10-HDoHE	10-HDoHE	Human	1Thr+5CRP	pmol/mg Protein	17.83353609	0.655816533
Lipid mediators	Docosanoid	10-HDoHE	10-HDoHE	Human	5CRP	pmol/mg Protein	36.94655956	2.244778881
Lipid mediators	Docosanoid	10-HDoHE	10-HDoHE	Human	0.01Thr	pmol/mg Protein	6.988050994	0.19930888

- Lack of defined, controlled terminology
- Changes to the file are not tracked / documented
- Names may be non-standard
- Species may be non-standard
- No information what the treatment values mean
- How was the data created?
- What protocols and machines were used?
- What software was used?
- ...
- This would not be interoperable!

(Data) standards – Nomenclature & Terminology



- We need to define what exactly we are talking about!
 - Controlled Vocabularies
 - Taxonomies

- We need to make sure that our information is complete and adequate to represent our knowledge!
 - Data formats and standards for reporting

Parsing & normalization of lipid nomenclature

Problem:

- Lipid nomenclature is standardized, but different dialects and conventions have evolved [1-3,6].
- To better handle long systematic names (also by humans), shorthand lipid nomenclatures were defined [4] and added to databases [3,5,6].
- For new lipid classes, nomenclature is often not defined. New information, like hydroxylations or other modifications or often not covered in current nomenclature.
- → Constant process of refinement.
- → Automated name resolution needed.

1. IUPAC-IUB Commission on Biochemical Nomenclature, **The nomenclature of lipids**, Journal of Lipid Research, 8:523–528, 1967.
2. MA Chester, IUPAC-IUB (JCBN) **Nomenclature of glycolipids**, European Journal of Biochemistry, 257(2):293–98, 1998.
3. Eoin Fahy *et al.*, **A comprehensive classification system for lipids**, Journal of Lipid Research, 46(5):839–862, 2005.
4. Liebisch *et al.*, **Shorthand notation for lipid structures derived from mass spectrometry**, Journal of Lipid Research, 54(6):1523–1530, 2013.
5. Aimo *et al.*, **The SwissLipids knowledgebase for lipid biology**, Bioinformatics, 31(17):2860–2866, 2015.
6. Wishart *et al.*, **HMDB: the Human Metabolome Database**, Nucleic Acids Research, 35(suppl_1):D521–D526, 2007.
7. Kopczynski *et al.*, **Goslin - A Grammar of Succinct Lipid Nomenclature**, BioRxiv preprint, April 18th, 2020; doi:10.1101/2020.04.17.046656

Example:

- Cer(d18:1/16:0)
- Cer (d18:1/16:0)
- d18:1/16:0 Cer
- Cer 18:1;2/16:0
- CER[N(16)S(18)]

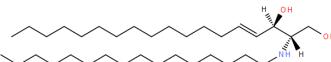


Image: LIPID MAPS LMSP02010004, 2020

Systematic name:

→ N-(hexadecanoyl)-sphing-4-enine

Category	<u>Sphingolipids [SP]</u>
Main Class	<u>Ceramides [SP02]</u>
Sub Class	<u>N-acylsphingosines (ceramides) [SP0201]</u>

Parsing & normalization of lipid nomenclature

Goslin – Grammar(s) of succinct lipid nomenclature:

- Context-free grammars for lipid names following LipidMaps, SwissLipids and Liebisch shorthand notations.
- Enables construction of lipid name parsers (left-to-right, leftmost derivation: LL^(*)) and defines common data structures for lipid level hierarchy.
- First step towards normalization of lipid names following different dialects.

```
1  lipid : lipid_eof EOF
2  ;
3  lipid_eof : lipid_pure
4  | lipid_pure adduct_info
5  ;
6  lipid_pure : gl // NT rule for glycerolipids
7  | pl // NT rule for phospholipids
8  | sl // NT rule for sphingolipids
9  | sterol
10 | mediator
11 ;
12 ...
13 gl : mgl // NT rule for monoacylglycerol
14 | dgl // NT rule for diacylglycerol
15 | sgl // NT rule for dgl with sugar head
16 | tgl // NT rule for triacylglycerol
17 ;
```



Level	Name	Description
Category (LM)	Glycerophospholipids	Lipid category
Class (LM)	Glycerophosphoethanolamine	Lipid class
Species (SL, LM Subclass)	Phosphatidylethanolamine (32:1), PE(32:1)	HG, FA summary
Molecular Subspecies (SL)	PE(16:0_16:1)	HG, two FAs
Structural Subspecies (SL)	PE(16:1/16:0)	HG, SN pos. for FA1 and FA2
Isomeric Subspecies (SL, LM)	PE(16:1(6Z)/16:0)	HG, SN pos., Stereo

Parsing & Harmonization of Lipid Nomenclature

Parsing, Normalization & Mapping

The screenshot shows the Goslin web application interface. On the left, three lipid names are listed: Cer(d18:1/16:0), Cer 18:1;2/16:0, and d18:1/16:0 Cer. To the right of these, a large green puzzle piece icon contains the letter 'G' and the text 'ANTLR'. Below the puzzle piece, a legend defines the columns: Normalized Name, LIPID MAPS Category, LIPID MAPS Main Class, Level, Struct. Properties, and Chem. Properties. The data for Cer 18:1;2/16:0 is shown:

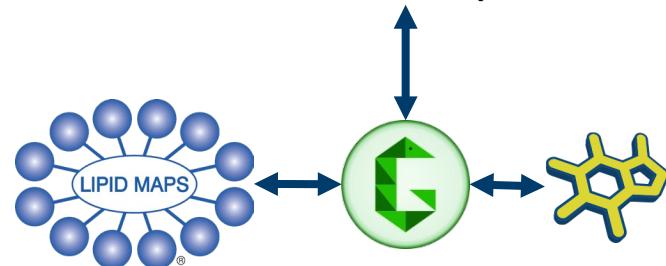
Normalized Name	Cer 18:1;2/16:0
LIPID MAPS Category	Sphingolipids [SP]
LIPID MAPS Main Class	Ceramides [SP02]
Level	Pos ₁ = LCB, 18xC, 1xDB, 2xOH
Struct. Properties	Pos ₂ = FA, 16xC, 0xDB, 0xOH
Chem. Properties	Sum Formula = C ₃₄ H ₆₇ NO ₃ Exact Mass = 537.5121

At the bottom of the interface, there are links for Home, Documentation, REST API, Source, Imprint and Privacy Policy, and a Download button.

→ Normalize lipid names to shorthand nomenclature using Goslin in Java, C++, Python & R

→ Cross-linking of normalized lipid names to LIPID MAPS, SwissLipids and ChEBI

Swiss**Lipids**



D. Kopczynski, N. Hoffmann, B. Peng, G. Liebisch, F. Spener, and R. Ahrends, "Goslin 2.0 Implements the Recent Lipid Shorthand Nomenclature for MS-Derived Lipid Structures," *Anal. Chem.*, vol. 94, no. 16, pp. 6097–6101, Apr. 2022

→ <https://apps.lifs-tools.org/goslin>

Parsing & normalization of nomenclature

1.0.16 [Home](#) [REST API](#) [Info](#) [Source](#) [Imprint and Privacy Policy](#)

Validated Lipid Names [Download](#)

12-HETE Isomeric Sub-Species [GOSLIN](#) 1/16

BMP 18:1-18:1 Molecular Sub-Species [GOSLIN](#) 2/16

LBPA 18:1-18:1 Molecular Sub-Species [GOSLIN](#) 3/16

Normalized Name	BMP 18:1_18:1																					
Original Name	LBPA 18:1-18:1																					
Grammar	GOSLIN																					
Lipid MAPS Category	Glycerophospholipid [GP] [?]																					
Lipid MAPS Main or Sub Class	Monoacylglycerophosphomoradylglycerols [GP0410] [?]																					
Swiss Lipids Entry	BMP(18:1_18:1) [?]																					
Functional Class Abbreviation	BMP																					
Functional Class Synonyms	[BMP, LBPA]																					
Level	Molecular Sub-Species																					
# of C atoms	36																					
# of hydroxyl groups	0																					
# of double bonds	2																					
Fatty Acids	<table border="1"><thead><tr><th>Name</th><th># C atoms</th><th># Double bonds</th><th># hydroxyl</th><th>HG FA</th><th>Long Chain Base</th><th>Double Bond Positions</th></tr></thead><tbody><tr><td>FA1</td><td>N.D.</td><td>18</td><td>1</td><td>0</td><td>Ester</td><td>false</td></tr><tr><td>FA2</td><td>N.D.</td><td>18</td><td>1</td><td>0</td><td>Ester</td><td>false</td></tr></tbody></table>	Name	# C atoms	# Double bonds	# hydroxyl	HG FA	Long Chain Base	Double Bond Positions	FA1	N.D.	18	1	0	Ester	false	FA2	N.D.	18	1	0	Ester	false
Name	# C atoms	# Double bonds	# hydroxyl	HG FA	Long Chain Base	Double Bond Positions																
FA1	N.D.	18	1	0	Ester	false																
FA2	N.D.	18	1	0	Ester	false																

Goslin Webapp

- Form-based user interface for submission of lipid name lists (text file + interactive form)
- REST API for programmatic translation.
- Cross-linking of normalized lipid names to LIPID MAPS and SwissLipids database

Practical Phase I

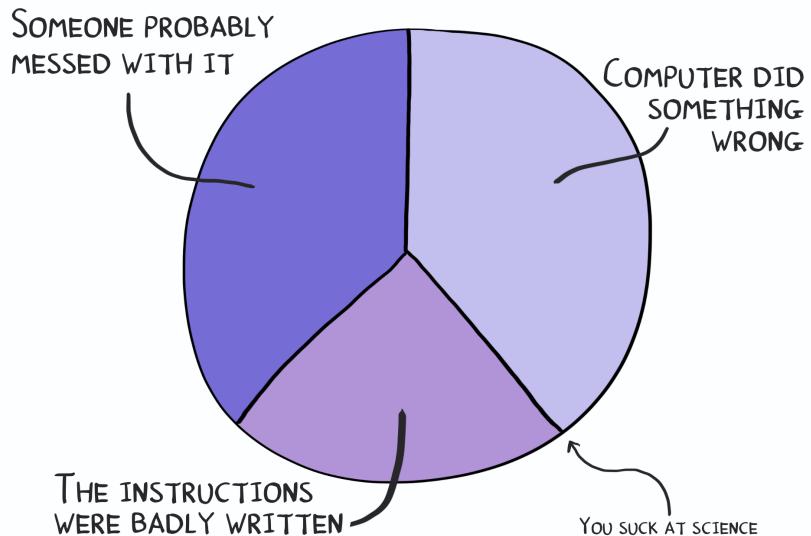
Normalizing Lipid Names with Goslin

Quality Control in Mass Spectrometry

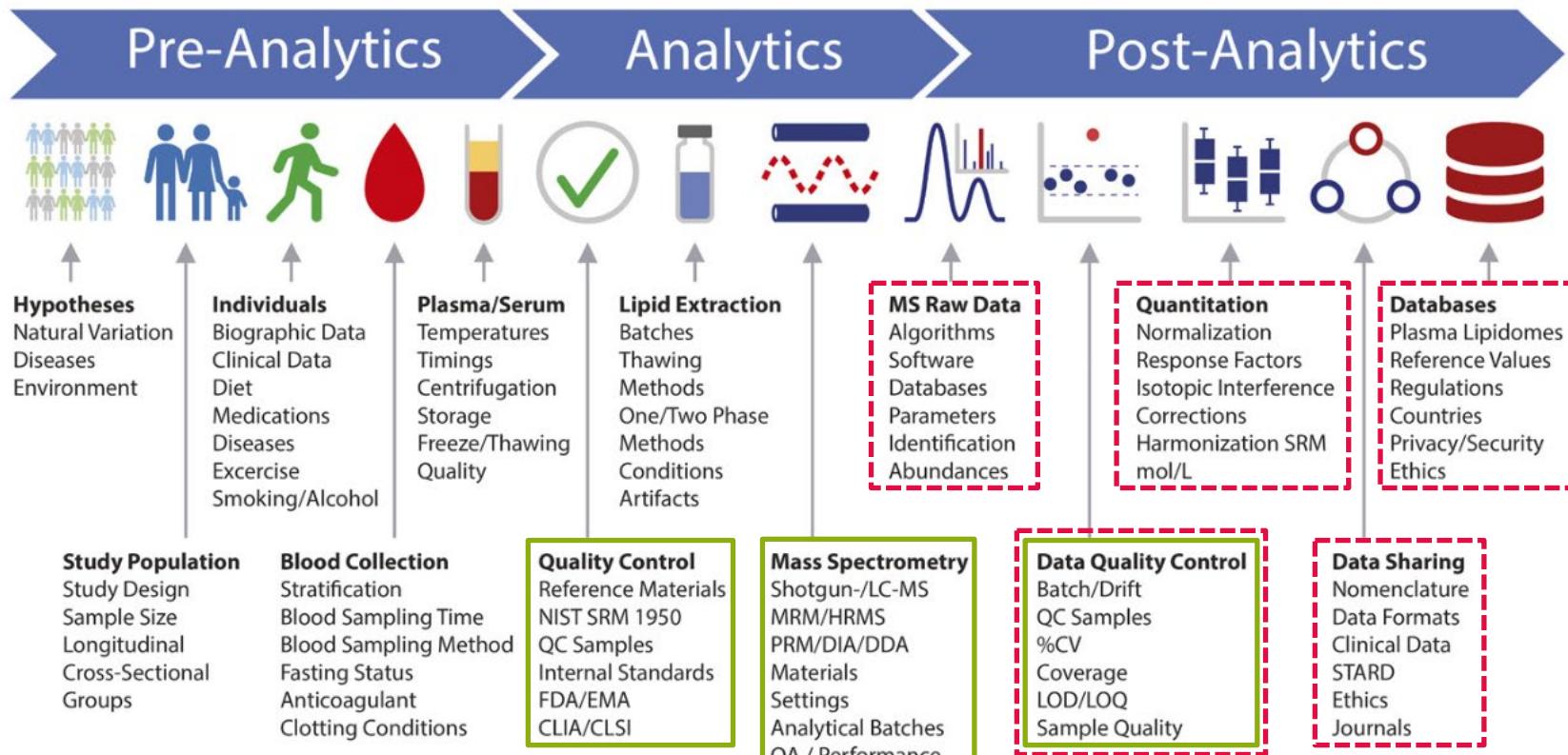
Work within HUPO-PSI MS

The mzQC Format

YOUR EXPERIMENT FAILS –
WHOSE FAULT IS IT? A PIE CHART



Variability in Clinical MS-Lipidomics*



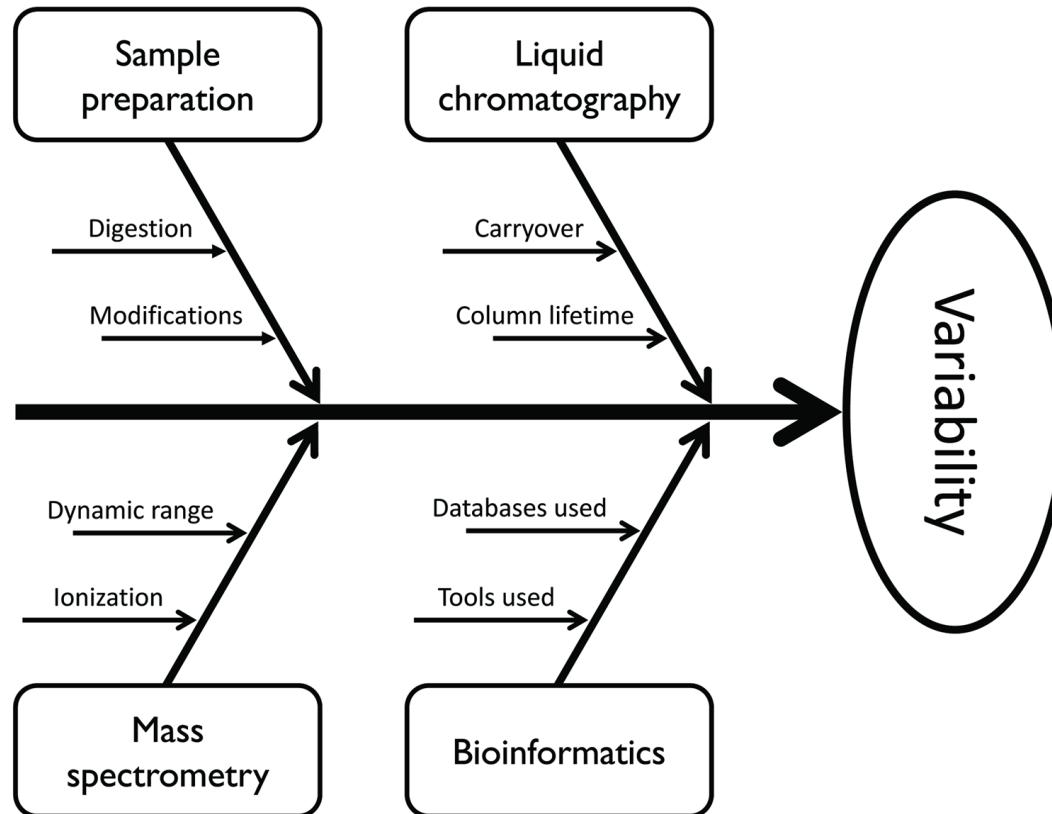
* just for blood!

many apply to other MS-omics, too

QC challenges

bioinformatics / statistics / legal challenges

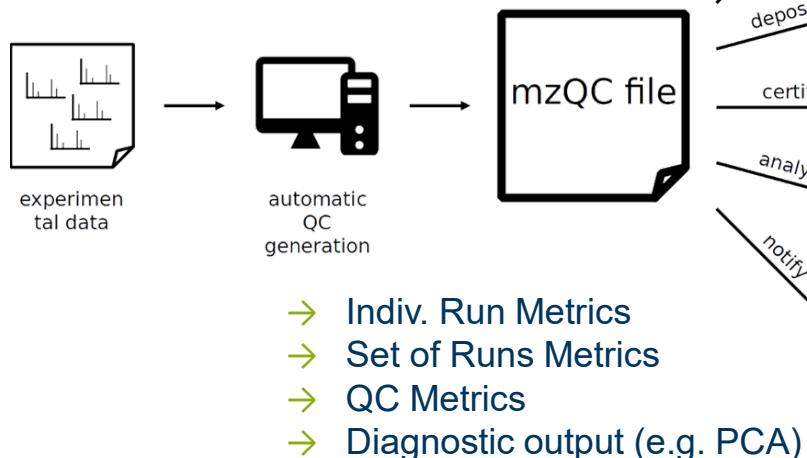
Sources of Variability and Errors in MS



The Quality Control Working Group creates mzQC for communicating QC information



- JSON Format (based on JSON schema)
- Uses CV terms (PSI-MS) and enables automatic (semantic) validation



HUPO-PSI mzQC WG:
Matthias Walzer, Wout Bittremieux,
David Tabb, Chris Bielow, Paul Brack,
Eralp Dogu, Jinmeng Jia, David
Jiminez-Morales, Reza Salek, Stefan
Tenzer, Julian Uszkoreit, Weimin Zhu



Implementations in
Python, R & Java for
reading and writing

→ <https://github.com/HUPO-PSI/mzQC>

Practical Phase II

Capturing QC Information with mzQC

Data SHARING

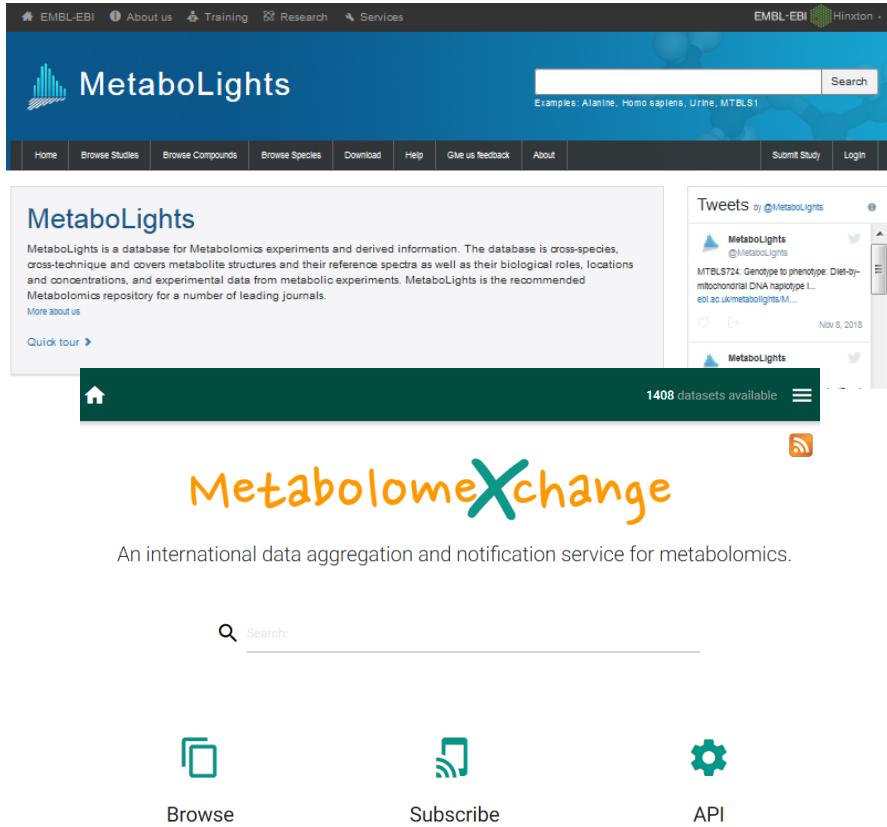
Data sharing entails

- making your data known
- share it with collaboration partners
- publish your data and share it with the global research community
- data sharing doesn't mean open data or public data!
- sharing data with restricted access or even closed access is sometimes mandatory (e.g. sensitive health data, patents, ...)
- data sharing can be done at any time during the research data life cycle but, at the latest, data should be made available at the time of publication of articles that use the data to make scientific conclusions
- open access, registered access or authentication procedure, controlled access or Data Access Committees (DACs), or access upon request (not recommended)
- metadata (data describing your data) should always be published to make it findable!

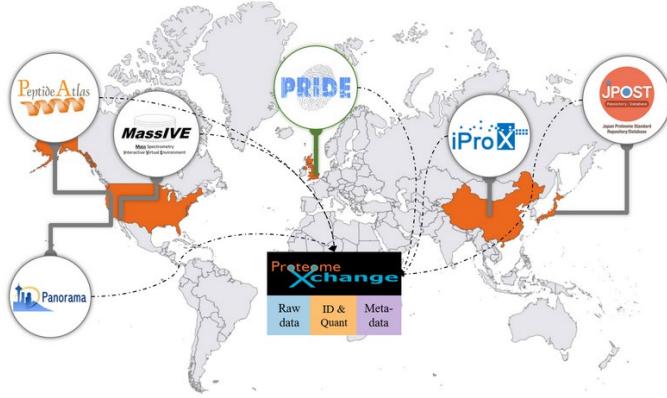
Why?

- Sharing of data is a cornerstone of good science.
- good research practice to ensure data underlying research is preserved
- data made available to the research community and society at large may be reused to gain new insight
- sharing data is a prerequisite for making your research reproducible
- **Facilitate FAIR**

Data Storage and Sharing



The image displays two screenshots of scientific databases. On the left is the MetaboLights website, featuring a search bar, navigation links like 'Home', 'Browse Studies', and 'Submit Study', and a sidebar with a tweet from the official account (@MetaboLights). On the right is the MetabolomeXchange website, which includes a search bar, a 'Browse' section with icons for 'Browse', 'Subscribe', and 'API', and a 'Panorama' section showing a world map with various data exchange points.



- Submitting data to public repositories makes them
 - Findable
 - Accessible
 - Indexable
 - Reusable
 - and citeable (e.g. via a Document Object Identifier, DOI)!

MetaboLights – Study Descriptors

PUBLICATIONS

LipidCreator workbench to probe the lipidomic landscape

✉ Bing Peng, Dominik Kopczynski, Brian S Pratt, Christer S Ejs...



Descriptors Protocols Samples Assays Metabolites Files

KEYWORDS

Targeted Metabolites Lipidomics Ultra-performance Liquid Chromatography-mass Spectrometry

Factors

Treatment : Treatment

Concentration : Concentration

MetaboLights – Protocols

Descriptors **Protocols** Samples Assays Metabolites Files

[Collapse all](#)

Sample collection

Blood from five individual healthy volunteers was collected in ACD-buffer and centrifuged at 200 x g for 20 mins. The obtained platelet-rich plasma was added to modified Tyrode-HEPES (N-2-hydroxyethyl-piperazine-N'-ethanesulfonic acid) buffer (137 mM NaCl, 2 mM KCl, 12 mM NaHCO₃, 5 mM glucose, 0.3 mM Na₂HPO₄, 10 mM HEPES, pH 6.5). After centrifugation at 900 x g for 10 mins and removal of the supernatant, the resulting platelet pellet was resuspended in Tyr

[▼ more](#)

Extraction

Lipid (except fatty acid and its derivatives) extraction was carried out according to Matyash et al. [1] with small modifications. In brief, 225 µl of MeOH (4 °C) were added to platelet cell pellet or platelet supernatant in an Eppendorf polypropylene tube that was placed on ice. After a few seconds of treatment with ultrasonication and vortexing, 8 µl of the SPLASH standard and 750 µl MTBE (4 °C) were added. The mixture was incubated for 1 h at 4 °C in a thermom

[▼ more](#)

[Post Extraction](#) [Derivatization](#)

Chromatography

For the reverse-phase liquid chromatography (LC), an UltiMate 3000-system from Thermo Fisher Scientific (Darmstadt, Germany) was employed. The chromatographic separation was performed according to Bird et al. [1] on an Ascentis Express C18 main column (150 mm × 2.1 mm, 2.7 µm, Supelco) fitted with a guard cartridge (5 mm × 2.1 mm, 2.7 µm, Supelco). The temperatures of the autosampler and the column oven were set to 10 °C and 30 °C, respectively. Solvent A was ACN/H₂O (3:7, v/v) and 0.1 % form

[▼ more](#)

[Chromatography Instrument](#) [Autosampler Model](#) [Column Model](#) [Column Type](#) [Guard Column](#)

Data available at <https://www.ebi.ac.uk/metabolights/MTBLS1381>

MetaboLights – Protocols

Mass spectrometry

The LC was coupled to a QTRAP 6500 (Applied Biosystems, Darmstadt, Germany) which was equipped with an electrospray ion source (Turbo V Ion Source). The following ESI source settings were used for negative mode: curtain gas 10 arbitrary units, temperature 525 °C, ion source gas I 30 arbitrary units, ion source gas II 55 arbitrary units, collision gas medium; ion spray voltage -4500 V, entrance potential -10 V, and exit potential 10 V.

Scan Polarity Scan M/z Range Instrument Ion Source Mass Analyzer

Data transformation

Wiff data files were acquired using Analyst (version 1.6.1). Data was converted to mzML using the ProteoWizard msConvert tool (version 3.0.11537). The data was centroided using vendor peak picking and MS1 and MS2 peaks were selected for export with 64 bit float encoding and scan-wise zlib compression.

Metabolite identification

Data analysis for native QTrap data (MRM) was performed with Skyline (64-bit, 4.2.0.18305). Metabolite identification and integration was performed using Skyline with custom MRM inclusion lists generated by LipidCreator. The final metabolite table reports representative quantities for each biological replicate, as reported in the Skyline documents HuPI_5donors_Mediators_SN_2019-07-24_15-27-24.sky.zip and HuPI_5donors_Mediators_pellet_2019-07-24_15-25-22.sky.zip, which are available for download from <https://panoramaweb.org/lipidcreator.url>. The absolutely quantified values (pmol/mg protein) are provided in a separate XLS file (HuPI_mediators_quantified.xls) in the MetaboLights study folder. Transition lists and integrated peak tables exported from Skyline, together with an R script to create the MetaboLights maf metabolite tables, are provided in the project directory.

▲ hide

MetaboLights – Samples

Descriptors	Protocols	Samples	Assays	Metabolites	Files																																																																																		
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MetaboLights – Assays

Descriptors Protocols Samples Assays Metabolites Files

Assay Sheet 1

File: a_MTBLs1381_LC-MS_negative_reverse-phase_metabolite_profiling.txt Items per page: 180 ▾ 1 – 180 of 180 | < < > > |

Filter

	Sample Name	Protocol REF	Parameter Value - Post Extraction	Parameter Value - Derivatization	Extract Name	Protocol REF	Parameter Value - Chromatography Instrument
	QTrap007483_031618-Blank ext	Extraction			QTrap007483_031618-Blank ext	Chromatography	Thermo Scientif Dionex UltiMate 3000 System
	QTrap007484_031618-STD ext	Extraction			QTrap007484_031618-STD ext	Chromatography	Thermo Scientif Dionex UltiMate 3000 System

MetaboLights – Metabolites

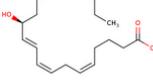
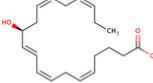
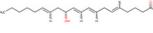
Descriptors Protocols Samples Assays Metabolites Files

MAF Sheet 1

File: m_MTBL1381_LC-MS_negative_reverse-phase_metabolite_profiling_v2_maf.tsv

Items per page: 47 | < < > > | 1 – 47 of 47

Filter

Structure	Database identifier	Chemical formula	SMILES	InChI
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	CHEBI:88345	C20H30O3	C(CC)=C\CC=C\CC(/C=C/C=C\CC(C=CCCC(=O)[O-])O	InChI=1S/C20H30O3 /c1-2-3-4-5-10-13-16-19(21)17-14-11-8-6 /h3-4,7-11,13-14,17,19,21H,2,5-6,12,15-1 /p-1/b4-3-,9-7-,11-8-,13-10-,17-14+
	CHEBI:19138	C20H32O3	[H]C(CCCC(=O)=O)=CCC([H])=CC([H])=CC(O)CC([H])=CCCCCC	InChI=1S/C20H32O3 /c1-2-3-4-5-10-13-16-19(21)17-14-11-8-6 /h7-11,13-14,17,19,21H,2-6,12,15-16,18H

Data available at <https://www.ebi.ac.uk/metabolights/MTBL1381>

MetaboLights – Files

Descriptors Protocols Samples Assays Metabolites Files

FTP Download Aspera Download ? Help

ISA METADATA Download

[a_MTBL1381_LC-MS_negative_reverse-phase_metabolite_profiling.txt](#) March 31 2020 23:47:08 Download

[i_Investigation.txt](#) April 08 2021 14:07:34 Download

[m_MTBL1381_LC-MS_negative_reverse-phase_metabolite_profiling_v2_maf.tsv](#) January 21 2020 17:51:12 Download

[s_MTBL1381.txt](#) March 31 2020 23:42:13 Download

RAW / DERIVED FILES

[search raw files](#)

[QTrap007483_031618-Blank ext.mzML](#) November 20 2019 15:40:18 Download

[QTrap007483_031618.wiff](#) November 20 2019 15:40:19 Download

[QTrap007483_031618.wiff.scan](#) November 20 2019 15:40:19 Download

[QTrap007484_031618-STD ext.mzML](#) November 20 2019 15:40:19 Download

[QTrap007484_031618.wiff](#) November 20 2019 15:40:19 Download

[QTrap007484_031618.wiff.scan](#) November 20 2019 15:40:19 Download

Data available at <https://www.ebi.ac.uk/metabolights/MTBL1381>

Practical Phase III

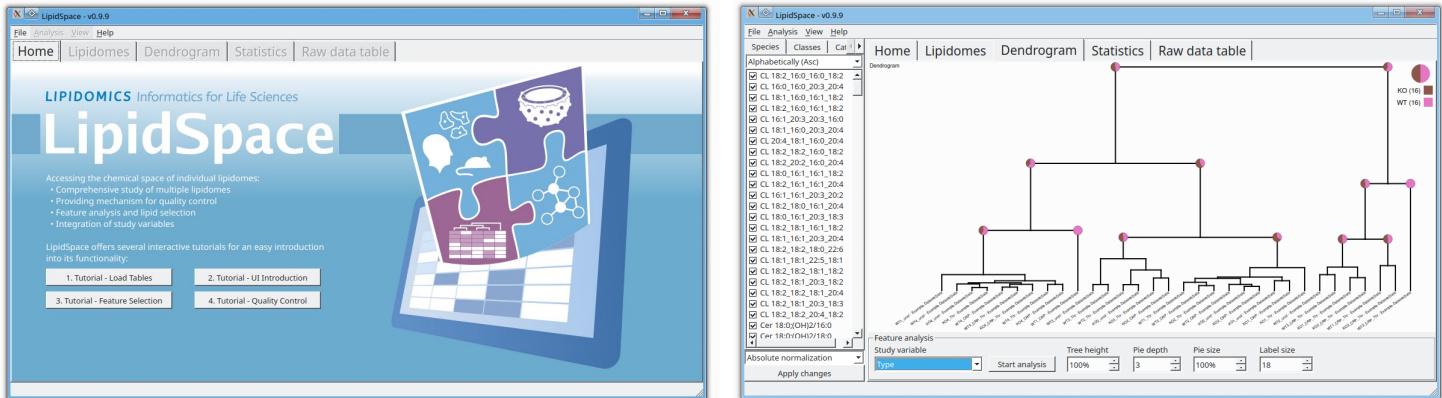
Transforming results to MetaboLights MAF format

Data Reuse and Reanalysis

Interactive Tools, Repositories and Search Engines

LIPIDSPACE FOR STRUCTURAL LIPID COMPARISON

- LipidSpace was designed to compare lipidomes on a structural basis
- All lipids are pairwisely compared and scored by similarity
- All lipidomes (a set of lipids) are compared with each other by distance
- The lipidomes are then hierarchically ordered

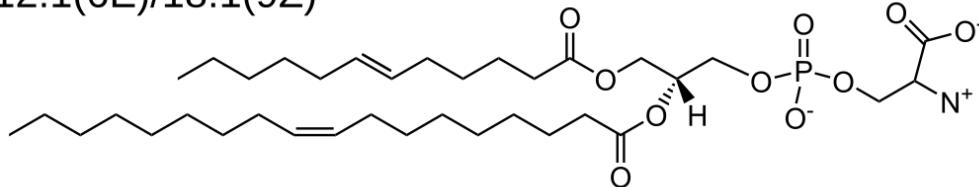


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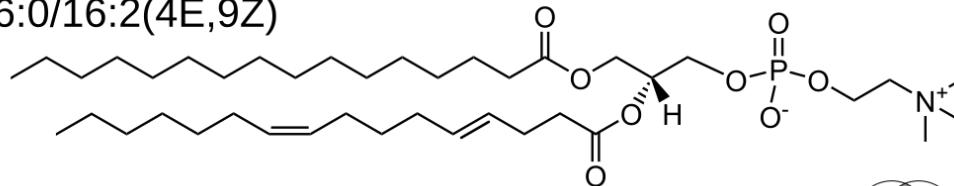


STRUCTURAL COMPARISON

PS 12:1(6E)/18:1(9Z)

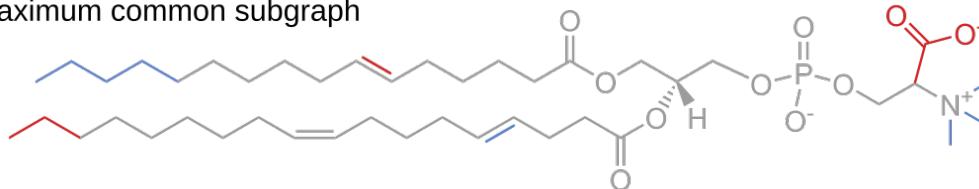


PC 16:0/16:2(4E,9Z)



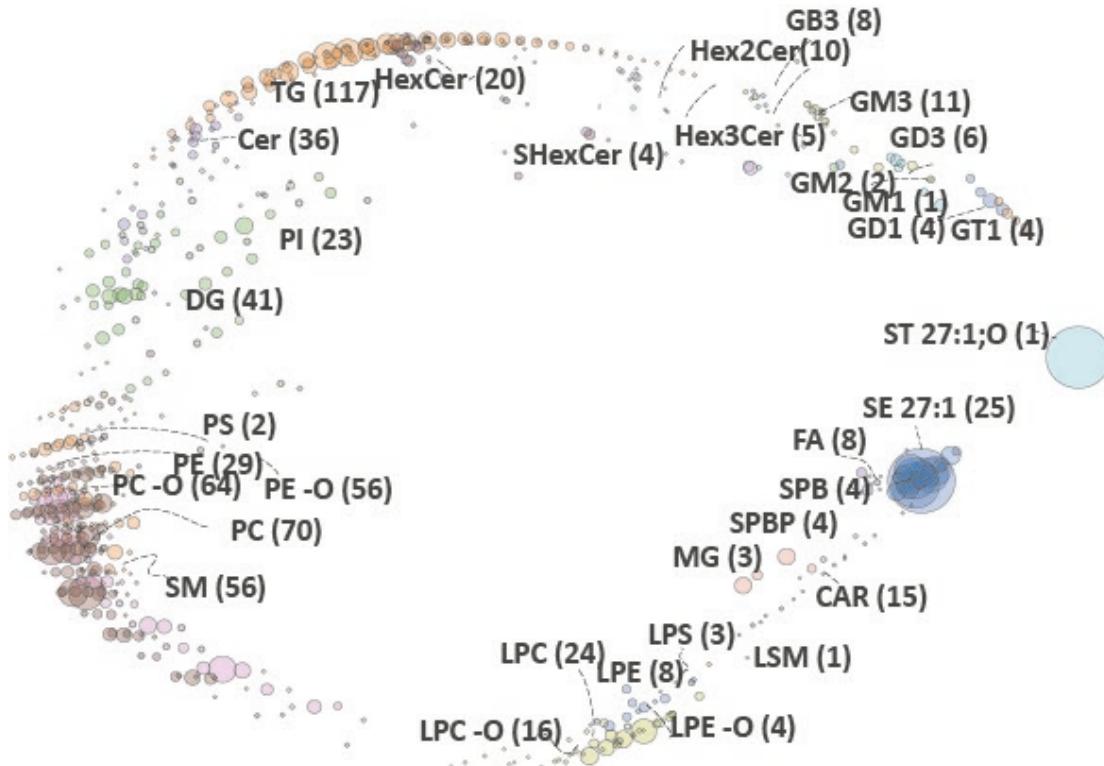
- PS 12:1(6E)/18:1(9Z) specific
- PC 16:0/16:2(4E,9Z) specific
- Maximum common subgraph

$$\text{Dist}(L_1, L_2) = 1 - \frac{|L_1 \cap L_2|}{|L_1 \cup L_2|} = 1 - \frac{\text{Area of intersection}}{\text{Area of union}}$$



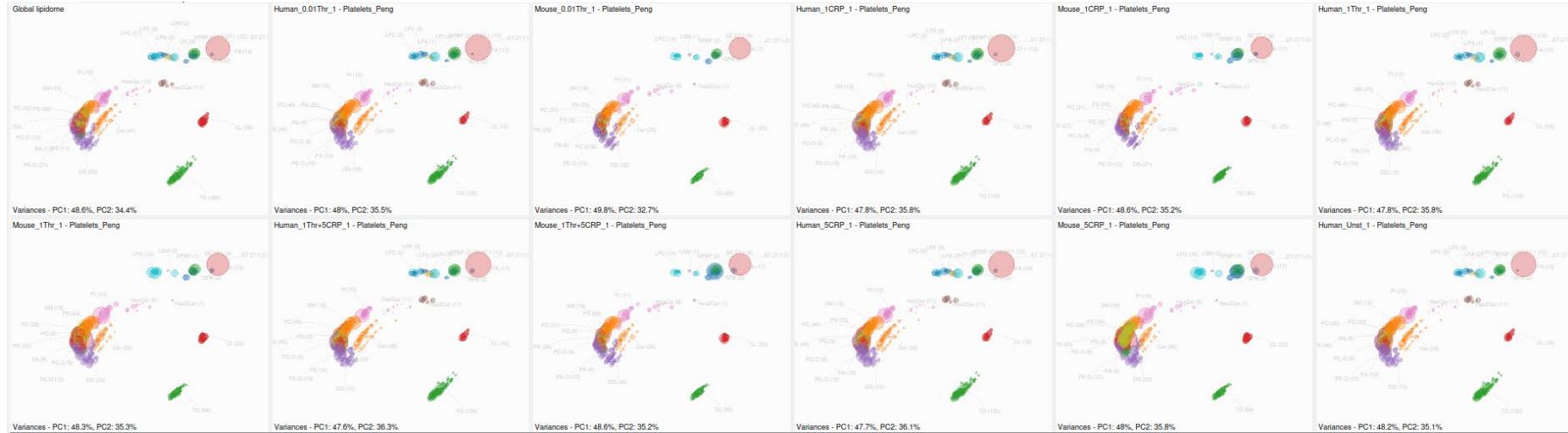
LIPID SPACE DIAGRAM

- The outcome of the pairwise lipid comparison is a global lipid space diagram



LIPID SPACE DIAGRAM

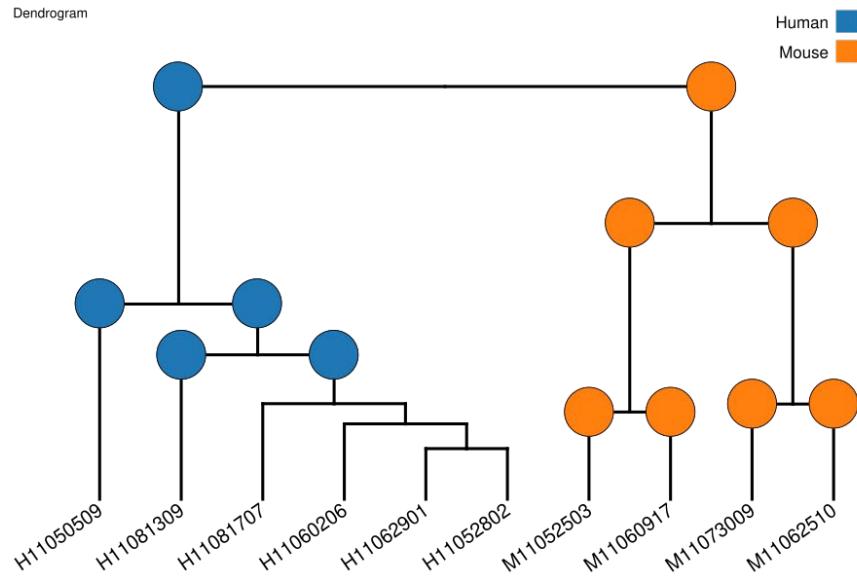
- This diagram can be further split back into the single lipidomes



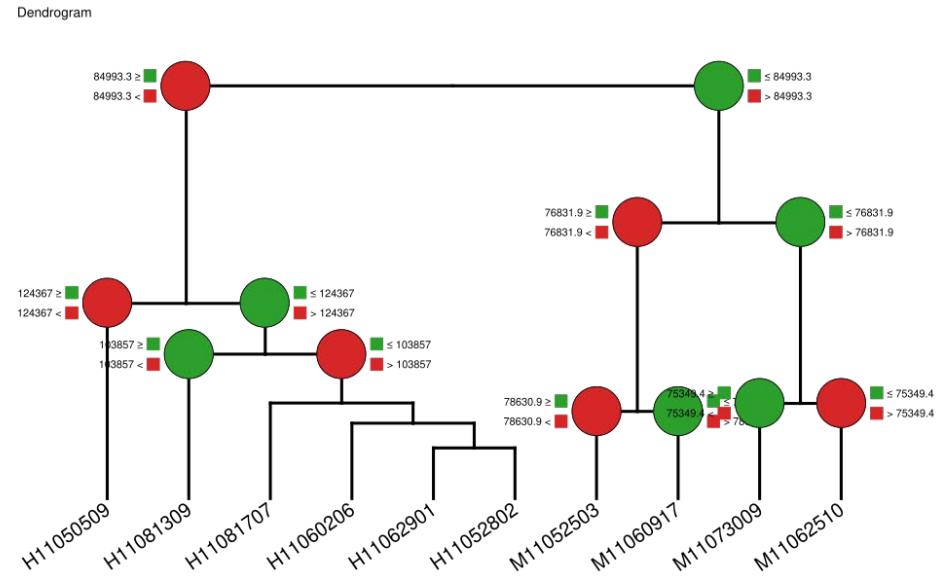
HIERARCHICAL LIPIDOME DIAGRAM

- Lipid spaces can further be structured in a hierarchical dendrogram with respect to their structural distance

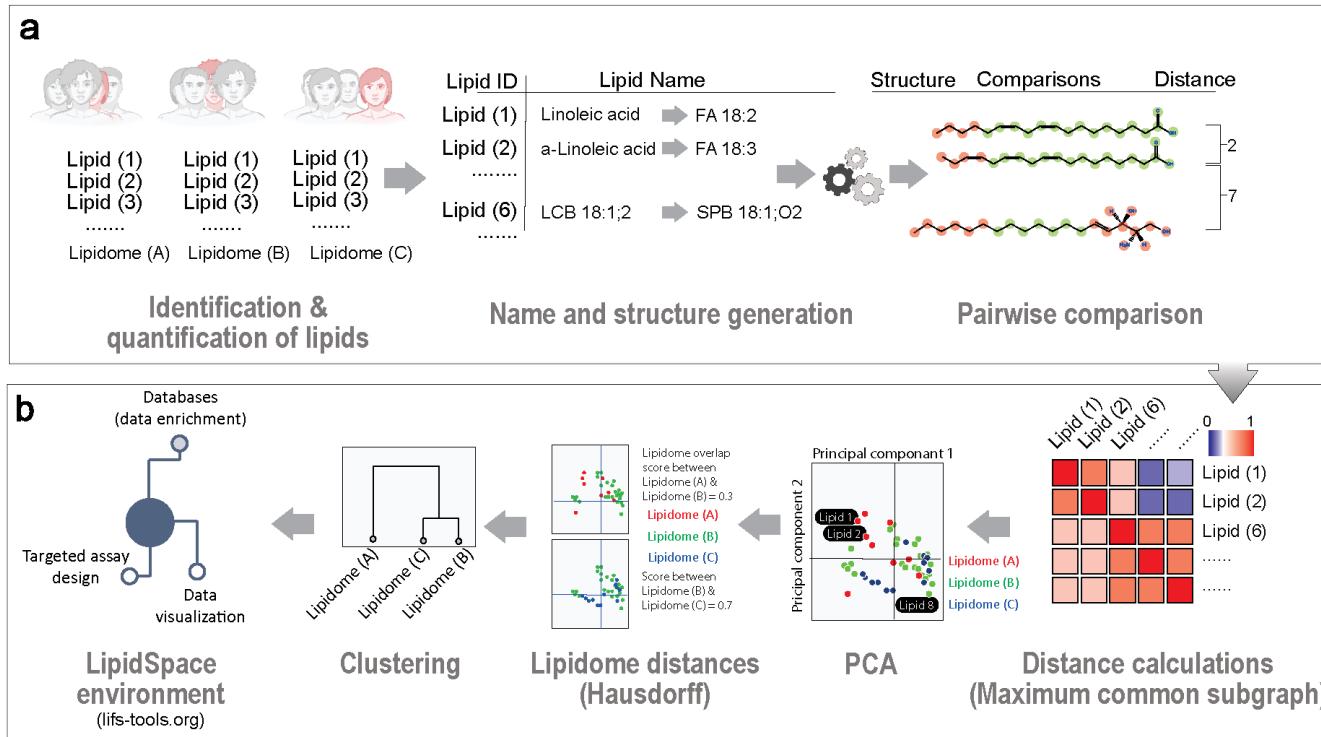
Dendrogram



Dendrogram



INTERNAL PROCESSING WORKFLOW



STATISTICAL COMPARISON

- LipidSpace is equipped with a powerful interactive statistical module



Data Reuse – Omics DI

<https://www.omicsdi.org>

The screenshot displays the OmicsDI platform interface. At the top, there's a navigation bar with links for OmicsDI, Browse, Submit Data, Databases, API, Help, and Login. Below the navigation is a search bar with the placeholder "MTBLS1381" and a "Loading" status message. To the right of the search bar are "Advanced" and "Search" buttons.

The main content area includes several data visualizations:

- A large circular bubble chart showing the distribution of datasets across various tissues, organisms, and diseases.
- A bar chart titled "Omics" showing the count of datasets categorized by type (Omics, Resources, Diseases) over time, with bars color-coded by update date.
- A section titled "Latest Datasets" listing recent publications and datasets, such as "Mar 28 '23 Venom proteome of two egg parasitic wasps".
- A section titled "Most Accessed Datasets" listing highly used datasets, such as "7804 58C" and "14725 Kholodenko1999 - EGFR signaling".
- A section titled "New Datasets Per Year" showing a line graph of new datasets added annually from 2020 to 2023.

- Datasets from different Omics repositories are findable via their exposed metadata
- Allows to find suitable datasets for re-use and re-analysis

Perez-Riverol Y, et al. Discovering and linking public omics data sets using the Omics Discovery Index. Nat Biotechnol. 2017 May 9;35(5):406-409

Data Reuse – Omics DI

OmicsDI Browse Submit Data Databases API Help ▾ Login

MTBLS1381 Advanced Search

12 Results Show all Save search Copy query

Show results for

M Metabolomics (7)
O Other (5)

Organisms

Find your Organisms
 standard reference vector pMCS (2)
 Saccharomyces cerevisiae (1)
 Homo sapiens (1)

Repository

Find your Repository
 MetaboLights (7)
 GNPS (5)

Technology Type

Find your Technology Type
 Mass spectrometry (7)

« Previous 1 2 Next » Sort by: Relevance Page size 10

LipidCreator workbench to probe the lipidomic landscape - Platelet isolation and stimulation, targeted lipid mediator profiling
...able to generate large targeted experiments to analyze blood and to dissect lipid-signaling pathways such as in human platelets.

In MTBLS1381, to validate the performance and accuracy of the transition lists provided by LipidCreator and their applicability on other MS platforms, we used t...
2020-04-15 | MTBLS1381 | MetaboLights Cite

LipidCreator workbench to probe the lipidomic landscape - Platelet isolation and stimulation - DIA lipid mediator validation
....

In MTBLS1382, to validate lipid mediator species identified with the Qtrap instrument (<https://www.ebi.ac.uk/metabolights/MTBLS1381>), the Thermo QEx HF was used to perform high resolution M...
2020-04-15 | MTBLS1382 | MetaboLights Cite

LipidCompass



How can we integrate and enrich existing and new data?



How can we include quality control in data acquisition, data processing and storage?



What is the range for a particular lipid species in sample material like Human plasma?

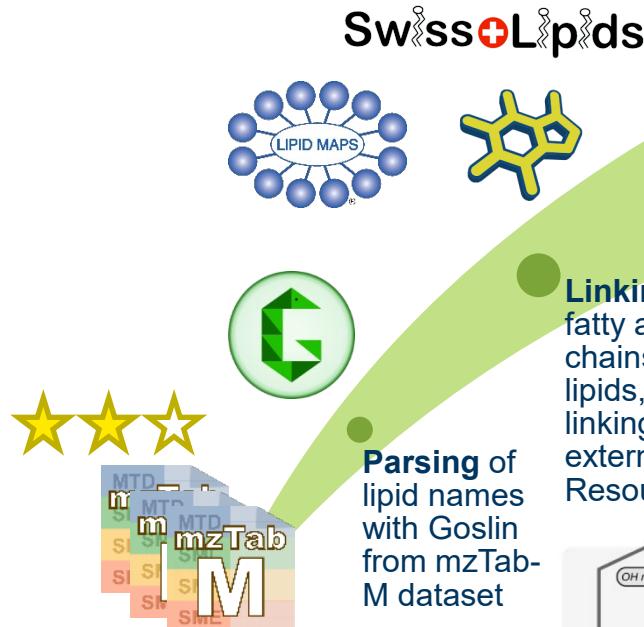


How can we compare and visualize lipid quantities across multiple studies, organisms and tissues?

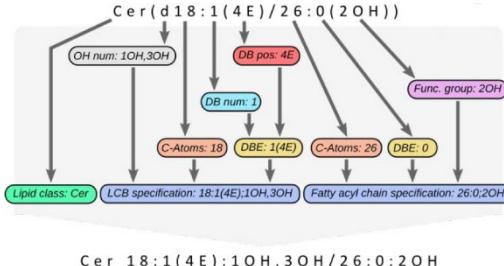


Goal: Create a Findable, Accessible, Interoperable, and Reusable (FAIR) data repository for quantitative lipidomes

Submission and Dataset Import



- Basic & advanced checks on import
- CV terms for semantic annotation, classification and enrichment
- Link to raw data (mzML) possible
- Optional Manual Curation



Current work with EMBL-EBI MetaboLights

- Convert mzTab-M + Lipidomics Checklist to ISA-Tab submission format
- Validation and QC for lipids in submission workflow
- Enrichment and Extension of ChEBI with Shorthand Nomenclature levels

In Preparation

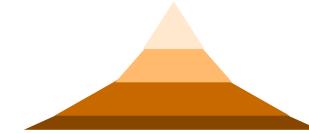
Exploring Datasets

Dataset Details

 Title	Singaporean Integrative Omics Study - Site 1	 PUBLISHED	Status
 Description	Establishing multiple omics baselines for three Southeast Asian populations in the Singapore Integrative Omics Study		Basic Dataset Information
 Contacts	Peter J. Meikle  Metabolomics Laboratory, Baker IDI Heart and Diabetes Institute, 75 Commercial Road, Melbourne 3004, Australia.		
	Markus Wenk  Department of Biochemistry, Center for Life Sciences, 28 Medical Drive, National University of Singapore, Singapore 117456, Singapore.		
 Publications	doi: 10.1016/j.clinms.2017.11.002  ¹ doi: 10.1038/s41467-017-00413-x  doi: 10.1038/srep19139 	CV Term Classification	
 Classifications	Nanomole per Liter quadrupole ion trap 6490 Triple Quadrupole LC/MS Electrospray Ionization Ethnic Group Homo sapiens blood plasma Body Mass Index Age Gender Current Smoker Performing Laboratory Institutional Review Board Diastolic Blood Pressure (mmHg) Serum Total Cholesterol Measurement (mmol/L) Serum Triglyceride Measurement (mmol/L) Serum HDL Cholesterol Measurement (mmol/L) Serum LDL Cholesterol Measurement (mmol/L) Fasting Glucose (mmol/L) Systolic Blood Pressure (mmHg) positive scan		
 Quantification Unit	Nanomole per Liter		
 Study Variables	3		 Quantities
 Samples	359	 Summary Entries	281
 Assays	359	 MS Features	0
 MS Runs	359	 MS Evidence	0

¹H. Begum *et al.*, Lipidomic profiling of plasma in a healthy Singaporean population to identify ethnic specific differences in lipid levels and associations with disease risk factors, *Clinical Mass Spectrometry*, vol. 6, pp. 25–31, Dec. 2017

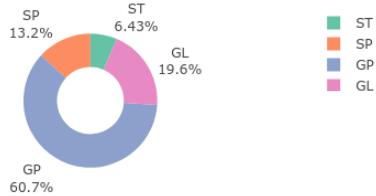
Exploring Dataset Lipidomes



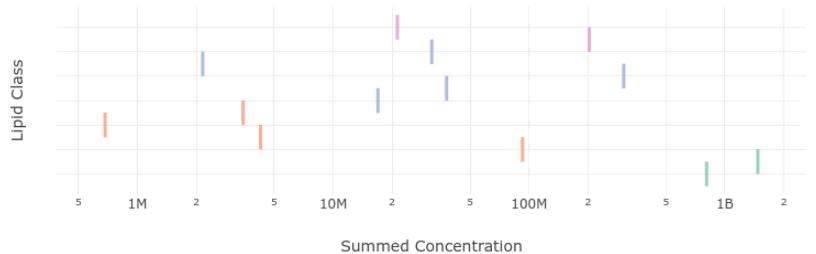
Category
Class
Species
...

Lipid
Category
Level

Lipid Counts on Category Level

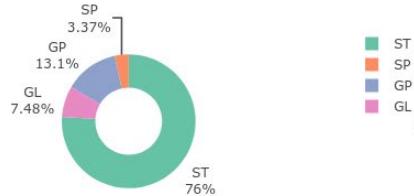


Total Lipid Concentrations on Class Level

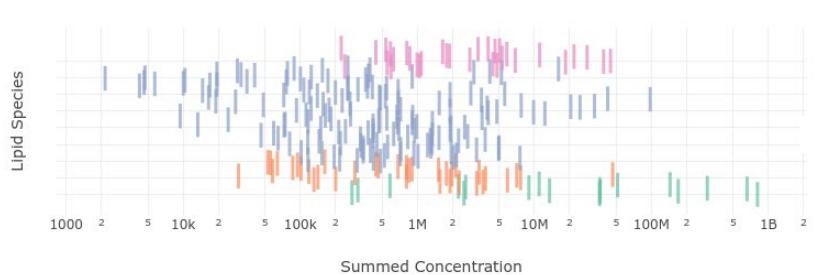


Lipid
Class
Level

Lipid Concentrations on Category Level



Lipid Concentrations on Species Level



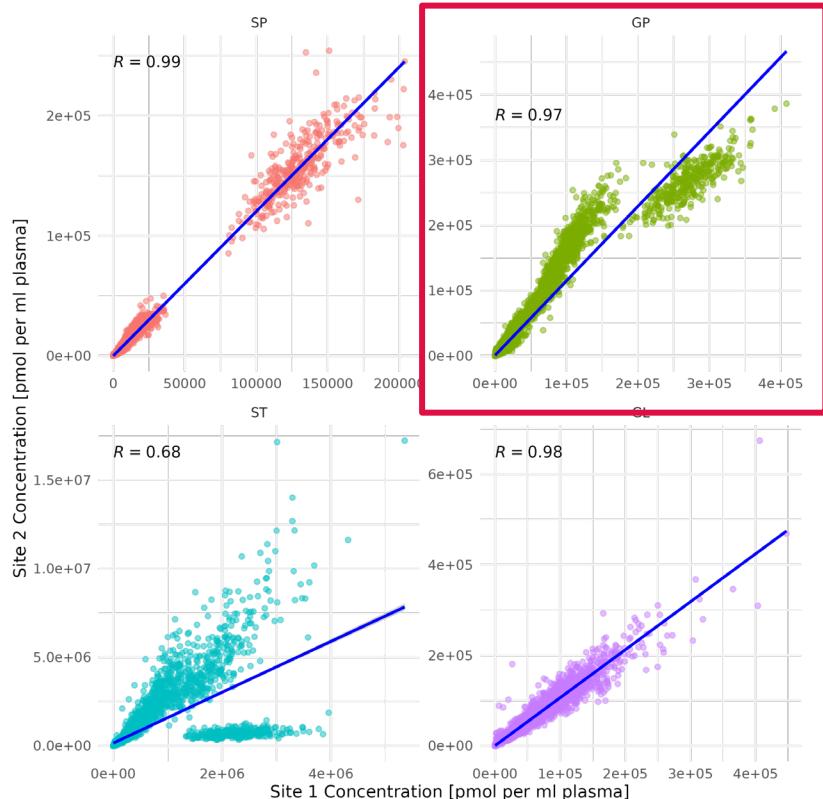
Lipid
Species
Level

In Preparation

Use-Cases in Clinical Lipidomics

1. Comparing Plasma Samples Between Sites
2. Comparing Selected Ceramides Across Labs - ILS Ceramide Ring Trial

Use Case 1: Plasma – Multiple Sites



Study details:

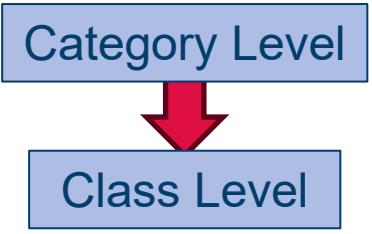
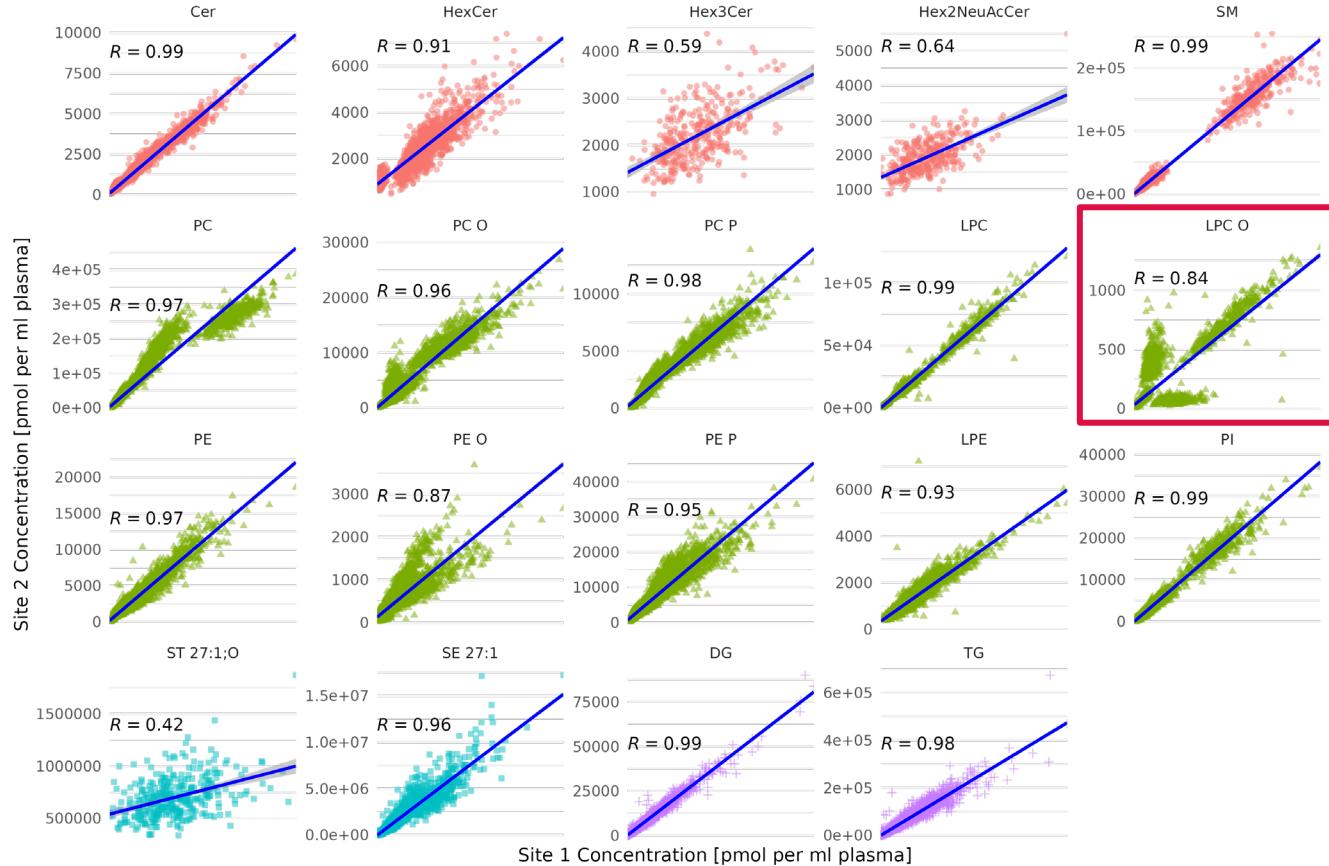
- 281 lipids (species & subspecies)
- 359 samples (one per participant)
- Mixed (gender, age, BMI, ...) population with Chinese, Malayan and Indian background
- Same samples (different aliquots) measured at both sites, same protocol
- Comparison of matched samples
- Agilent 6490 (Site 1) vs 6460 (Site 2) QQQ LC-MS, MRM

LipidMaps.Category

- SP
- GP
- ST
- GL

¹H. Begum *et al.*, Lipidomic profiling of plasma in a healthy Singaporean population to identify ethnic specific differences in lipid levels and associations with disease risk factors, *Clinical Mass Spectrometry*, vol. 6, pp. 25–31, Dec. 2017

Use Case 1: Plasma – Multiple Sites

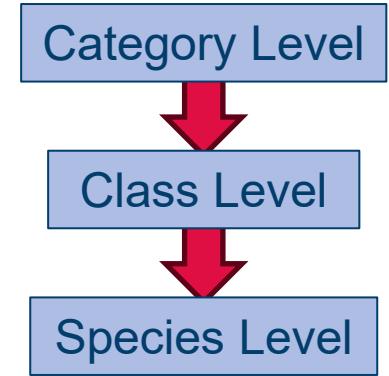
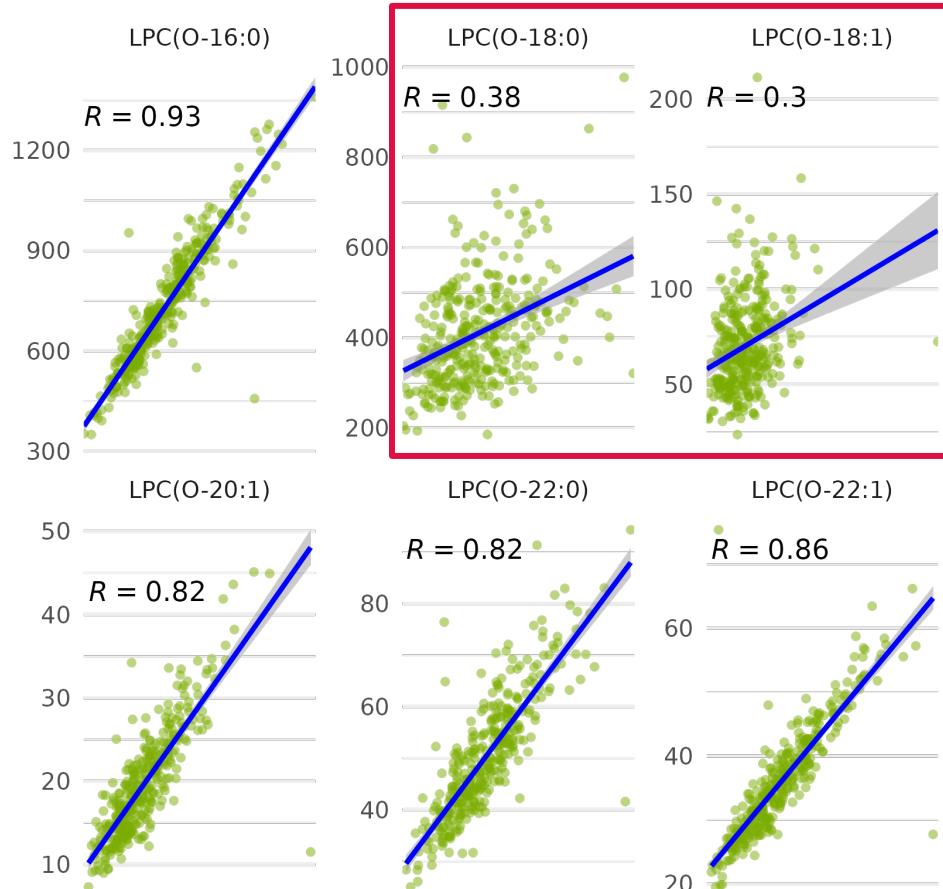


Lipid.Maps.Category

- SP
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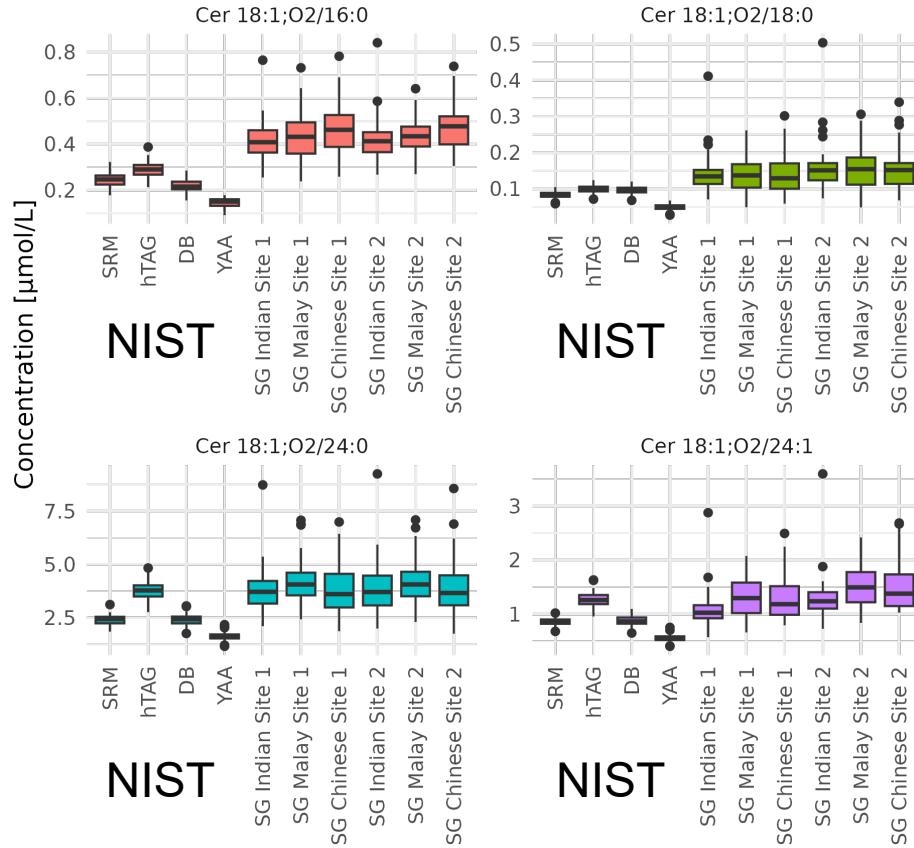
In Preparation

Use Case 1: Plasma – Multiple Sites



- Different visualizations highlight other data characteristics
- Requires matching of Samples!

Use Case 2: Ring Trial & Human Plasma



¹Torta, F., Hoffmann, N., Burla, B. et al. Nature Communications 15, 1, 2024: 8562.

- Ring Trial¹: Quantification with labeled matched standards for each Ceramide in 23 labs with SOP (of 39 reports from 34 different labs)
- Multi Site: Quantification with one class-specific internal standard for Ceramides: Cer 18:1;O2/17:0
- NIST samples were pooled from samples of multiple people, but with strict selection criteria (e.g. age [40, 50] for SRM 1950)
- Use of class specific internal standard has large effect on variability for final quantities. Need for renormalization!
- More quantitative studies needed to study influence factors and effect sizes!

Thanks!

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ILS: IG Lipidomics Standards Initiative ([minimal reporting check list](#)), IG Reference Materials and Biological Reference Ranges ([Ceramide ring trial](#)), IG Clinical Lipidomics, IG Applied Bioinformatics

DGMS: Fachgruppe Lipidanalytik und Lipidomics

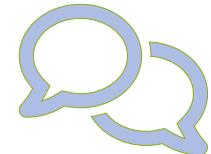
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<https://lipidcompass.org>

<https://lifs-tools.org>

<https://github.com/lifs-tools>



[Public Lipidomics Datasets at EBI MetaboLights](#)

MTBLS1333, MTBLS1334, MTBLS1369,
MTBLS1375, MTBLS1376, MTBLS1381, MTBLS1382



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