

Lipid metabolic network analysis for inferring mechanistic changes in enzyme activity

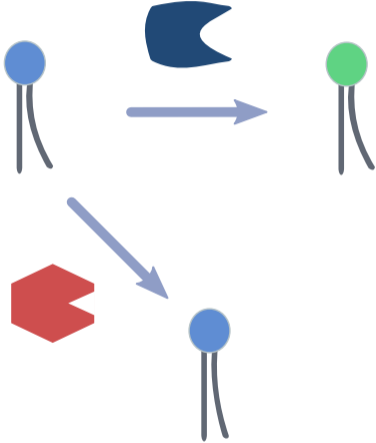
10th Workshop in Lipidomics

Nikolai Köhler

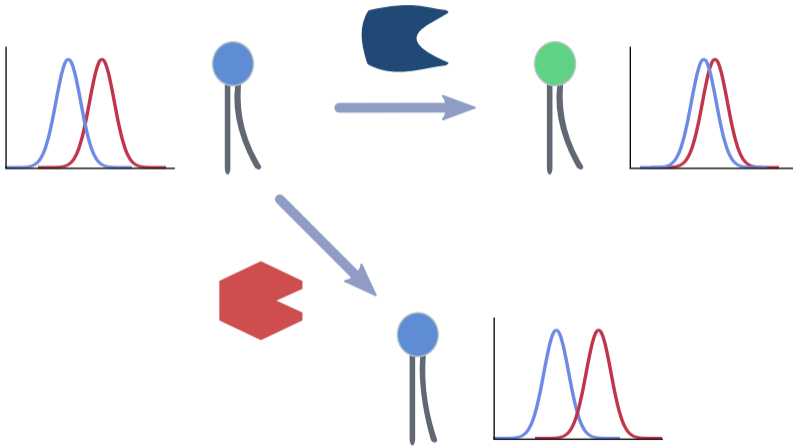
bidt Junior Research Group LipiTUM
Chair of Experimental Bioinformatics
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23rd March 2022

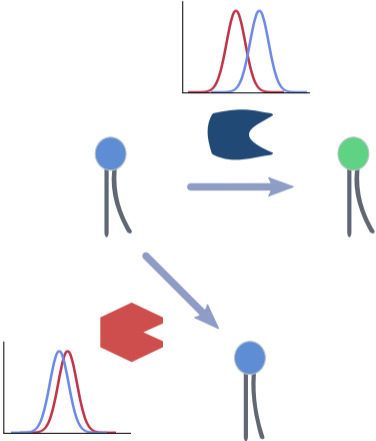
Motivation



Motivation

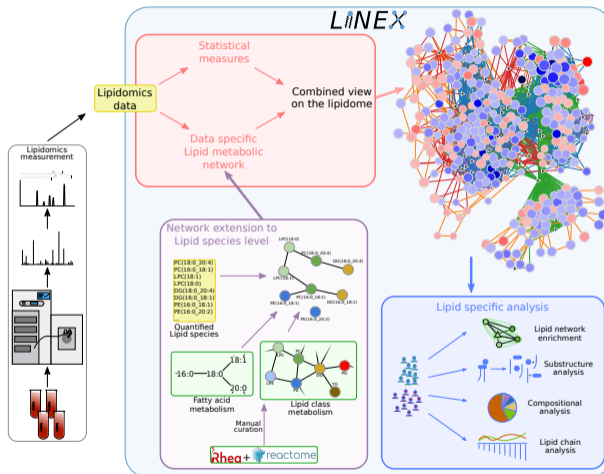


Motivation



⇒ **our aim:** analysis platform to look at both

The LINEX Platform



freely available at:

exbio.wzw.tum.de/linex

Open Access Article

Investigating Global Lipidome Alterations with the Lipid Network Explorer

by  Nikolai Köhler [†] ,  Tim Daniel Rose [†] ,  Lisa Falk  and  Josch Konstantin Pauling ^{*} 




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Köhler and Rose et al.

New Results

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Lipid network and moiety analyses reveal enzymatic dysregulation and altered mechanisms from lipidomics

 Tim D. Rose,  Nikolai Köhler, Lisa Falk, Lucie Klischat,  Olga E. Lazareva, Josch K. Pauling

doi: <https://doi.org/10.1101/2022.02.04.479101>

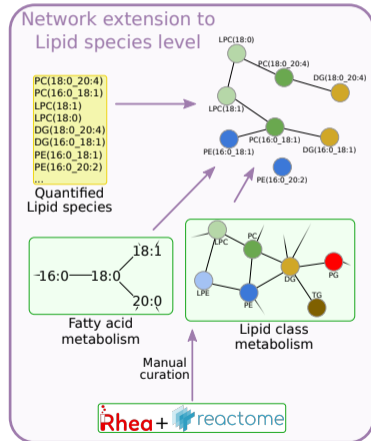
This article is a preprint and has not been certified by peer review [what does this mean?].

Rose and Köhler et al. (under review)

Lipid Metabolic Networks

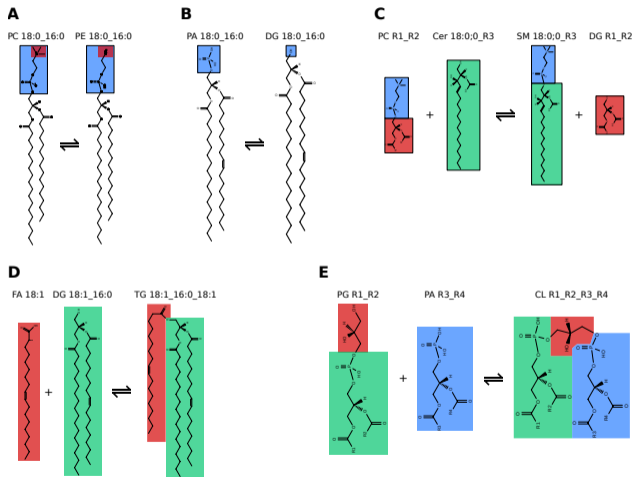
Network Generation

- lipid class metabolism: databases
 - matching fatty acids required
- fatty acid metabolism: metabolic rules
 - matching lipid classes required
- sum species internally converted



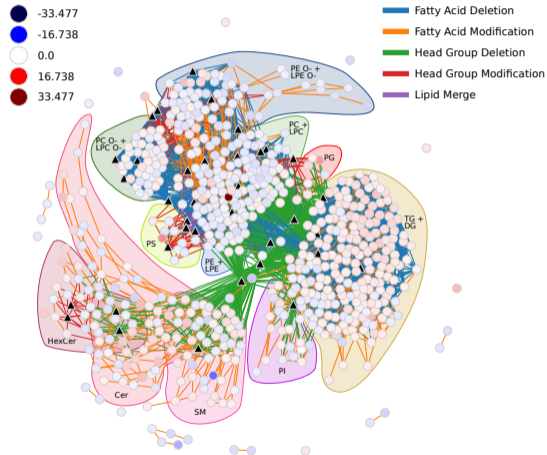
Lipid Metabolic Networks

Class Reactions



Lipid Metabolic Networks

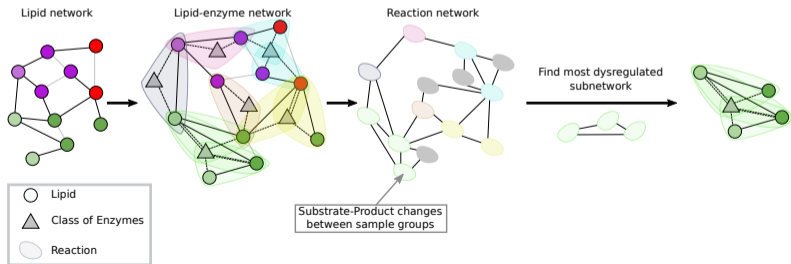
Example Network



Lipid Network Enrichment

Basic Rationale

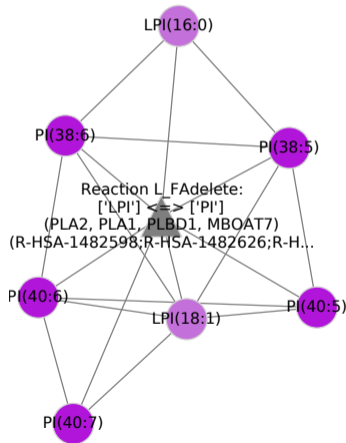
- compute the substrate - product relations for each lipid reaction
- compute the ratio between two experimental for each lipid reaction
- find an 'optimal' subnetwork with two optimization objectives
 - large change between groups (i.e. maximum ratio)
 - small number of reactions



Lipid Network Enrichment

Proof of Principle

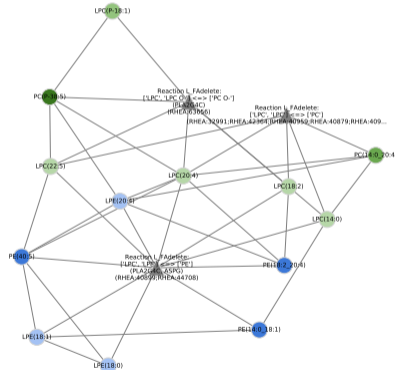
- MBOAT7 Knock-out (Thangapandi et al.)
- two mouse genotypes
 - wild-type
 - MBOAT7 deletion (hepatocyte-specific)
- 253 lipid species from 15 lipid classes



Lipid Network Enrichment

Clinical Data

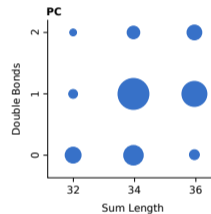
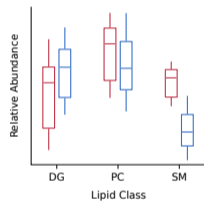
- AdipoAtlas (Lange et al.): quantitative lipidomes of white adipose tissues
 - visceral and subcutaneous
 - obese and lean samples
- 674 lipids from 17 lipid classes



LINEX Webtool

Quantitative Lipid Analyses

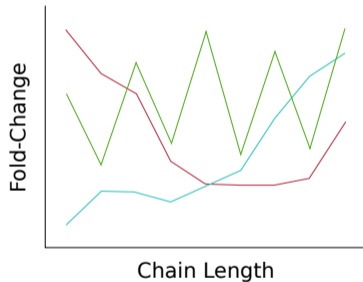
■ summary statistics



LINEX Webtool

Quantitative Lipid Analyses

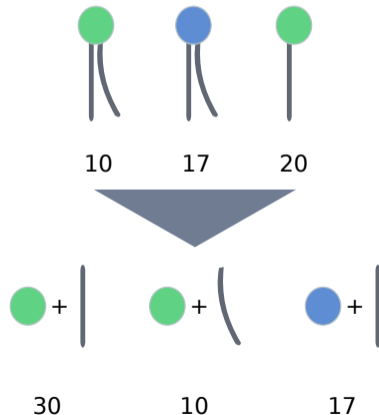
- summary statistics
- chain length analysis



LINEX Webtool

Quantitative Lipid Analyses

- summary statistics
- chain length analysis
- substructure analysis



LINEX Webtool

Contribute!

Contribute

LINEX 2 uses curated reactions from the [Rhea](#) and [Reactome](#) databases. We are constantly extending the LINEX reaction and lipid class database, but are happy to take user contributions into account. If you are an expert in the field or found publications with new information that should be considered, please let us know.

Use the following form to submit details about lipid classes and reactions, including references (publications, database identifiers or other), that should be added to LINEX 2. We will consider your contribution and contact you again. So please also leave your email address.

You can also reach us via email directly (See the [About](#) page).

Contribution Form

Email

Contribution

(Max 800 characters, for longer texts send us an email directly)

 Submit

Acknowledgements

- Dr. Josch K. Pauling
- LipiTUM Group
- Lisa Falk & Lucie Klischat
- Olga Lazareva



ExBio

bidt

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