Lipid metabolic network analysis for inferring mechanistic changes in enzyme activity

10th Workshop in Lipidomics

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Chair of Experimental Bioinformatics
TUM School of Life Sciences
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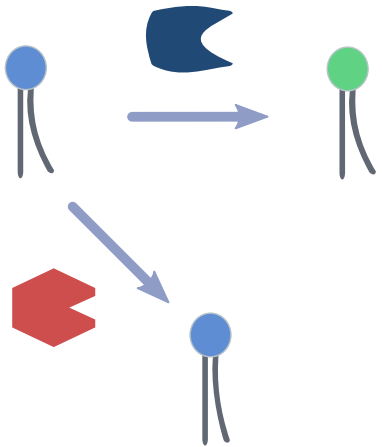
Motivation



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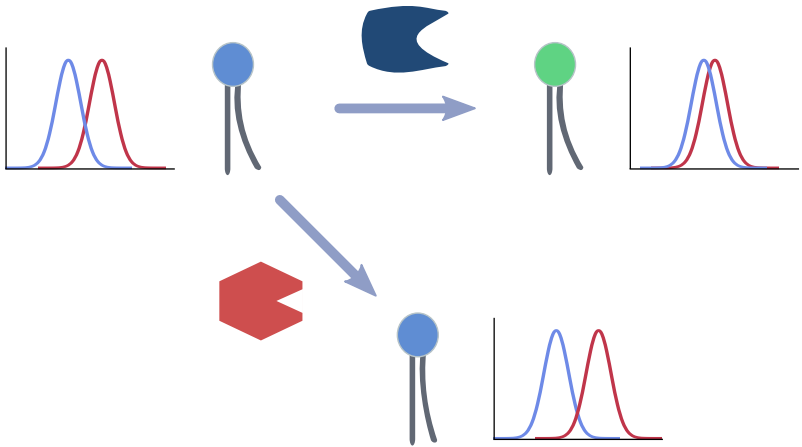

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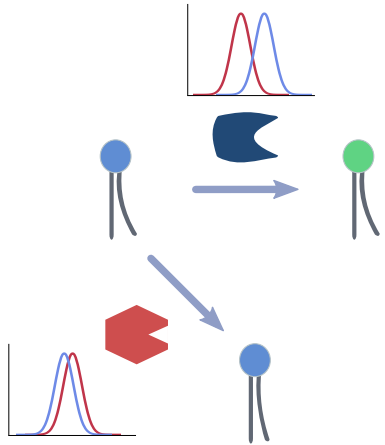
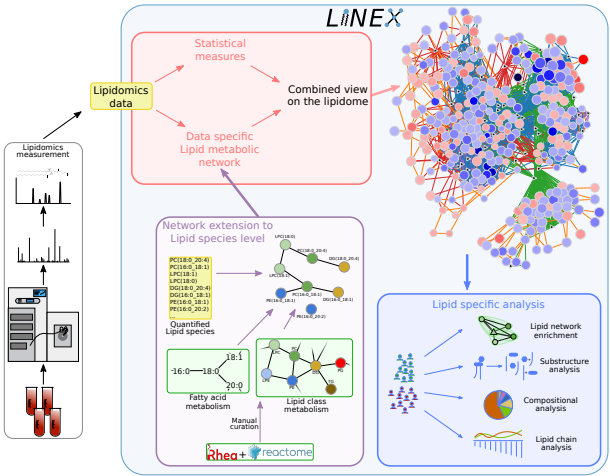


Motivation

LipiTUM

$\Rightarrow$ **our aim:** analysis platform to look at both

The LINEX Platform

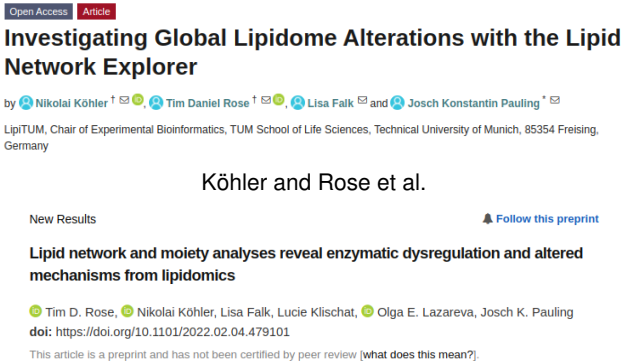


The LINEX Platform

freely available at:

exbio.wzw.tum.de/linex

The LINEX Platform



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

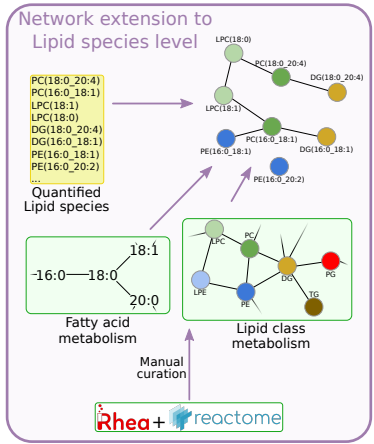
doi: https://doi.org/10.1101/2022.02.04.479101

This article is a preprint and has not been certified by peer review [what does this mean?].

Rose and Köhler et al. (under review)

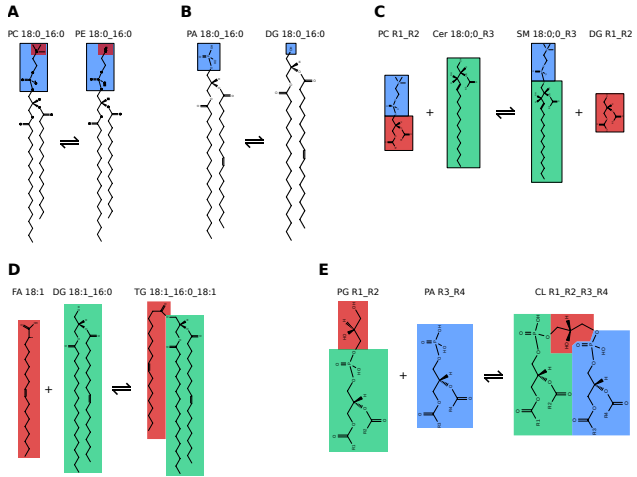
Lipid Metabolic Networks
Network Generation

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



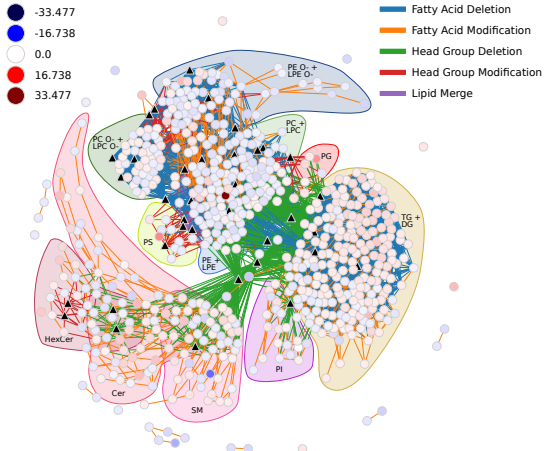
Lipid Metabolic Networks

Class Reactions



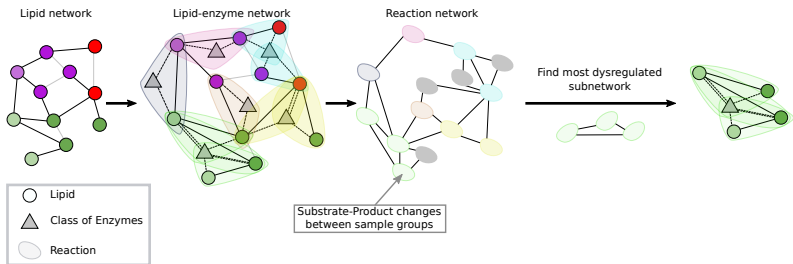
Lipid Metabolic Networks

Example Network



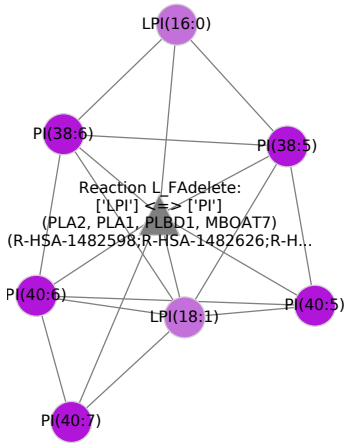
Lipid Network Enrichment
Basic Rationale

- 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



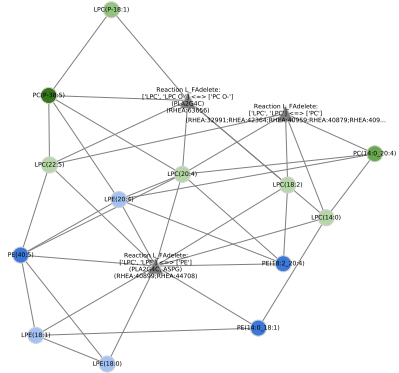
Lipid Network Enrichment
Proof of Principle

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



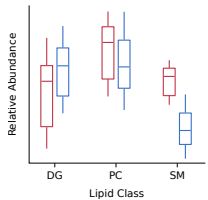
Lipid Network Enrichment
Clinical Data

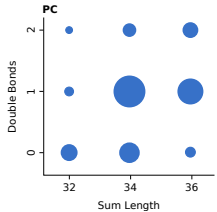
- AdipoAtlas (Lange et al.): quantitative lipidomes of white adipose tissues
  - visceral and subcutaneous
  - obese and lean samples
- 674 lipids from 17 lipid classes



LINEX Webtool
Quantitative Lipid Analyses

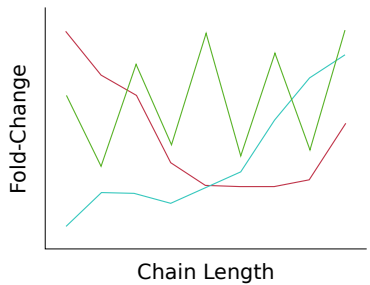
- summary statistics





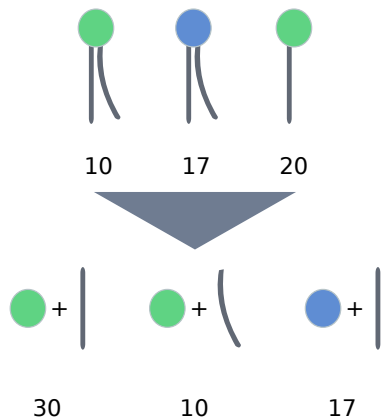
LINEX Webtool
Quantitative Lipid Analyses

- summary statistics
- chain length analysis



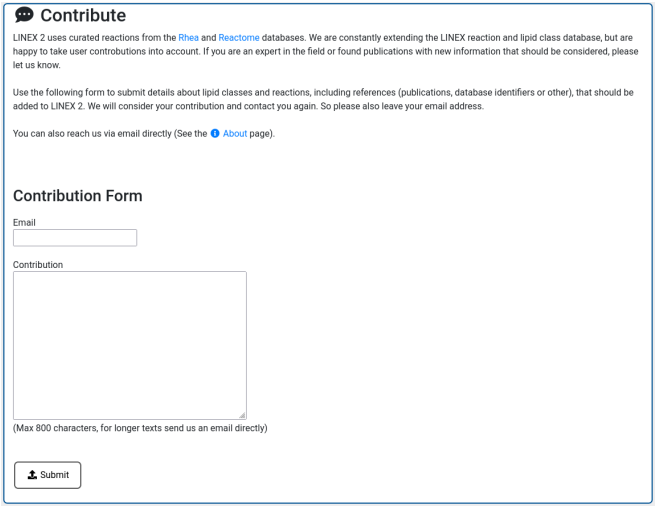
LINEX Webtool
Quantitative Lipid Analyses

- summary statistics
- chain length analysis
- substructure analysis



LINEX Webtool

Contribute!



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