

Investigating Global Lipidome Alterations with the Lipid Network Explorer

Nikolai Köhler, Tim Rose, Lisa Falk, Dr. Josch Konstantin Pauling

1st International Lipidomics Society annual conference and 7th Lipidomics Forum

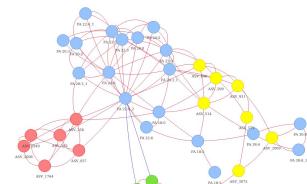
bidt-Junior Research Group LipiTUM
Chair of Experimental Bioinformatics
TUM School of Life Sciences Weihenstephan
Technical University of Munich
Germany

Why Lipid Networks?

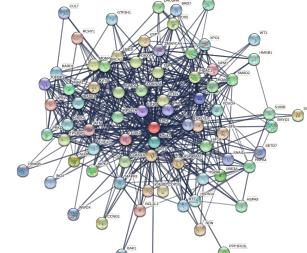


- Usefulness in other omics analysis
- Caveat: Biochemical Meaningfulness

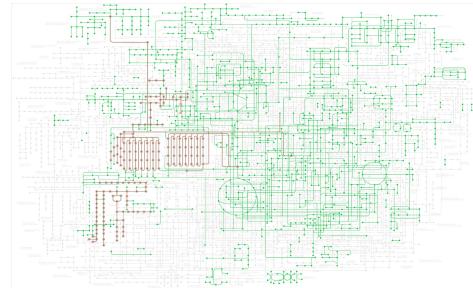
Correlation Networks



PPI Networks



Metabolic Networks



Aim: biochemically valid lipid species networks

- The ‘Lipid Network Explorer’
- Combined Lipid Metabolic Networks
- ...and Statistical Metrics



Article

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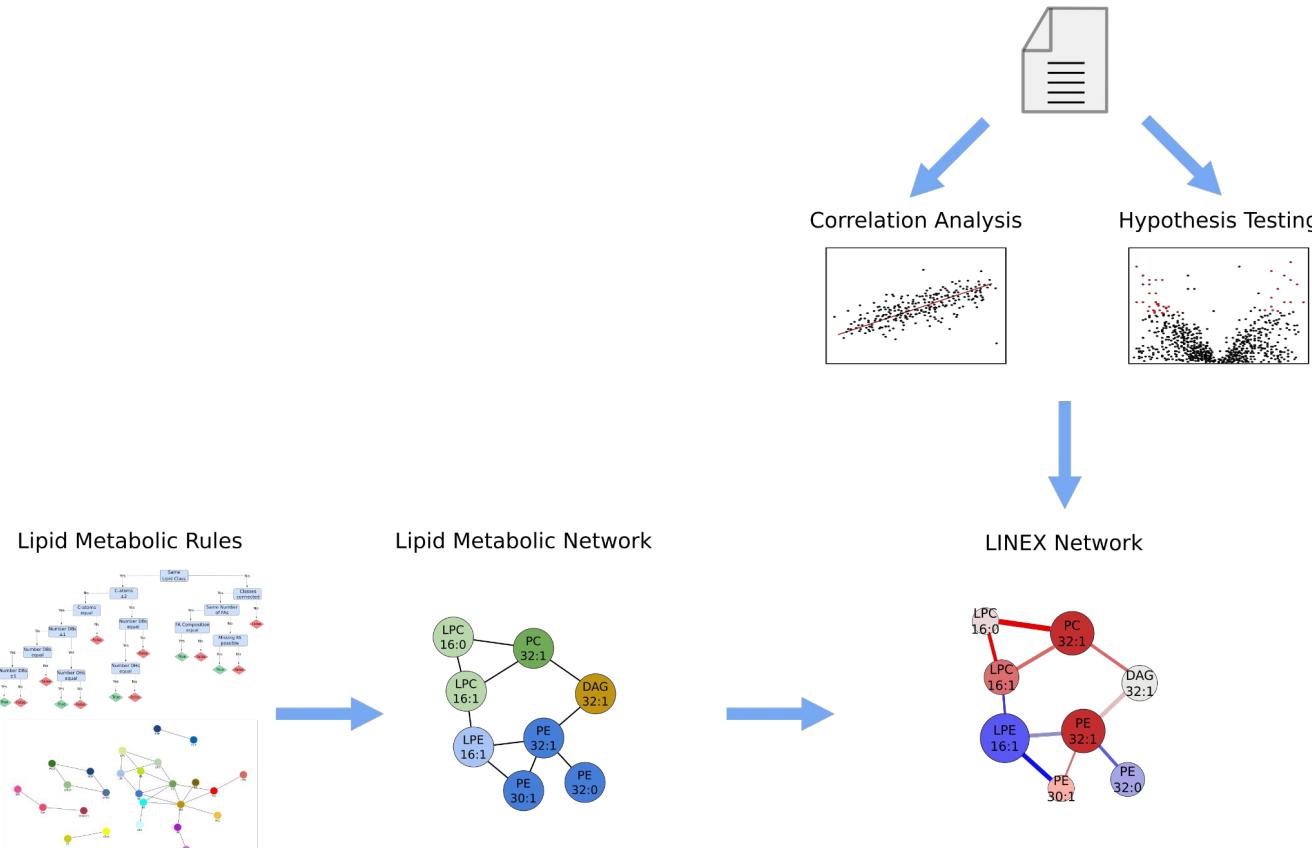
† These authors contributed equally to this work.

<https://doi.org/10.3390/metabo11080488>



<https://exbio.wzw.tum.de/linex/>

LINEX Network Generation



modified from Köhler and Rose et al., Metabolites 2021

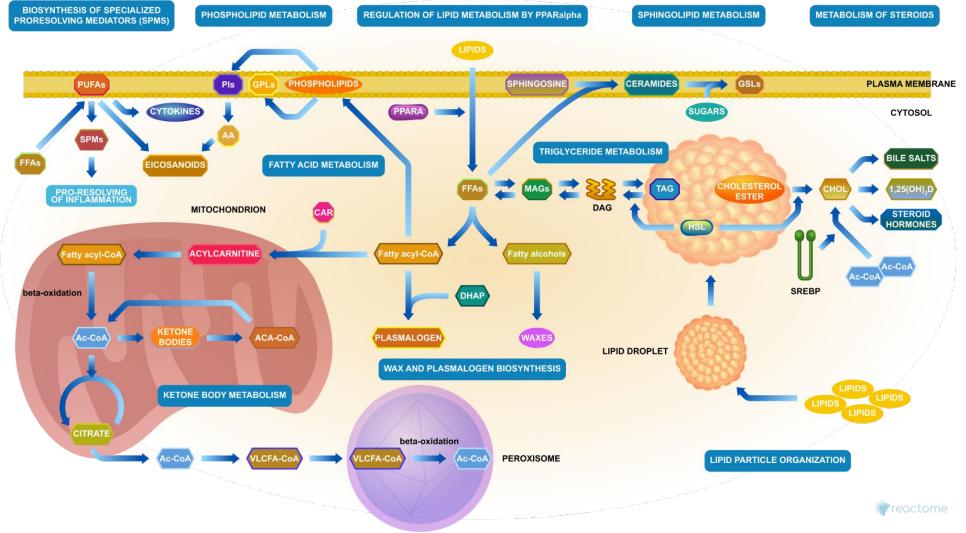
LINEX Network Generation



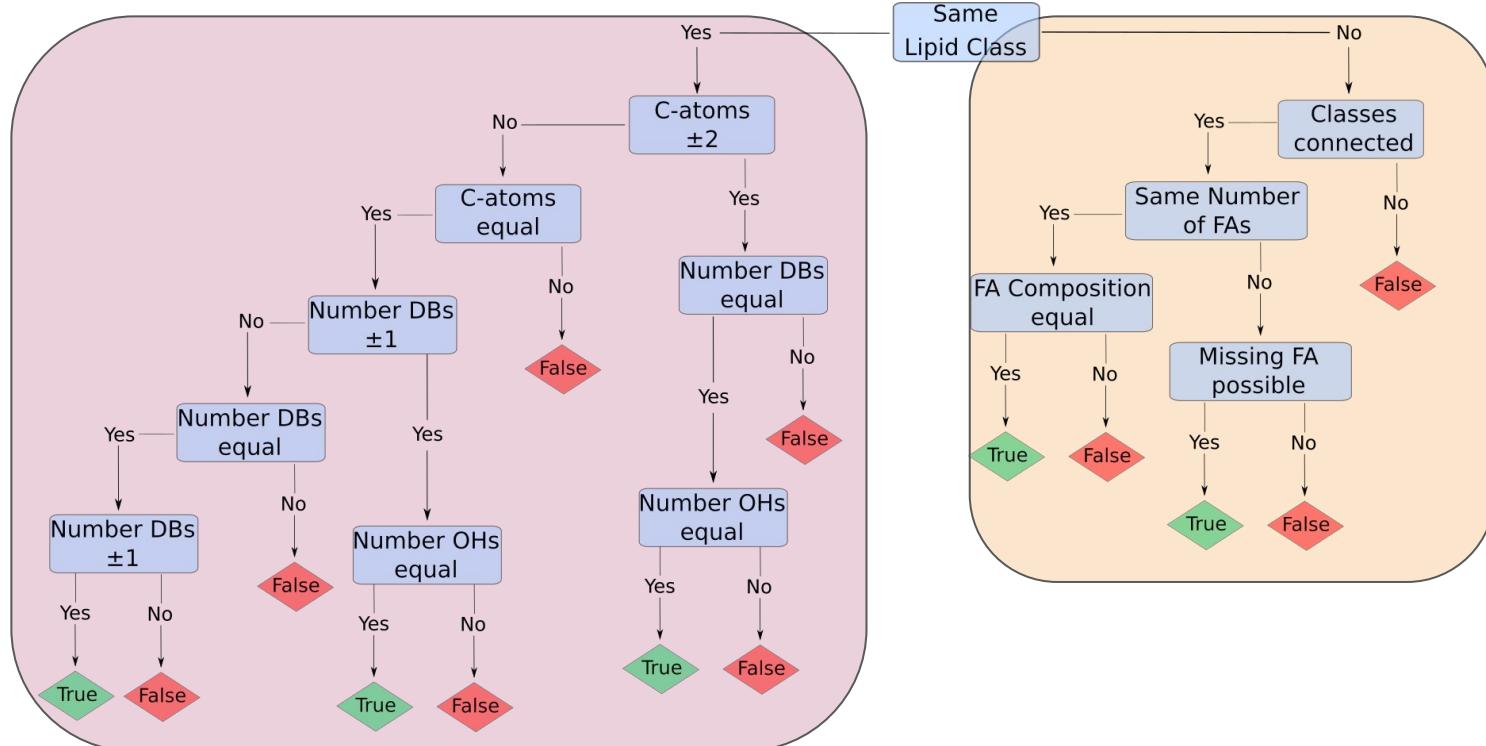
Fully rule-based

- Lipid class level
 - Head group modifications
 - Only one-to-one reactions
- Fatty acid level
 - Elongation/Oxidation
 - Desaturation
 - Hydroxylation
 - Restrictions

=> entirely customizable

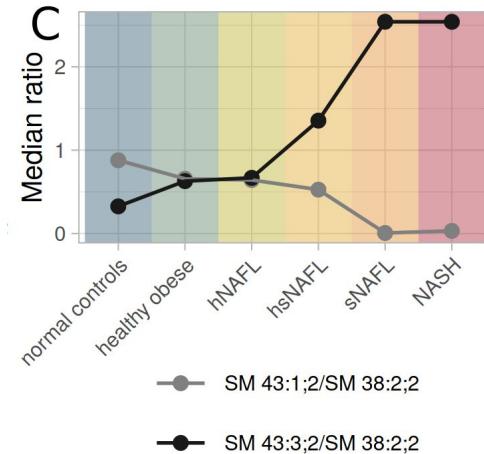


LINEX Network Generation



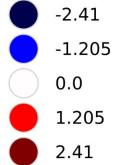
Example - NAFLD

- Data from Vvedenskaya and Rose et al.
(<https://doi.org/10.1016/j.bbalip.2011.06.009>)
- 316 lipids
- 22 lipid classes
- NAFL subtypes identified



hNAFL vs. sNAFL

Fold Changes

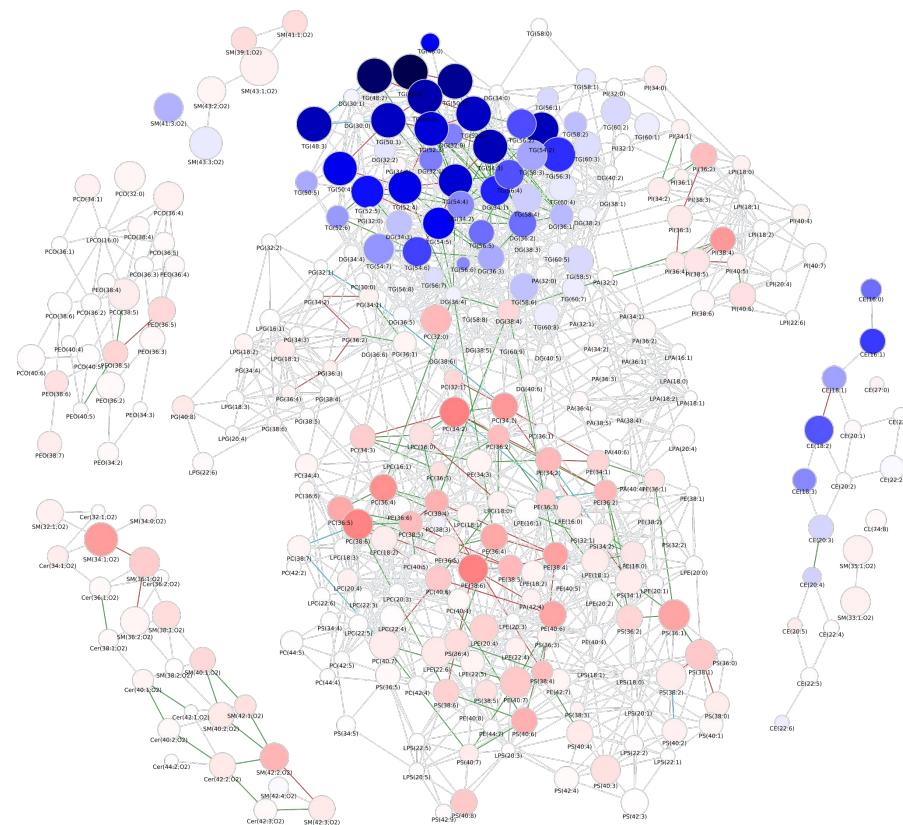


-log10(FDR)



Correlation Changes

- significant to unsignificant (cyan)
- unsignifcant to significant (green)
- unchanged significant (red)
- unsignifcant (gray)
- positive to negative (blue)
- negative to positive (orange)



hNAFL vs. sNAFL

Fold Changes

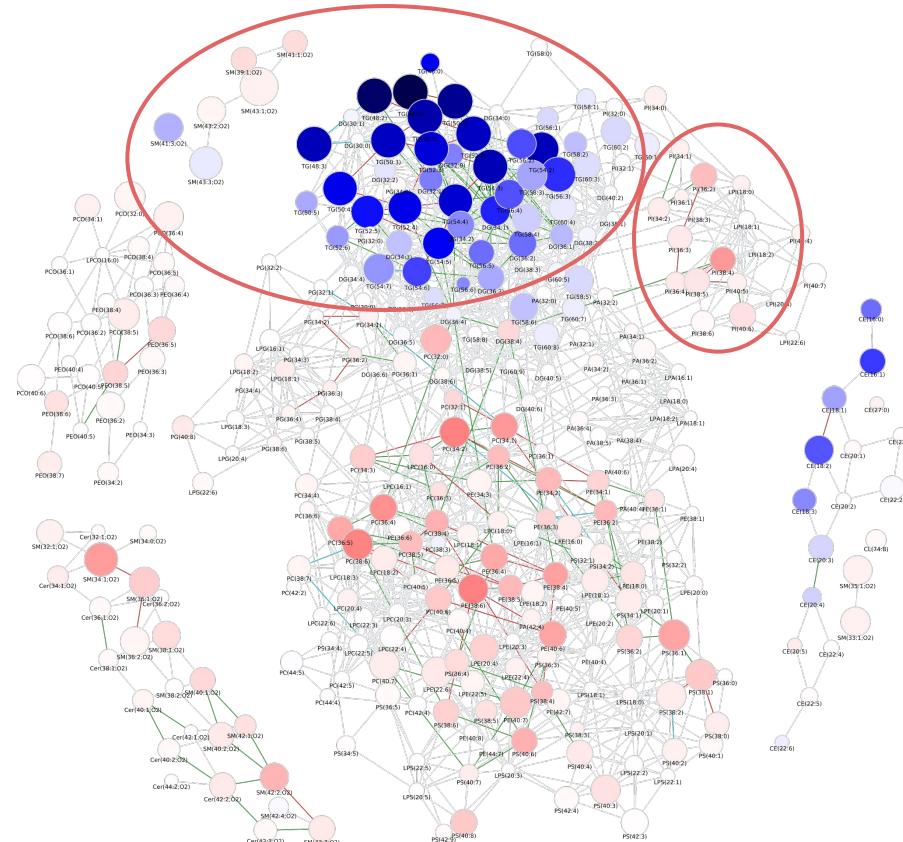
- -2.41
- -1.205
- 0.0
- 1.205
- 2.41

-log10(FDR)

- 0.0
- 2.362
- 4.723
- 7.085
- 9.447

Correlation Changes

- significant to unsignificant
- unsignificant to significant
- unchanged significant
- unsignificant
- positive to negative
- negative to positive



hNAFL vs. sNAFL

Fold Changes

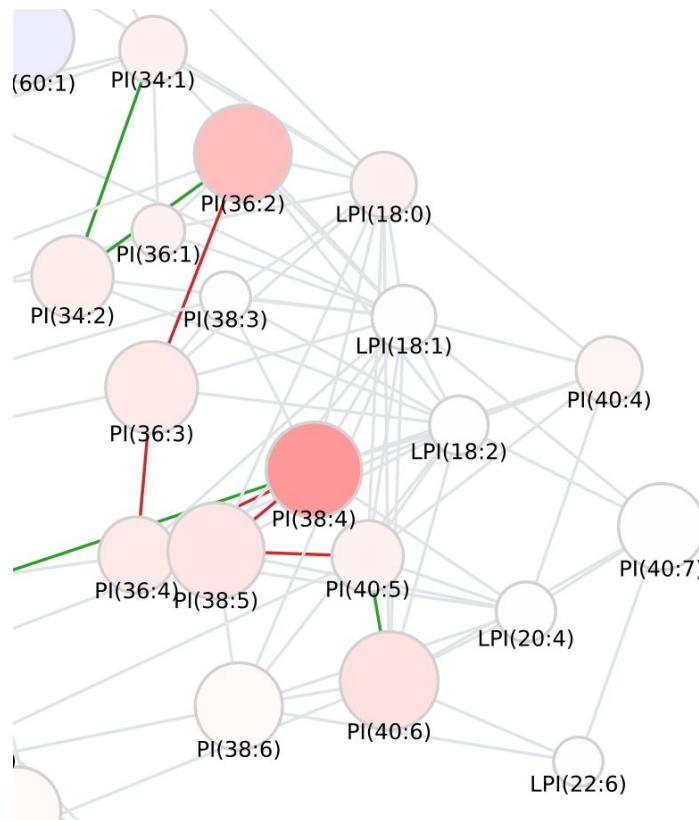
- 2.41
- 1.205
- 0.0
- 1.205
- 2.41

-log10(FDR)

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Correlation Changes

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hNAFL vs. sNAFL

Fold Changes

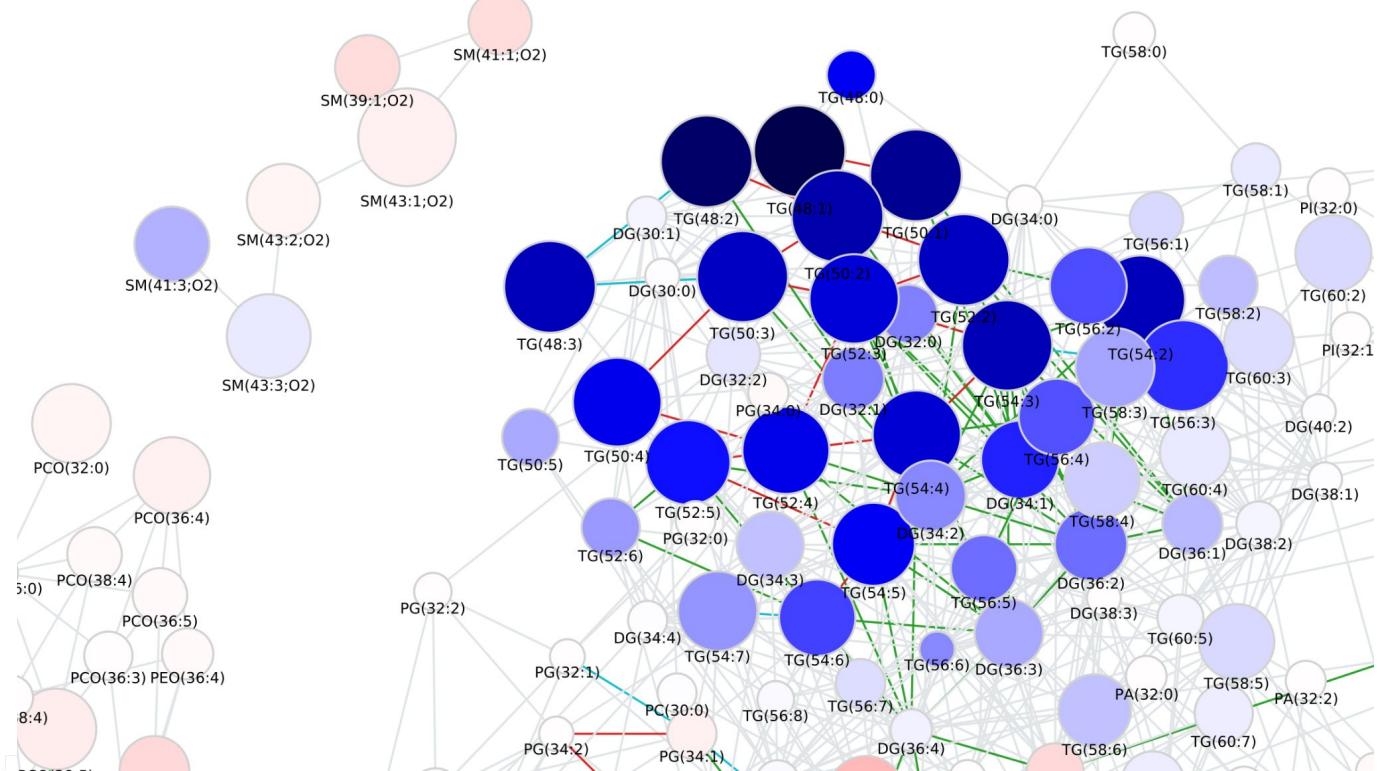
- -2.41
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-log10(FDR)

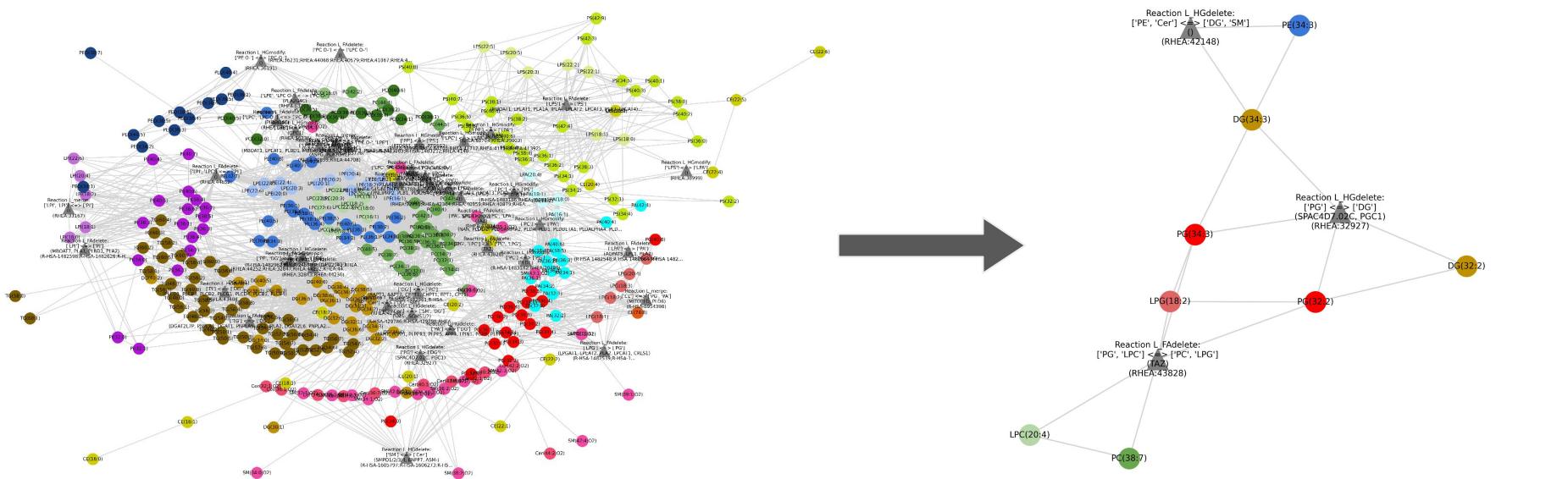
- 0.0
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Correlation Changes

- significant to unsignificant
- unsignificant to significant
- unchanged significant
- unsignificant
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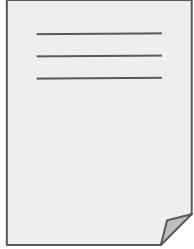


Network Enrichment



Web Interface

Your Quantified
Lipidomics Data



Upload

NOTE: You can only have one data set per session uploaded.
If you want to analyze multiple datasets please download the current one before uploading a new one.

Required Input Data

Select a lipid data file
 No file selected.

Optional Sample Data

Select a sample group file (optional)
 No file selected.

Optional Model Settings

Select Lipid Class Settings (optional)
 No file selected.

Select Fatty Acid Settings (optional)
 No file selected.

Computation Options

Data is log-transformed
 Fold changes as logratios
 Convert to Lipid and Nomenclature
NOTE: converting names may take up to several minutes

Molecule Species — Lipid Resolution
 Setting the highest resolution to consider:
 Please only change if all lipids are sum species or some are confident or specific specifications.

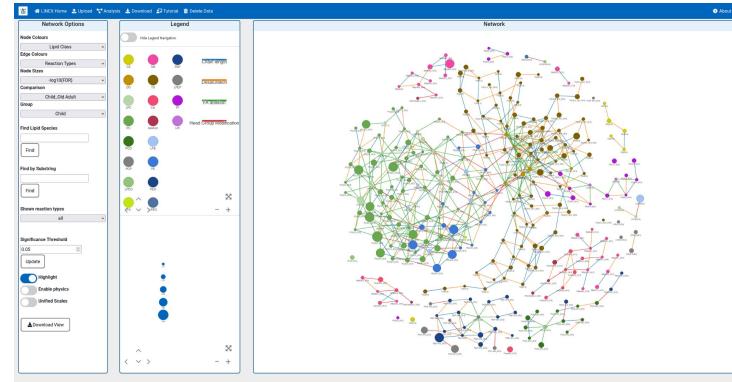
Correlations/Correlation Changes
 Partial Correlations/Correlation Changes
 0.05

Fold Changes
 Reference Group
 Reference Group to compute fold-changes against

p-values (binary statistical test)

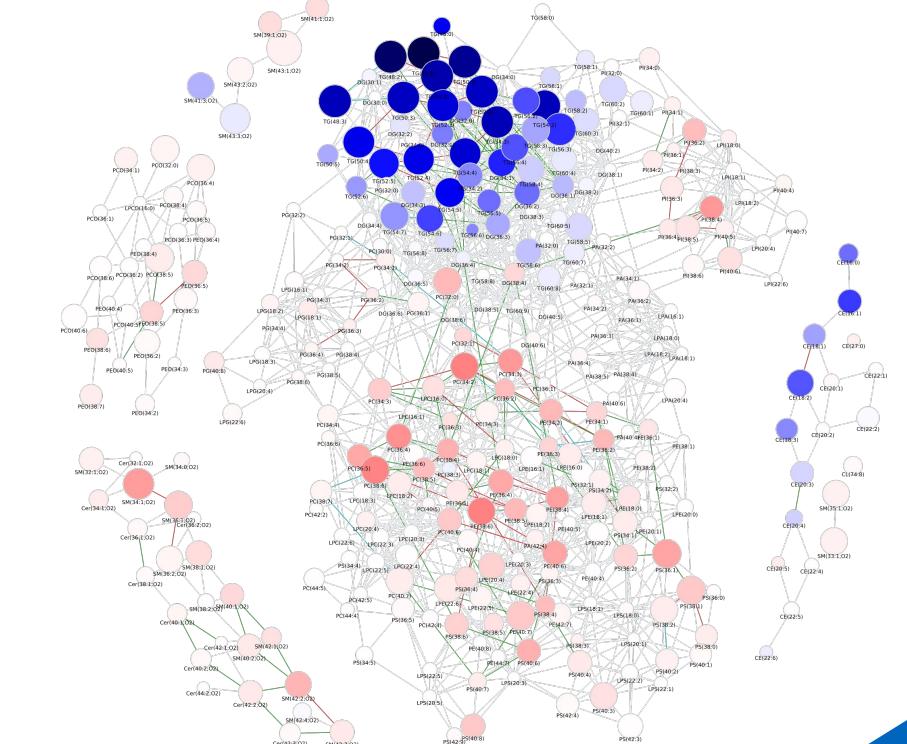
Statistical Test

Directed Graph
NOTE: directed edges increase memory and processor uptake

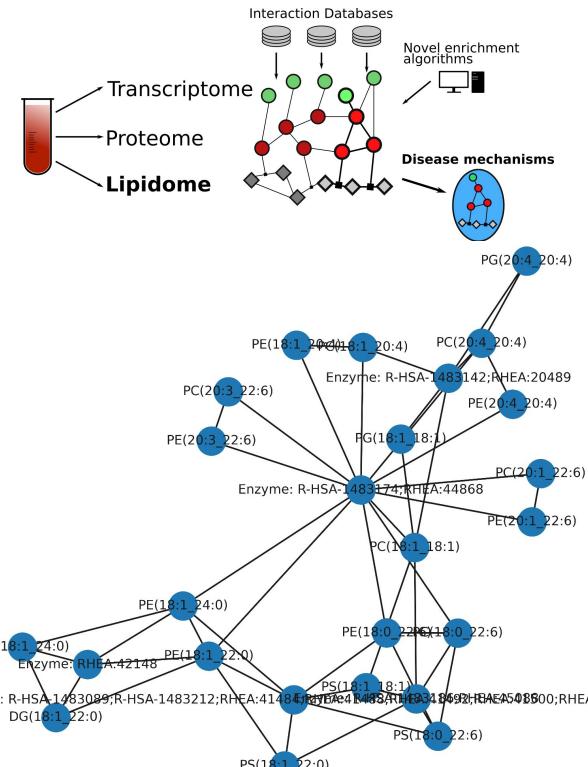


Conclusion

- Novel rule-based way to generate lipid metabolic networks
- Basis for hypothesis generation and data exploration
- Web-tool for easy accessibility



- Database connections
 - Support for ~100 lipid classes
 - Enzyme IDs
 - Reactions with multiple lipid substrates/products
- Bipartite networks
 - Reaction Networks
 - Enzyme-Lipid Networks
- Network enrichment
=> explainable lipid selection



Acknowledgments

- Dr. Josch K. Pauling
- LipiTUM Group
- Dr. Michael Witting



Link to slides, workshop and web-app
<https://exbio.wzw.tum.de/ils2021/>



lipitum.de

twitter.com/LipiTUM

gitlab.lrz.de/lipitum-projects