Computational stratification and subtyping on NAFLD liver lipidomics

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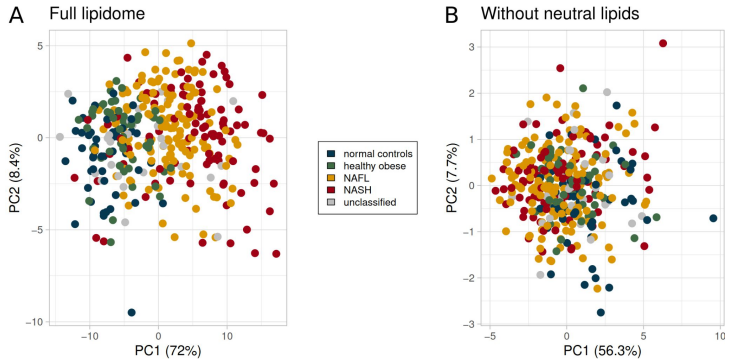
Computational analysis of NAFLD liver lipidomics

- Liver lipidomics of 365 patients
- Quantified 316 lipid species
  - From 22 lipid classes



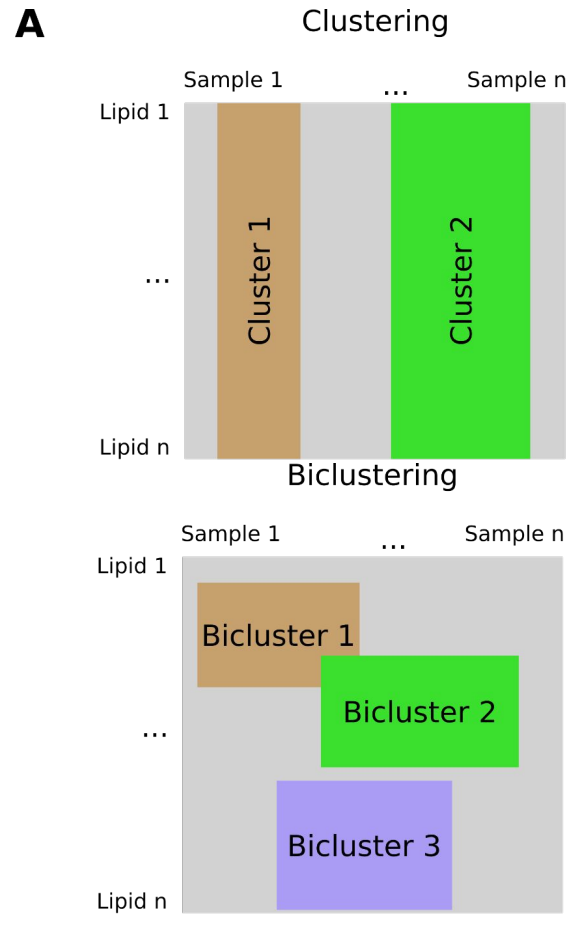
Vvedenskaya and Rose et al. (2021)
https://doi.org/10.1016/j.jlr.2021.100104

- How can we access the lipidome beyond neutral lipids?

- Novel workflow to access clinical (lipid-) omics data
  - Based on **biclustering**

Why biclustering?

- Clustering finds sample groups
  - Based on all features
  - Global similarity
- Biclustering extracts sample subgroups & molecular signatures
  - Disease phenotype usually manifested in local pathway alterations
  - More suitable for disease subtyping



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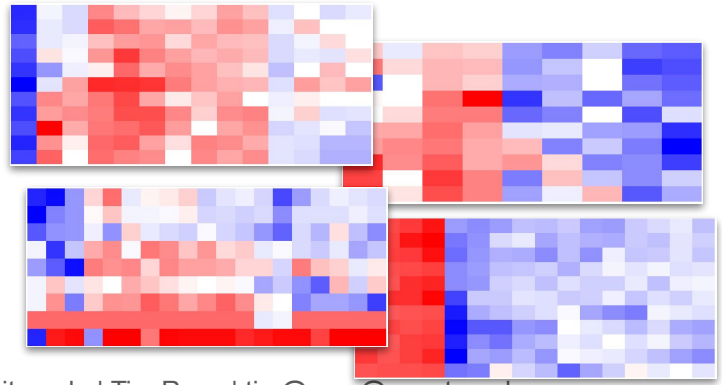
Application of biclustering in practice

- Many biclustering algorithms available
- Different objectives and heuristics
- Extensive parameterization necessary

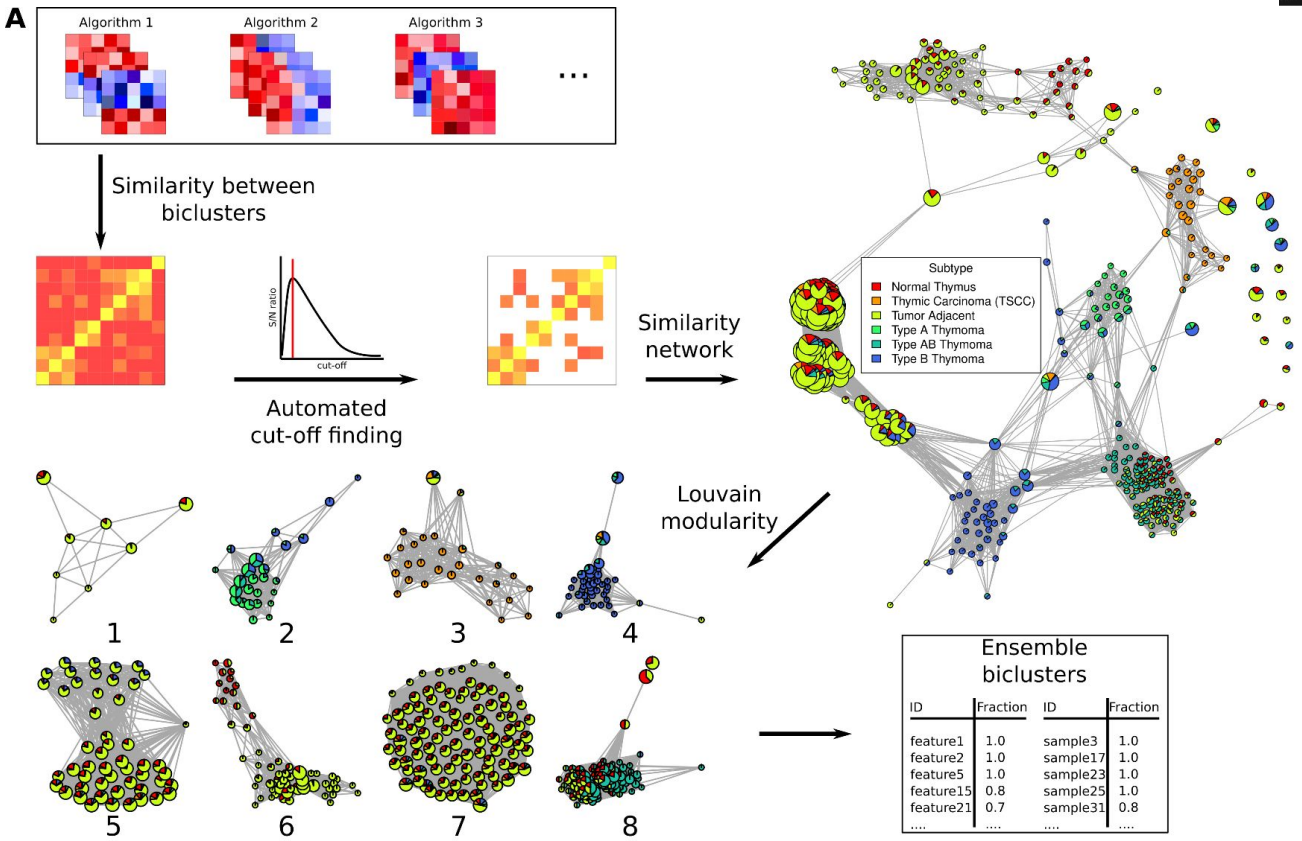
- Which algorithm should be used?



Molecular signatures from Biclustering - **MoSBi**

- Ensemble biclustering method
  - Commonly used in machine learning
- Integrating the results of multiple biclustering algorithms
  - More robust predictions
  - Overcoming specificities of single algorithms

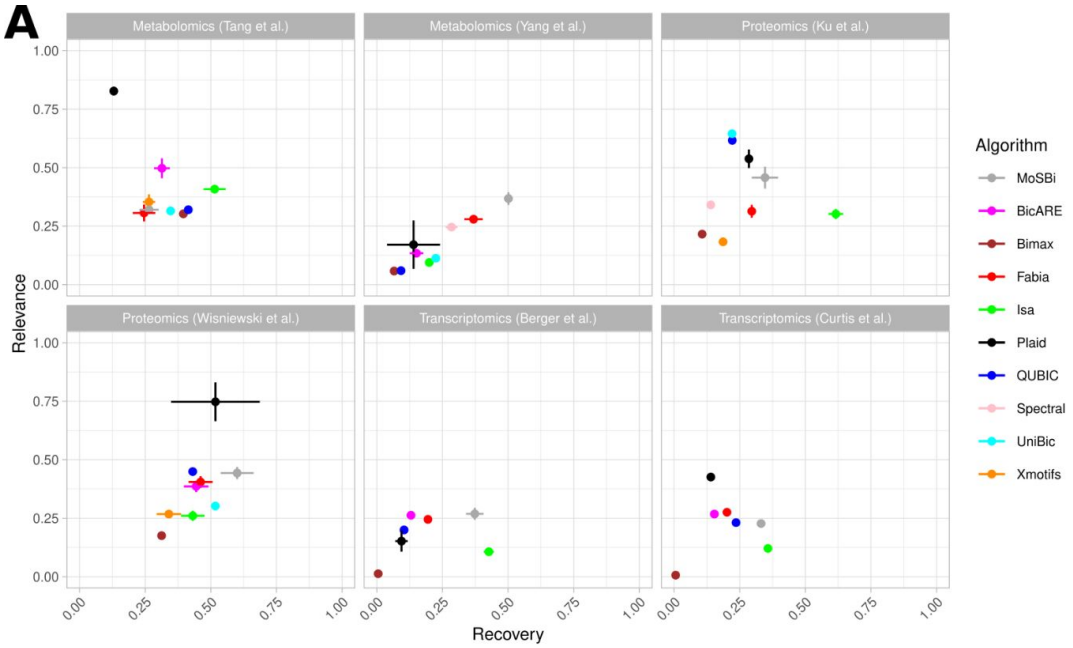
MoSBi workflow



Rose et al. (2021), bioRxiv https://doi.org/10.1101/2021.09.30.462567

MoSBi performance

- Algorithm performance on cancer *omics* studies
  - Robust results of MoSBi
  - Heterogeneous outcomes of most algorithms
- Metrics:
  - Relevance: predicted biclusters correspond to known labels
  - Recovery: labels were recovered by predictions



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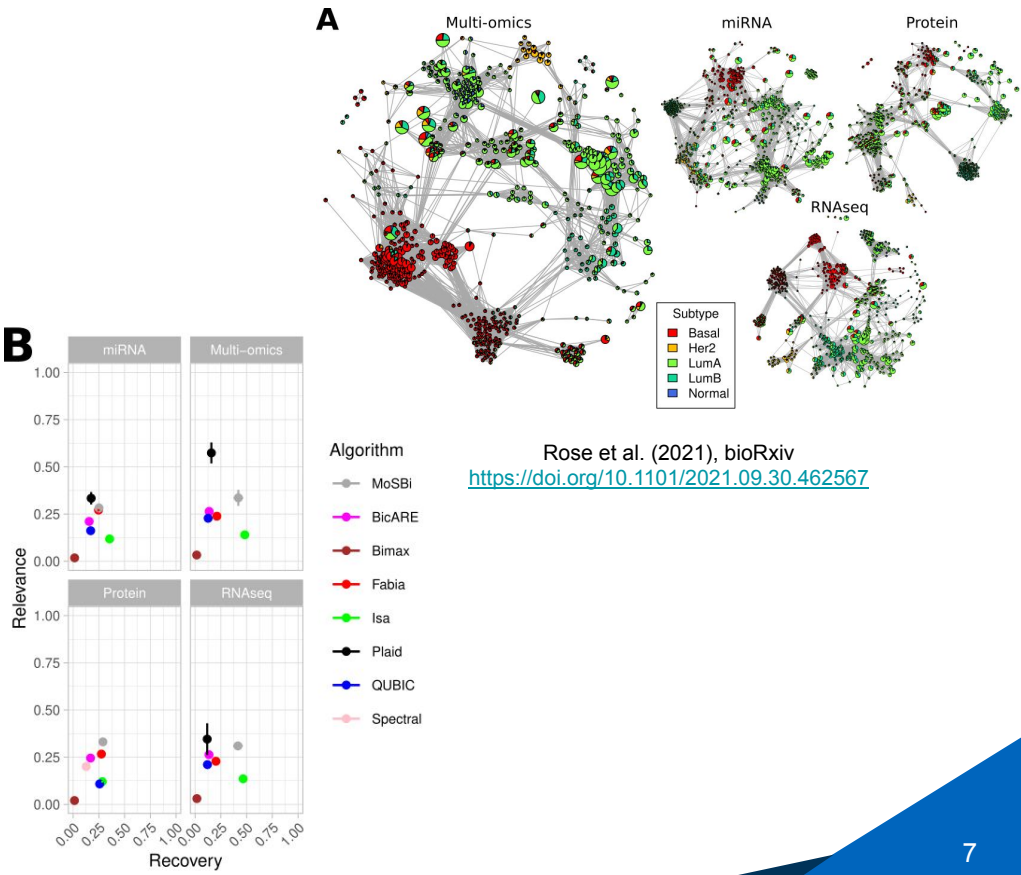
MoSBi in for multi-omics

- TCGA breast cancer data
- 484 samples with miRNA, RNAseq & Protein data
  - Analyzed independently and combined



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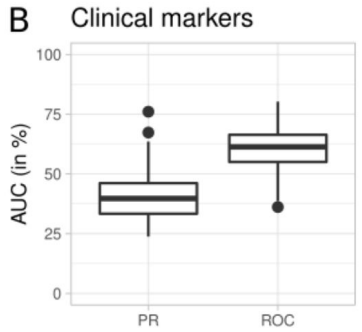
Back to non-alcoholic fatty liver disease



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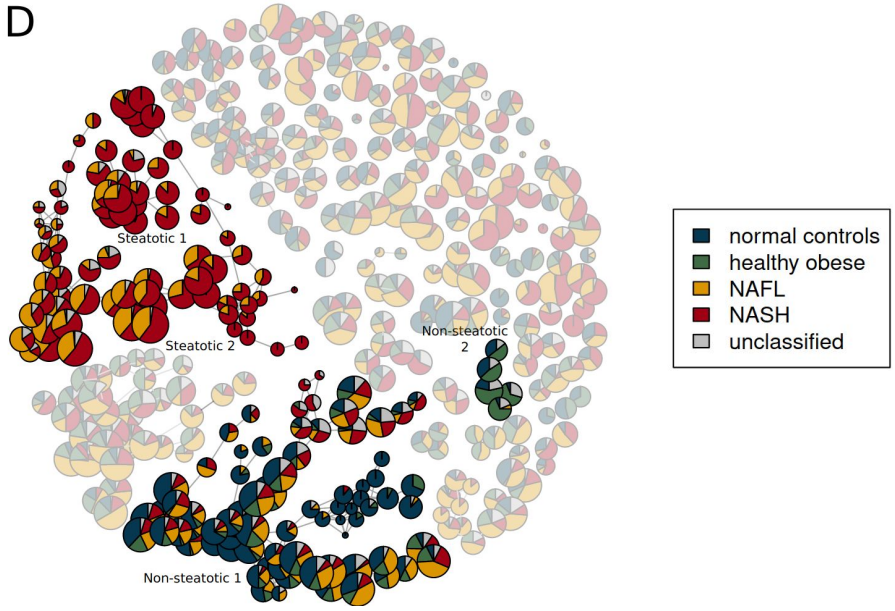
- Biclustering on clinical NAFL lipidomics
- Network communities enriched of steatotic and non-steatotic samples



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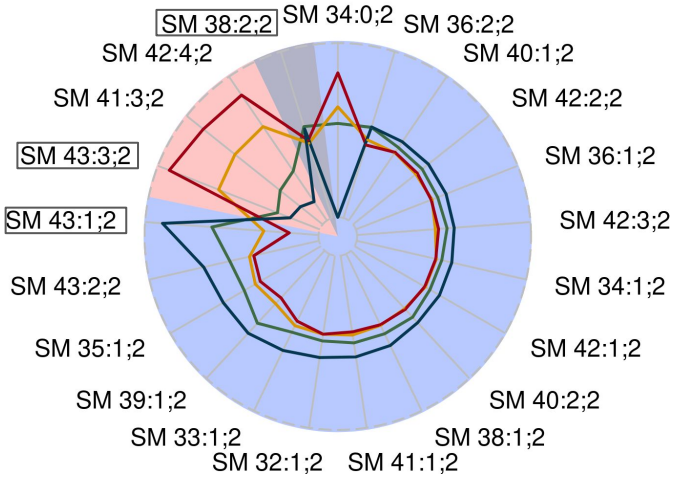
Patient groups

Lipid signatures

Lipid signatures

- Bi-directional SM changes
- SM ratios for disease classification
  - Problems with HO vs. NAFL & NAFL vs. NASH classifications



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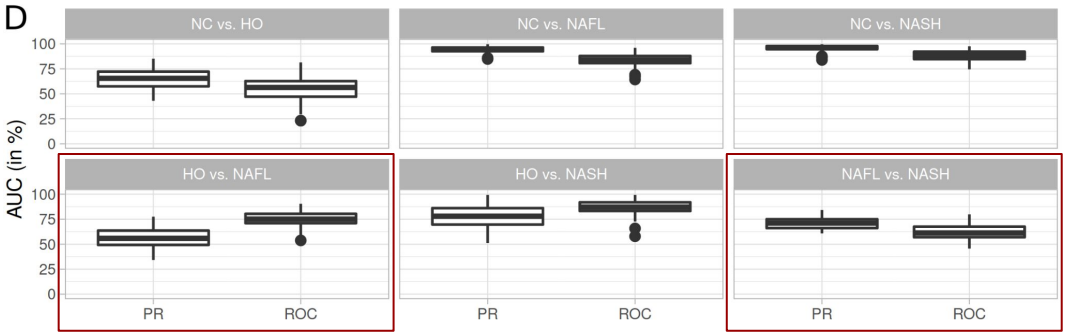
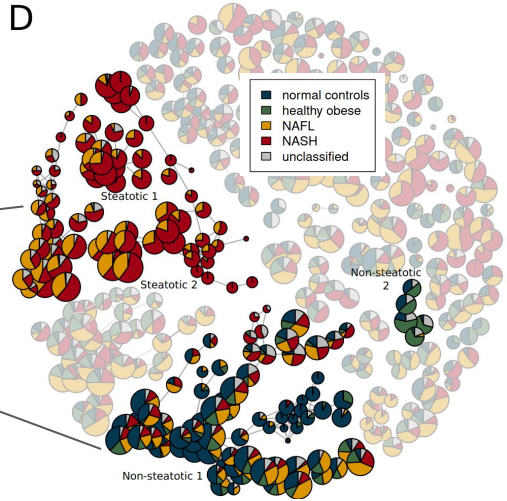
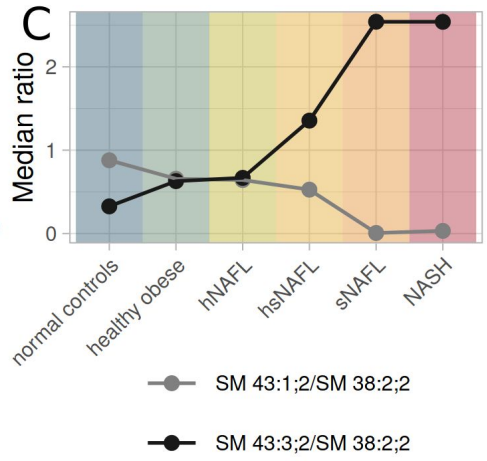
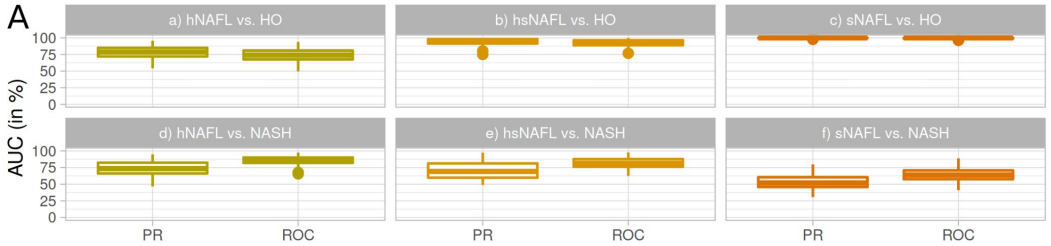


Subgrouping

- Defining subgroups based on biclusters
  - hNAFL
  - hsNAFL
  - sNAFL







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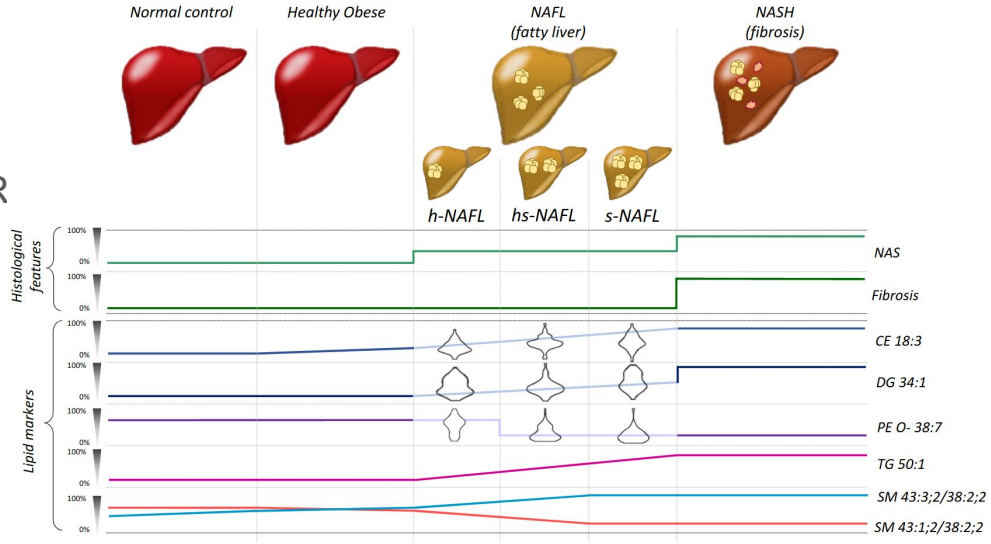
Conclusion

- Novel biclustering-based stratification method
  - Available as web-app (https://exbio.wzw.tum.de/mosbi/) and R package
- Successful application in NAFLD liver lipidomics
- Identified NAFL subgroups with bi-directional SM alterations



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Link to slides, workshop, web-app & publications:
https://exbio.wzw.tum.de/ils2021

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