



Molecular Gatekeepers bridge the exposome and health

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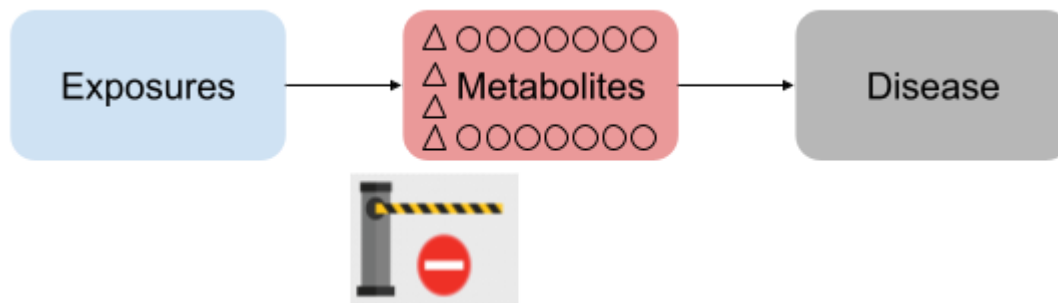
Exposome Data Analysis Challenge
2021-04-29

Exposures-Metabolites-Disease (EMD) model



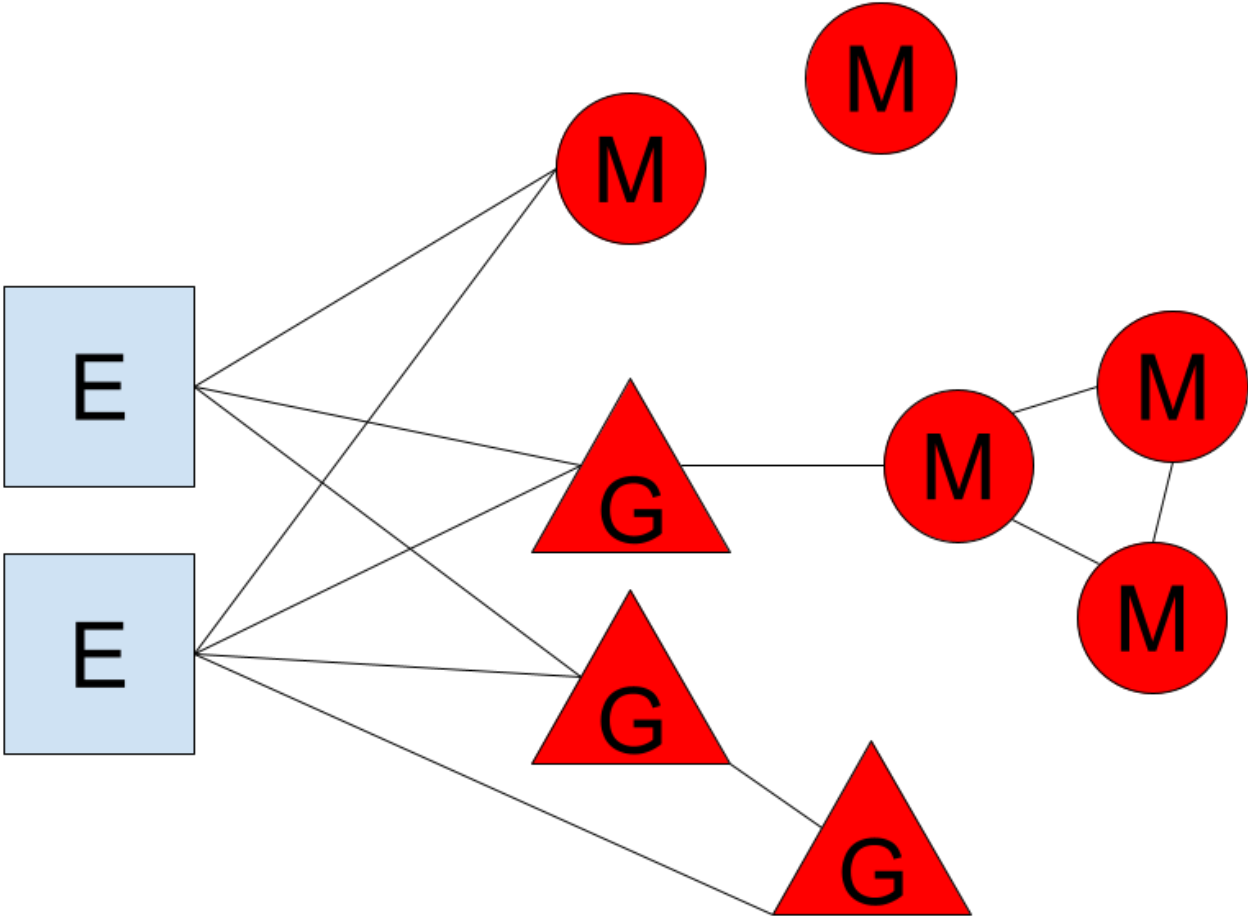
- What's the relationship between small molecule and health outcome?
- What's the relationship between exposures and metabolites?
- Which metabolites are the most important?

Gatekeeper theory for EMD model



- The small molecule linked both exposures and other small molecule should be the frontier of biological process
- Such molecules may regulate the adverse influences of exposures

Metabolites classes



Gatekeeper molecular discovery

Step 1: Correlation among metabolites

Step 2: Association between metabolites and exposures

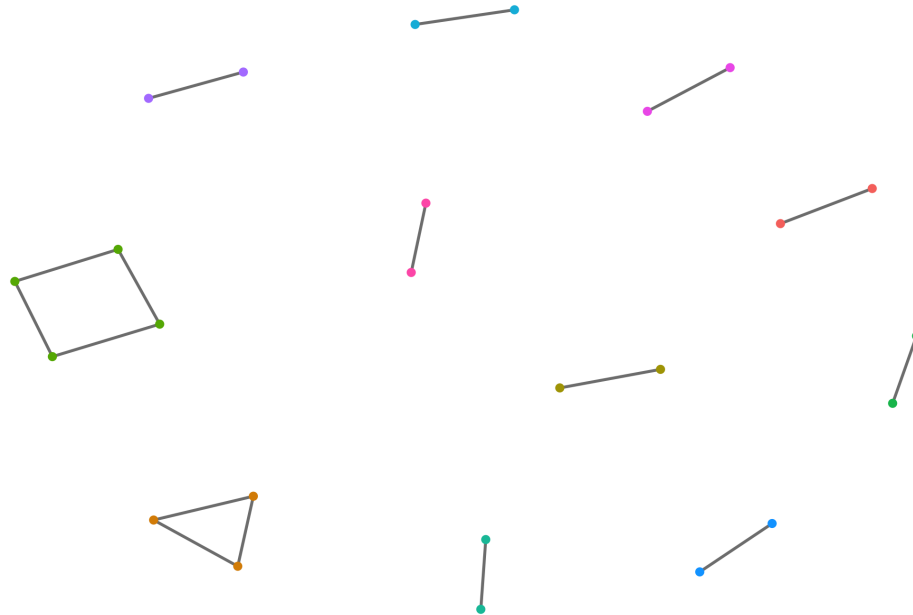
Step 3: Association between gatekeeper and health outcome

Samples summary

- HELIX subcohort database
- Serum Metabolome: 1198 individuals and 177 metabolites.
- Exposures: 170 continuous variables
- Health outcome: asthma or not

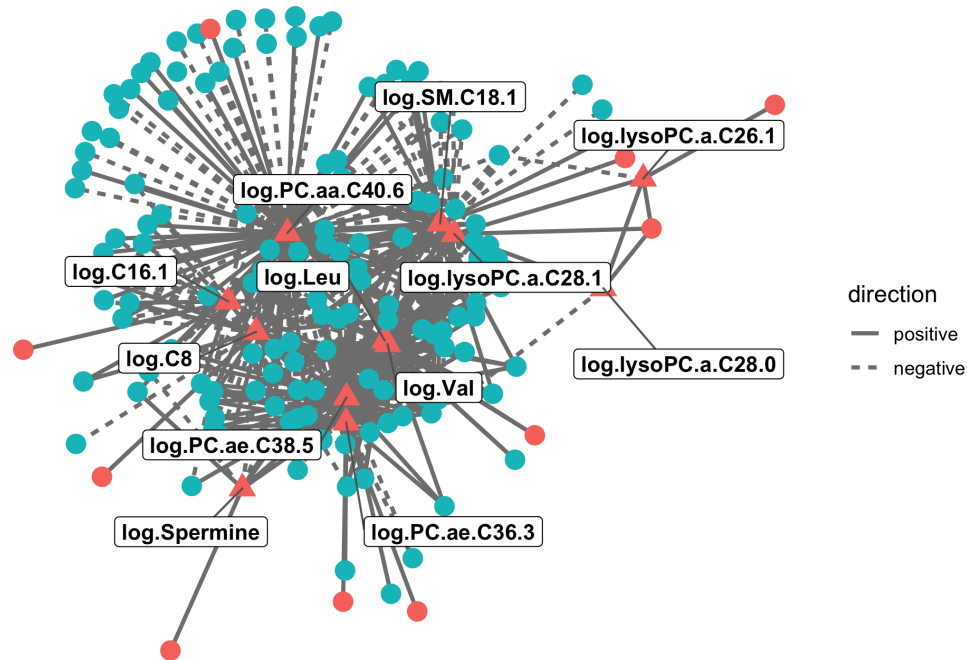
Step 1: Correlation among metabolites

Serum Metabolites network



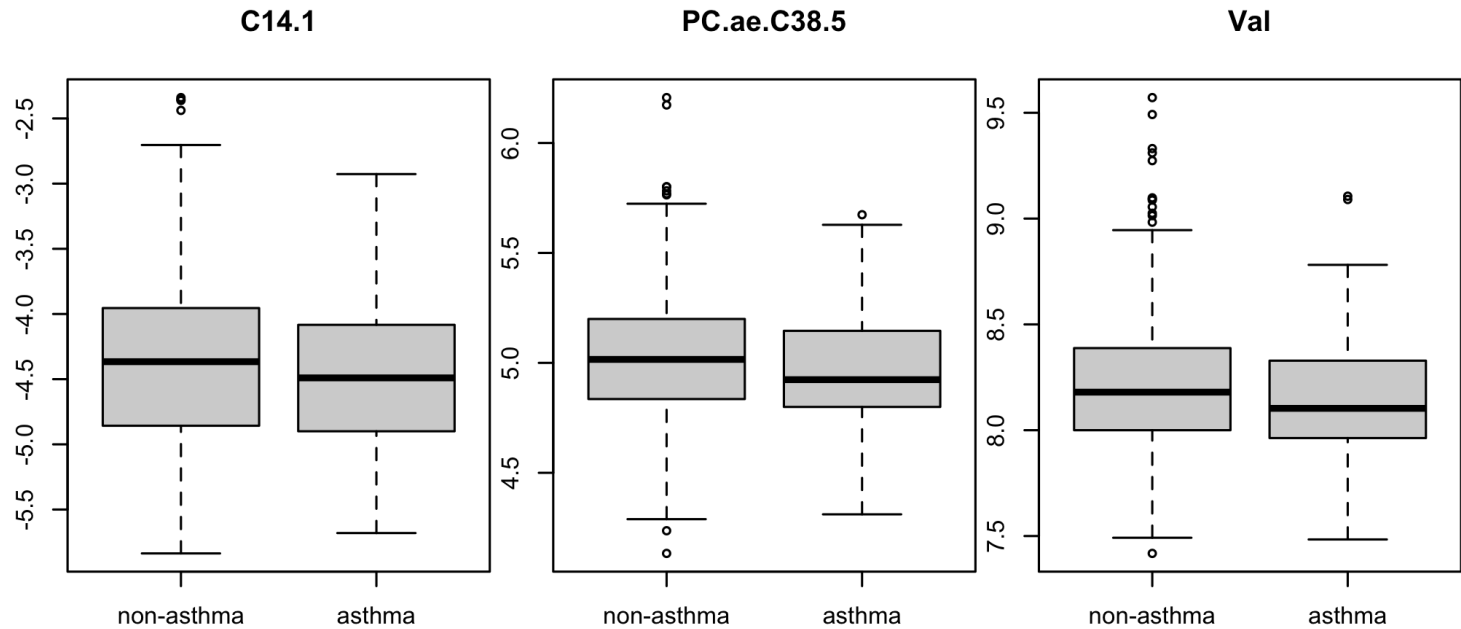
- Cutoff for correlation: Pearson's $R > 0.9$
- 9 metabolites correlation network clusters found
- 155 out of 177 metabolites have no correlation with other metabolites

Step 2: Association between metabolites and exposures



- 22 peaks connected with other peaks and exposures
- 155 peaks connected with exposures only

Step 3: Association between gatekeeper and health outcome



Conclusion

- Gatekeepers are **battlefront** metabolites between exposures and other metabolites
- Some gatekeepers are sensitive to multiple environmental exposures
- Gatekeepers might reveal mechanistic aspects of relationships between exposome and health outcomes to generate hypothesis for future studies
- Gatekeeper can be metabolites, genes, proteins, etc.

Acknowledgement

- Dr. Petrick's research group
- Lam-ha Dang
- Prof. Mary Wolff
- Prof. Susan Teitelbaum
- **Molecular gatekeeper discovery for multiple exposure groups in adolescent girls**

Funding

- NIEHS P30ES23515
- CHEAR pilot program
- U2C ES026561
- 1U2CES030859



Thanks

Q&A

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