

Decoding links between the exposome and health outcomes by multi-omics analysis

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➤ Exposome affect human health

Ecosystems

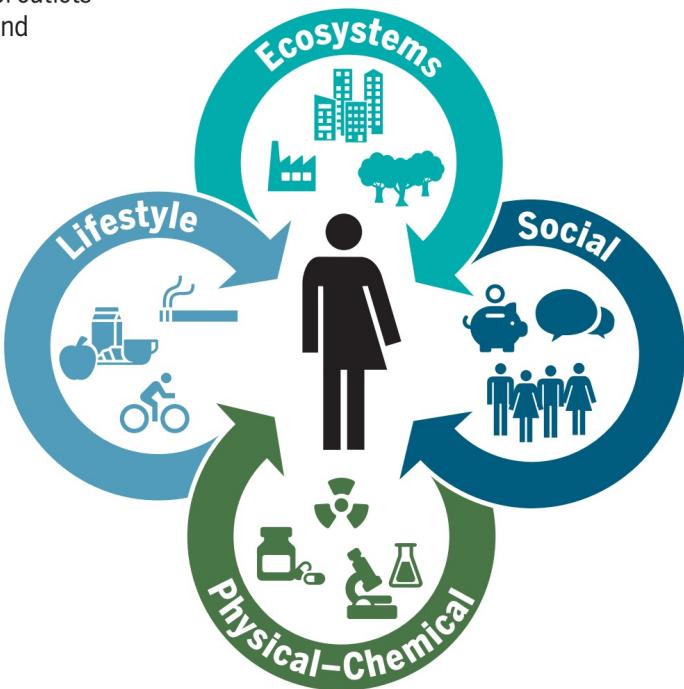
Food outlets, alcohol outlets
Built environment and urban land uses
Population density
Walkability
Green/blue space

Lifestyle

Physical activity
Sleep behavior
Diet
Drug use
Smoking
Alcohol use

Social

Household income
Inequality
Social capital
Social networks
Cultural norms
Cultural capital
Psychological and mental stress

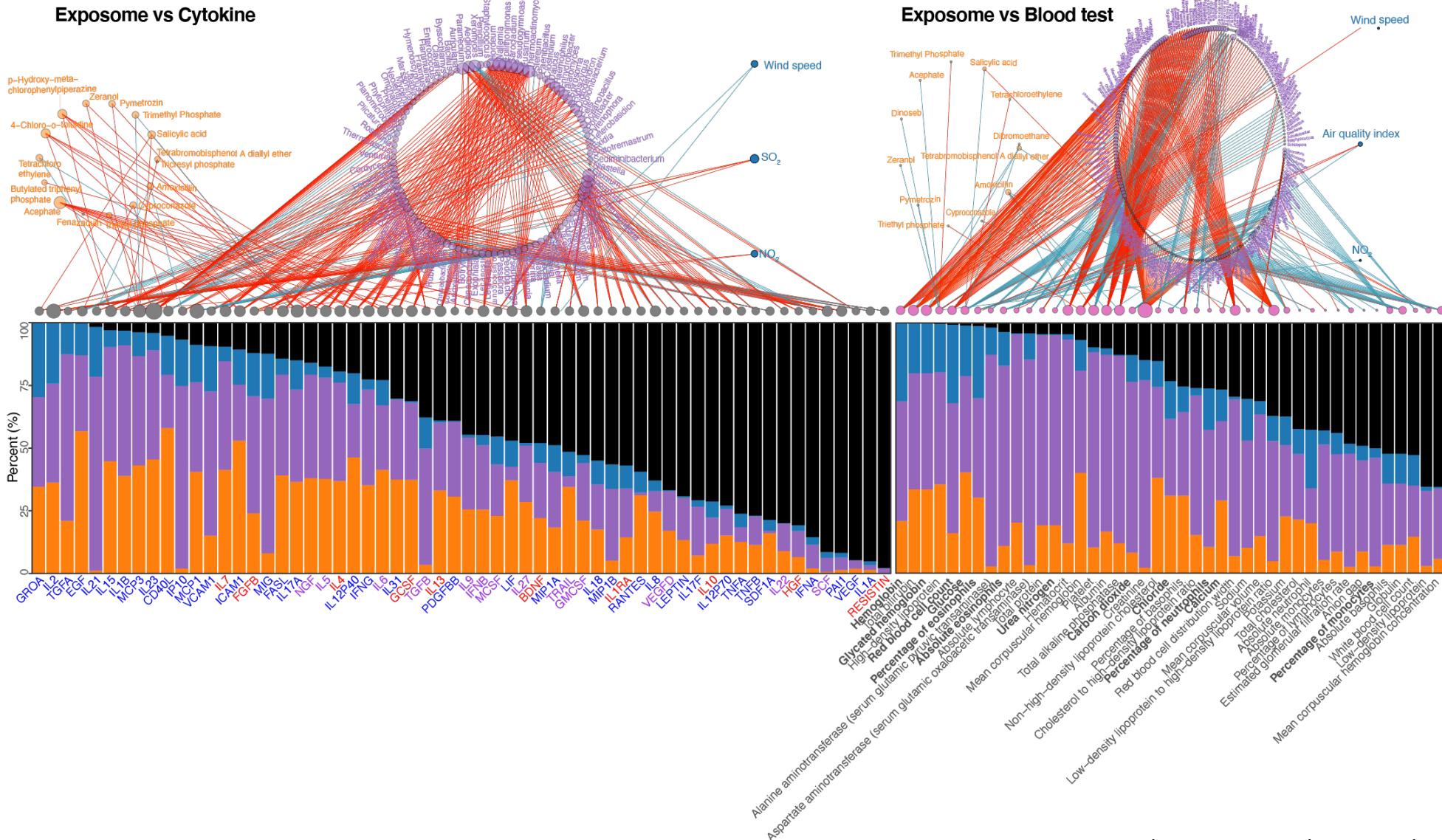


Physical-Chemical

Temperature/humidity
Electromagnetic fields
Ambient light
Odor and noise
Point, line sources, e.g., factories, ports
Outdoor and indoor air pollution
Agricultural activities, livestock
Pollen/mold/fungus
Pesticides
Fragrance products
Flame retardants (PBDEs)
Persistent organic pollutants
Plastic and plasticizers
Food contaminants
Soil contaminants
Drinking water contamination
Groundwater contamination
Surface water contamination
Occupational exposures

Exposome + genetics = health outcome (Phenotype)

➤ Exposome affect human health

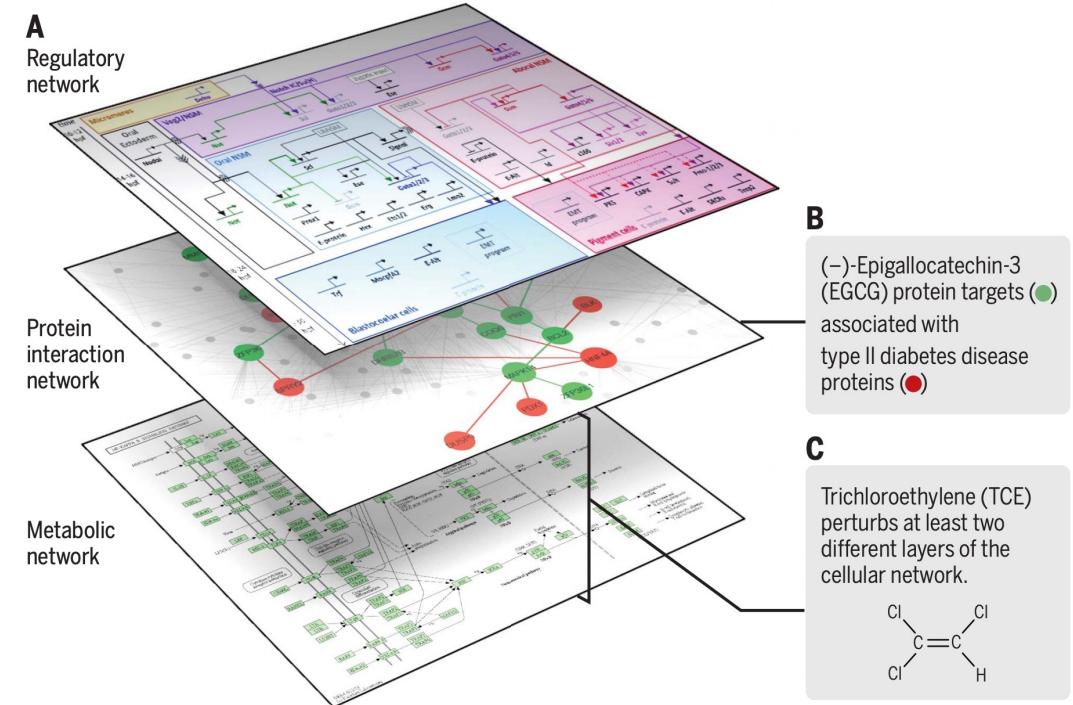


Peng et al., 2021, Submitted

➤ Exposome affect human health

“The challenge in understanding the role of the exposome on our health lies not only in the large number of chemical exposures in our daily lives, but also in the complex ways that they interact with cells.”

The cell as a multilayer network



➤ Motivations and analysis plan



<https://www.betterplace.org/>

Only the childhood data

1. Exposome affect the health outcomes (phenotypes).

Internal-ome
(Transcriptome, Proteome,
Serum/urine metabolome)

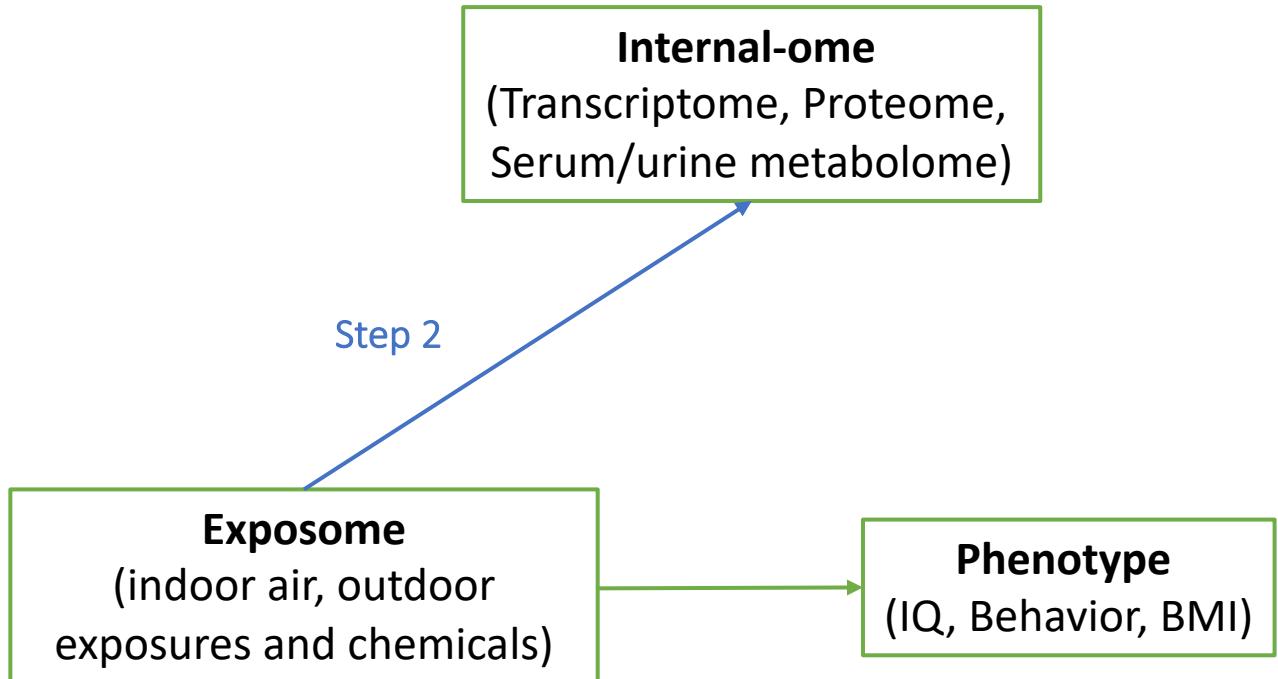


➤ Motivations and analysis plan



<https://www.betterplace.org/>

1. Exposome affect the health outcomes (phenotypes).
2. Exposome affect Internal-ome (transcriptome, proteome, metabolome).

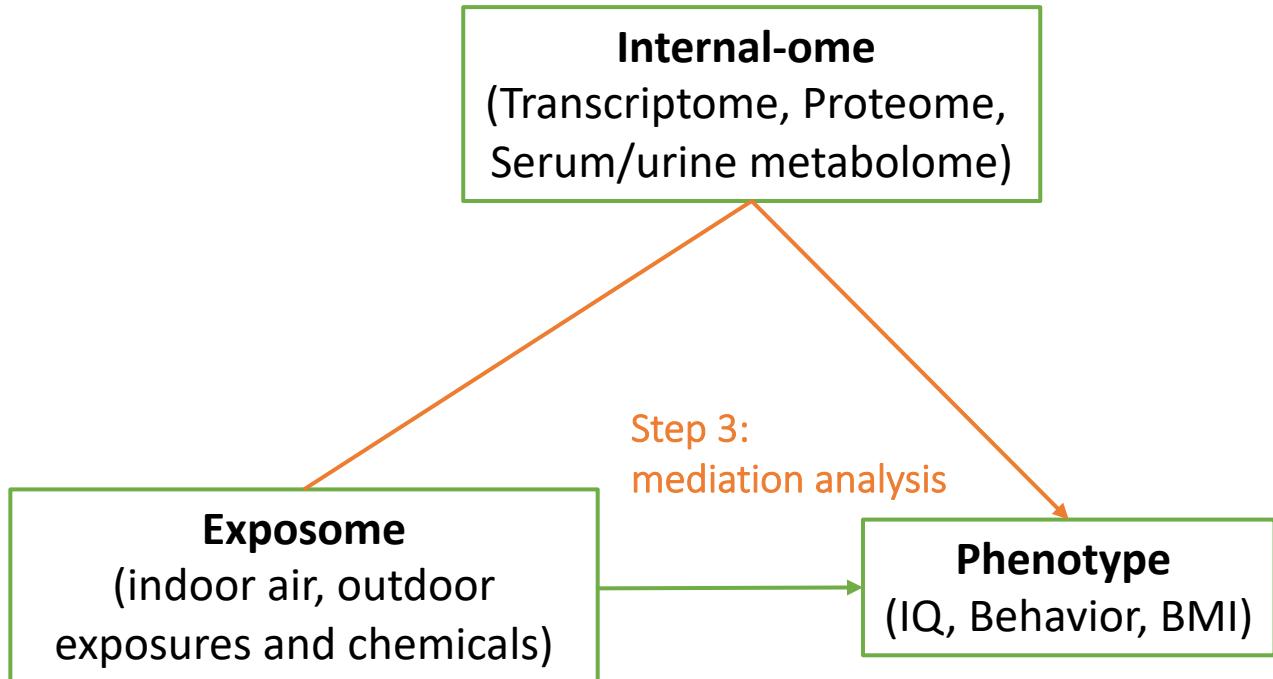


➤ Motivations and analysis plan

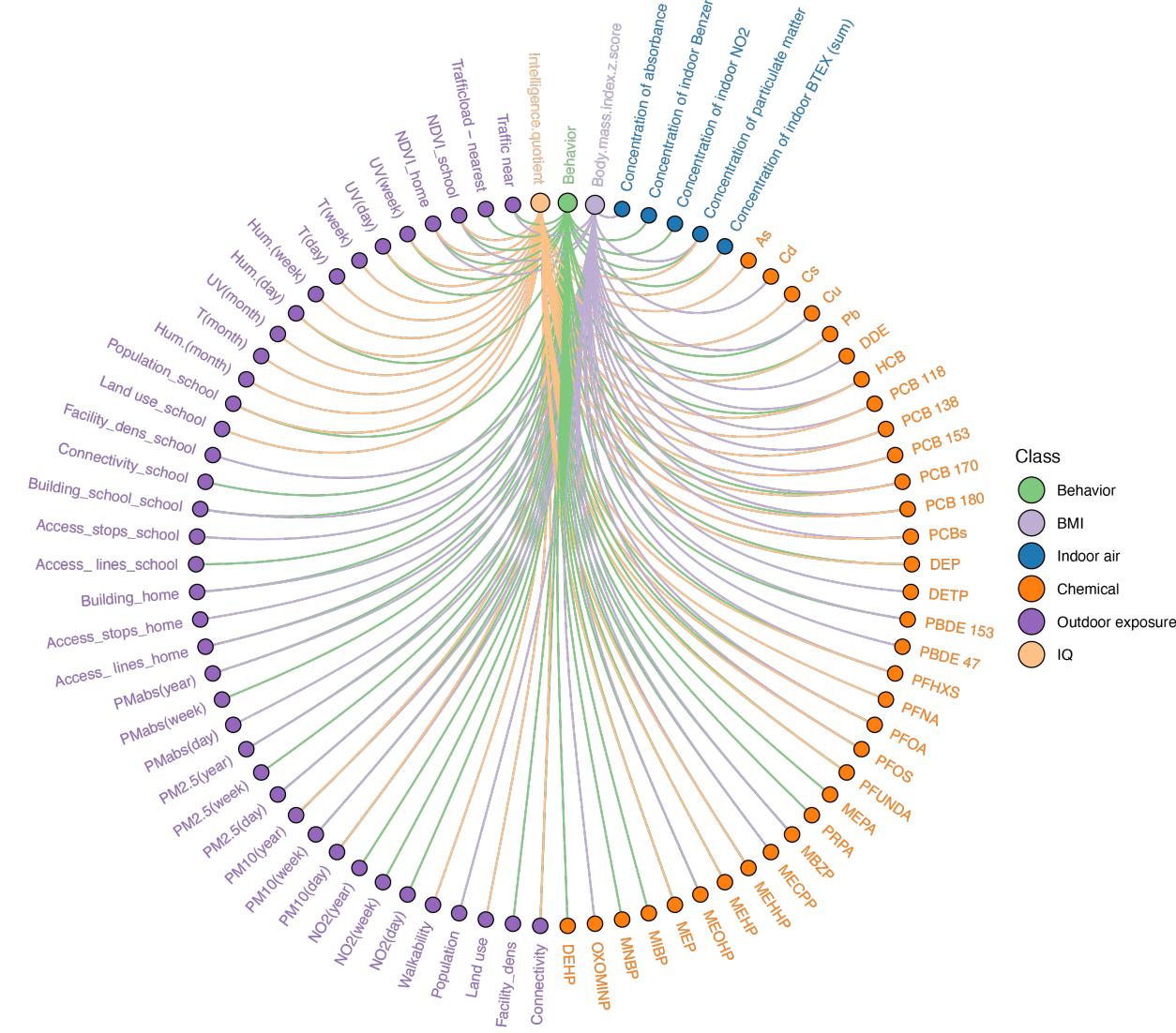


<https://www.betterplace.org/>

1. Exposome affect the health outcomes (phenotypes).
2. Exposome affect Internal-ome (transcriptome, proteome, metabolome).
3. Exposome affect the phenotype via internal-ome (mediation analysis).



➤ Exposome are associated with phenotypes



Linear mixed model to find the association between exposome and phenotype

(Child sex, Year of birth, Mother BMI, Gestational age at birth, Maternal age, child height, child weight, birth weight as covariates)

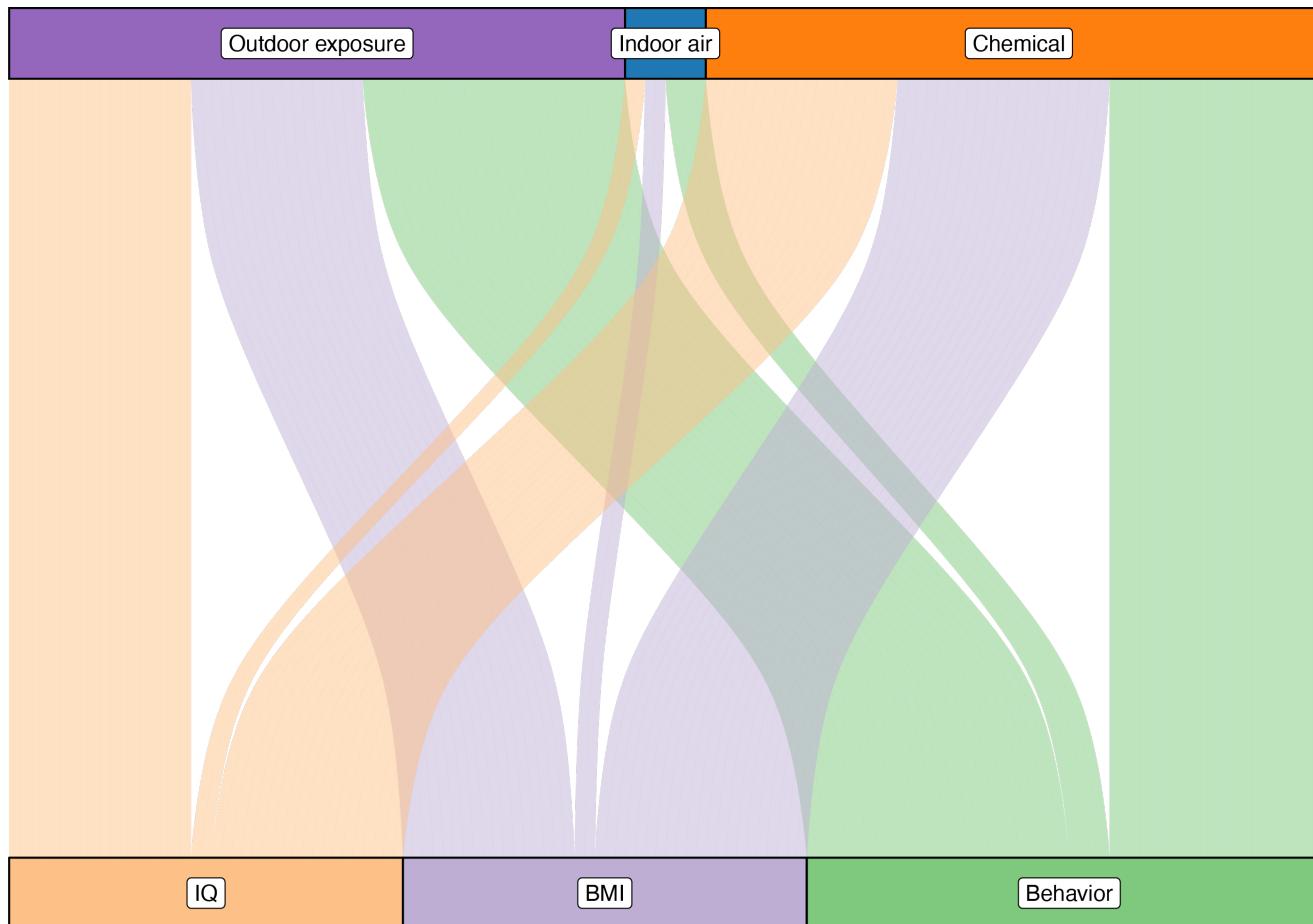
Summary

131 associations in total involving **3 phenotypes** and **79 exposome** features that were significant at $p.\text{adjust} < 0.05$ (BH).

➤ Exposome are associated with phenotypes

Association distribution

Exposome (Outdoor exposure, indoor air, chemical)



Most of the associations are from **outdoor exposures** and **chemicals**.

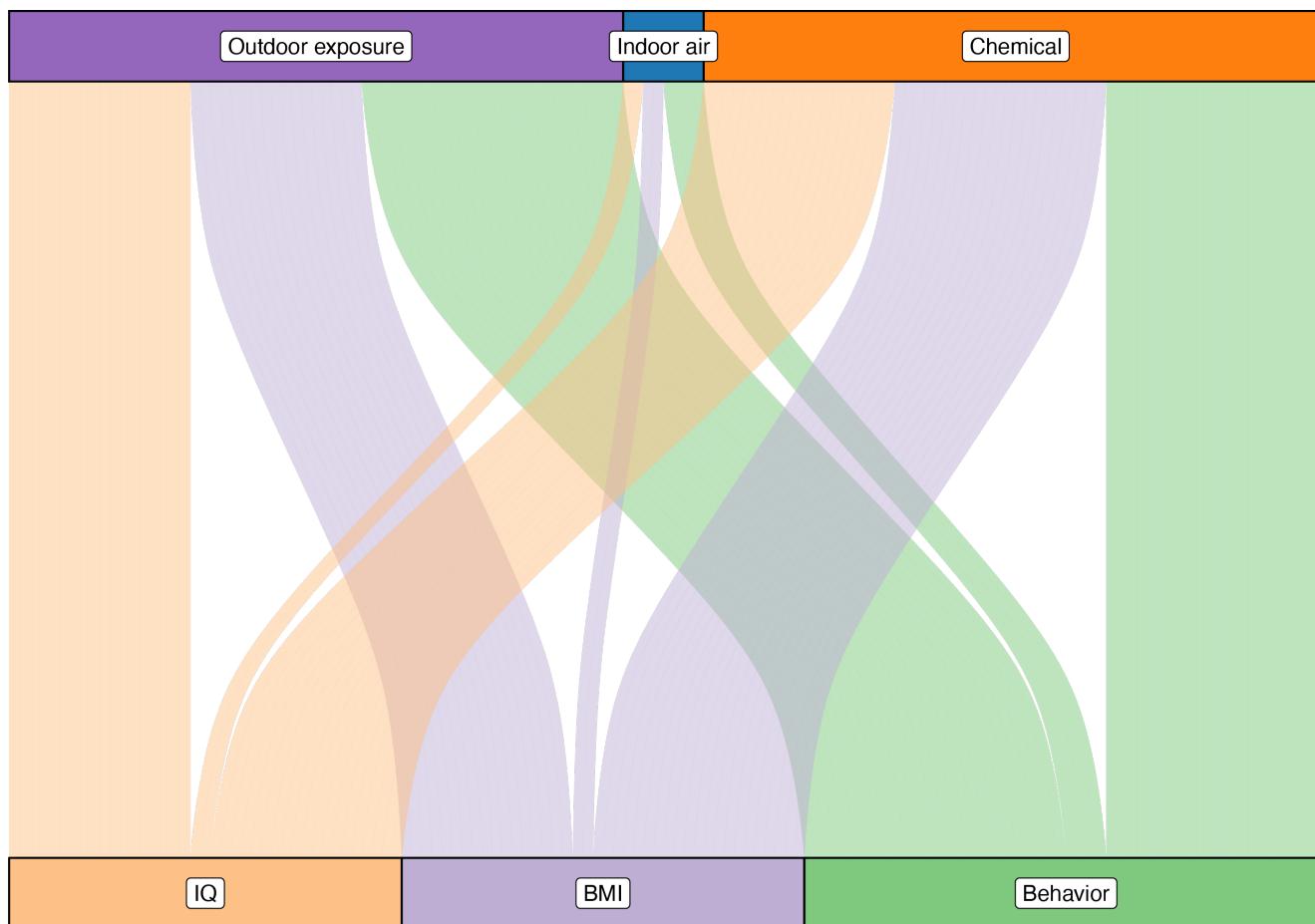
Phenotypes, IQ, BMI and Behavior have very similar number of associations with exposome.

Phenotype (IQ, BMI, Behavior)

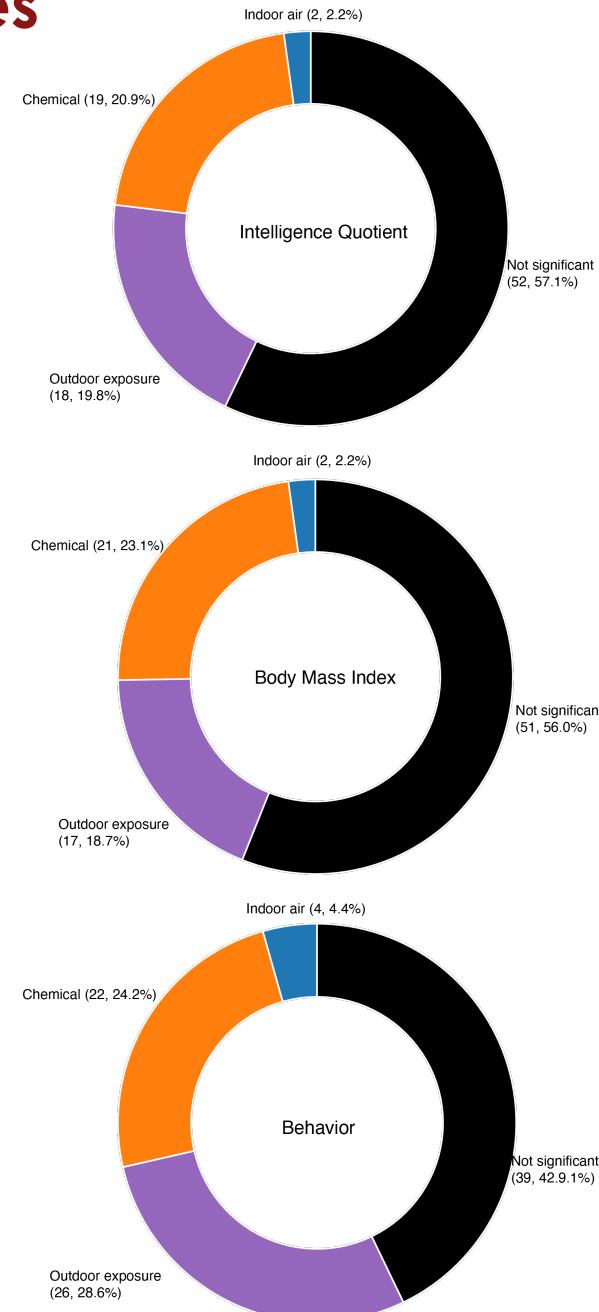
➤ Exposome are associated with phenotypes

Association distribution

Exposome (Outdoor exposure, indoor air, chemical)



Phenotype (IQ, BMI, Behavior)



Intelligence quotient (IQ):
39 exposome features

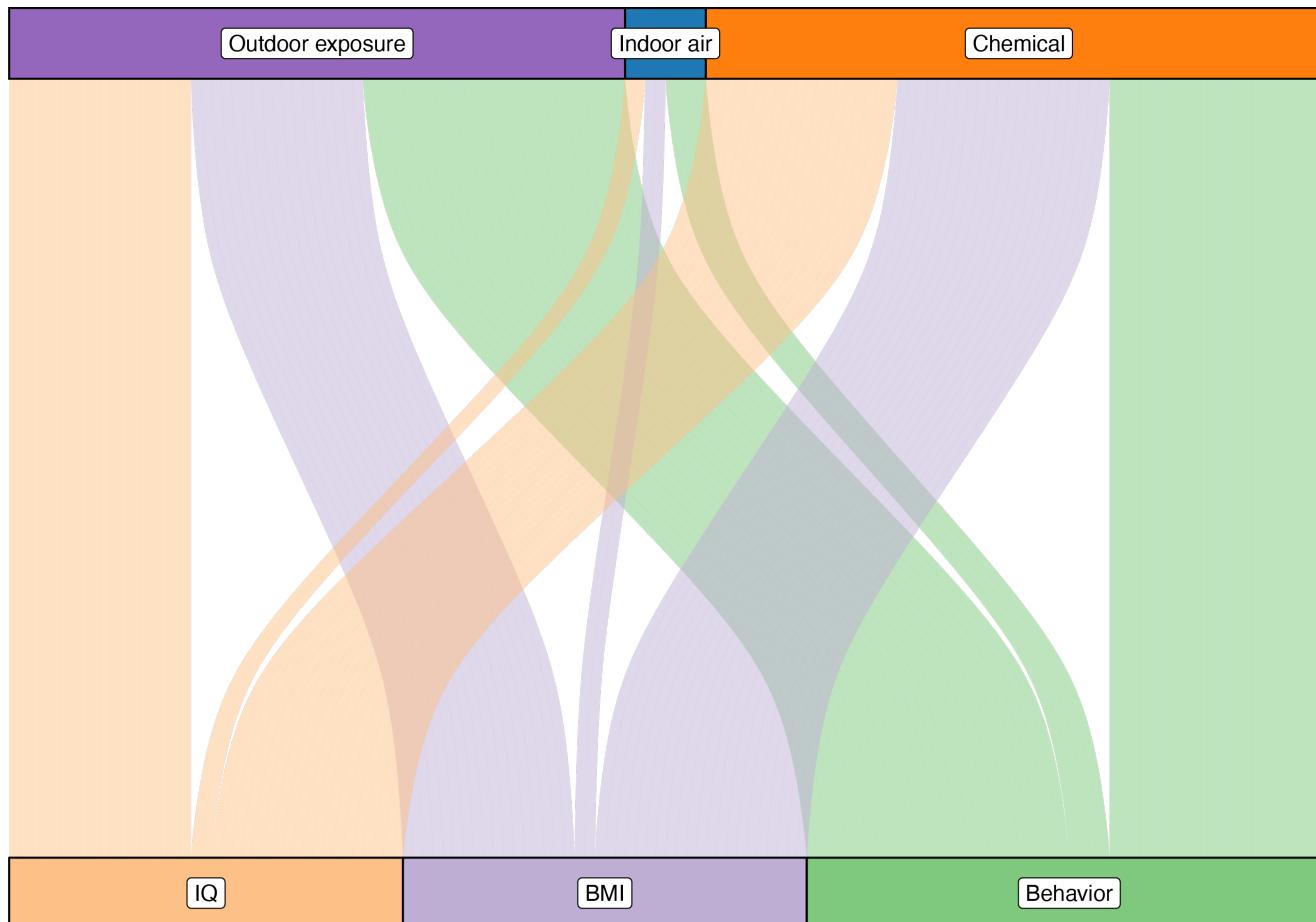
Body mass index (BMI):
40 exposome features

Behavior:
52 exposome features

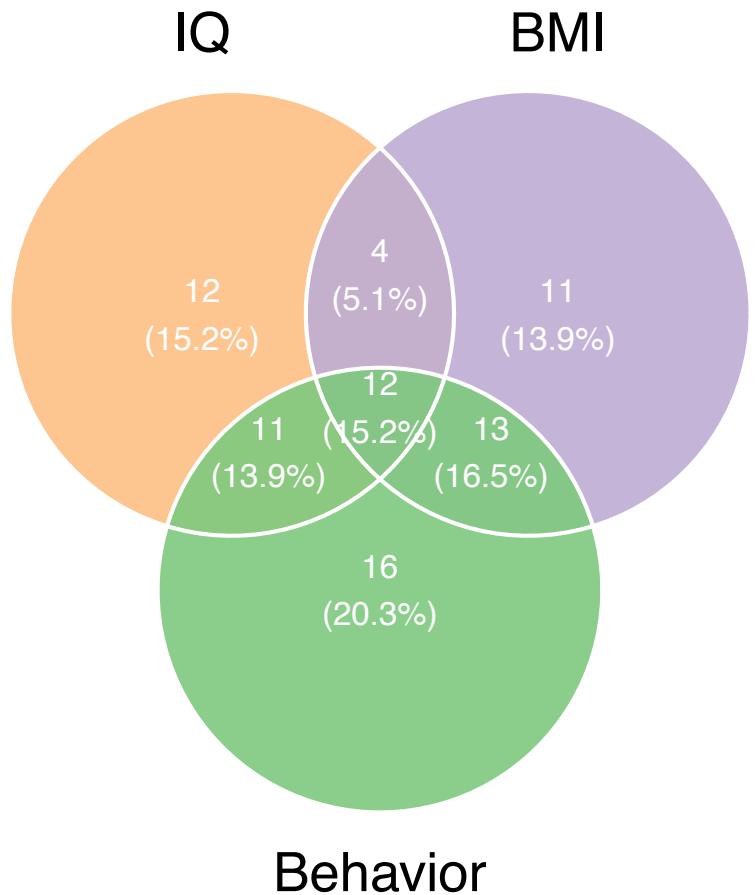
➤ Exposome are associated with phenotypes

Association distribution

Exposome (Outdoor exposure, indoor air, chemical)



Phenotype (IQ, BMI, Behavior)



Overlap between IQ, BMI and behavior's associations with exposome **are not big (< 50%)**.

➤ Exposome are associated with phenotypes

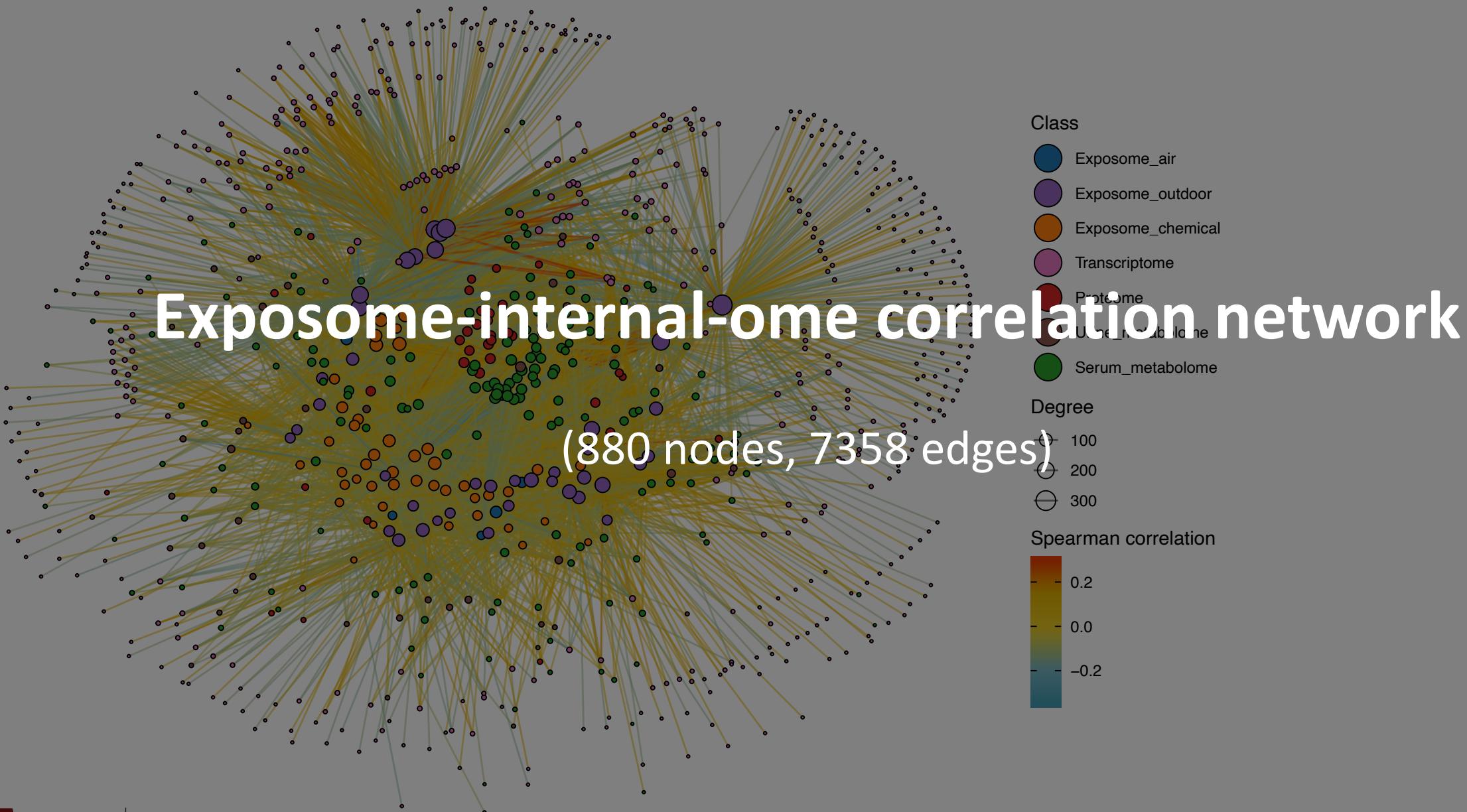
Exposome has significant associations with phenotypes

71 out of 110 (64.5%) measured exposome features have significant associations with at least one phenotype.

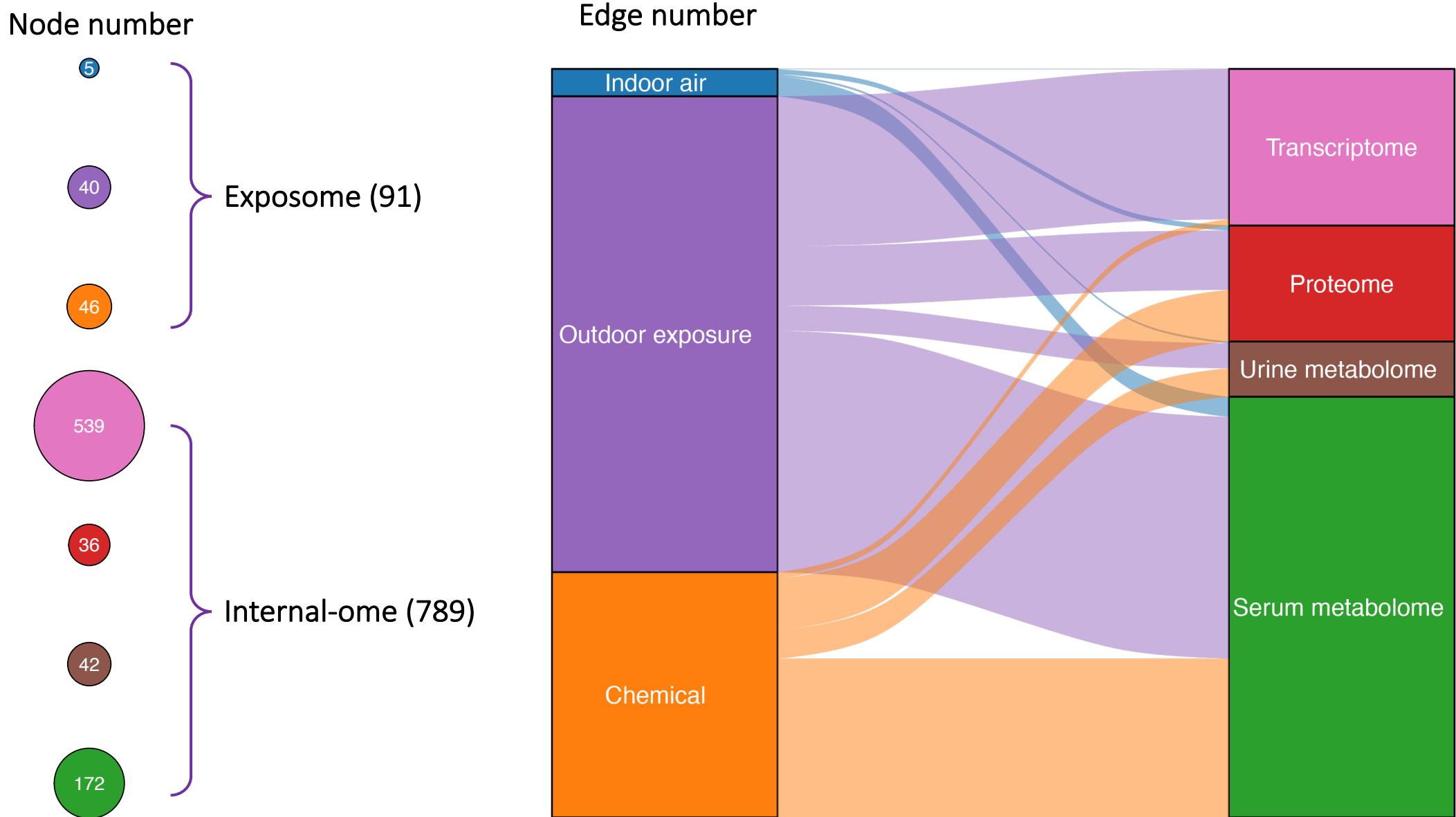
➤ Assumption/Hypothesis

To further understand the potential mechanisms by which the exposome could affect phenotype, we hypothesized that internal-ome are an important class of molecules that are involved in the exposome-phenotype interaction.

► Exposome are associated with internal-omics data

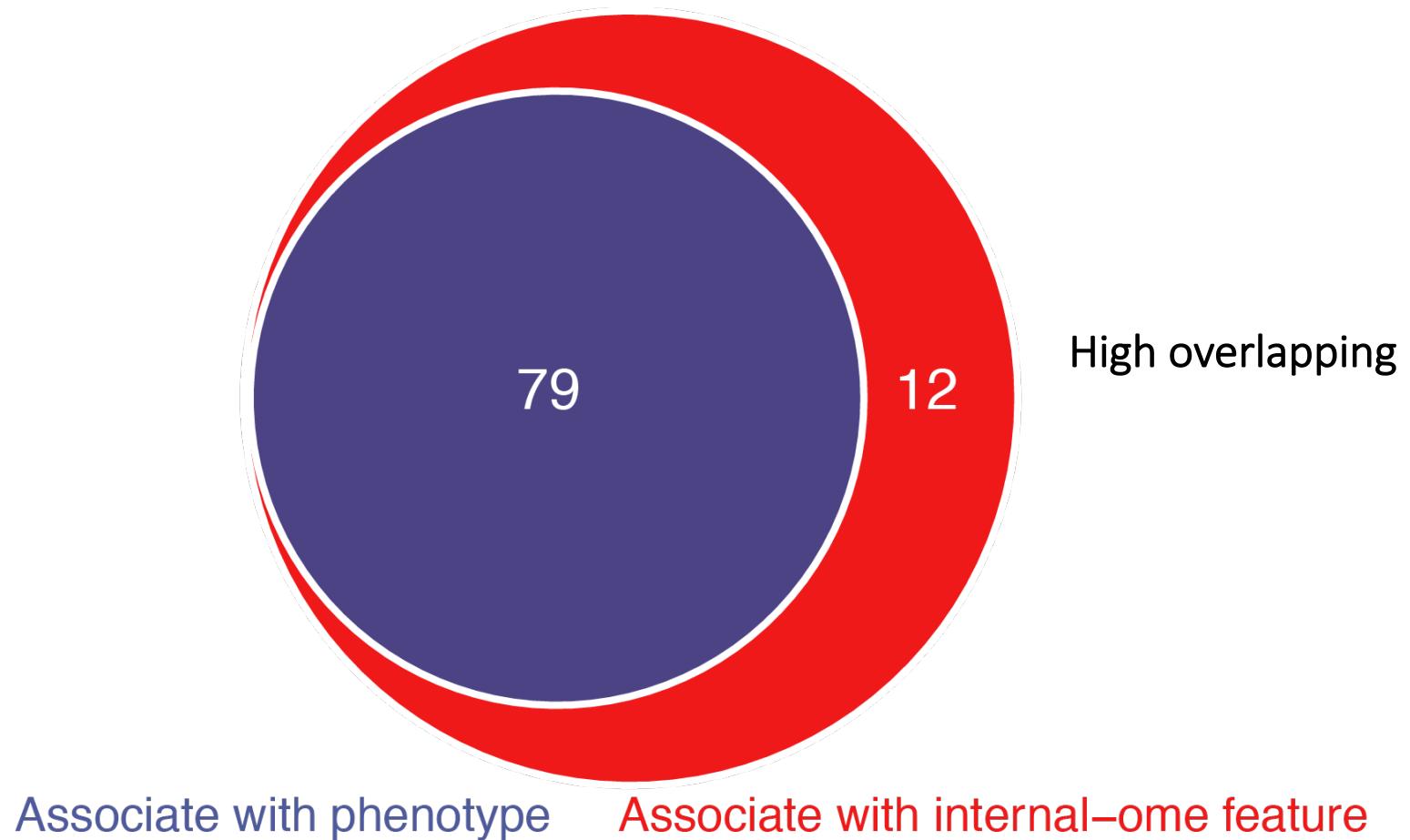


➤ Exposome are associated with internal-omics data



➤ Exposome contributes to phenotypic changes through internal-ome

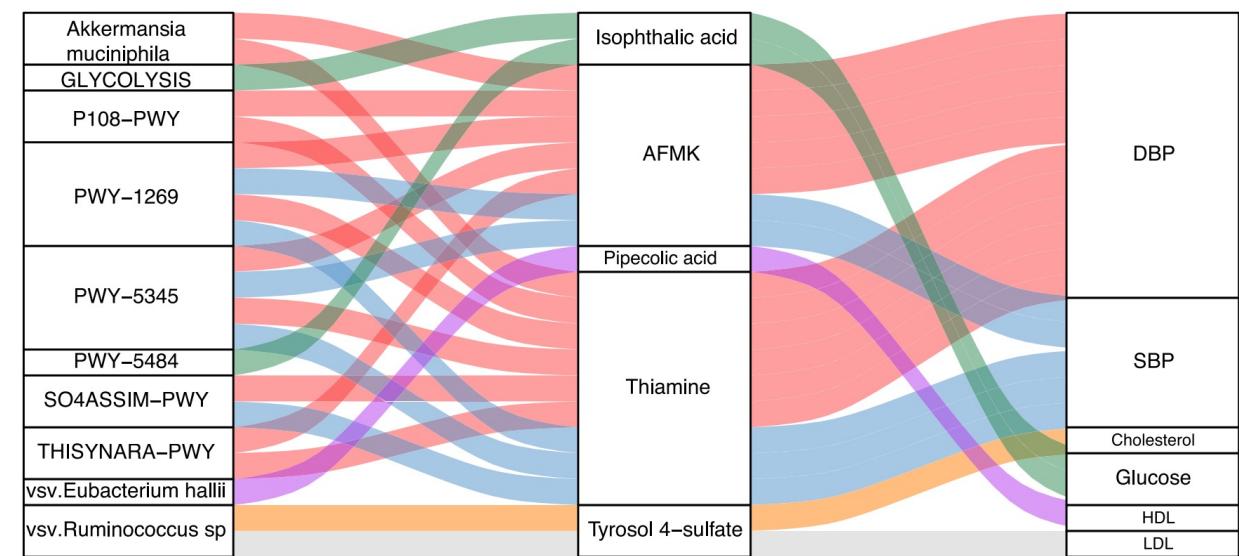
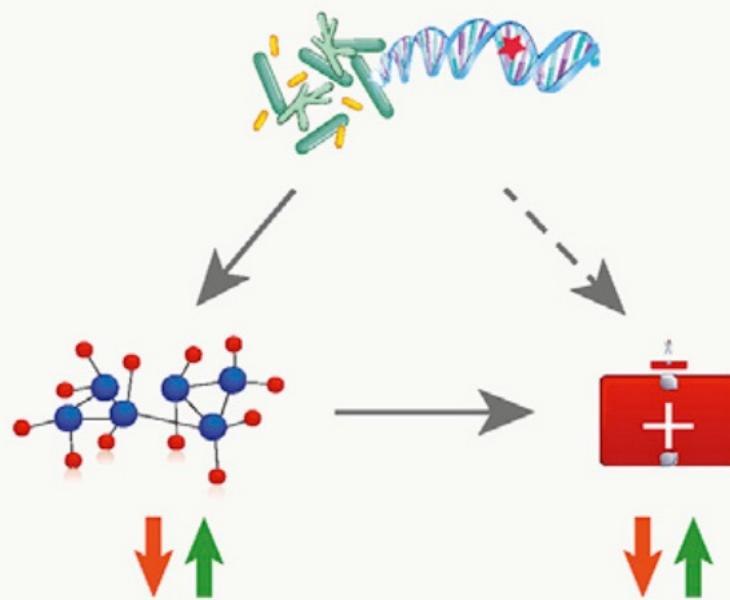
1. 79 out of 110 exposome features are associated with phenotypes.
2. 91 out of 110 exposome features are associated with internal-ome features.



➤ Exposome contributes to phenotypic changes through internal-ome

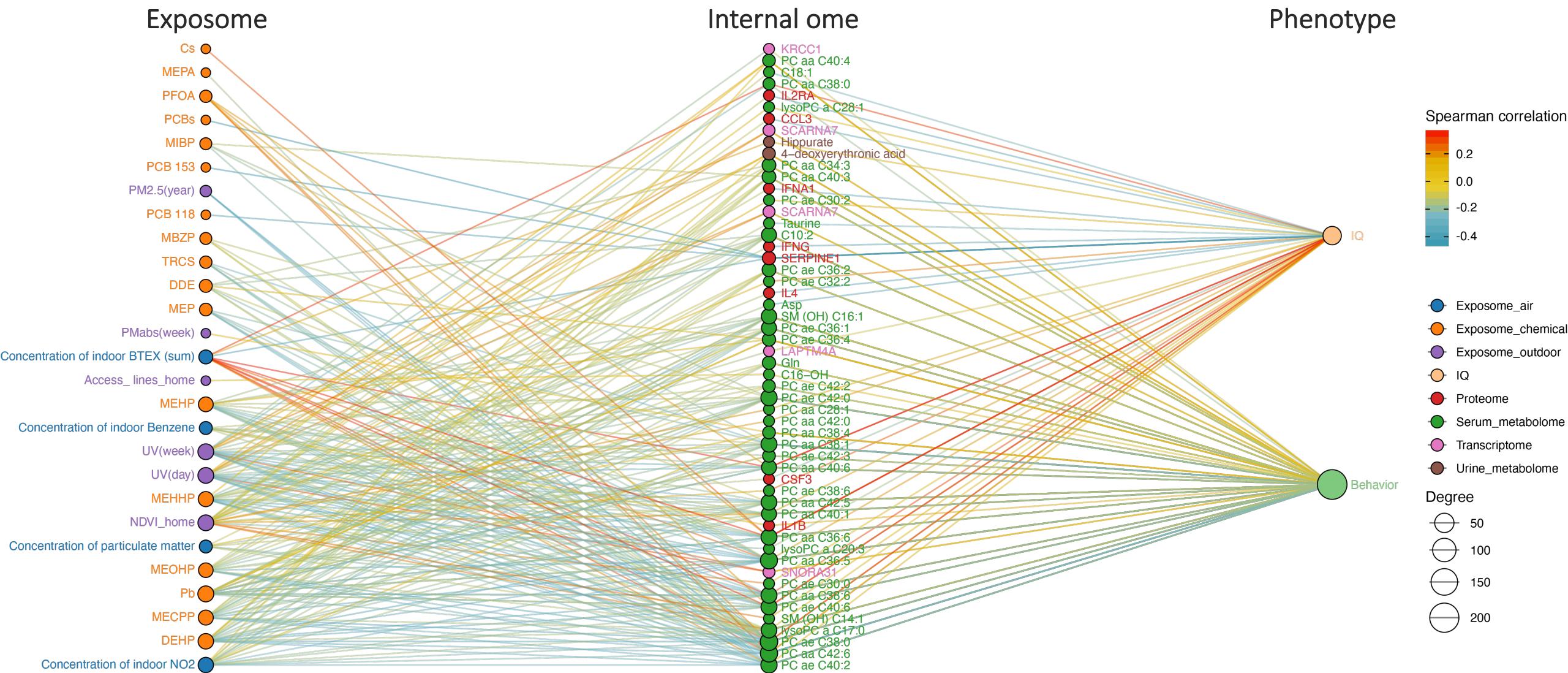
To evaluate whether internal-ome features can mediate the exposome impact on phenotypes, we applied **bi-directional mediation analysis**.

Microbial impacts on host phenotypes are mediated by metabolites



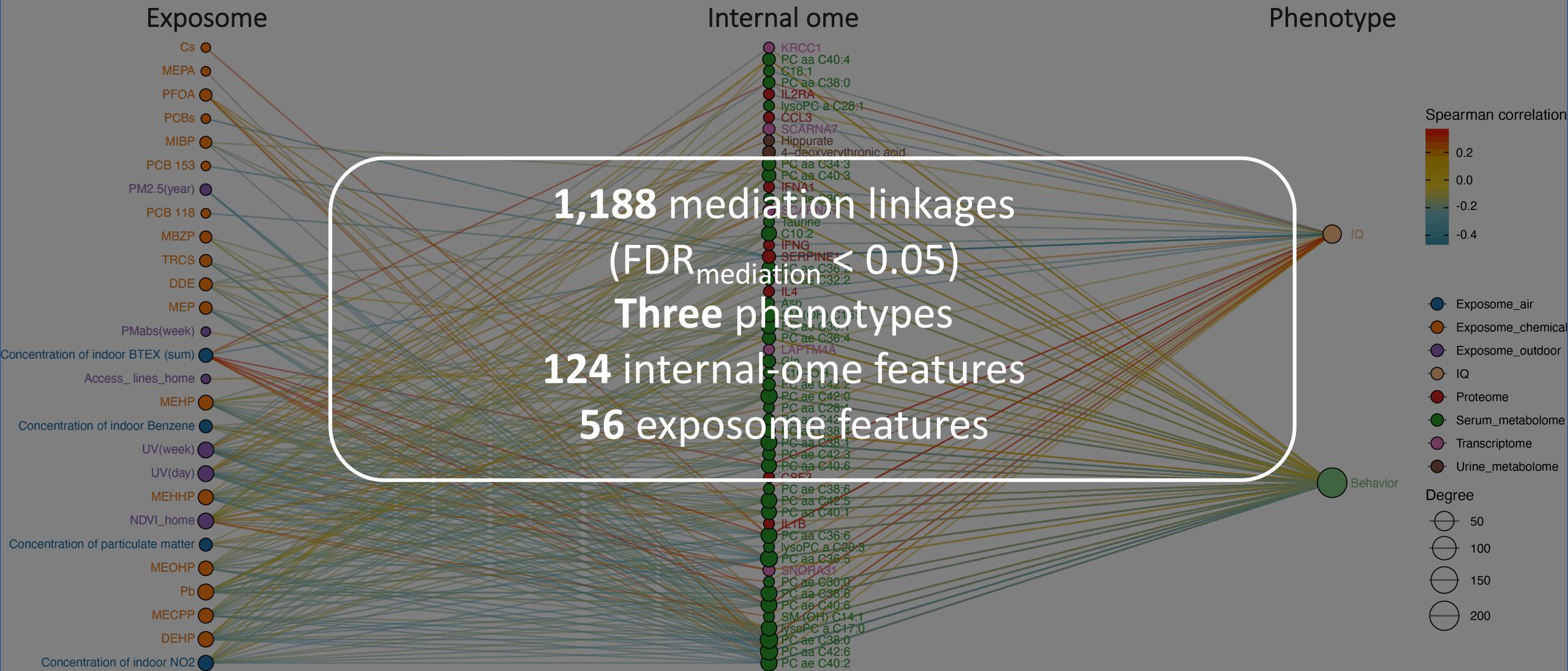
Chen et al., 2021, Cell 184, 1–14

➤ Exposome contributes to phenotypic changes through internal-ome

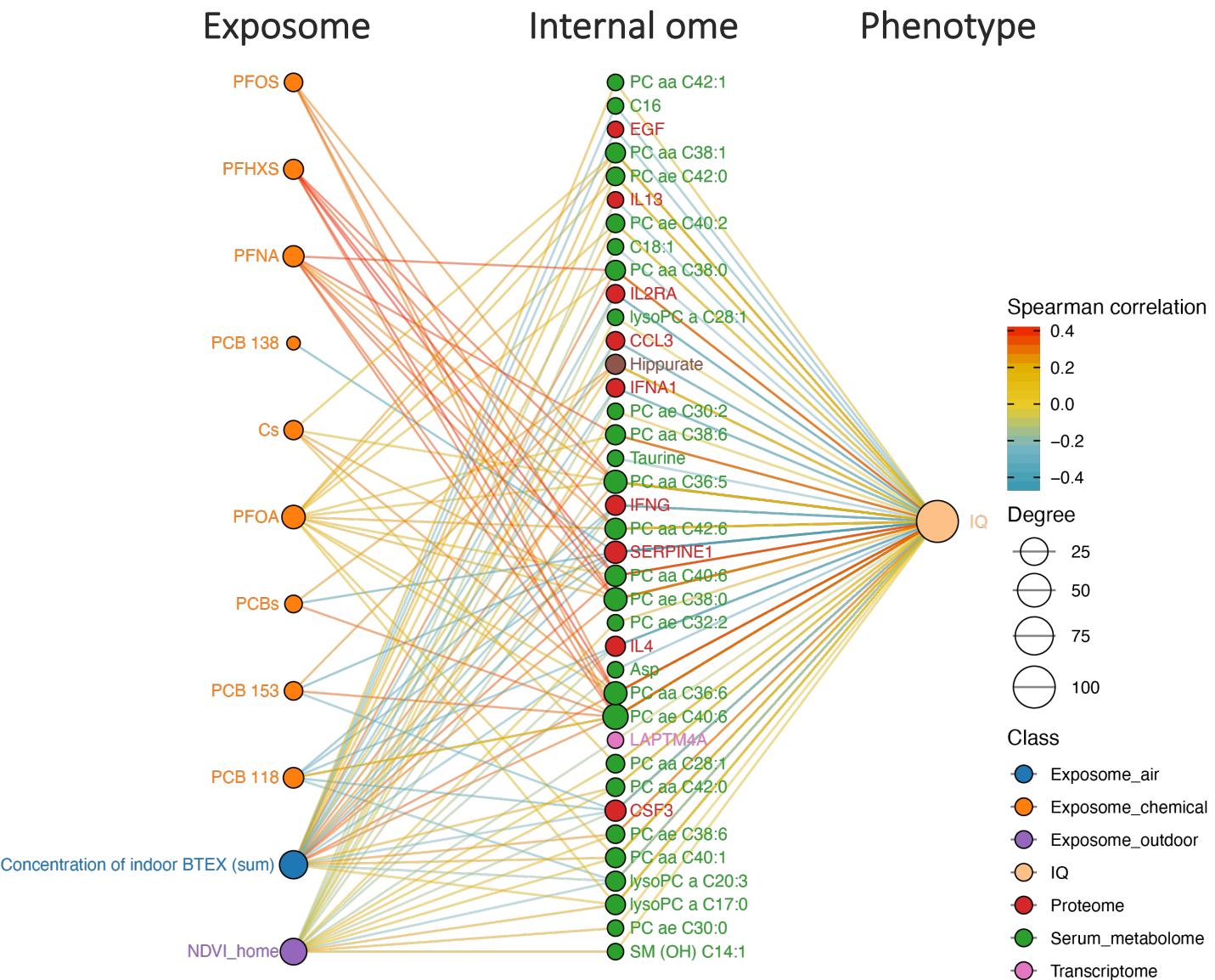


Example network illustration: Top 250 average causal mediation effects (ACME)

Exposome contributes to phenotypic changes through internal-ome



➤ Exposome contributes to IQ changes through internal-ome

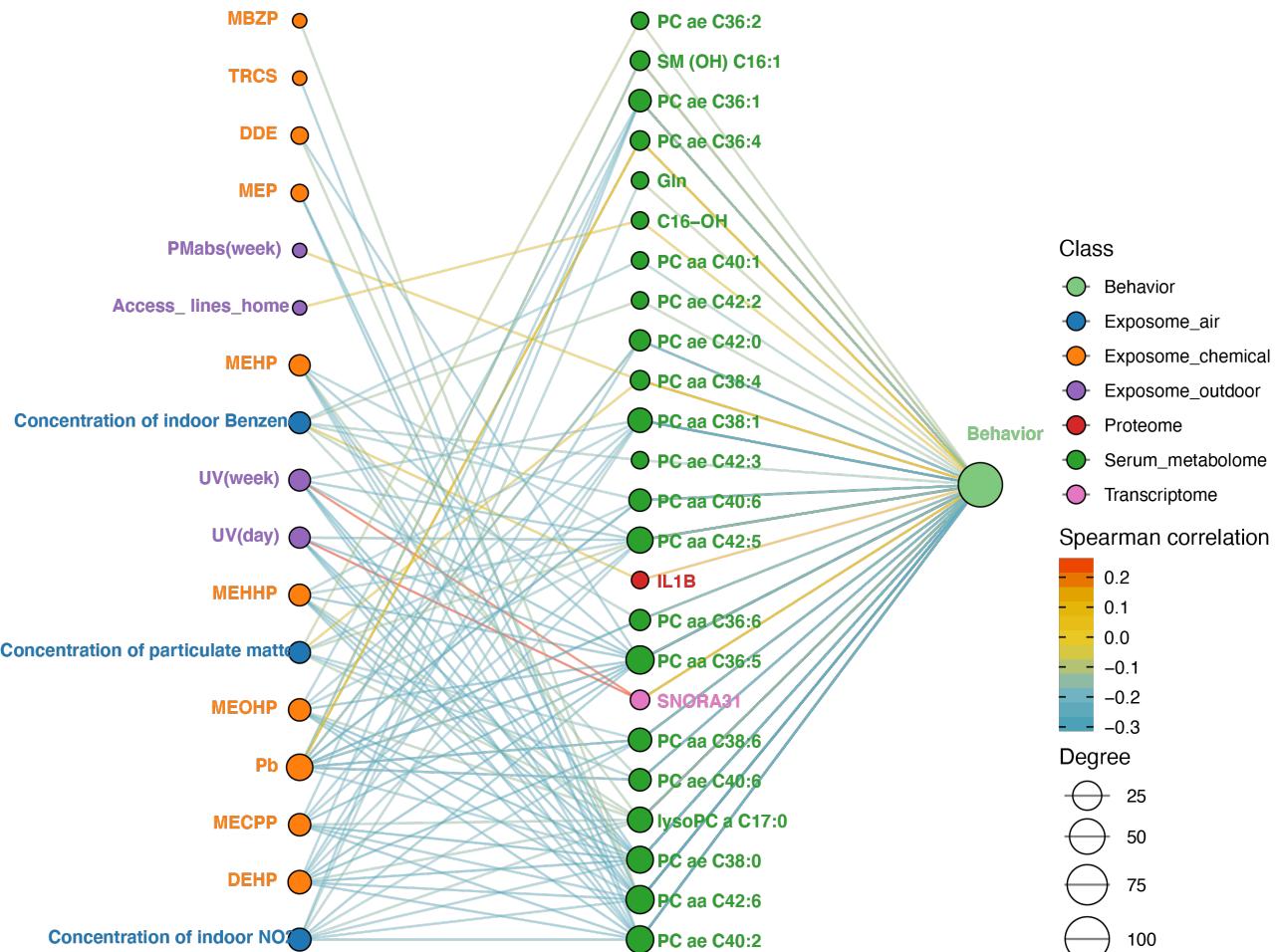


➤ Exposome contributes to Behavior changes through internal-ome

Exposome

Internal ome

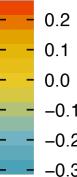
Phenotype



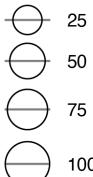
Class

- Behavior
- Exposome_air
- Exposome_chemical
- Exposome_outdoor
- Proteome
- Serum_metabolome
- Transcriptome

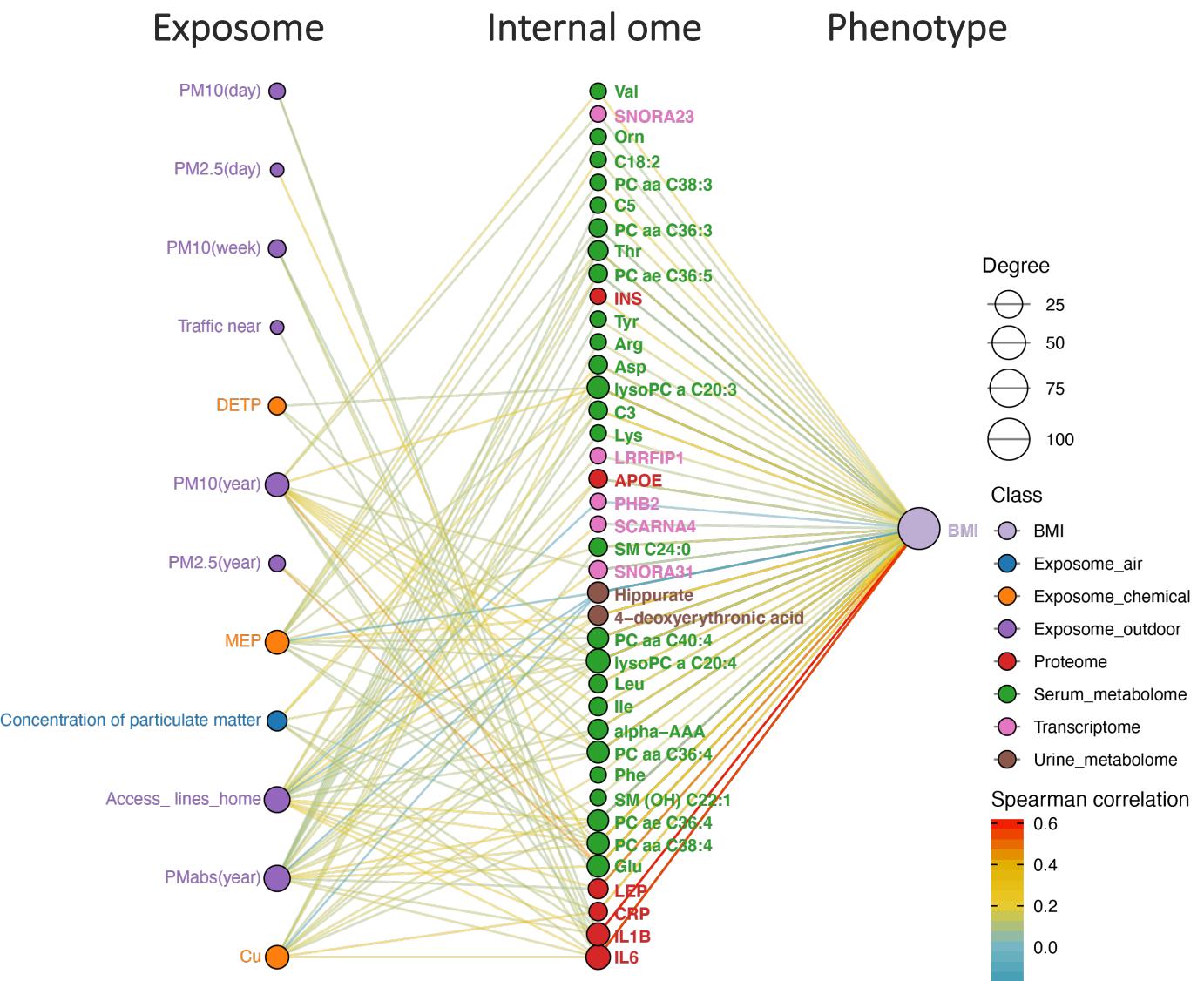
Spearman correlation



Degree



➤ Exposome contributes to BMI changes through internal-ome



➤ Summary

› ACKNOWLEDGEMENT

Our team



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Thanks for your attention!

Q&A

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