

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

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# Exposome affects human health outcome

Exposome x Genome = Health outcome (Phenotype)

## Ecosystems

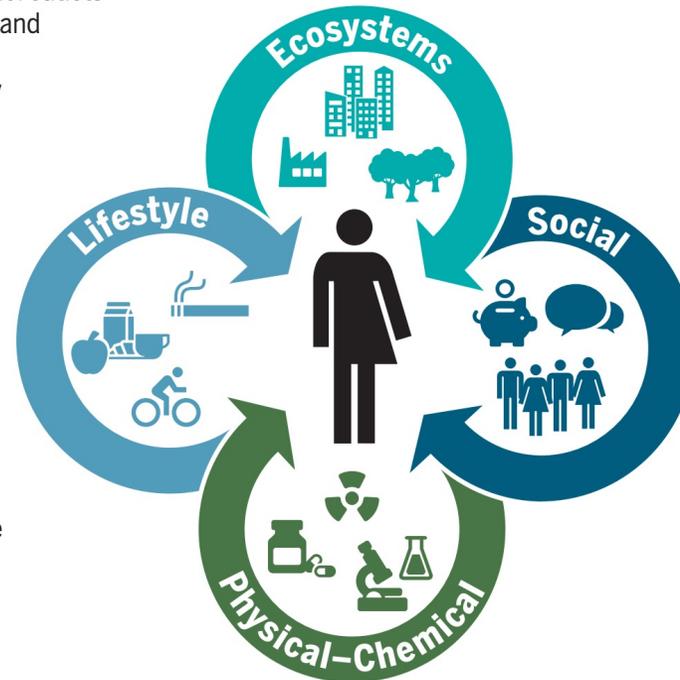
Food outlets, alcohol outlets  
Built environment and urban land uses  
Population density  
Walkability  
Green/blue space

## 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

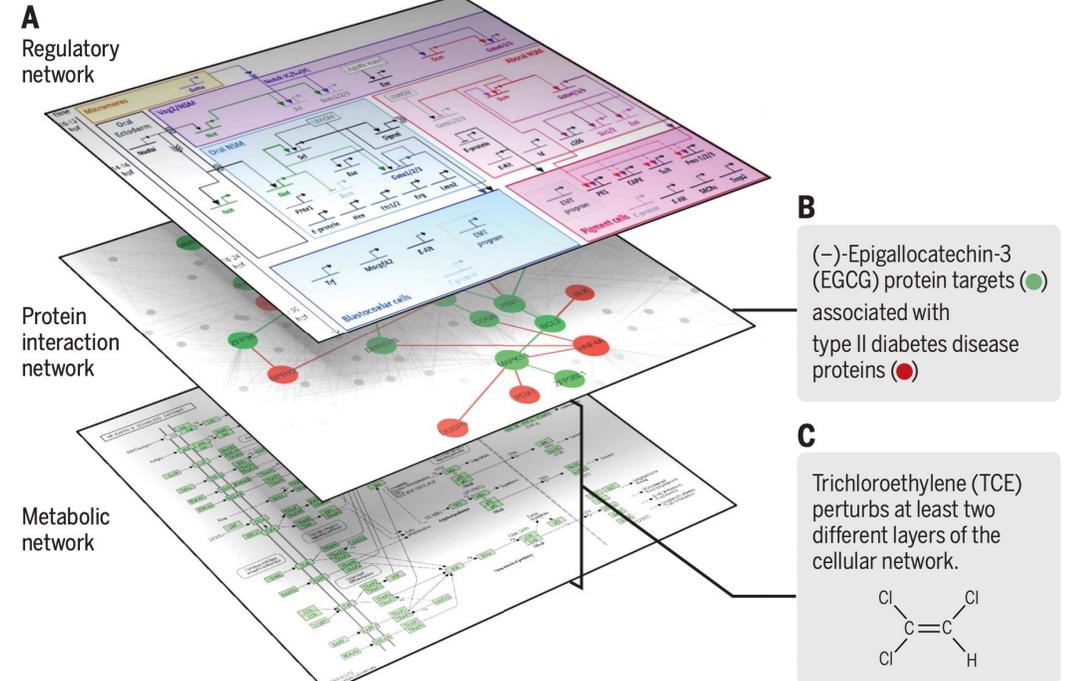
Vermeulen et al., 2020, Science



# Challenges in exposome research

“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



## Hypothesis

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

# ➤ Motivations and analysis strategy

1. Exposome affect the health outcomes (phenotypes).



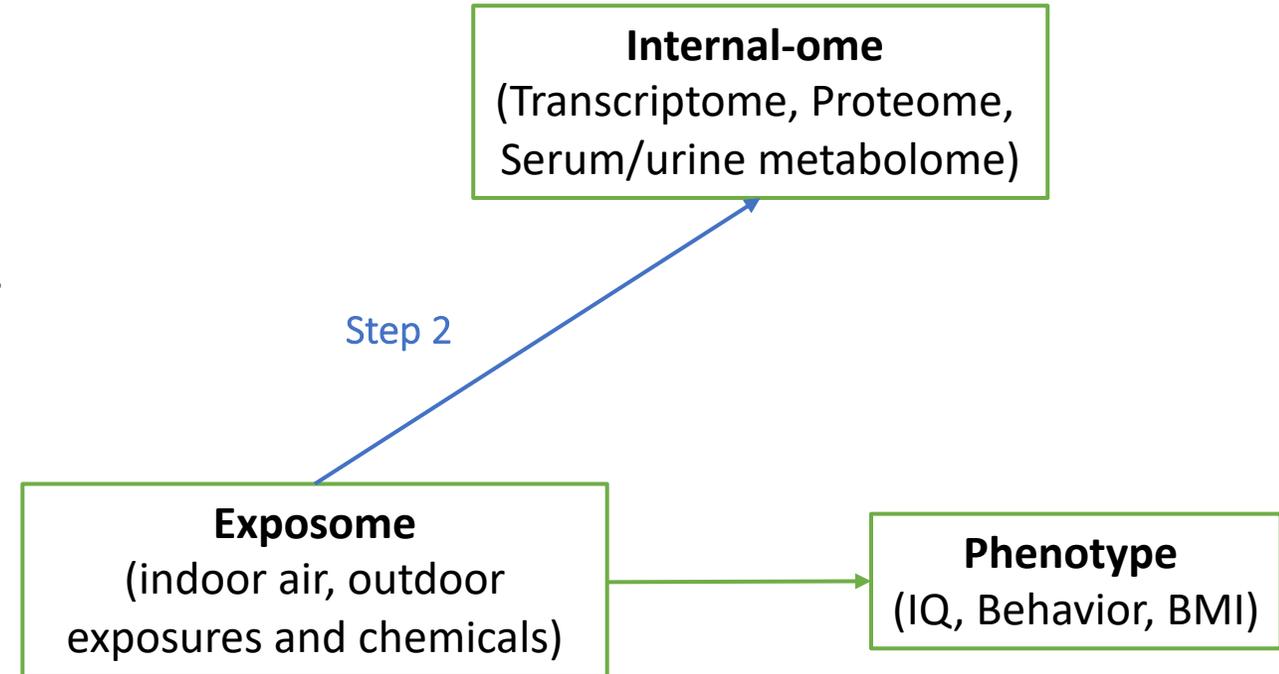
**Internal-ome**  
(Transcriptome, Proteome,  
Serum/urine metabolome)



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

## ➤ Motivations and analysis strategy

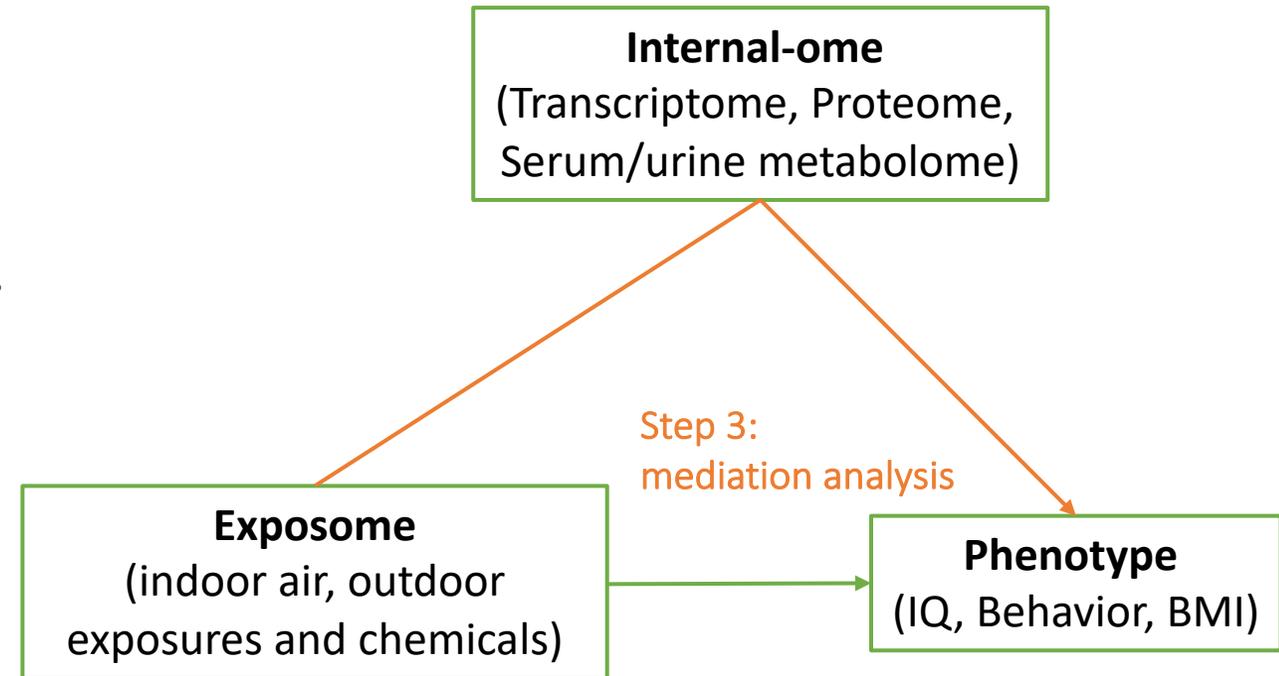
1. Exposome affect the health outcomes (phenotypes).
2. Exposome affect Internal-ome (transcriptome, proteome, metabolome).



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

## ➤ Motivations and analysis strategy

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).



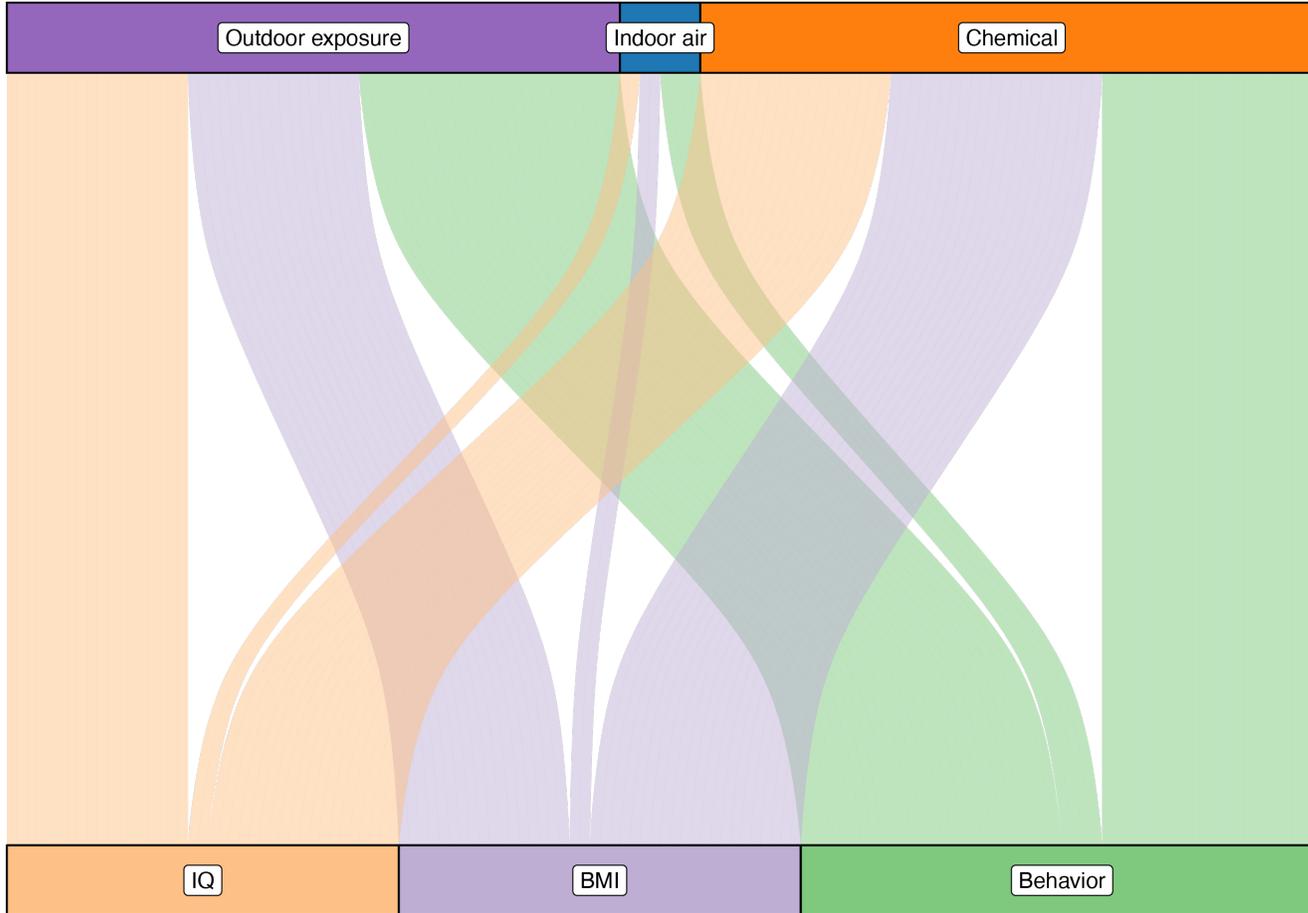
<https://www.betterplace.org/>



# Exposome are associated with phenotypes

## Association Distribution

Exposome (Outdoor exposure, indoor air, chemical)



Phenotype (IQ, BMI, Behavior)

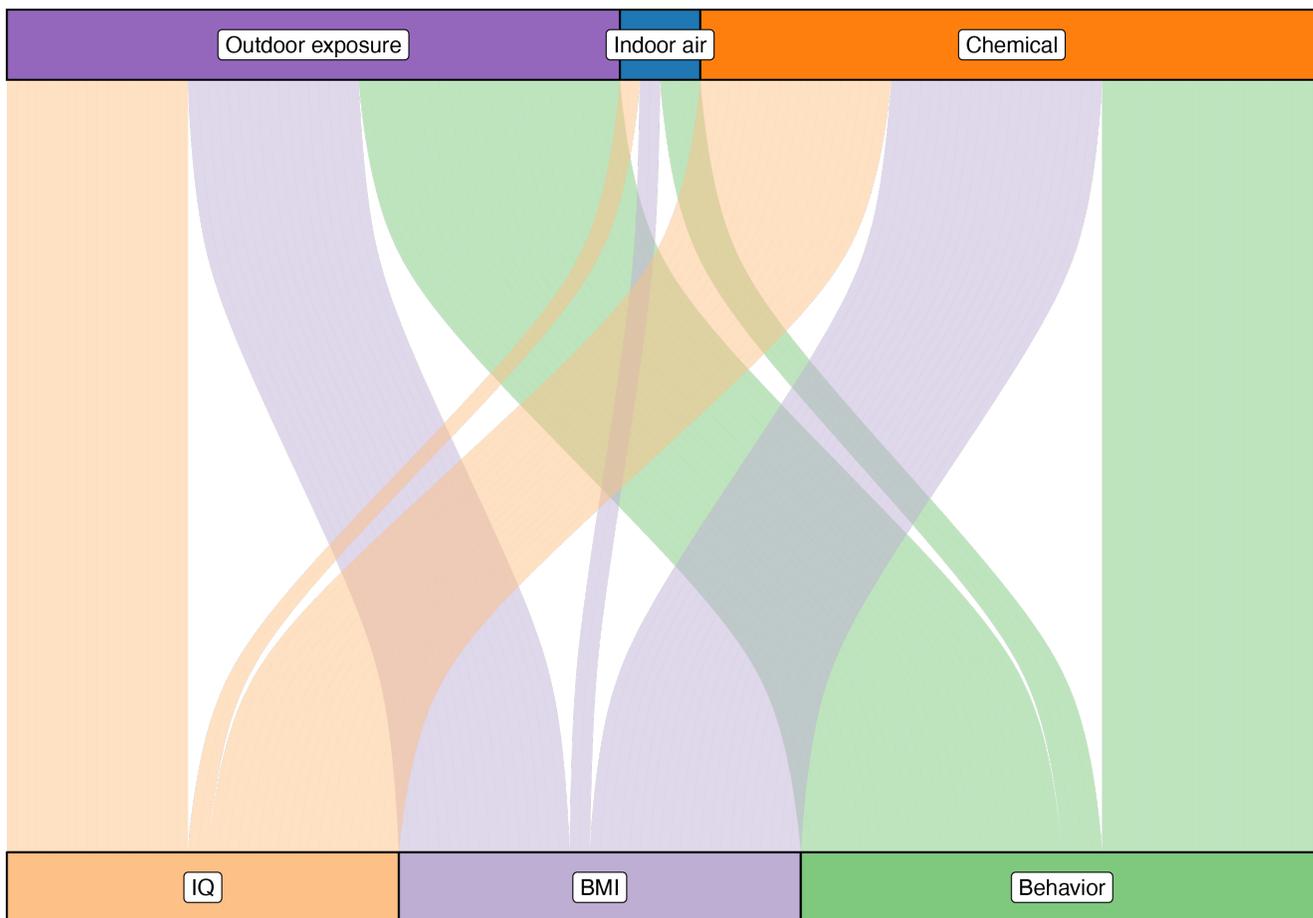
Most of the associations are from **outdoor exposures and chemicals**.

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

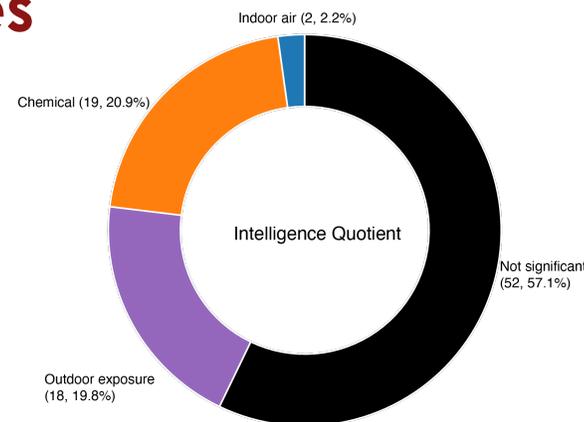
# Exposome are associated with phenotypes

## Association Distribution

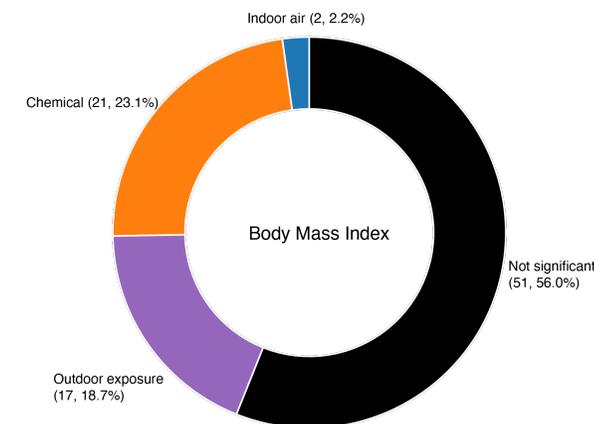
Exposome (Outdoor exposure, indoor air, chemical)



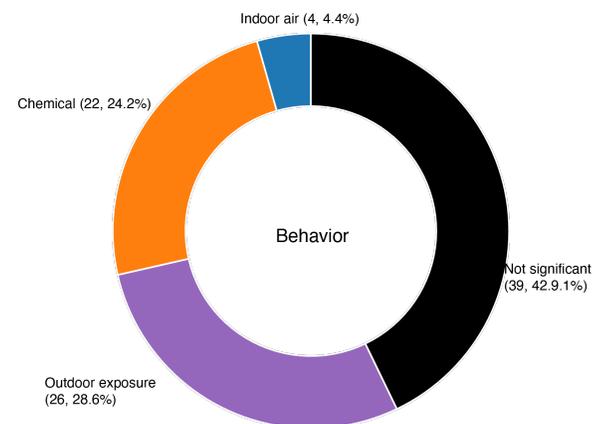
Phenotype (IQ, BMI, Behavior)



**Intelligence quotient (IQ):**  
39 exposome features



**Body mass index (BMI):**  
40 exposome features

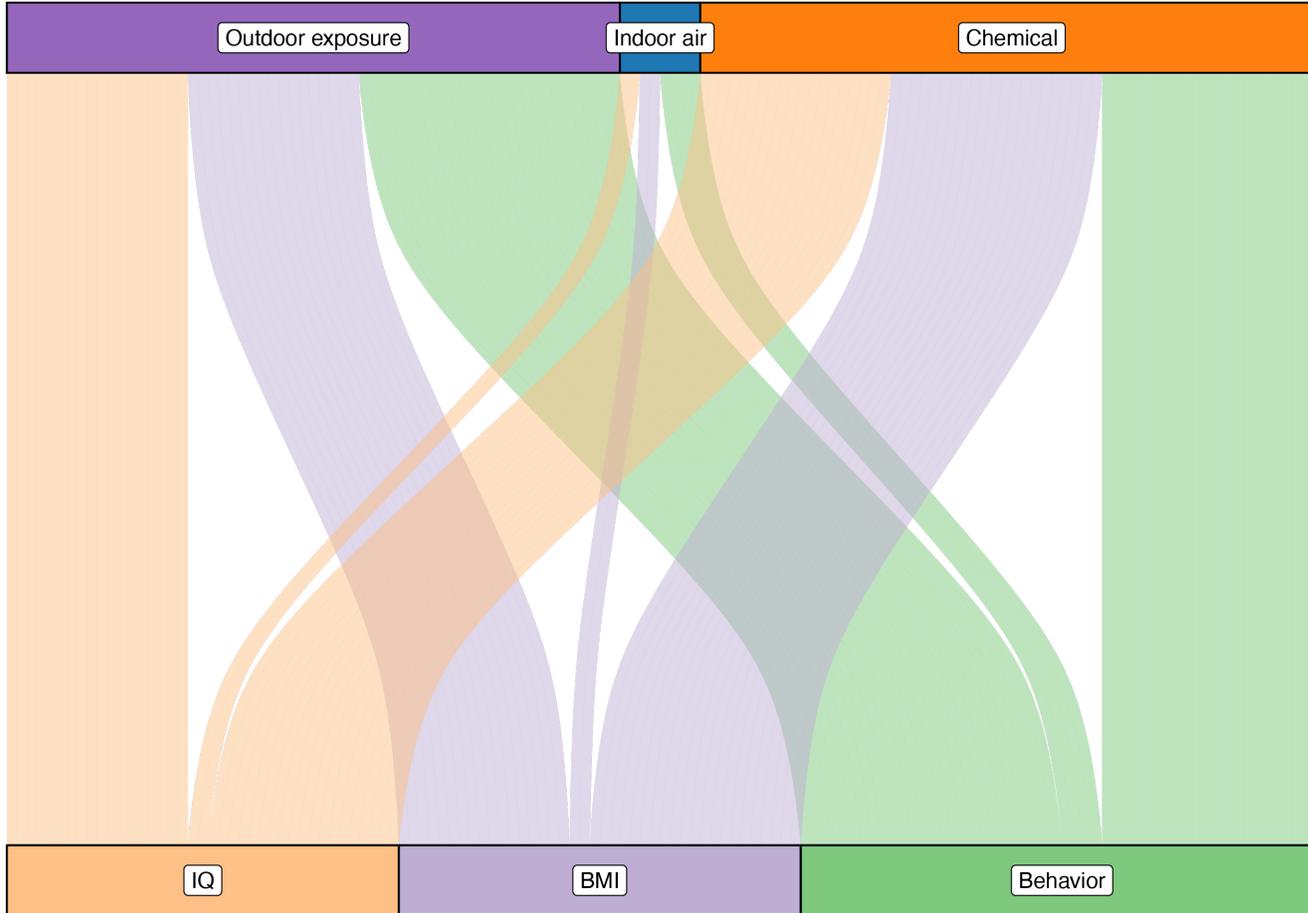


**Behavior:**  
52 exposome features

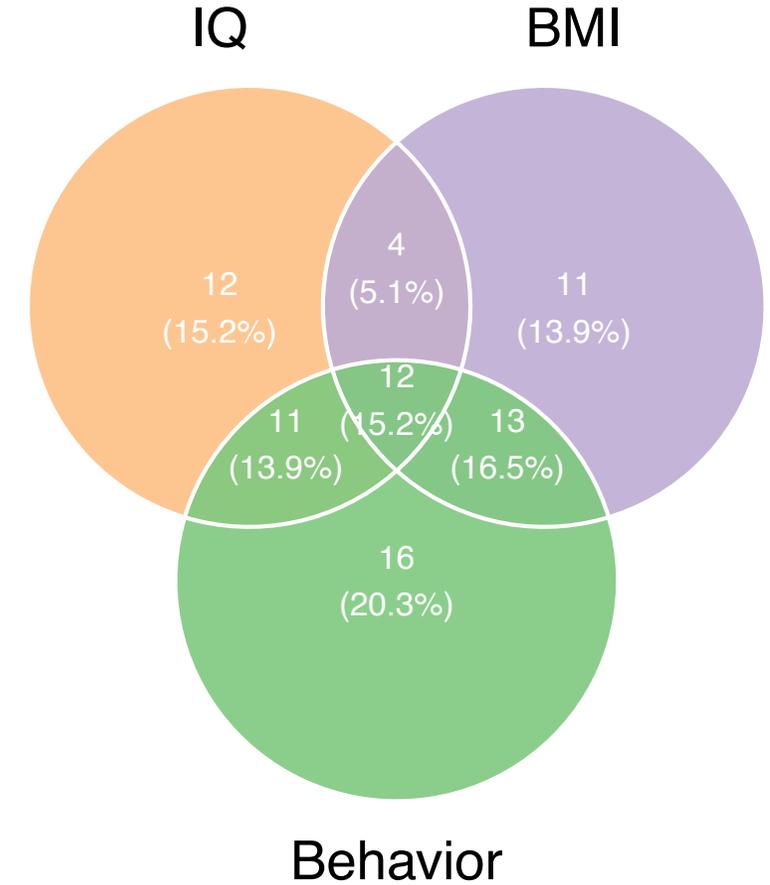
# Exposome are associated with phenotypes

## Association Distribution

Exposome (Outdoor exposure, indoor air, chemical)



Phenotype (IQ, BMI, Behavior)

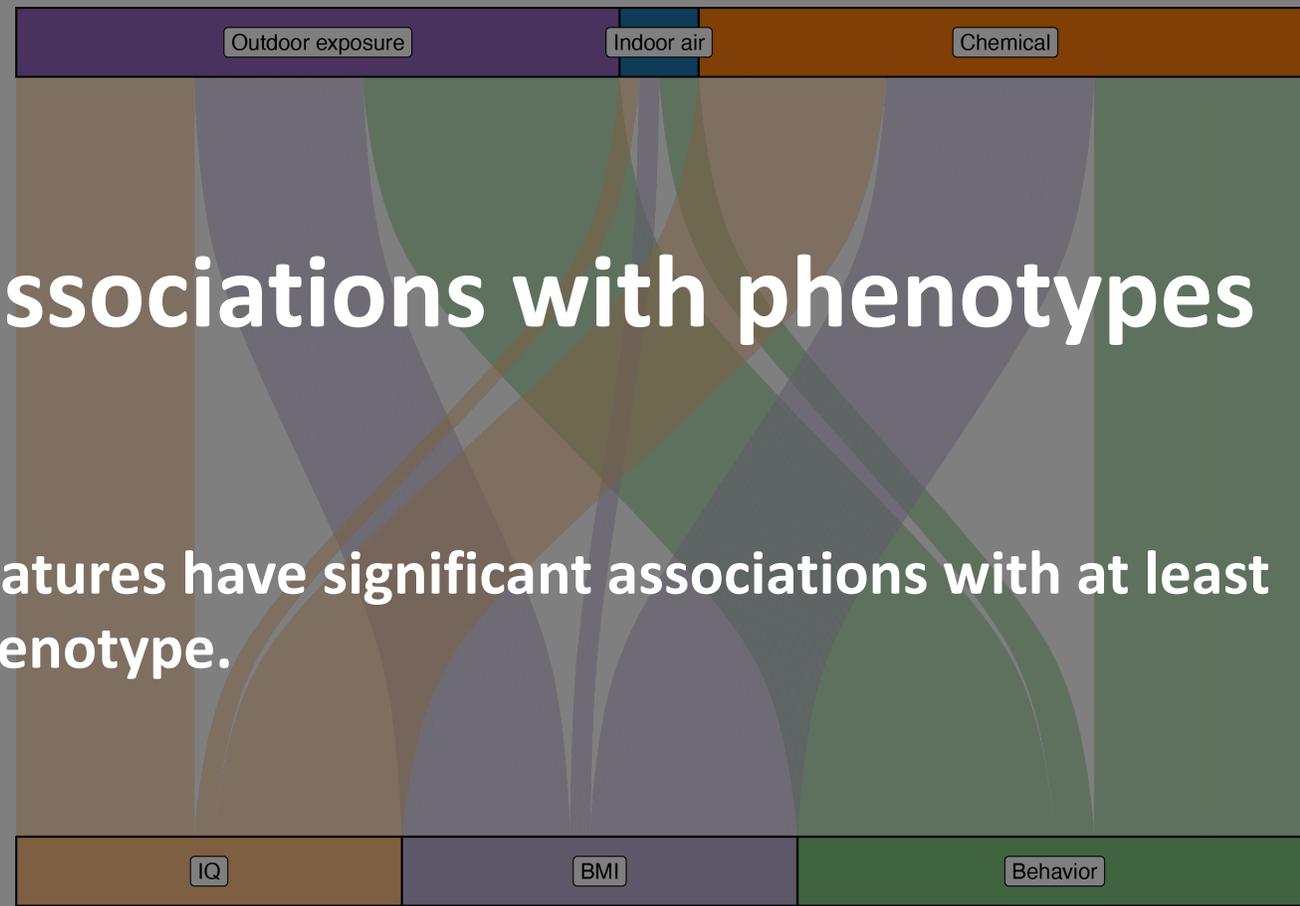
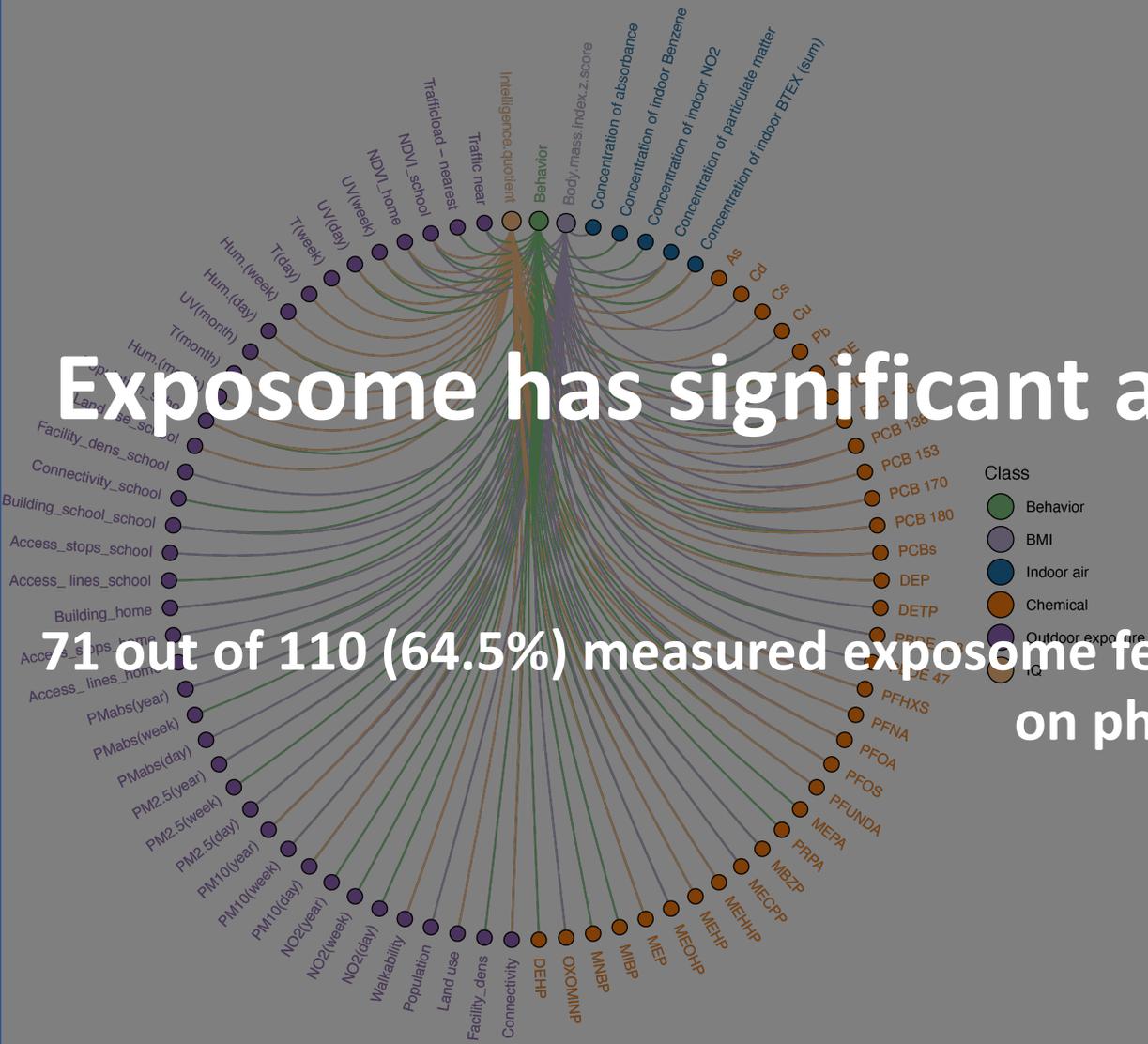


Overlap between IQ, BMI and behavior's associations with the exposome are modest (< 50%).

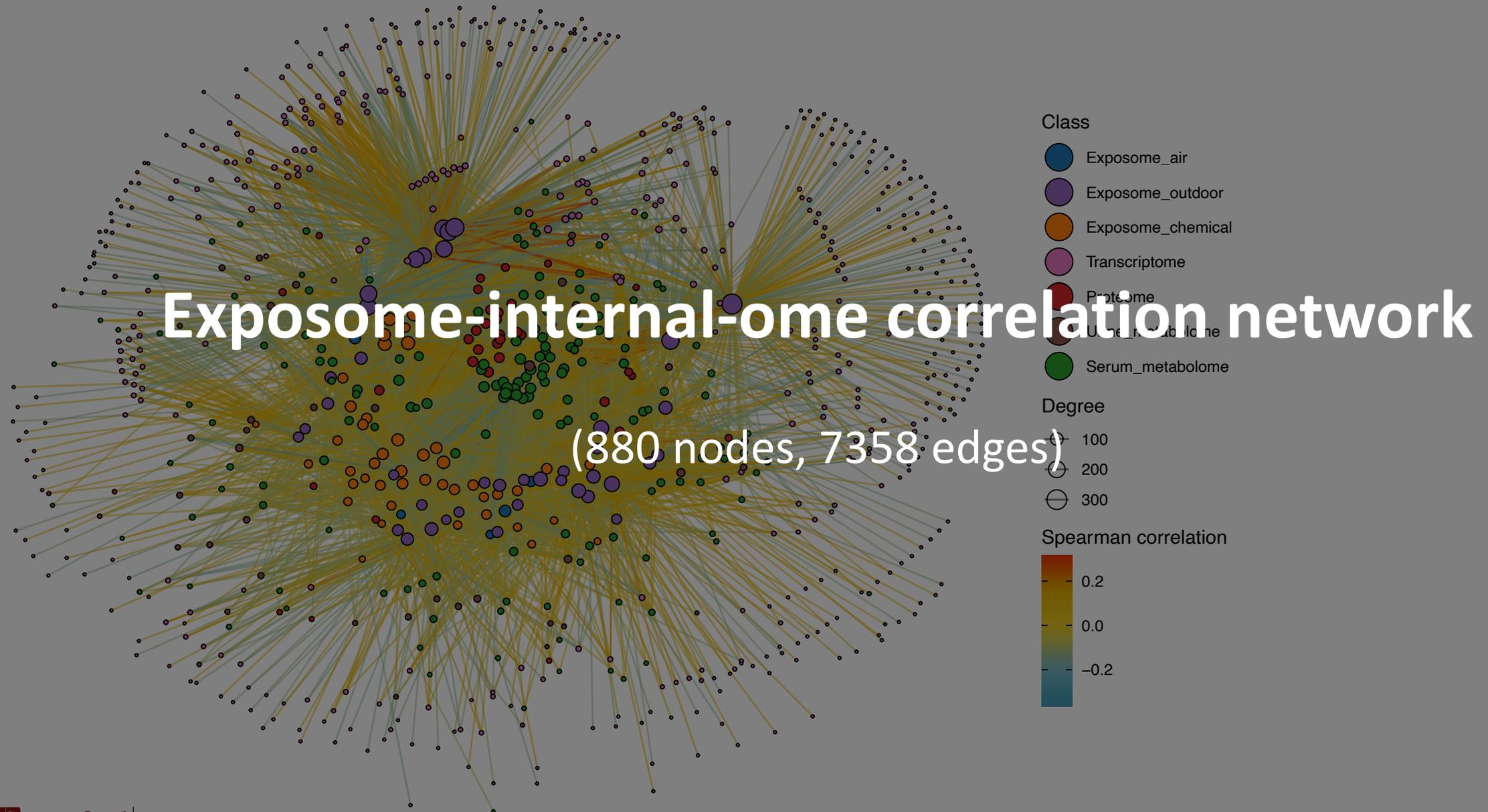
# Exposome are associated with phenotypes

## Exposome has significant associations with phenotypes

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



## Exposome are associated with internal-omics data



# Exposome are associated with internal-omics data

Node number

5

40

46

539

36

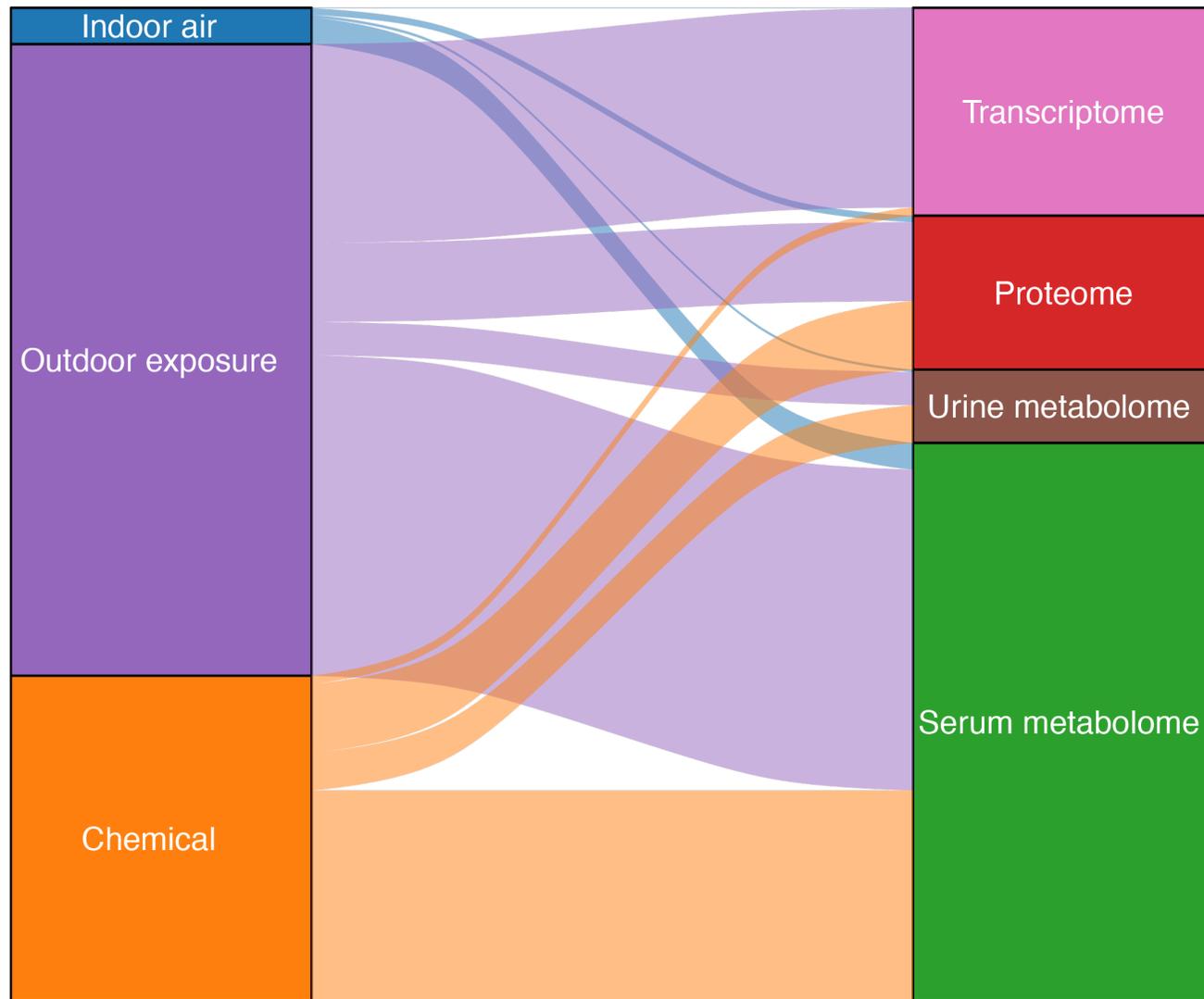
42

172

Exposome (91)

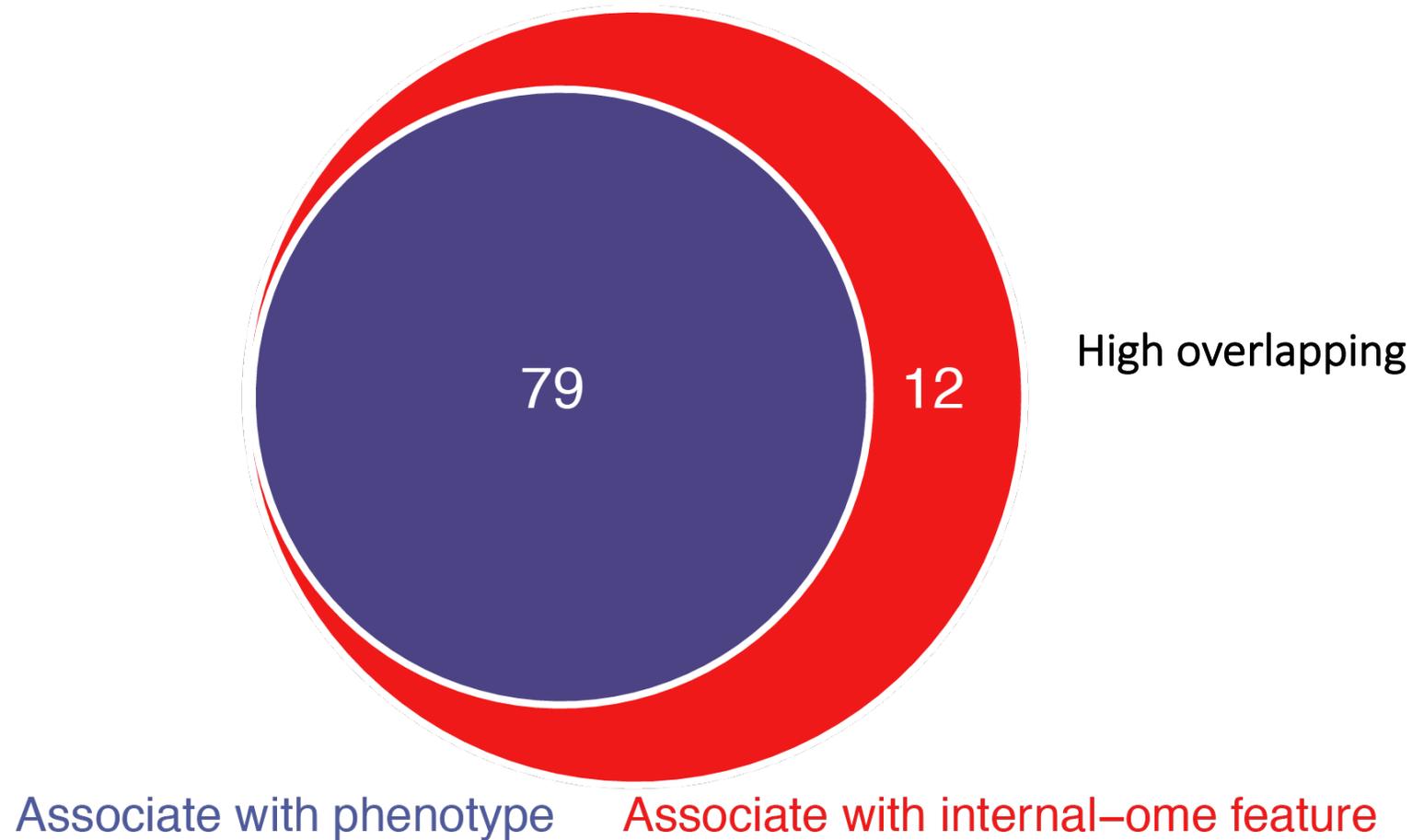
Internal-ome (789)

Edge number



## ➤ Exposome contributes to phenotypic changes through internal-ome

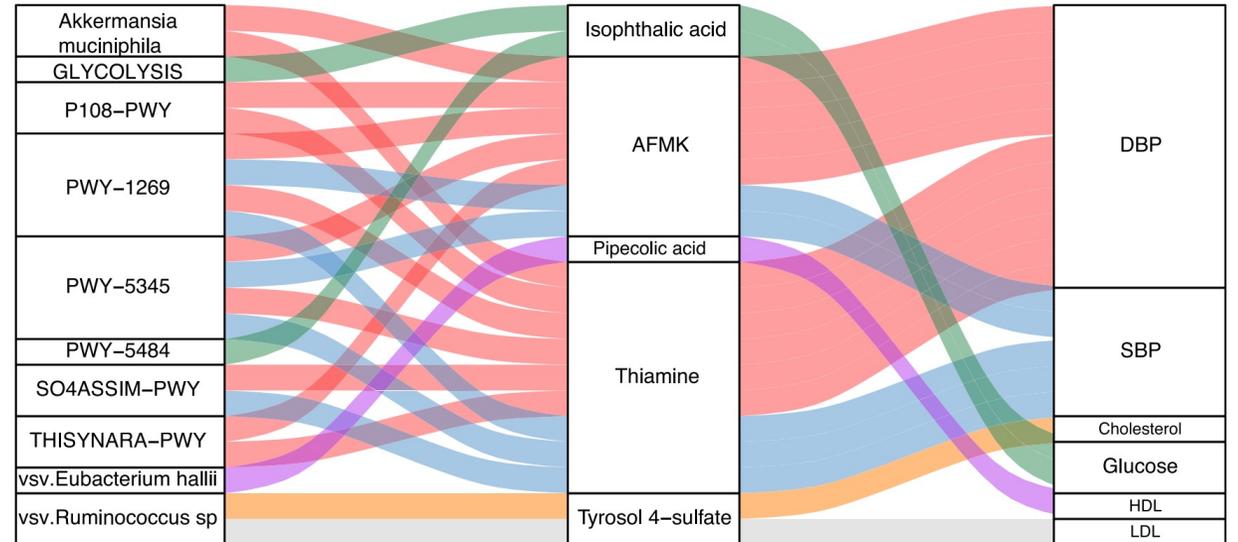
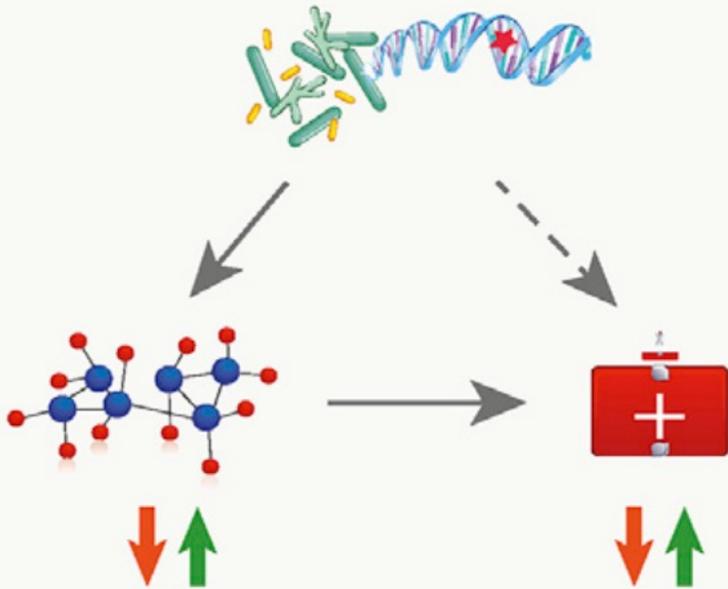
1. 79 out of 110 exposome features are associated with phenotypes.
2. 91 out of 110 exposome features are associated with internal-ome features.



# Exposome contributes to phenotypic changes through internal-ome

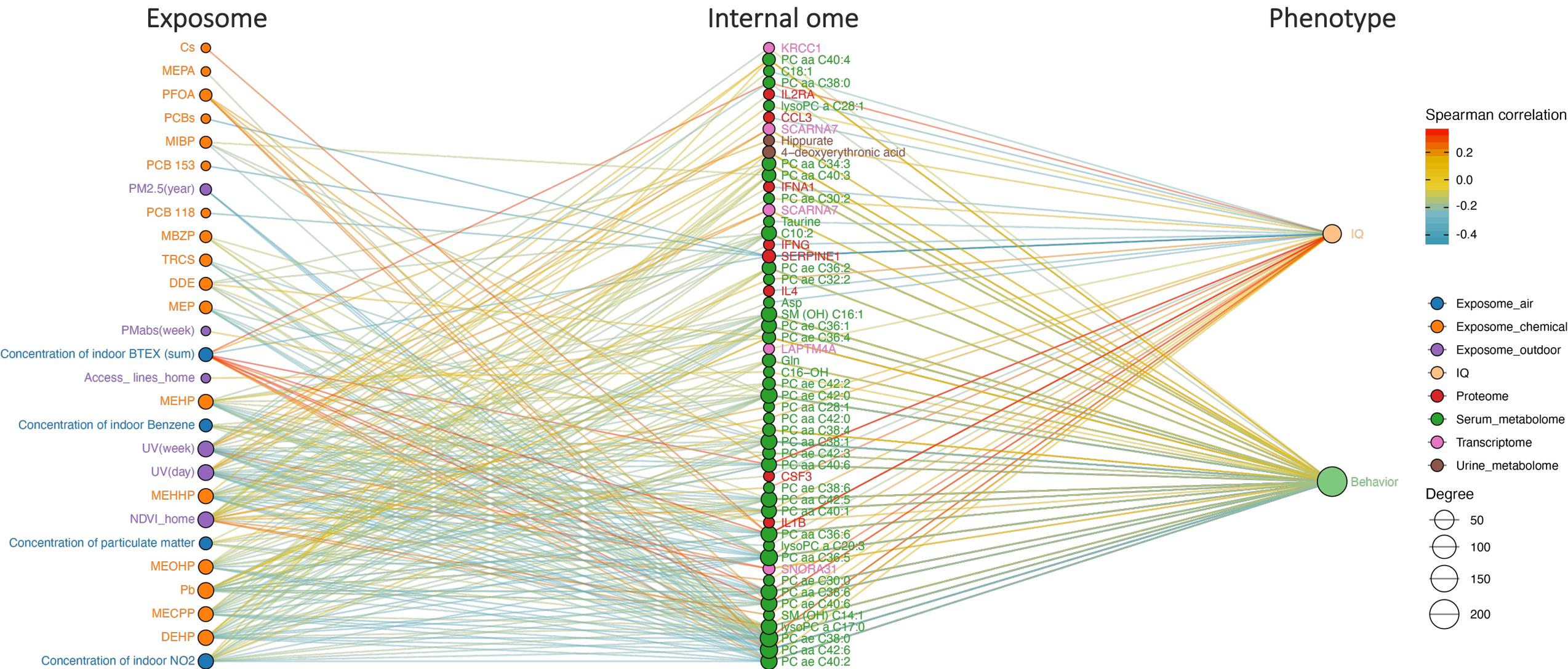
To evaluate whether internal-ome features can mediate the exposome impact on phenotypes, we applied **bi-directional mediation analysis**.

Microbial impacts on host phenotypes are mediated by metabolites



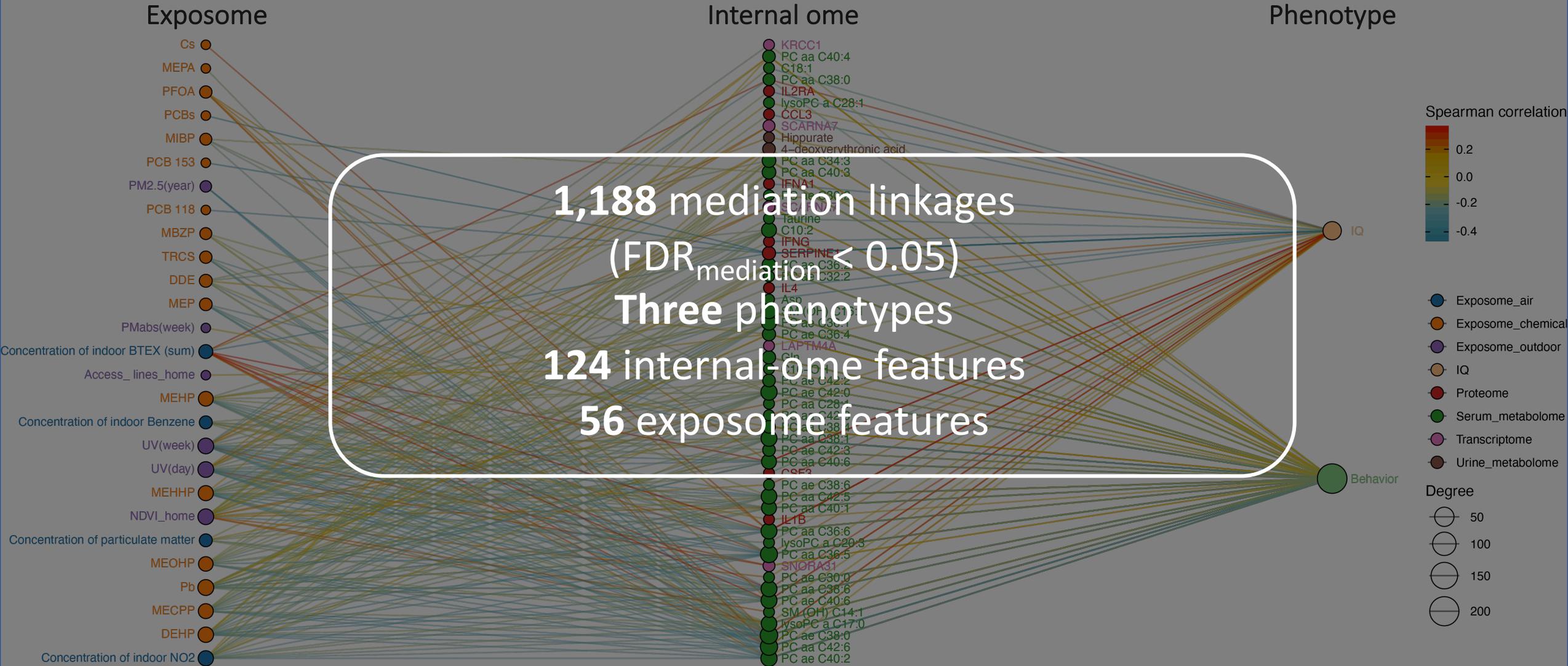
Chen et al., 2021, Cell 184, 1–14

# Exposome contributes to phenotypic changes through internal-ome



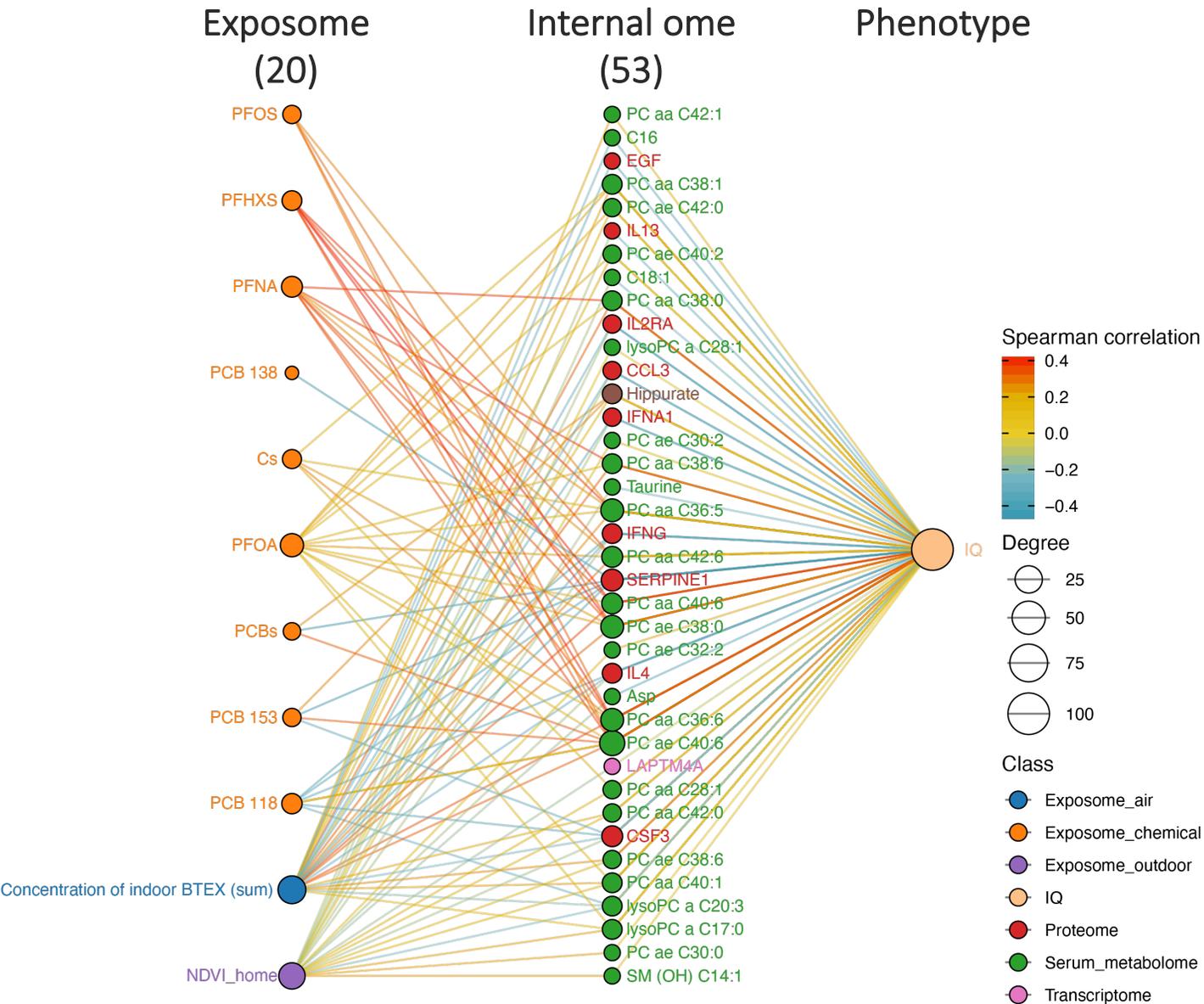
Example network illustration: Top 250 average causal mediation effects (ACME)

# Exposome contributes to phenotypic changes through internal-ome



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

# Exposome contributes to IQ changes through internal-ome



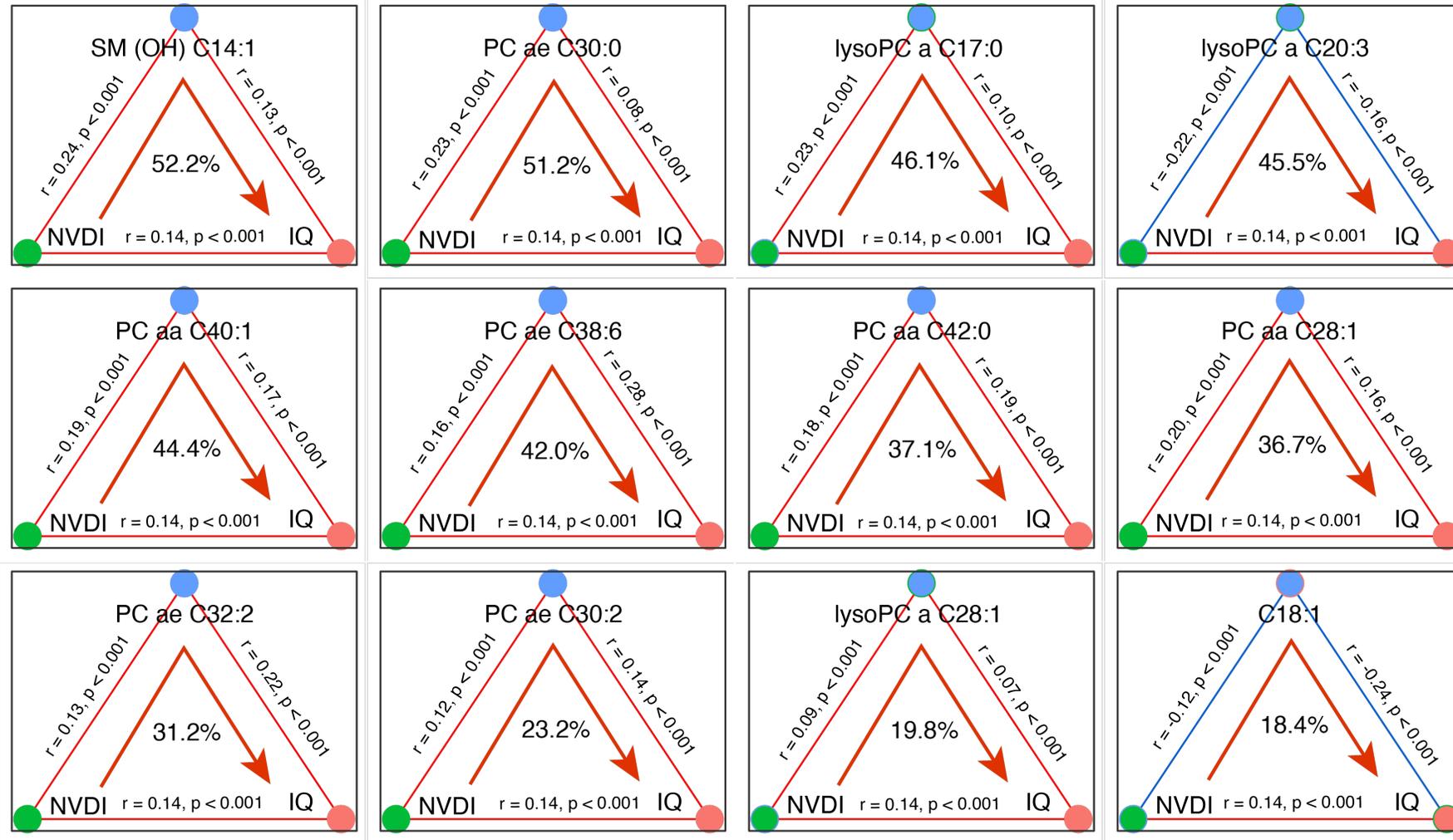
Almost of 25 out of 26 lipids from serum are positively associated with children IQ which has been well documented.

NVDI (normalized difference vegetation index) is positively associated with IQ for urban kids. But the mechanism is not clear.

Uauy et al. 2003, JN.  
Bijnens et al., 2020, PLOS Medicine.

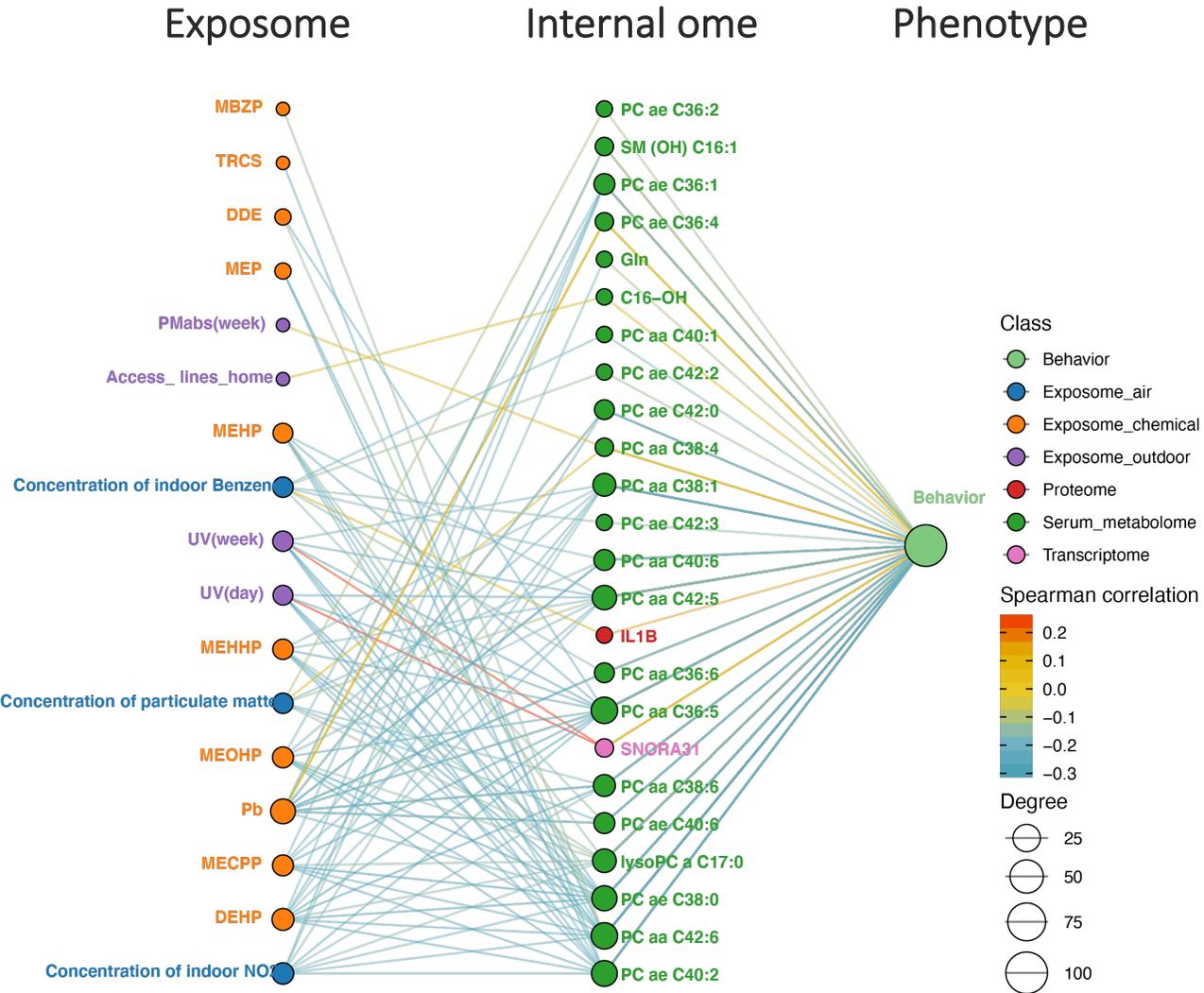
Example network illustration: Top 100 average causal mediation effects (ACME)

# Exposome contributes to IQ changes through internal-ome



NVDI (normalized difference vegetation index) positively affect IQ via lipids (PC, lysoPC and SM. 34%).

# Exposome contributes to Behavior changes through internal-ome



Blood Pb concentrations, even at mean levels of 6.4  $\mu\text{g}/\text{dL}$ , were associated with increased risk of behavioral problems in preschool children, including internalizing and pervasive developmental problems.

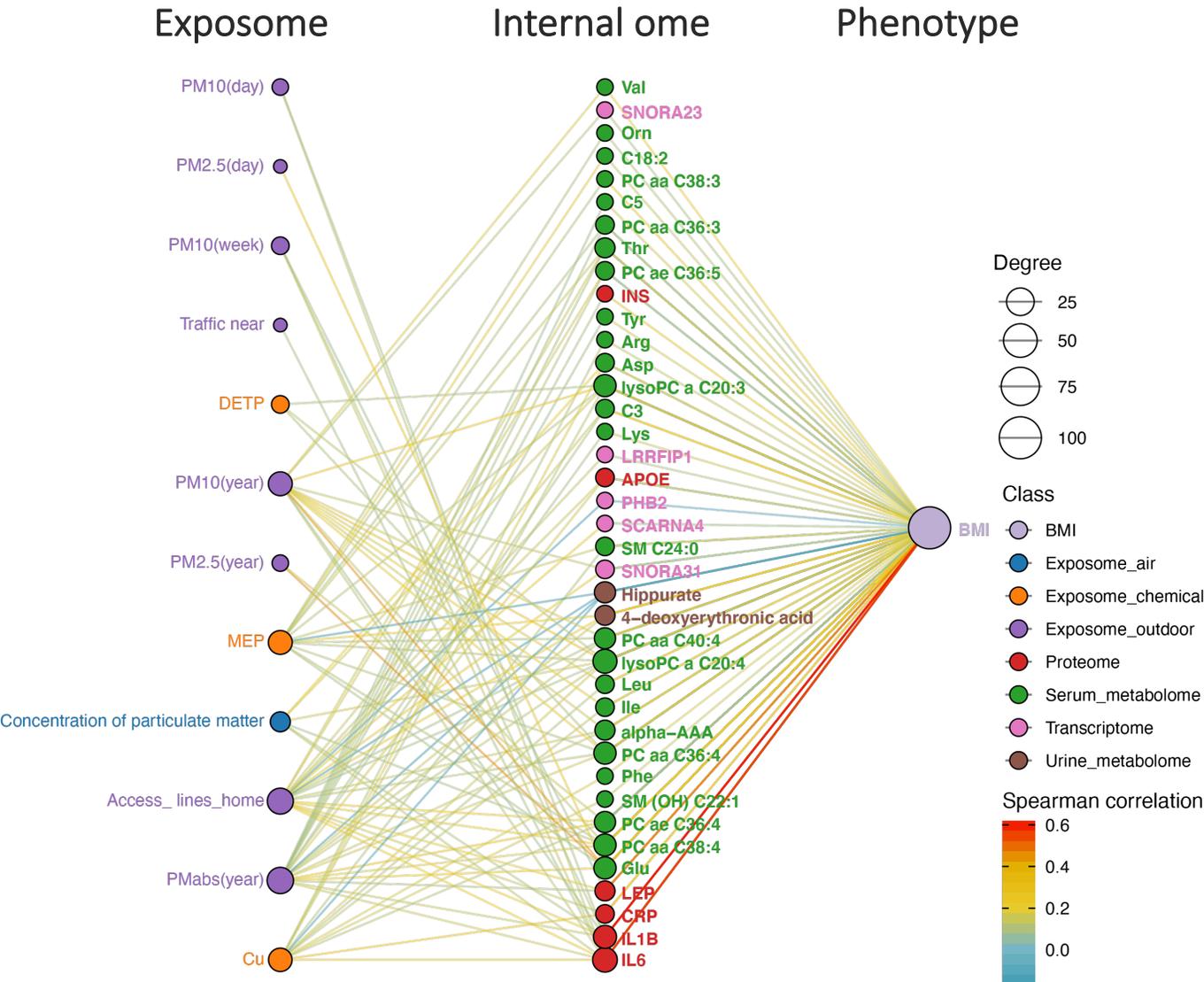
Liu et al., 2014

Several studies suggested that phthalate exposure may increase behavioral problems in childhood.

Braun et al., 2014

Example network illustration: Top 100 average causal mediation effects (ACME)

# Exposome contributes to BMI changes through internal-ome



A study found an inverse association between the daily PM<sub>10</sub> exposure and the DNA methylation of inflammatory genes, measured in peripheral blood of healthy overweight/obese subjects.

Cantone et al., 2017

Significant associations were found between the highest quartile of copper concentrations in blood with obesity status (OR = 9.27, 95% CI: 5.43, 15.82, pfor trend < 0.001) and cholesterol (OR = 3.08, 95% CI: 1.43, 6.63, pfor trend < 0.001).

Fan et al., 2017

Example network illustration: Top 100 average causal mediation effects (ACME)

## > Summary

- ❖ The exposome is associated with internal –omes and further associated with phenotypes
- ❖ Internal –omes mediated the interactions of exposome and phenotypes

## Our team



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**Supervisor:**  
Michael Snyder, PhD

# Thanks for your attention!

## Q&A

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