



Next generation chemicals and drugs: towards effective, safe, and sustainable products.

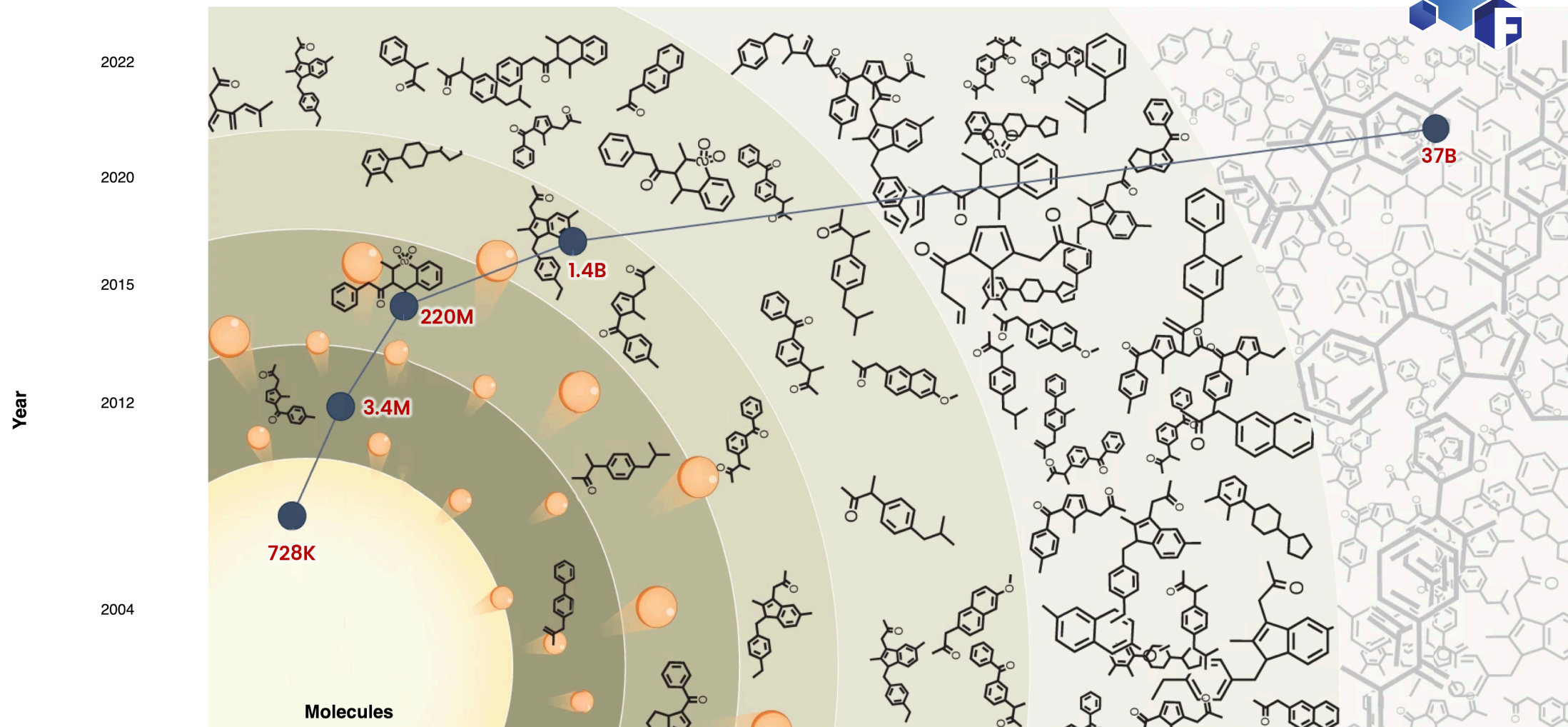
Dario Greco, PhD

Professor of Pharmaceutical Bioinformatics
Division of Pharmaceutical Biosciences
Faculty of Pharmacy
University of Helsinki
Finland

Professor of Bioinformatics, Director
FHAIVE
Faculty of Medicine and Health Technology
Tampere University
Finland



The “Big Bang” of the chemical universe



Cherkasov Nat Chem Bio 2023

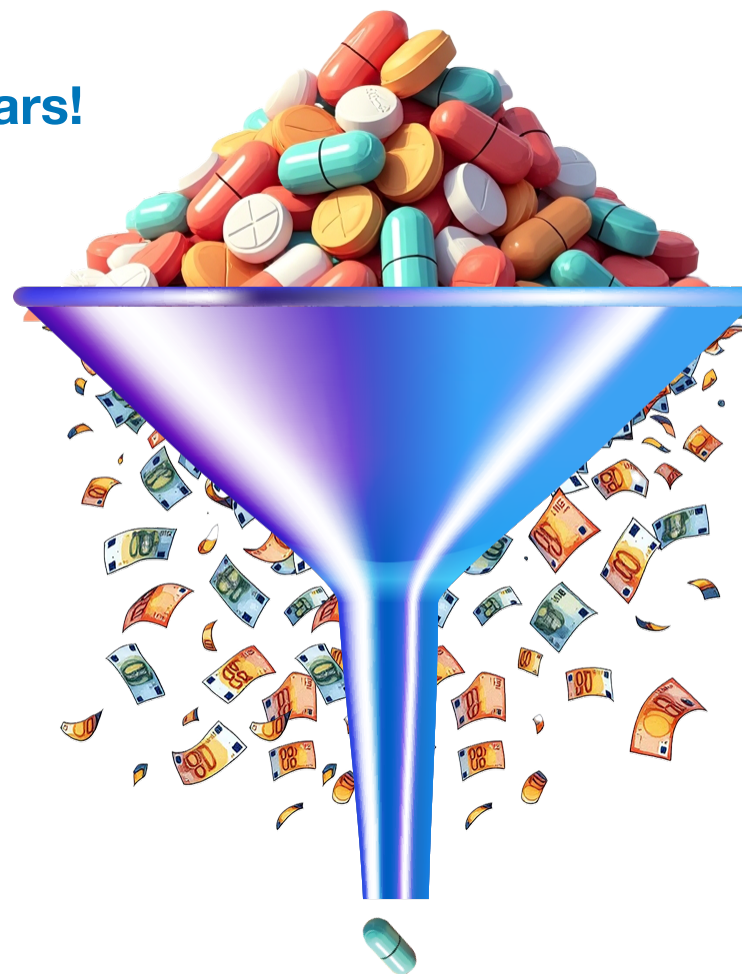
Too many chemicals, too few drugs!



1 new chemical
every 4 hours!



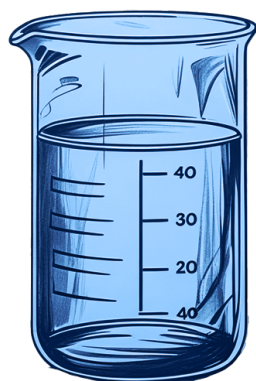
1 new drug
every 10 years!



Traditional Toxicology



Traditional toxicology

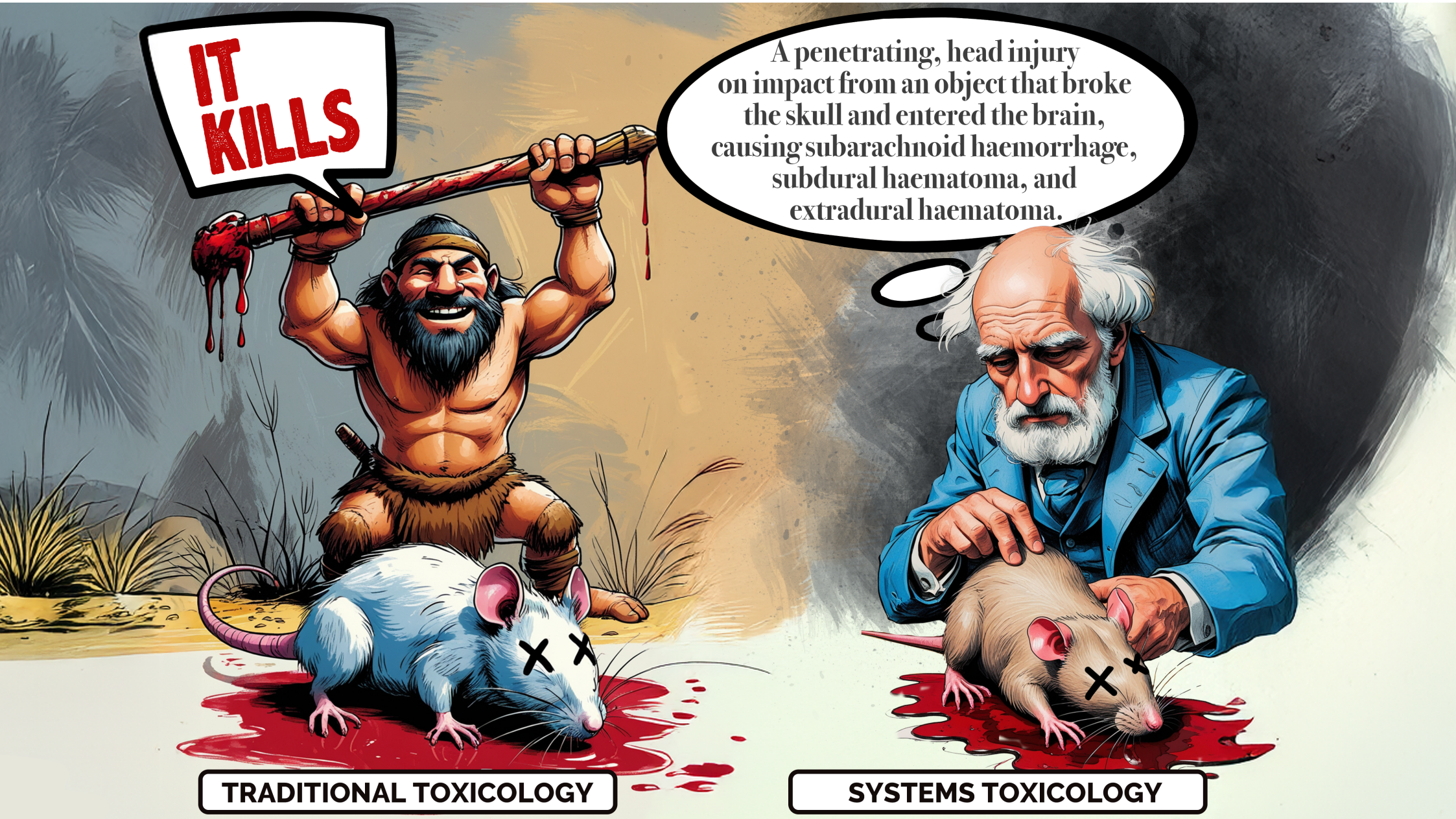


**IT
KILLS**

A penetrating, head injury
on impact from an object that broke
the skull and entered the brain,
causing subarachnoid haemorrhage,
subdural haematoma, and
extradural haematoma.

TRADITIONAL TOXICOLOGY

SYSTEMS TOXICOLOGY



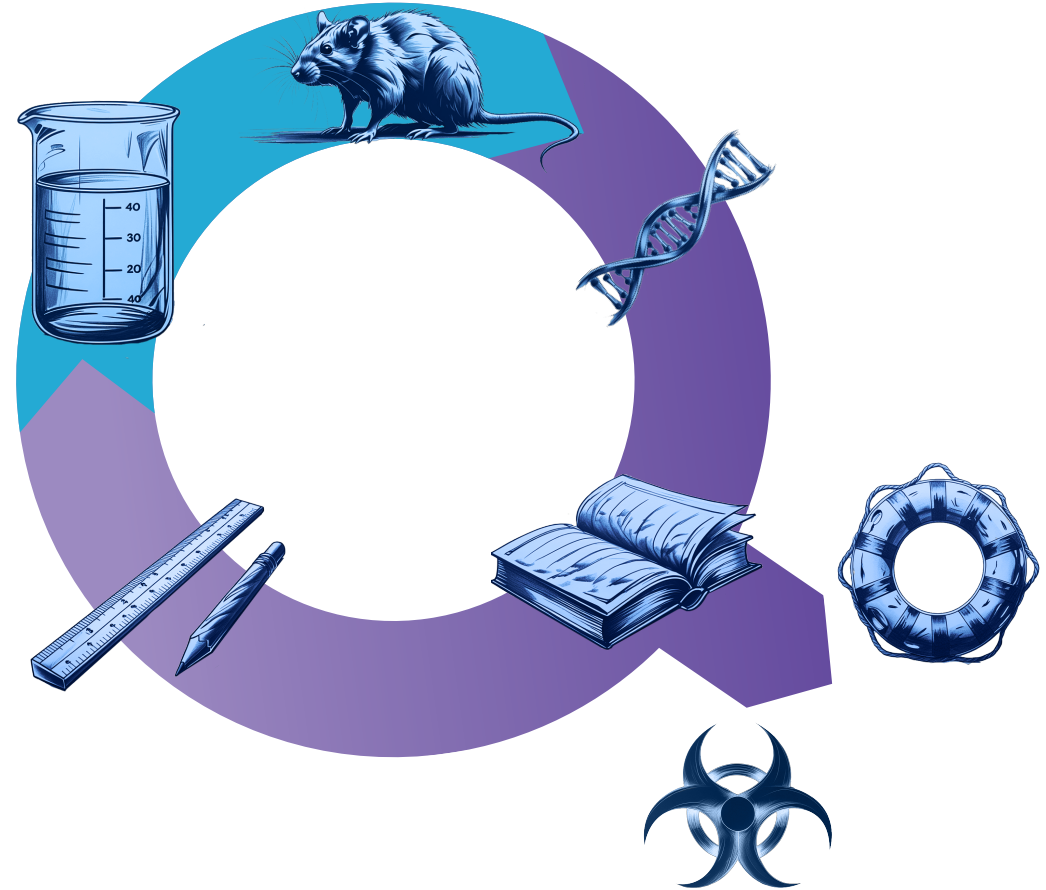
Current paradigms in Toxicology



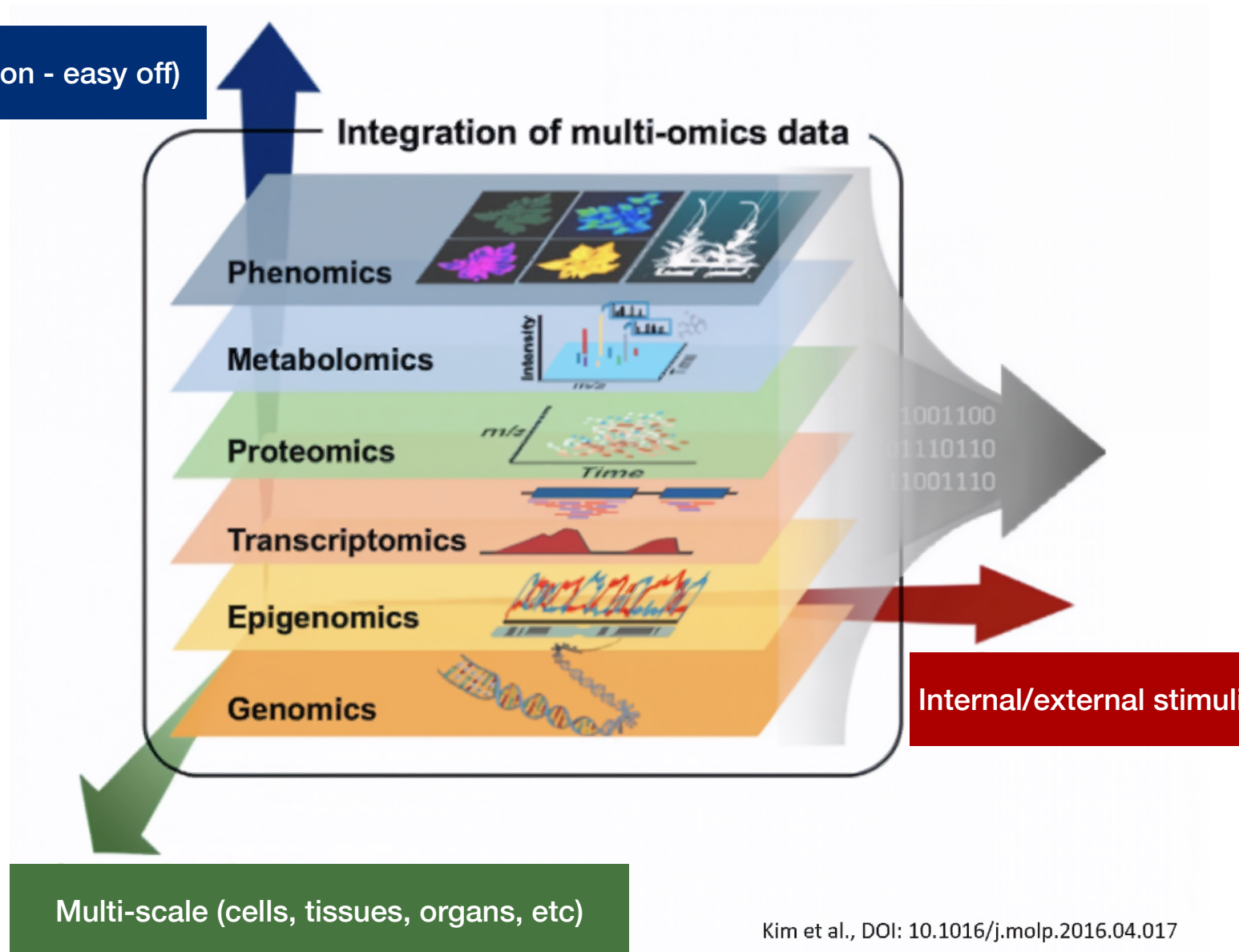
Traditional toxicology



Systems toxicology

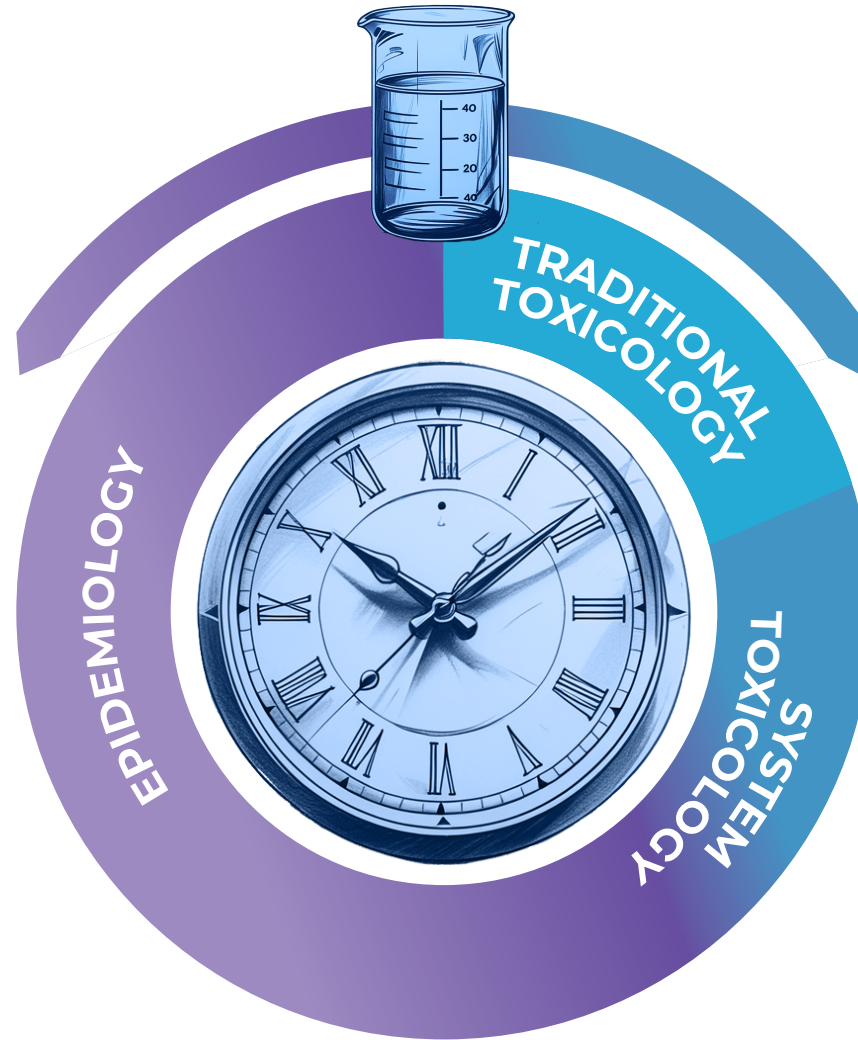


Instability (fast on - easy off)

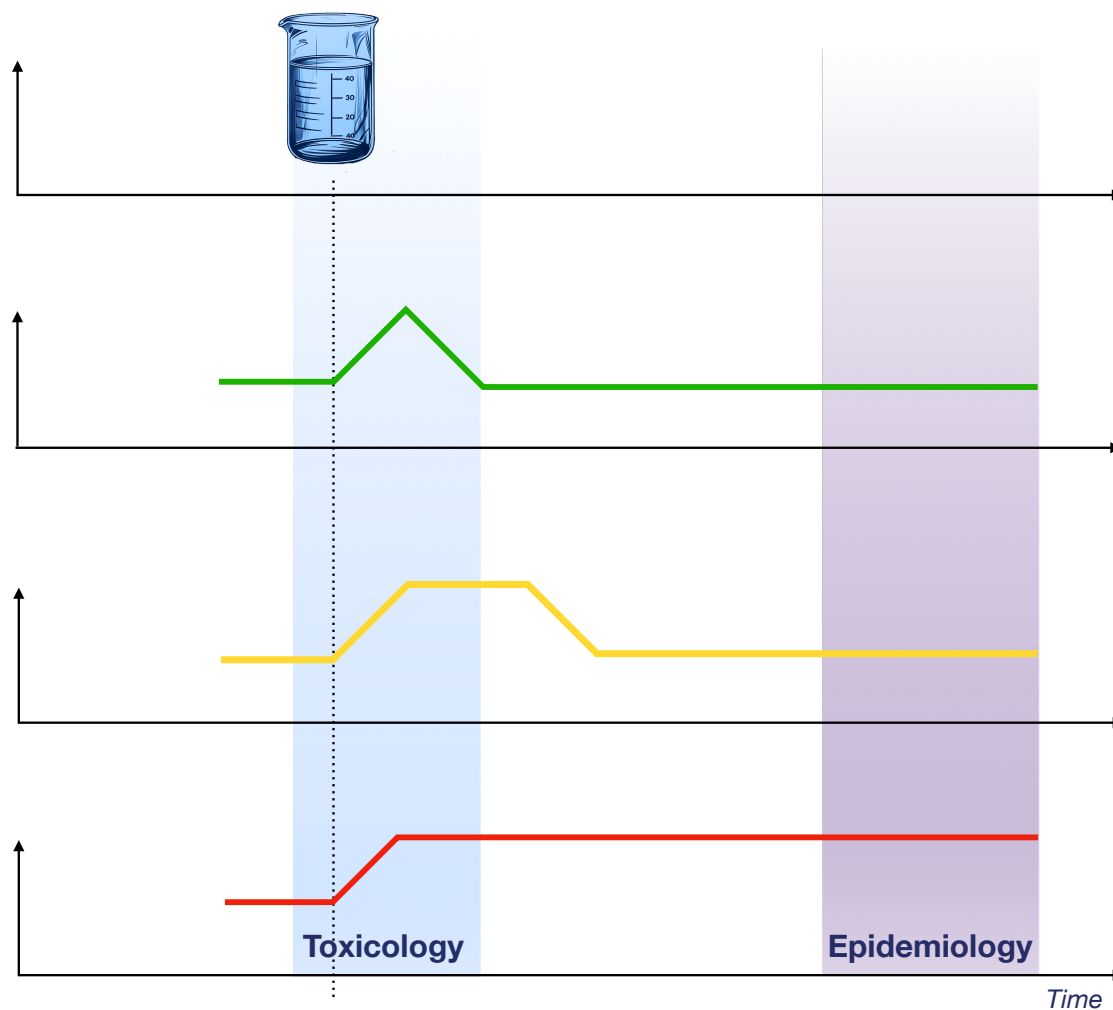


Kim et al., DOI: 10.1016/j.molp.2016.04.017

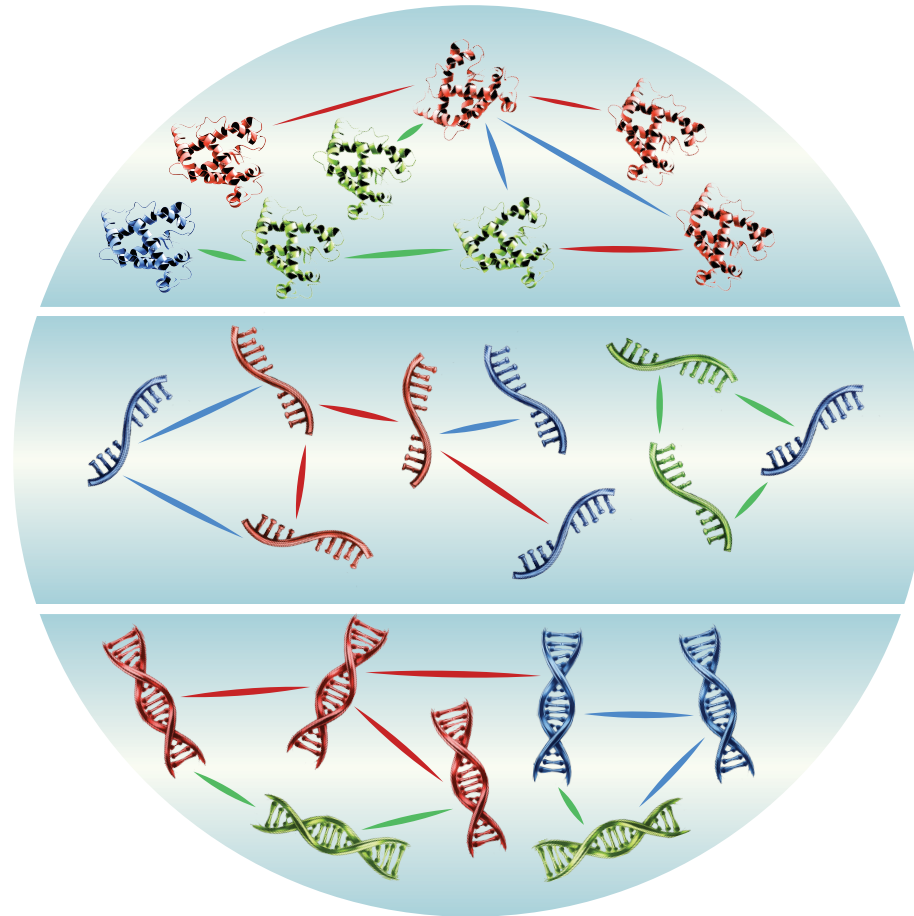
Predicting the future vs retrospective analysis



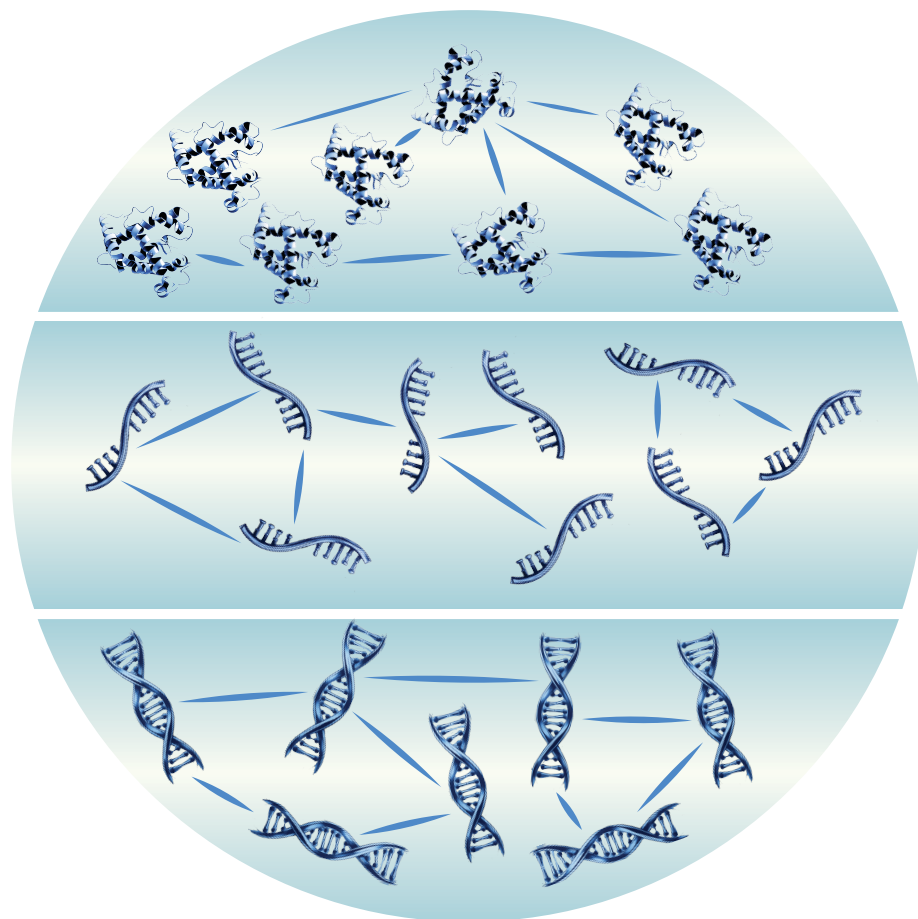
Acute vs long-term effects



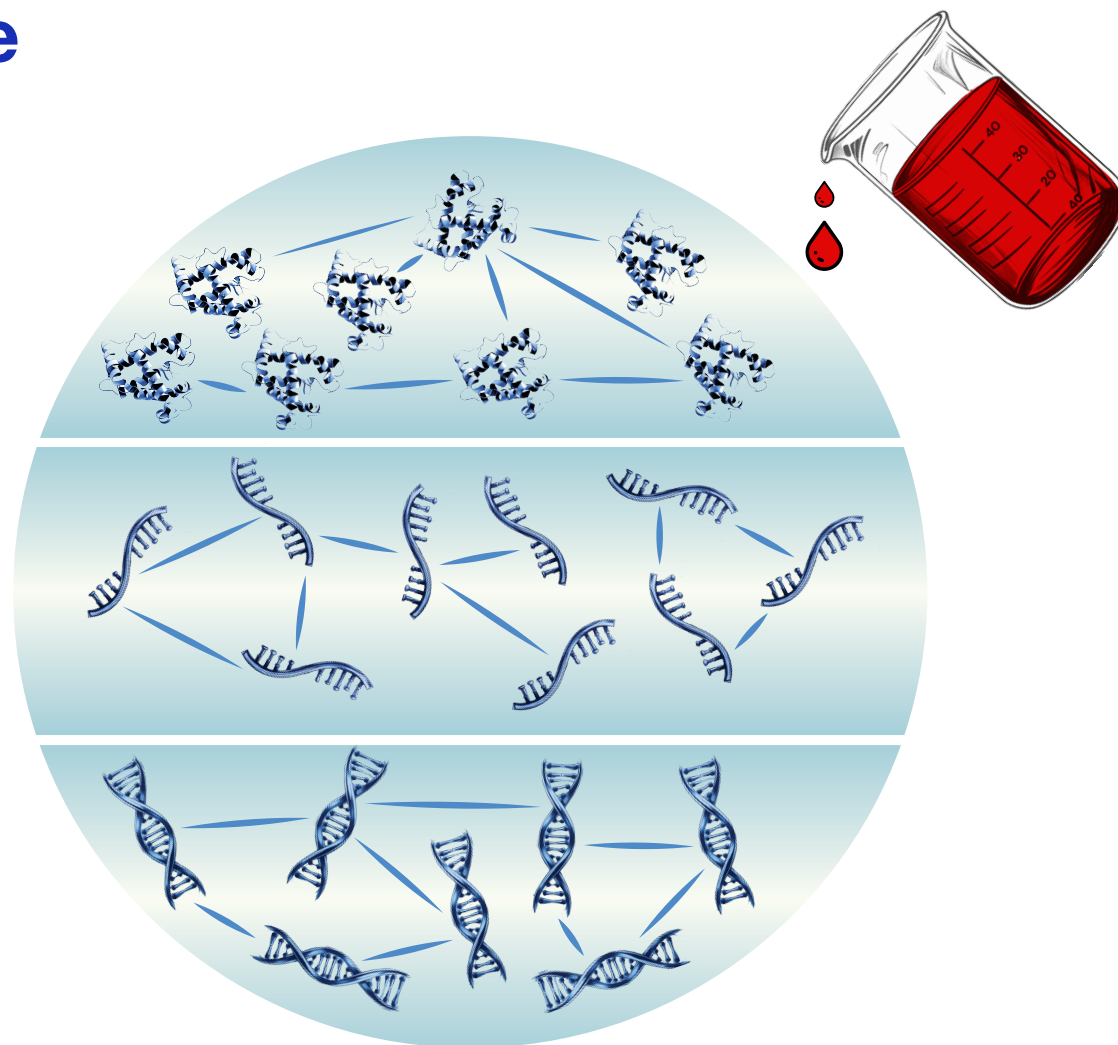
Multiple overlapping signatures



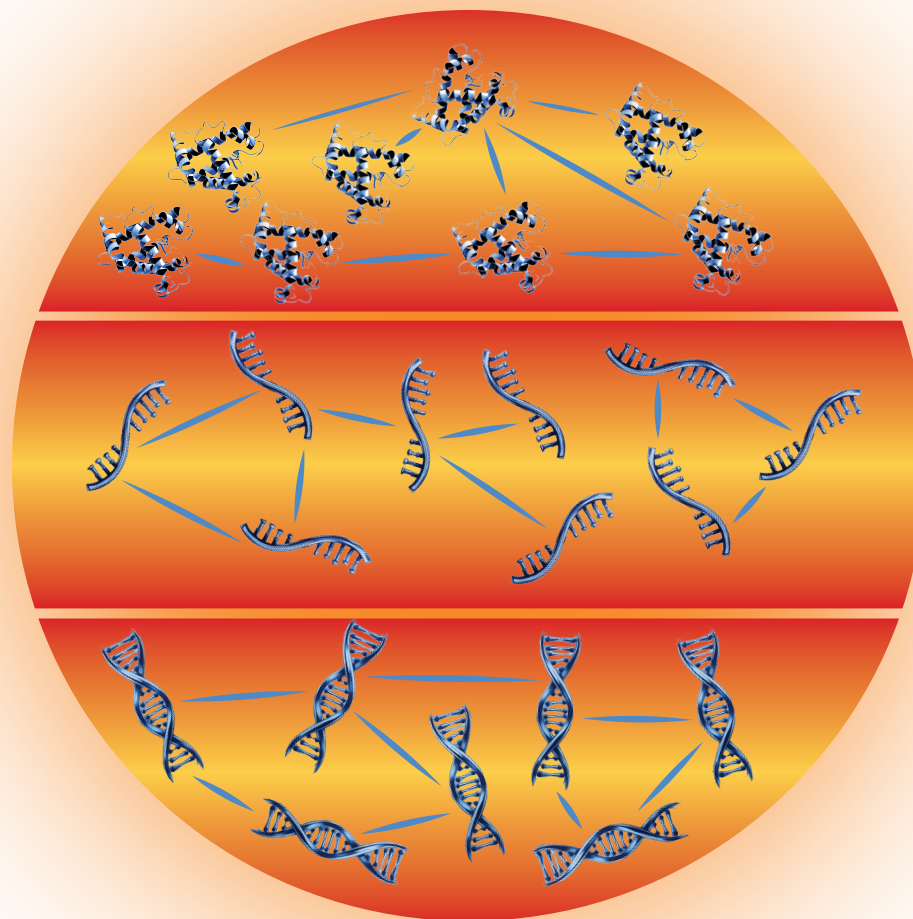
Initial steady state



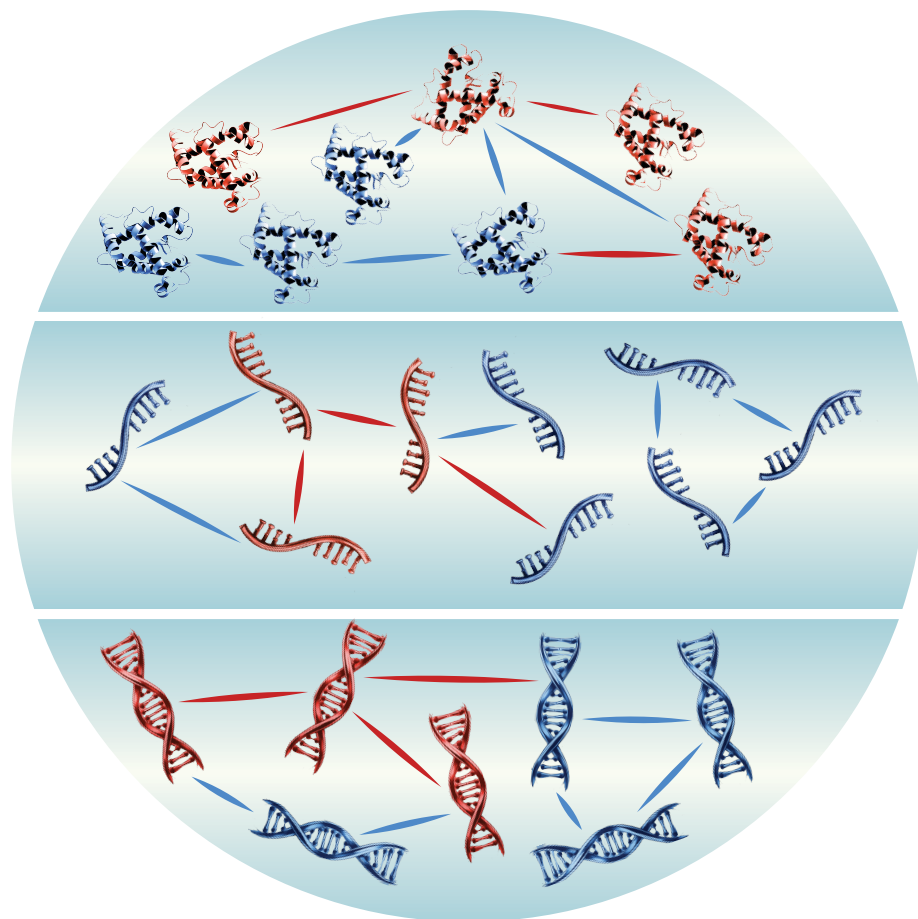
Earlier exposure



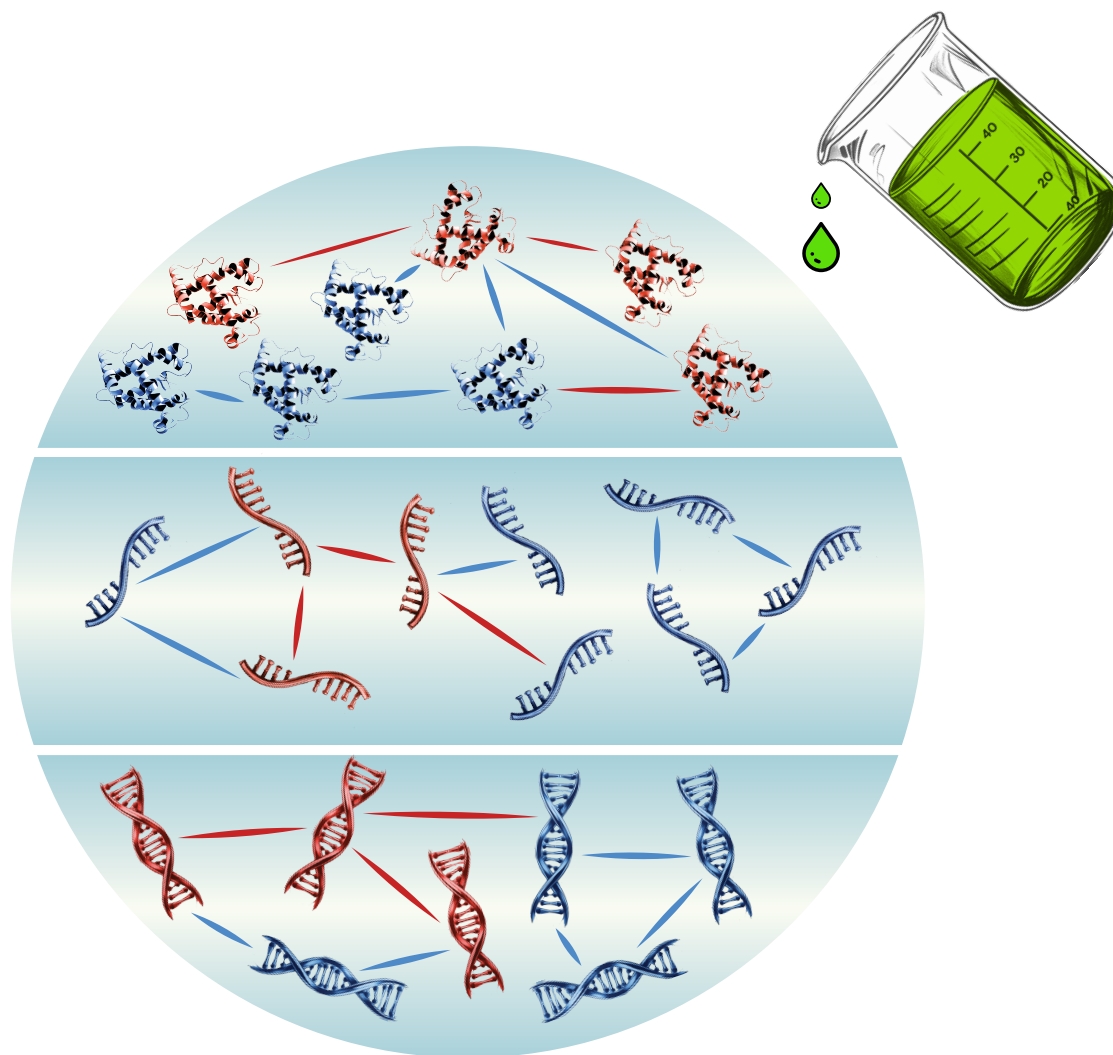
Response to earlier exposure



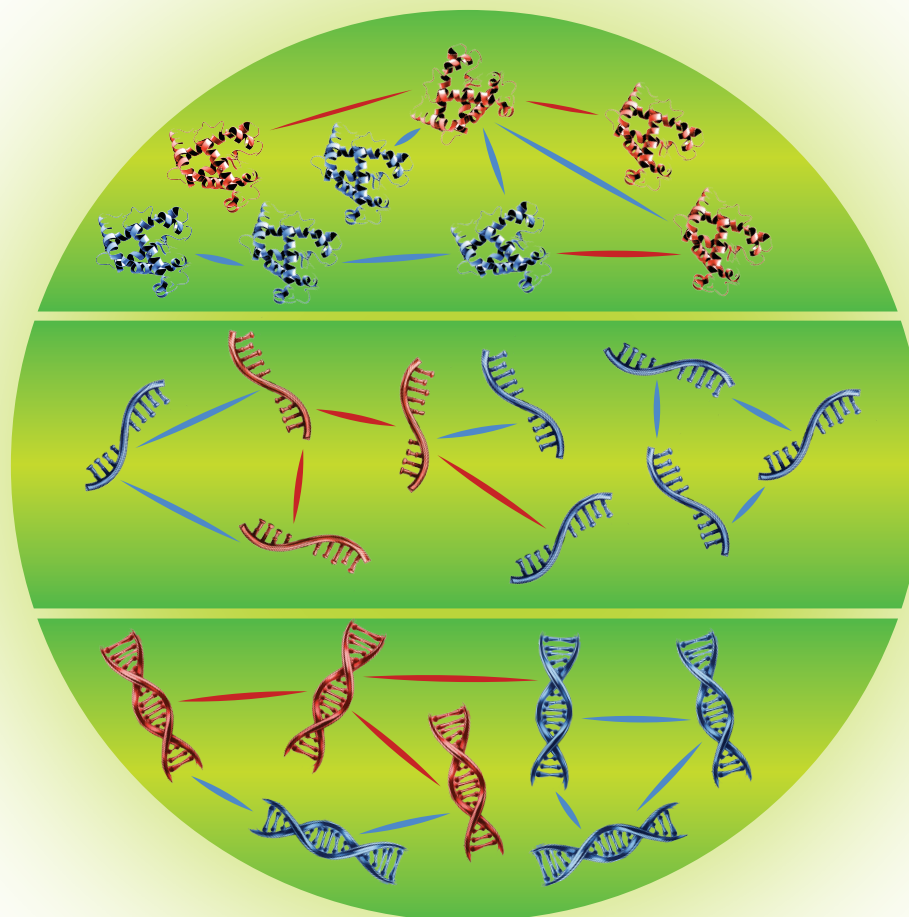
New steady state



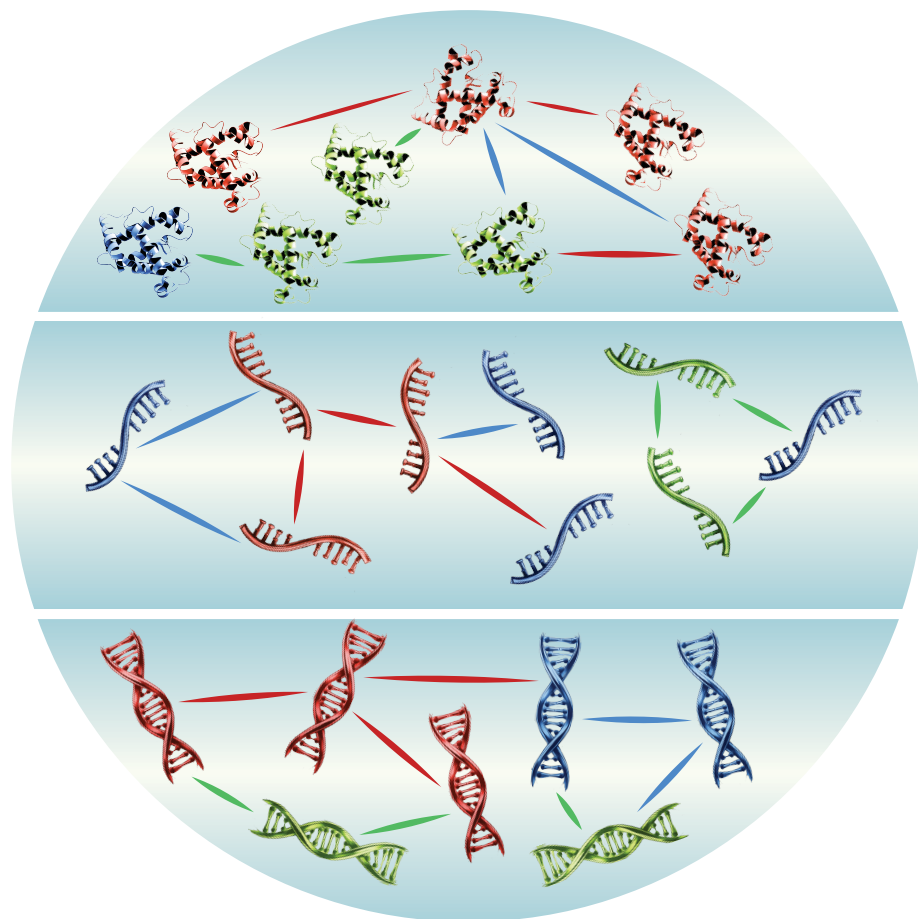
Later exposure

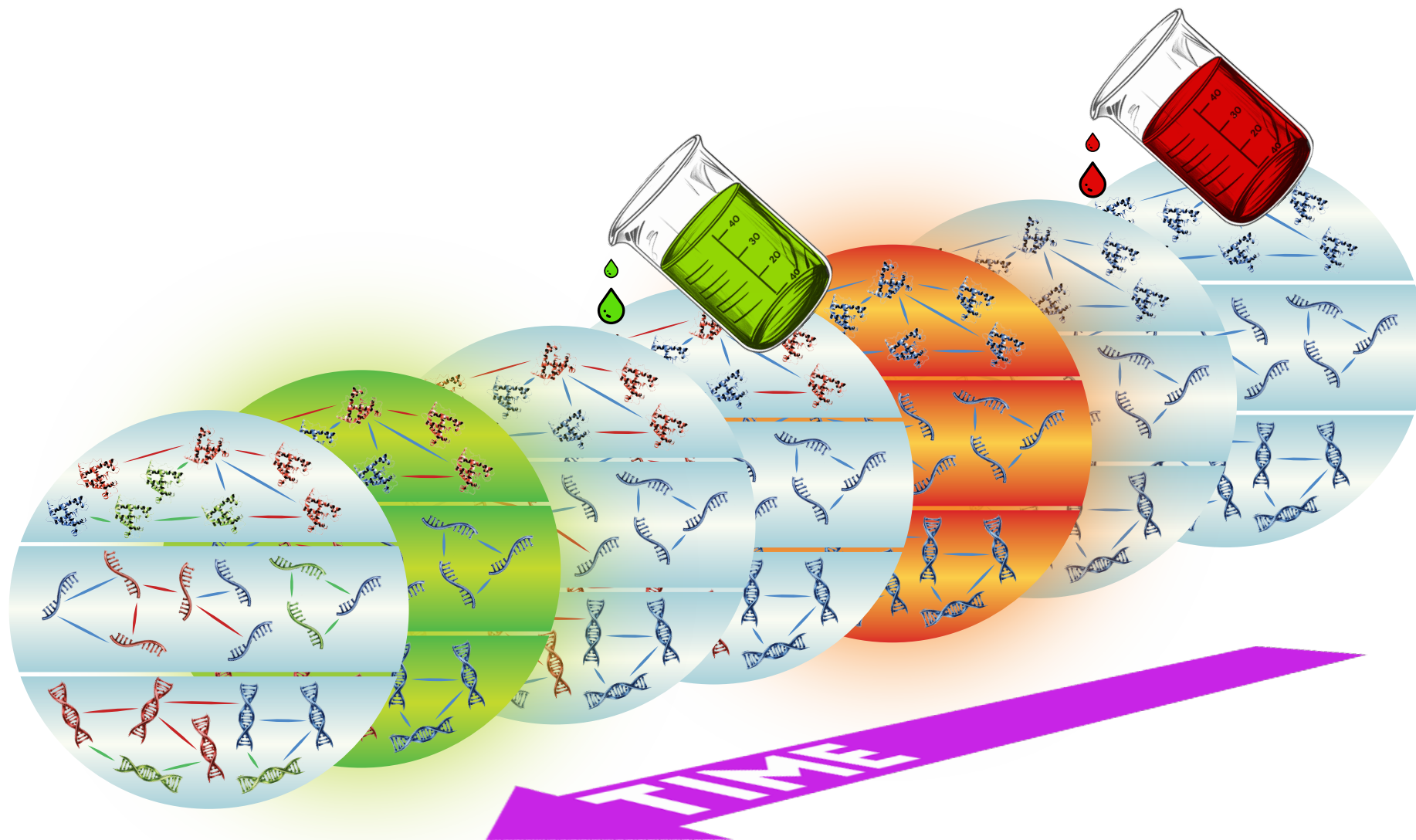


Response to later exposure



New steady state







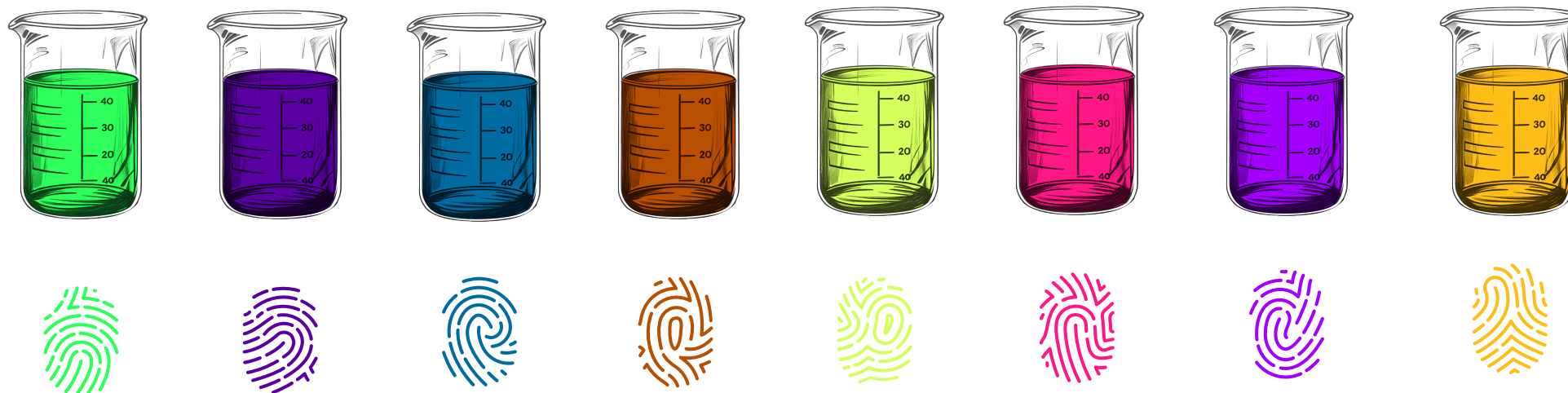
One chemical - one signature



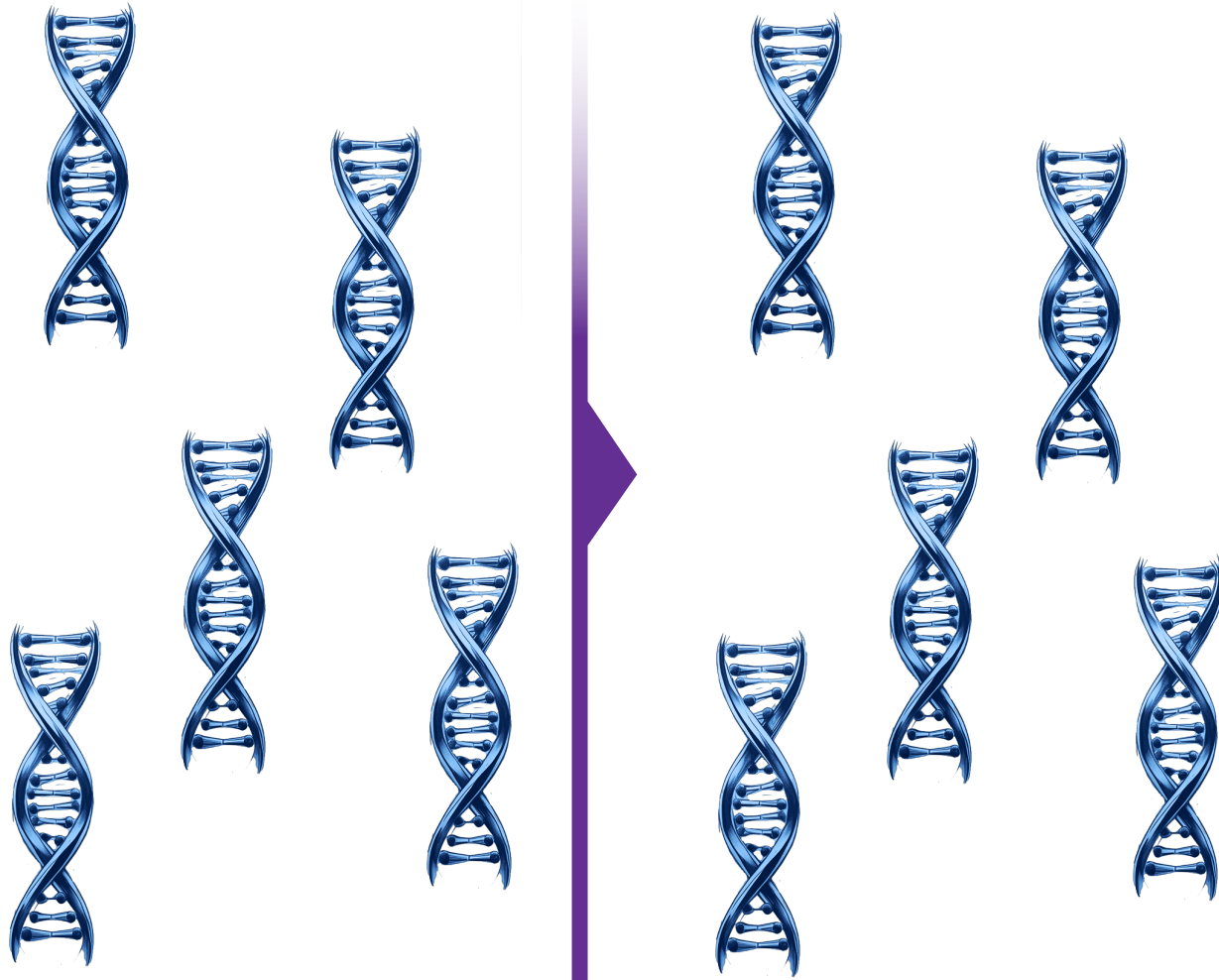
One exposure - one signature paradigm



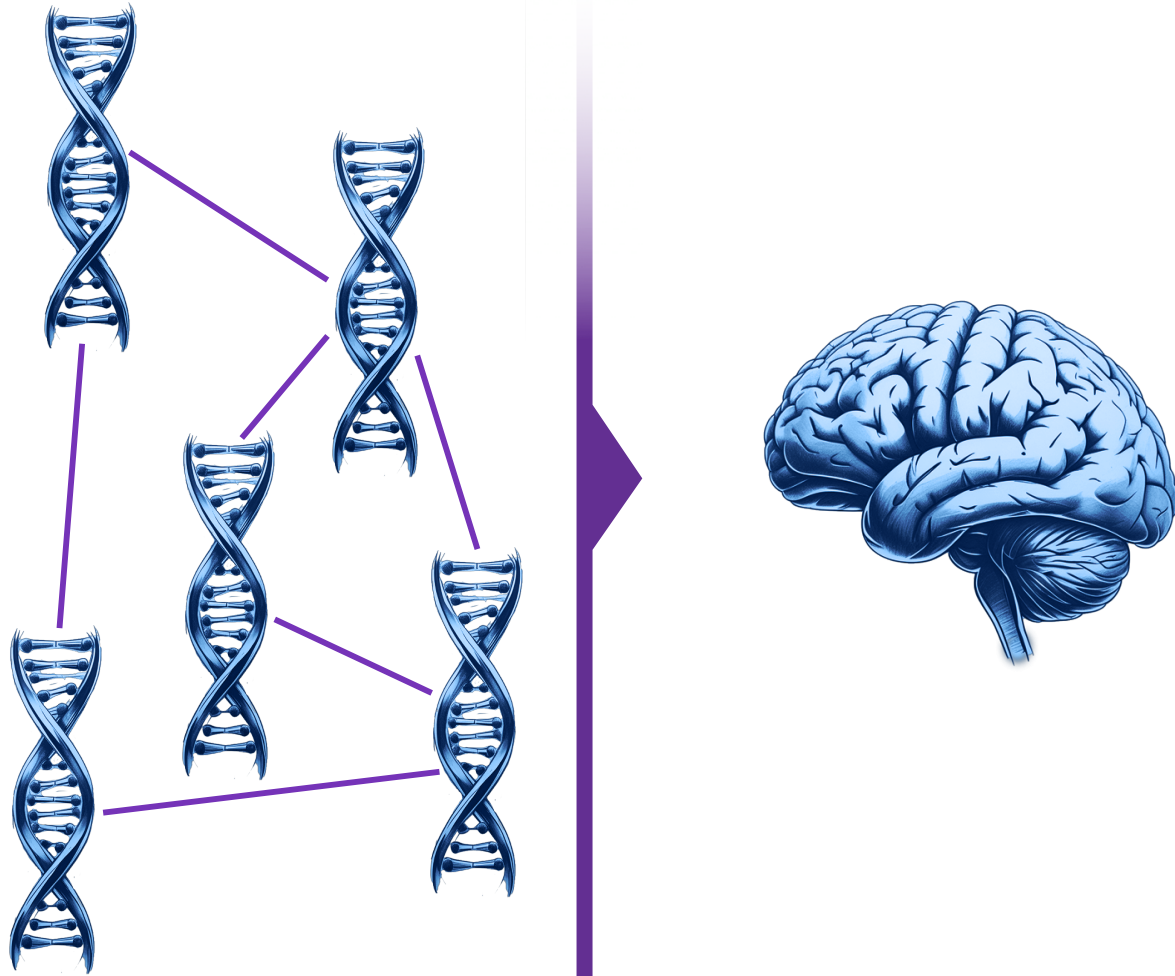
One exposure - one signature paradigm



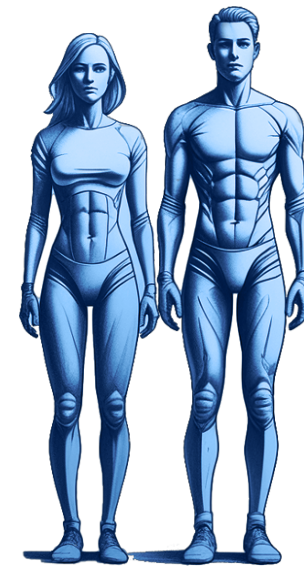
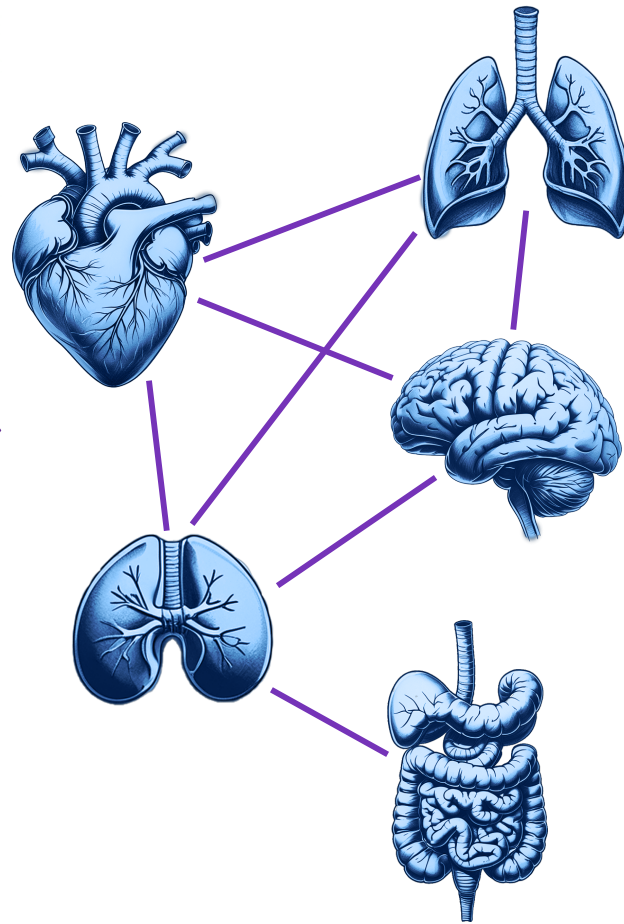
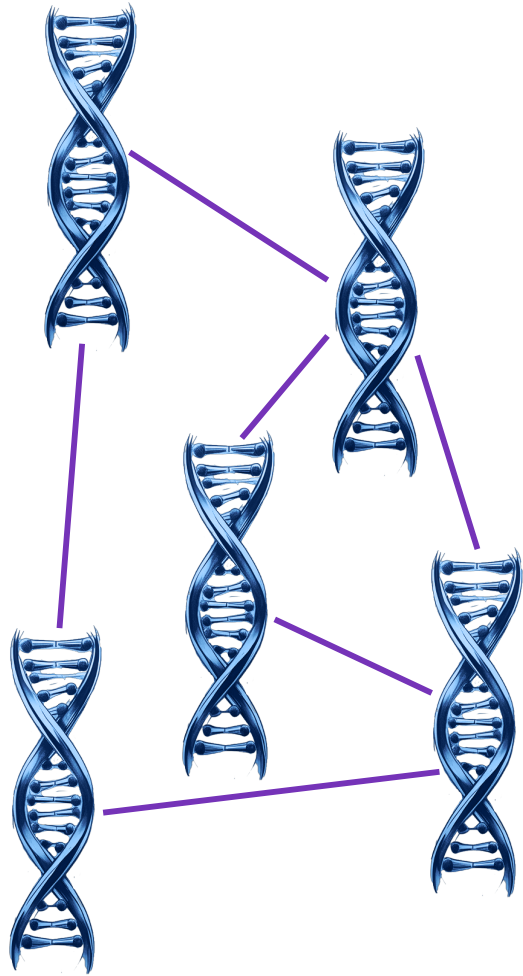
Gene lists will remain gene lists



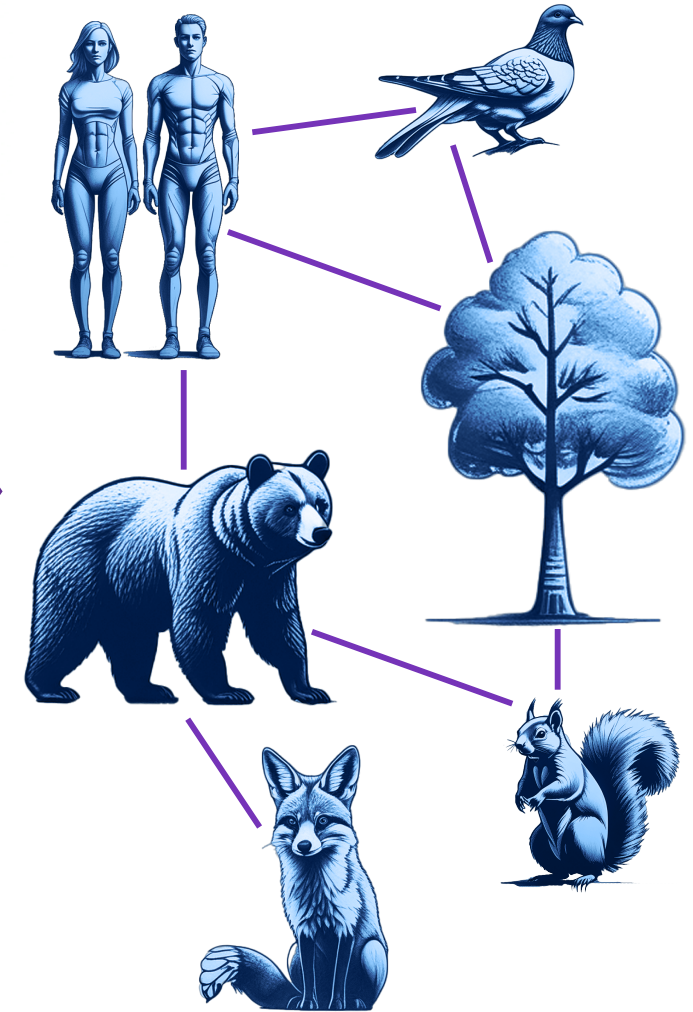
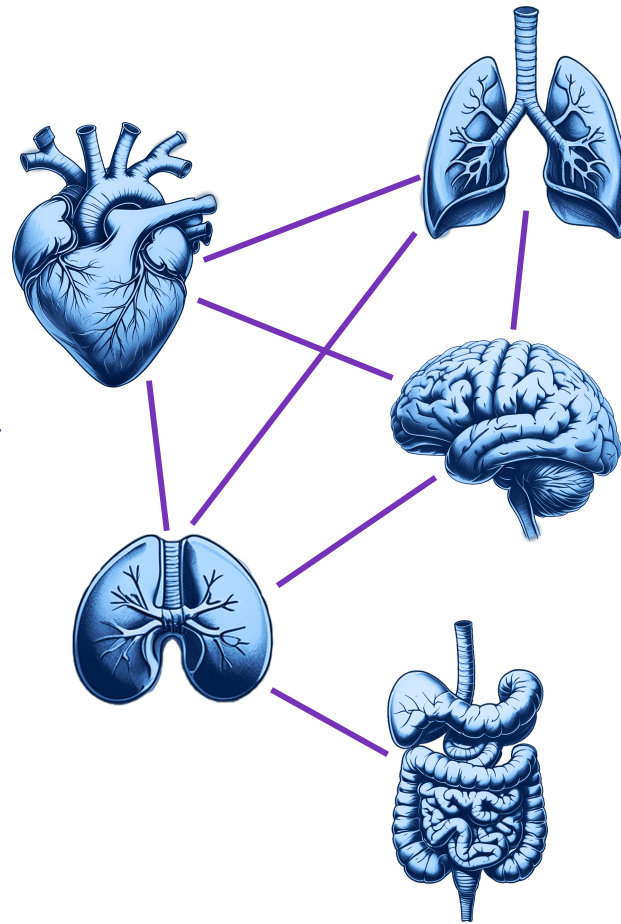
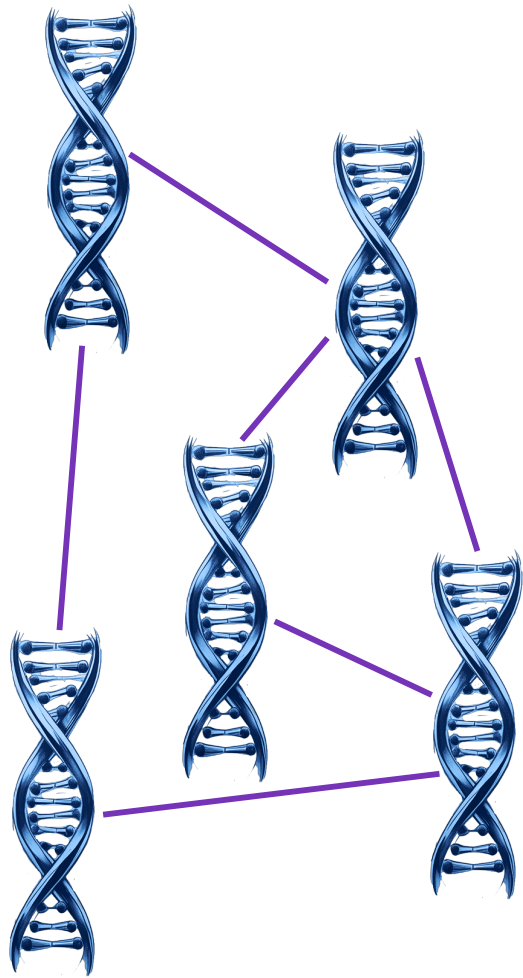
Interactions imply emerging complexity



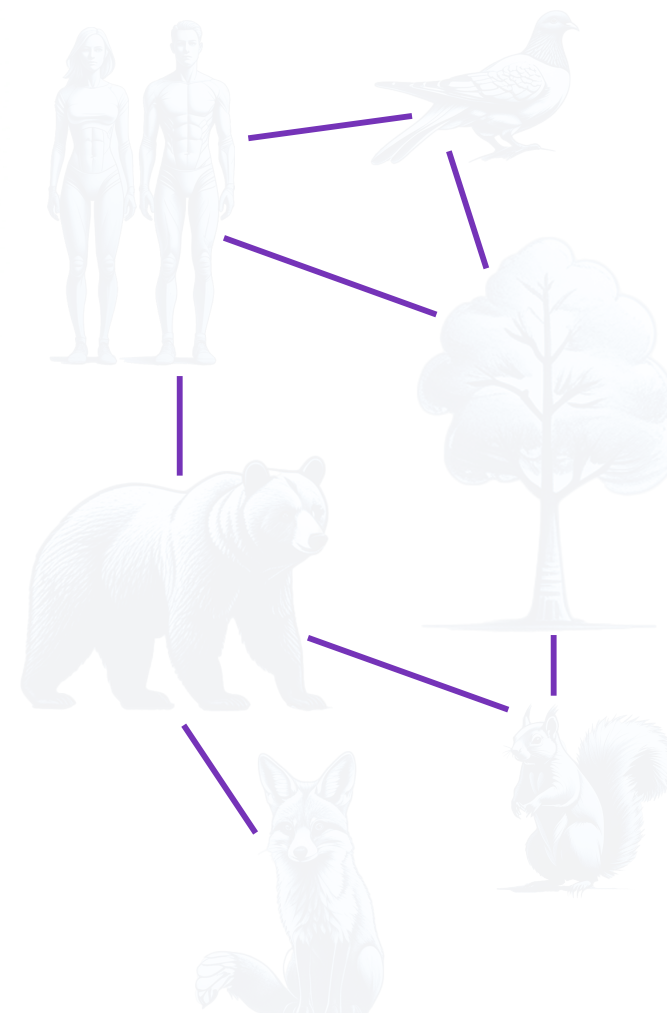
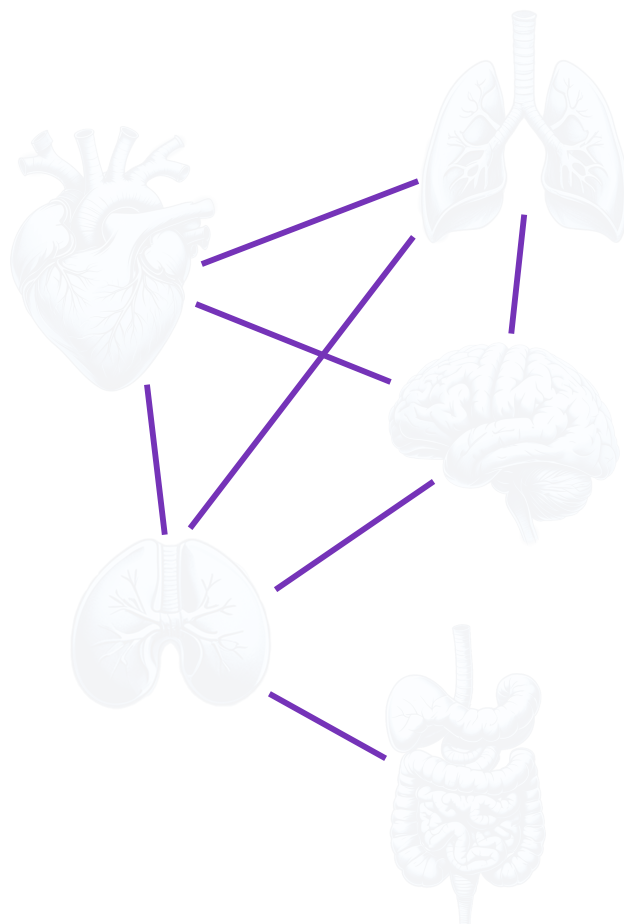
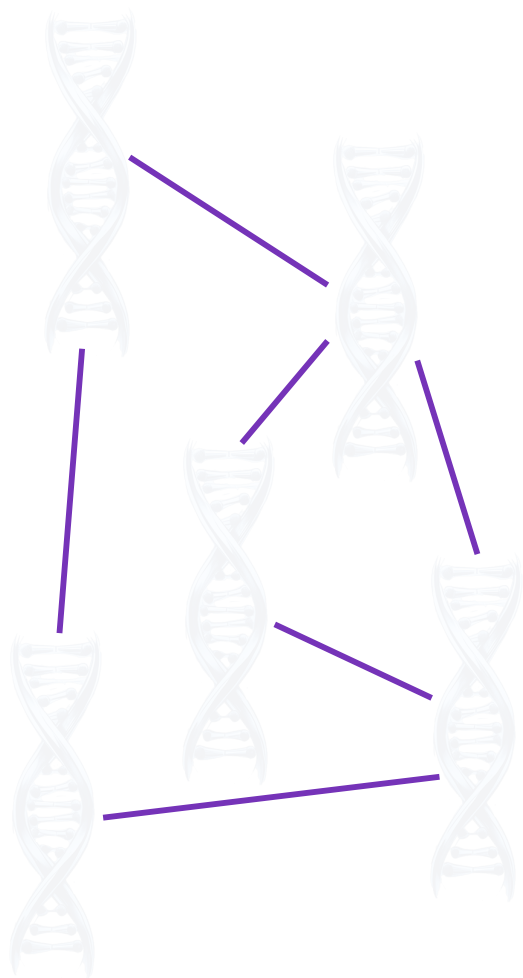
Interactions imply emerging complexity



Interactions imply emerging complexity



Focus on the fabric of life!





**Molecular networks are
highly conserved in the evolution**



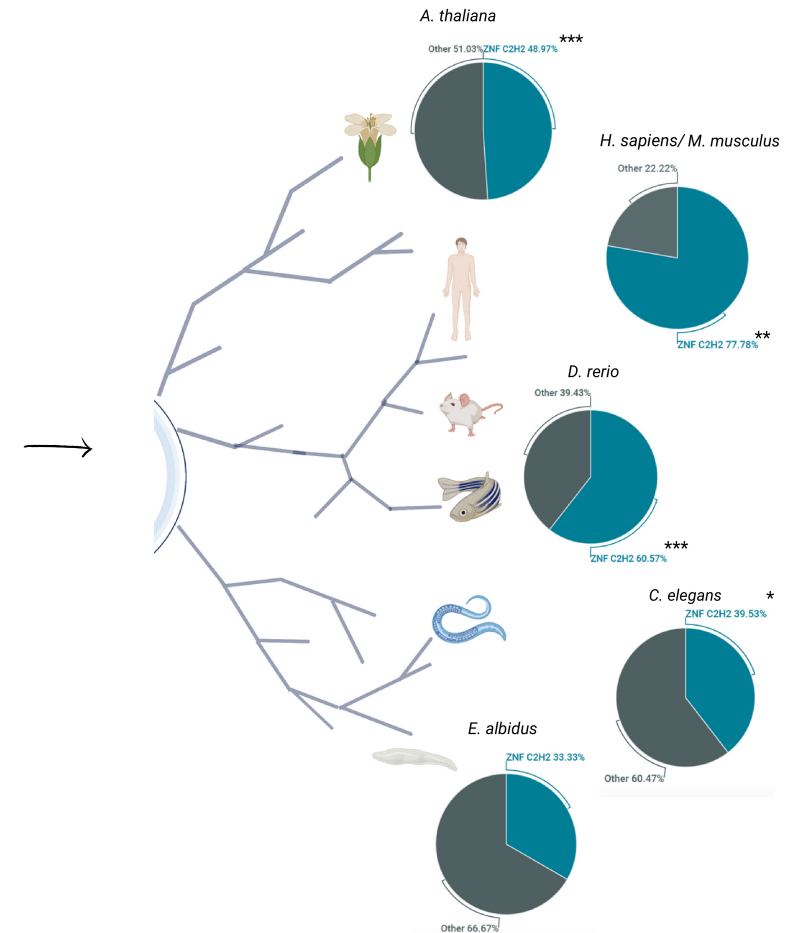
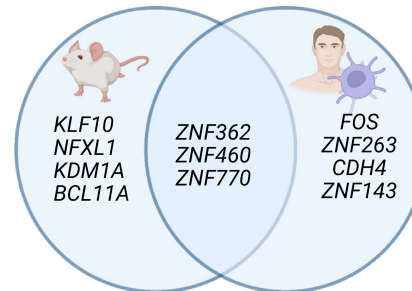
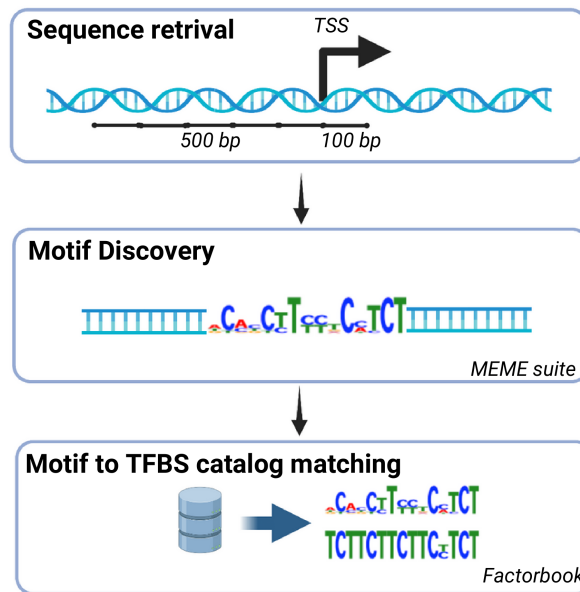
Response to nanomaterials in multiple species



Over 150 NM exposures across multiple biological systems



First One Health model of nano-bio interactions



del Giudice *et al.*, Nature Nanotech 2023



**Data can be connected
to form large networks**



Knowledge Graph as learning platform

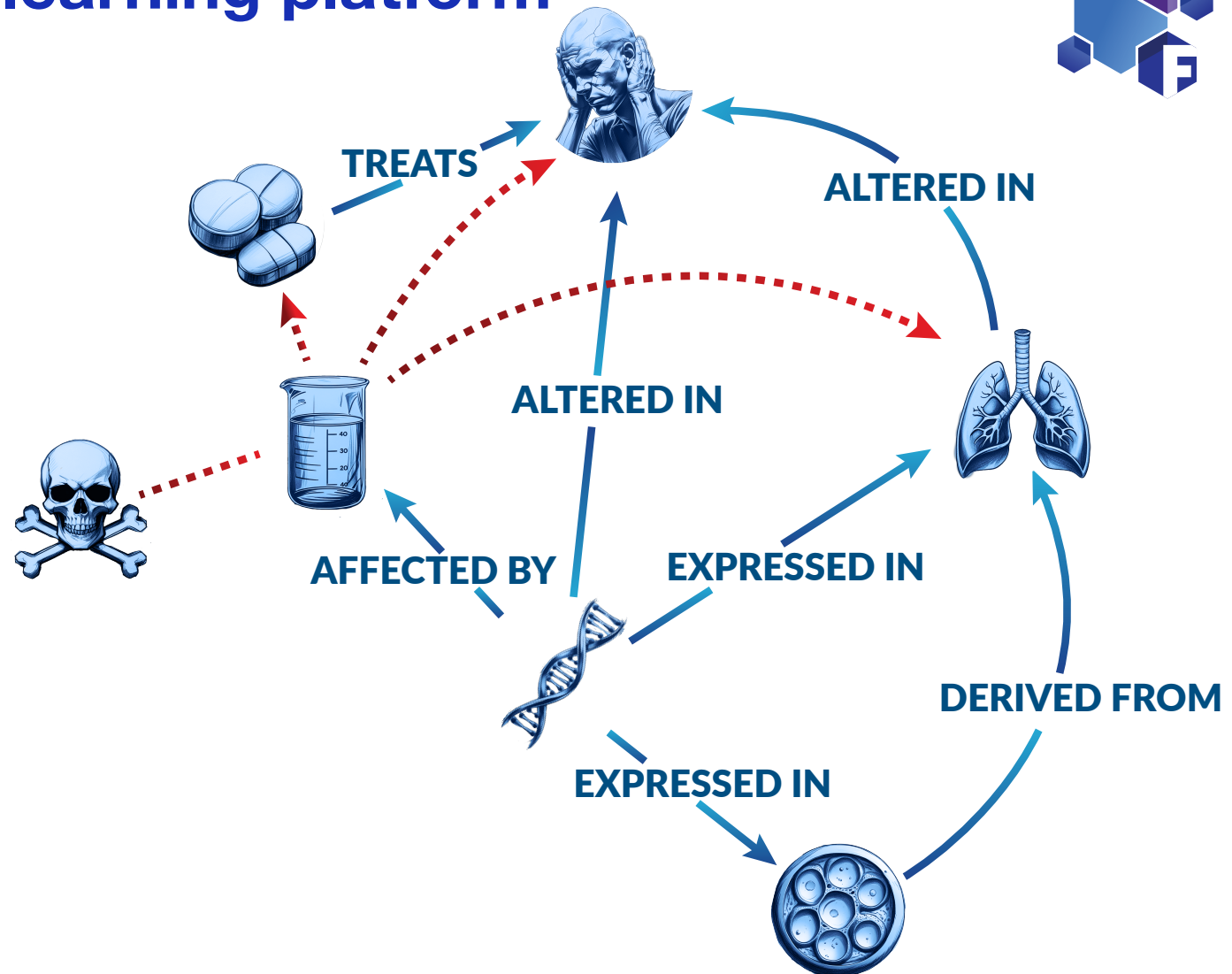


AI-based prediction of:

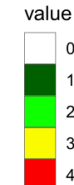
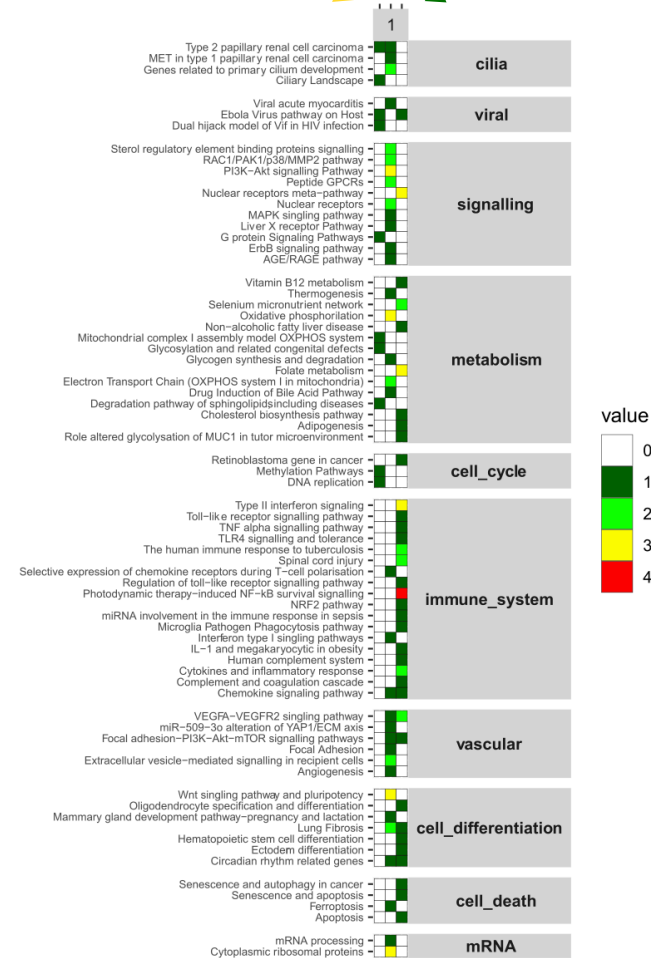
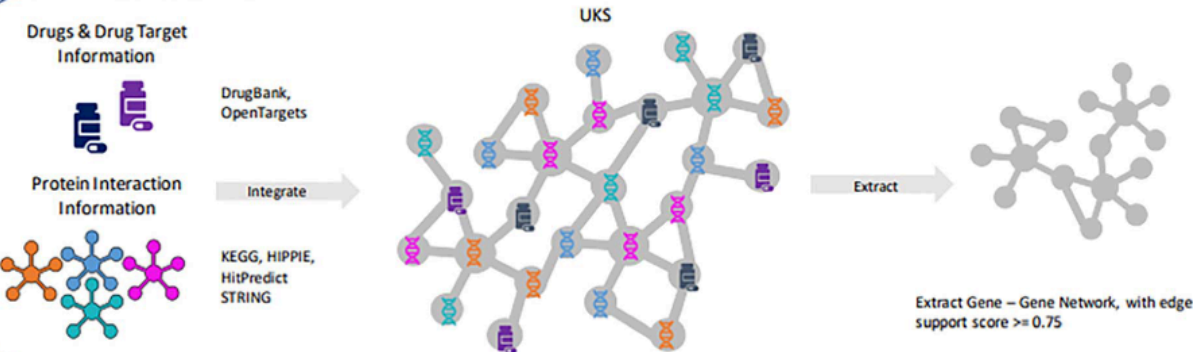
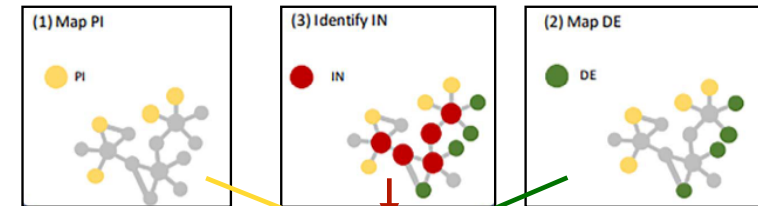
- Node properties
- New connections

UKS at FHAIVE:

- Over 70M data points
- Over 50 curated databases
- Over 80 curated datasets



Knowledge Graph for COVID-19





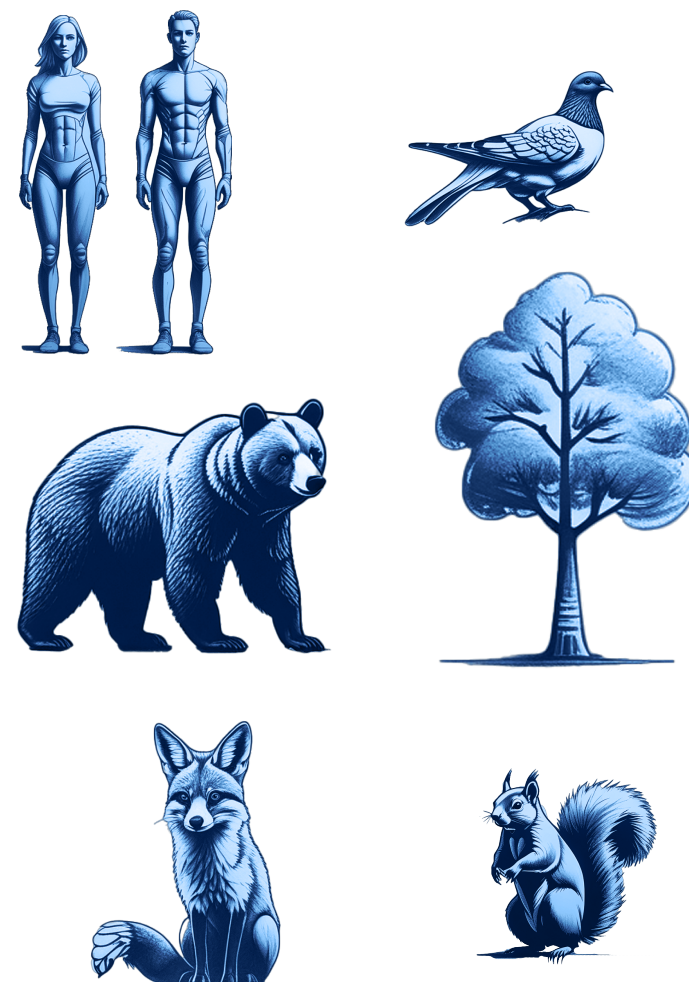
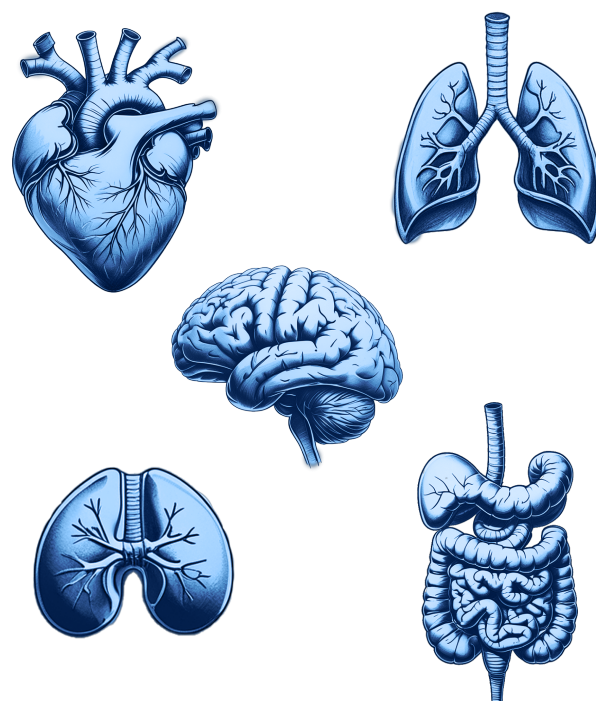
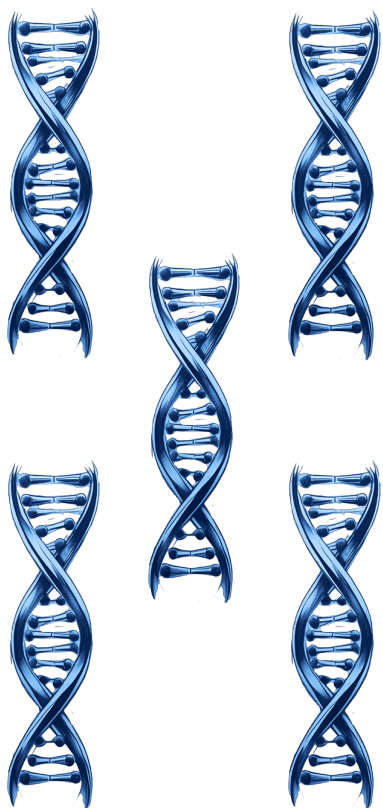
Multiscale modeling in spacetime



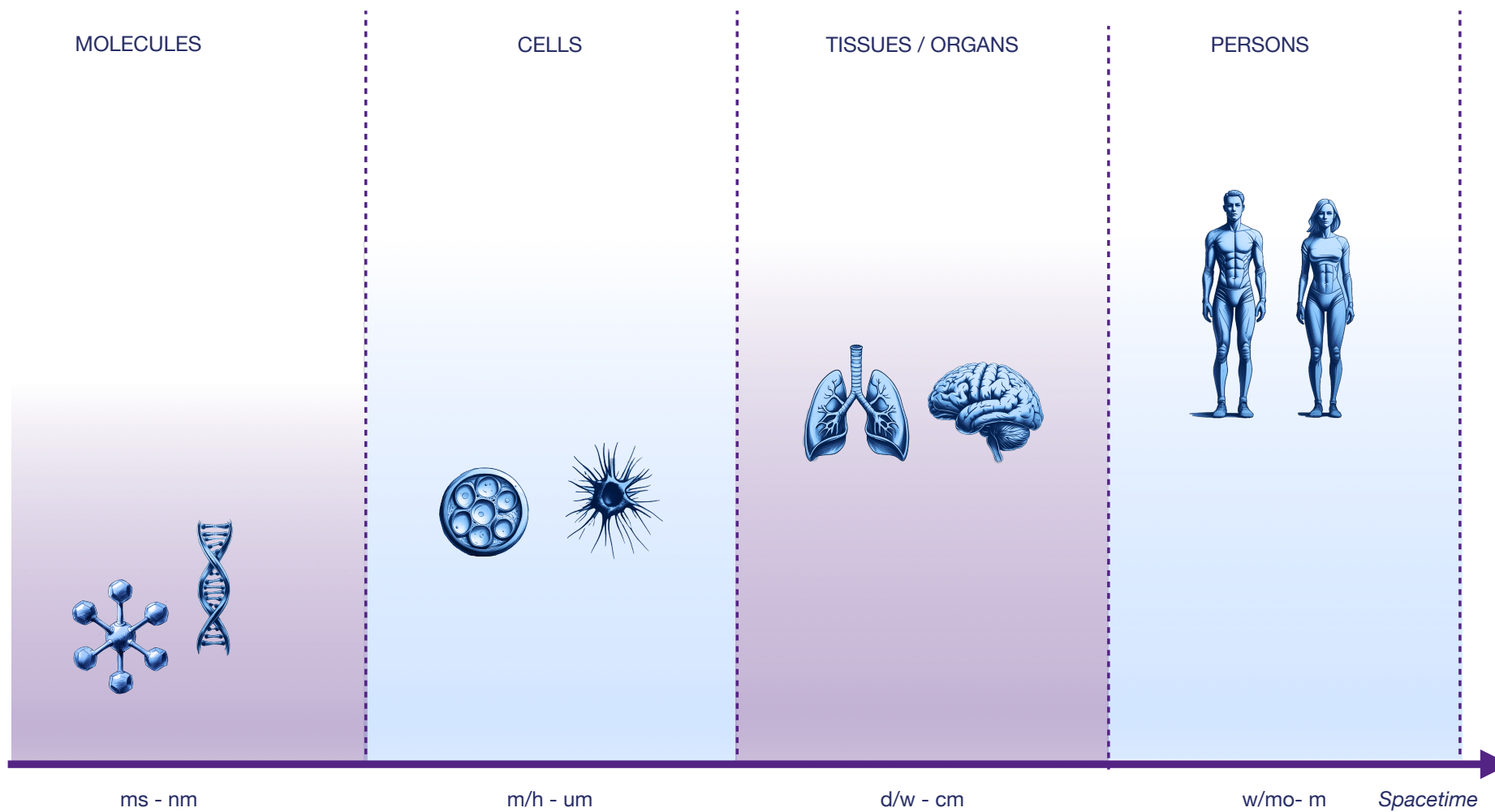
Spacetime travel



Multiscale chemical-biological interactions



Spacetime in toxicology

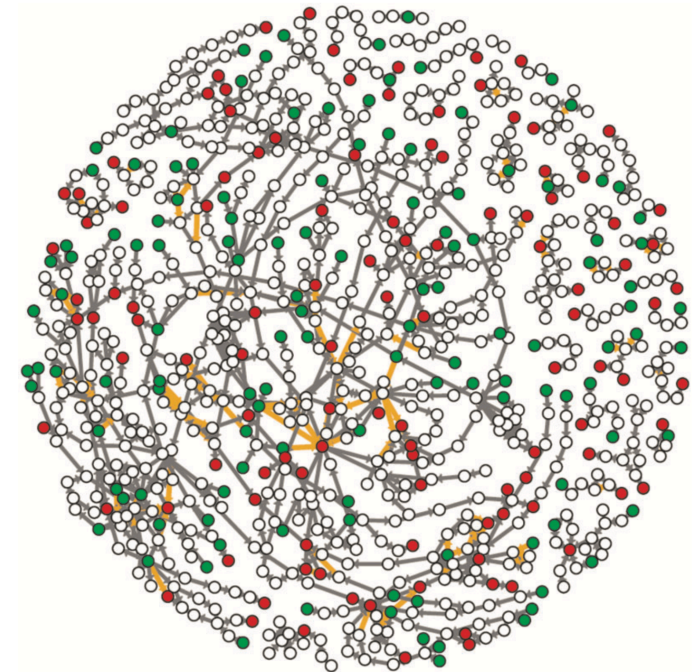
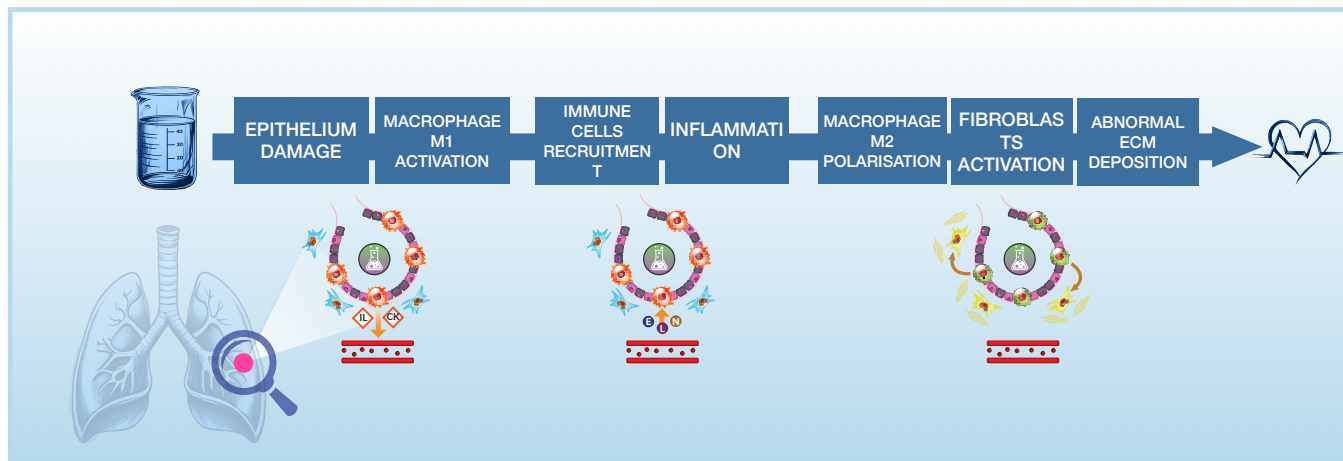


AOP / TOP as mechanistic models in biomedicine

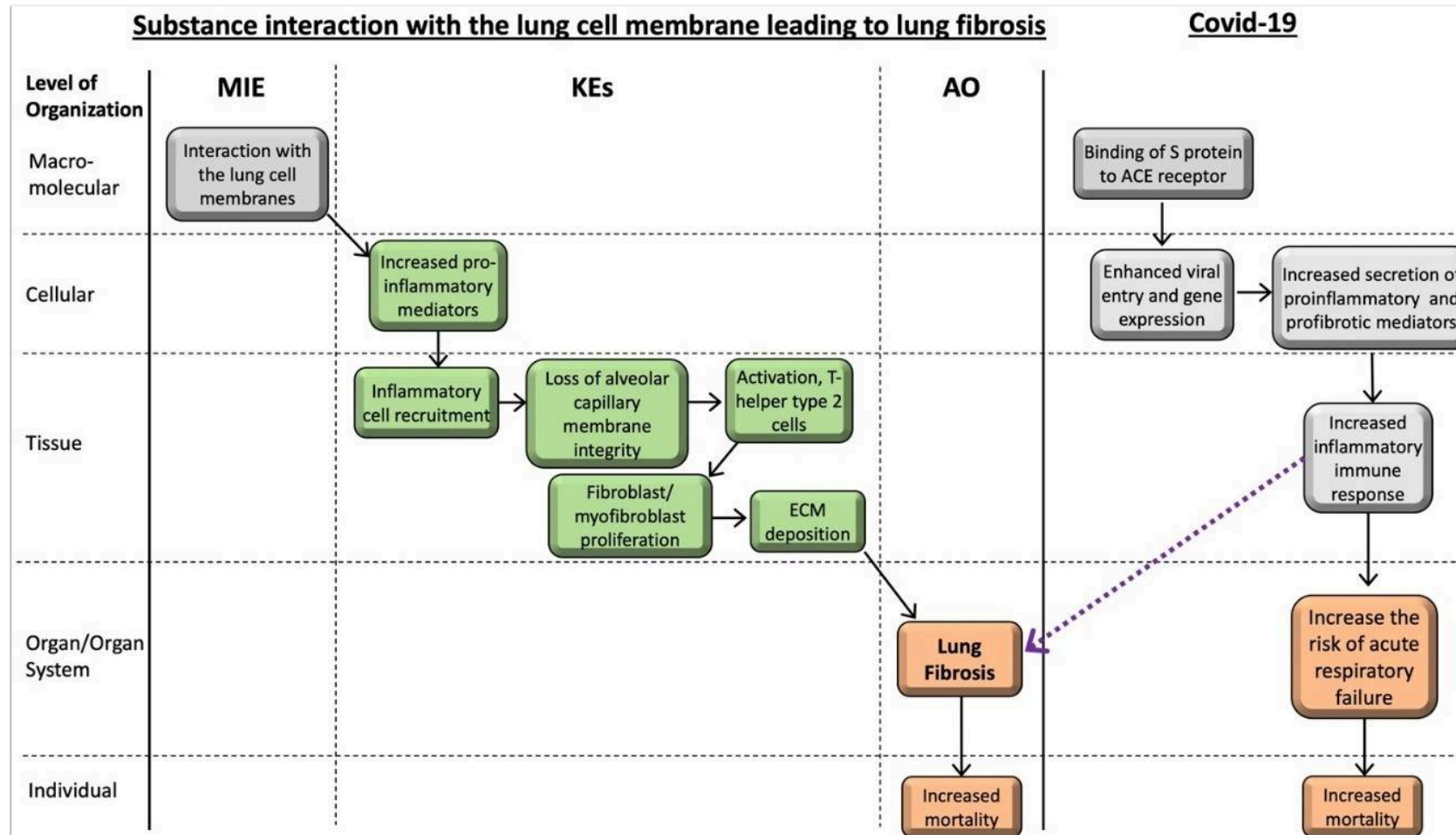


ADVERSE OUTCOME PATHWAYS (AOP)

- Multi-scale cause-effect models in biomedicine (chemicals, drugs, diseases)
- Chains of related key events
- OECD regulatory acceptance

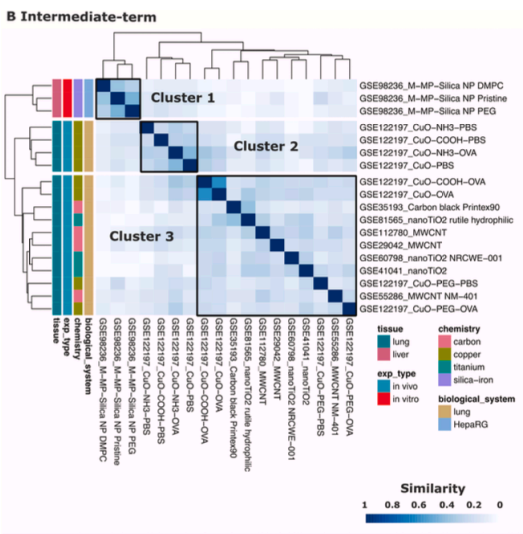
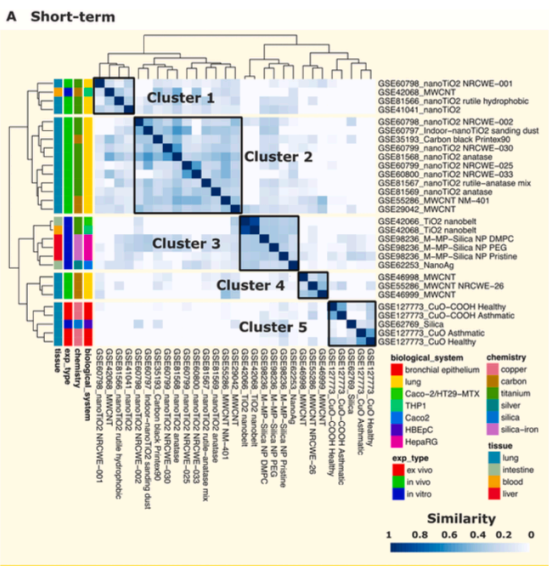
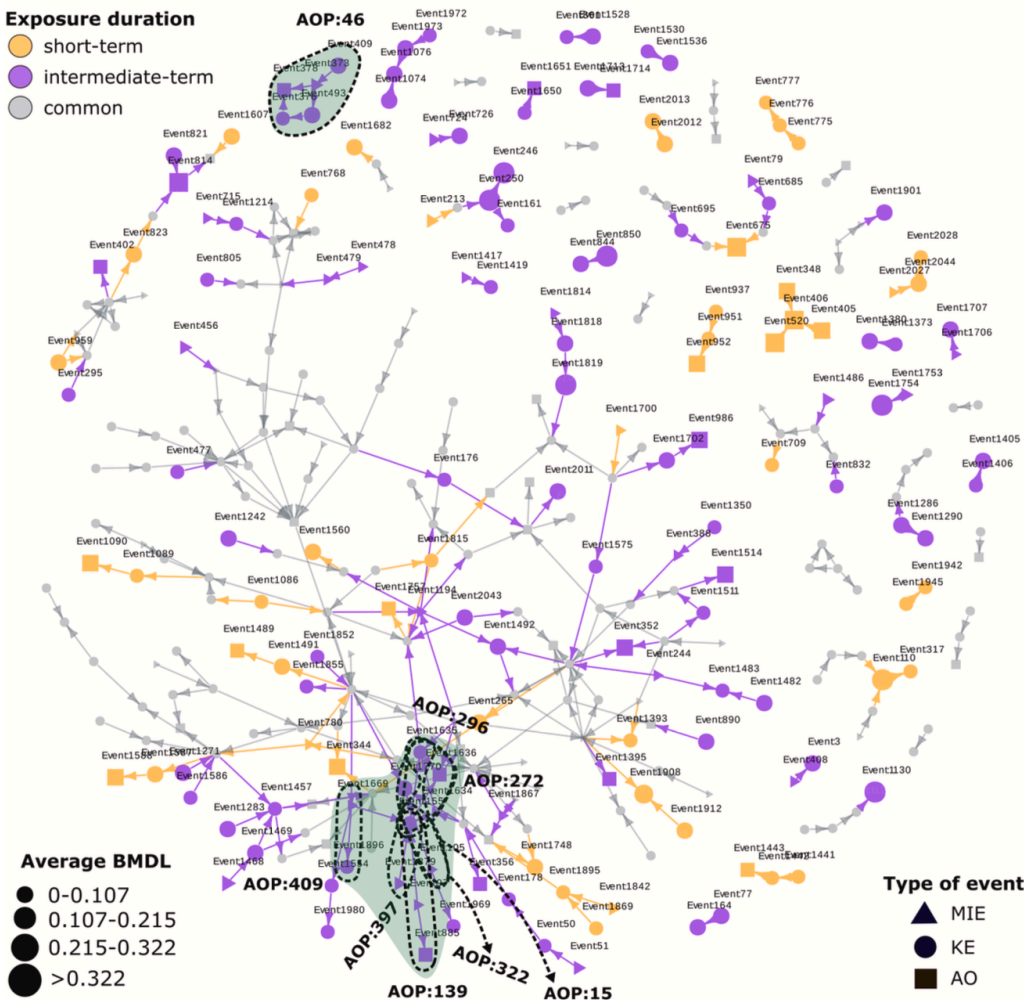


COVID-19 and lung fibrosis



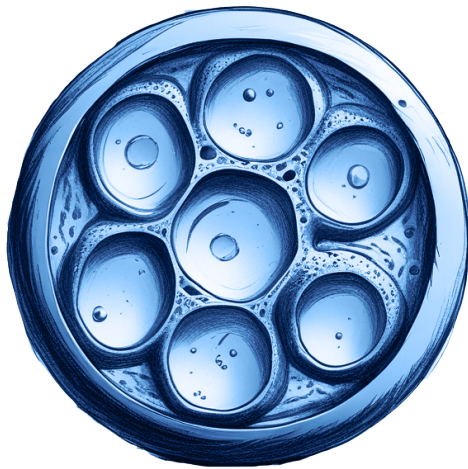
AOP-based NM grouping

- Specific functional effect**
- genotoxicity
- Exposure duration**
- short-term
 - intermediate-term
 - common



Torres Maia et al., Nano Today, 2025

Can we replace animal experiments with in vitro models?

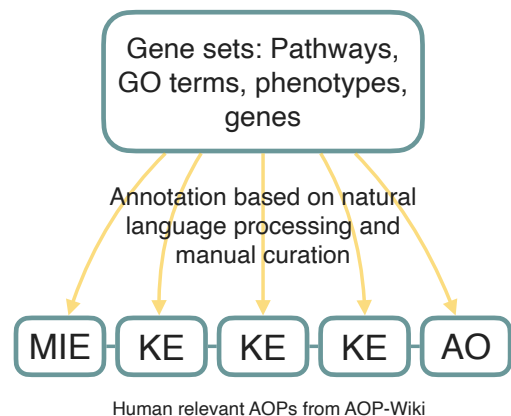


=



- More affordable
- Faster
- More ethical

AOP fingerprint for MWCNT exposure *in vitro* and *in vivo*

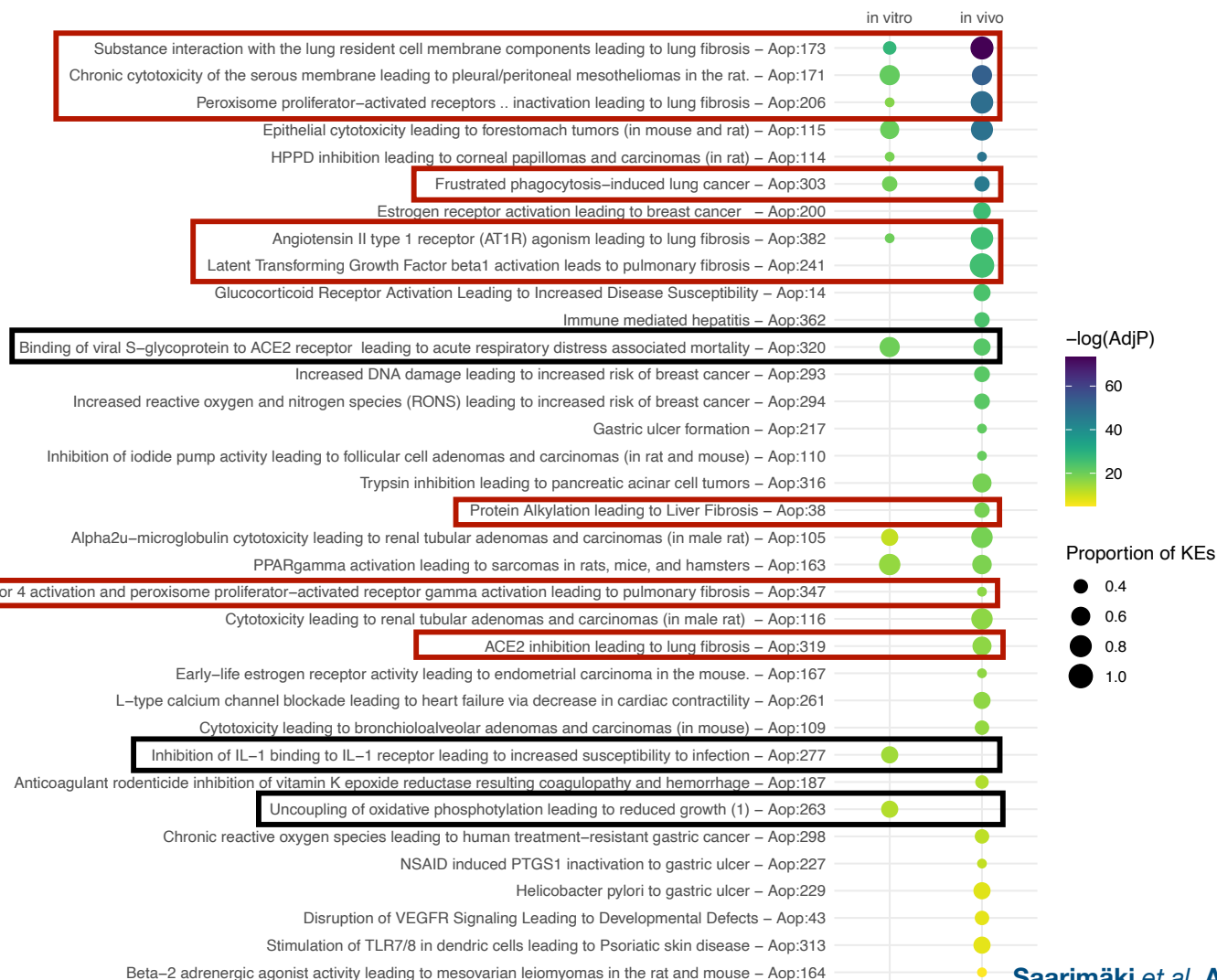


MWCNTs

Enrichment analysis

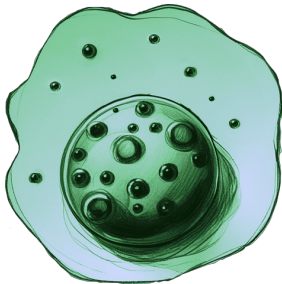
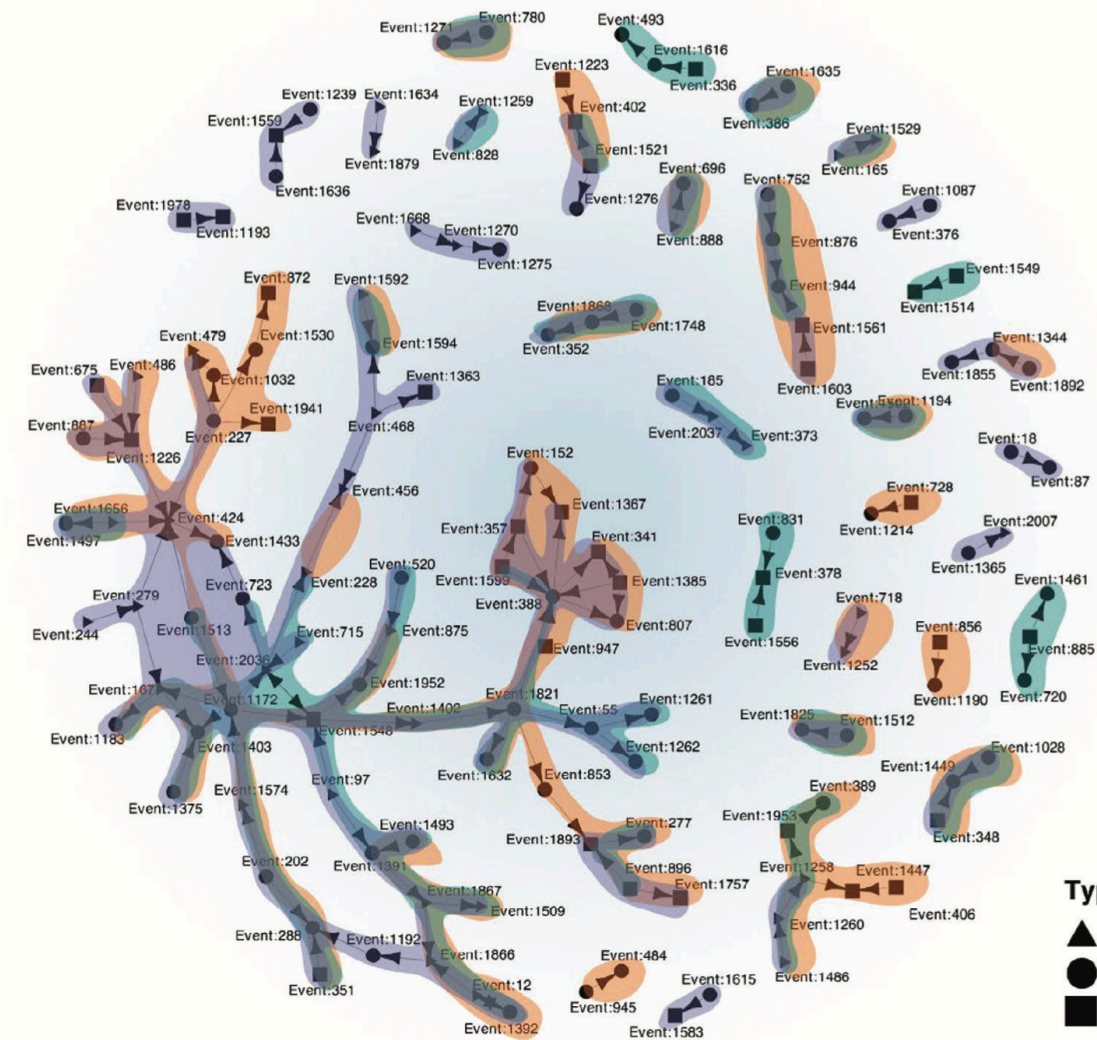
KEs AOPs

AOP
fingerprint



Saarimäki et al. Adv. Sci. 2023

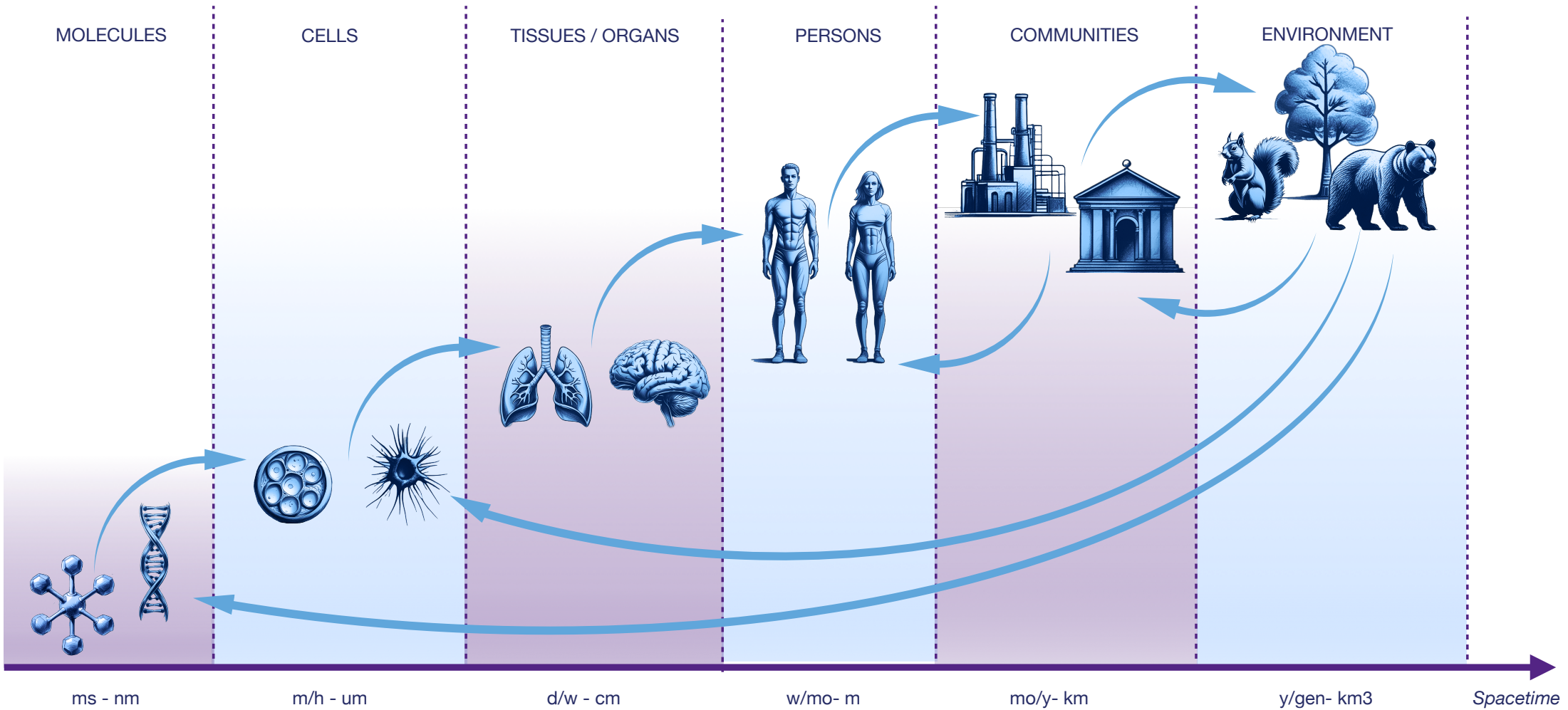
AOP-based applicability domain of TGx experiments



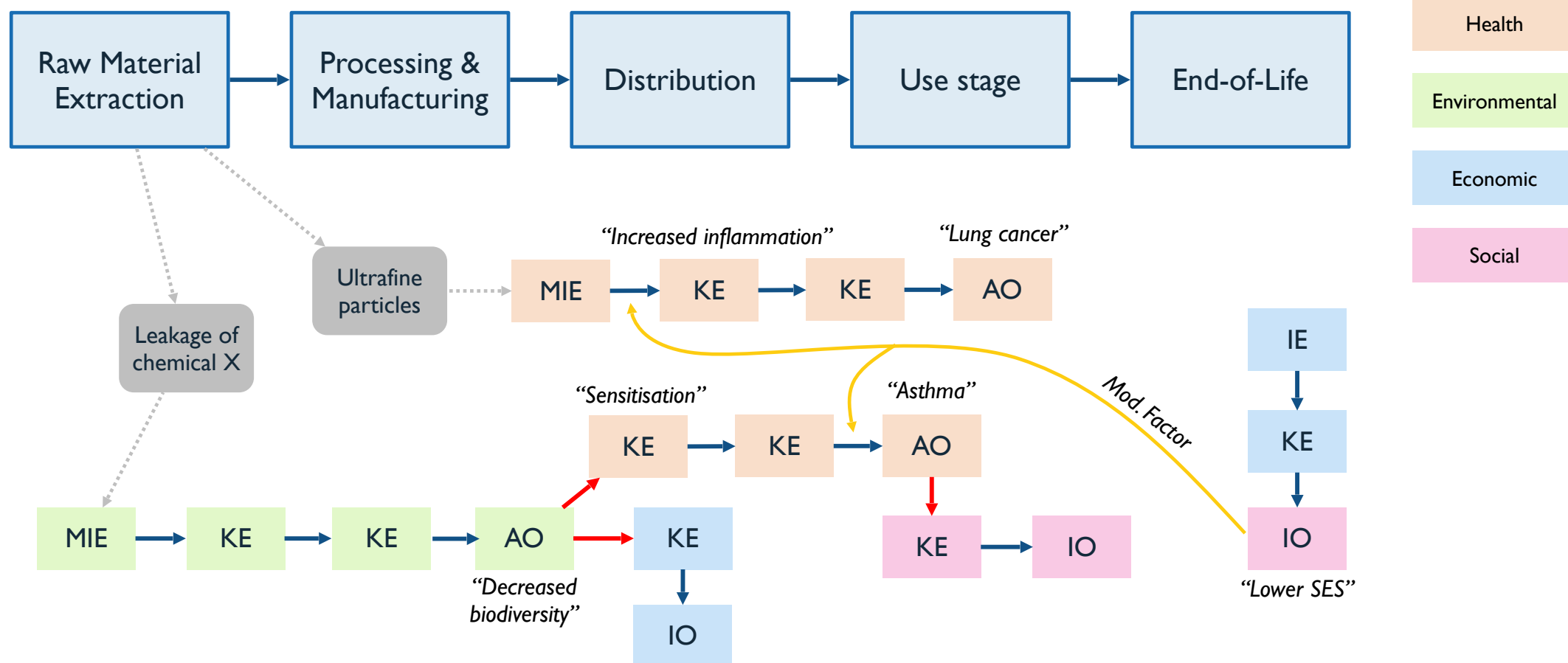
Type of Event	Biological system
▲ MIE	● Lung
● KE	● THP1
■ AO	● BEAS2B

del Giudice et al., Advanced Science 2024

Spacetime in SSbD

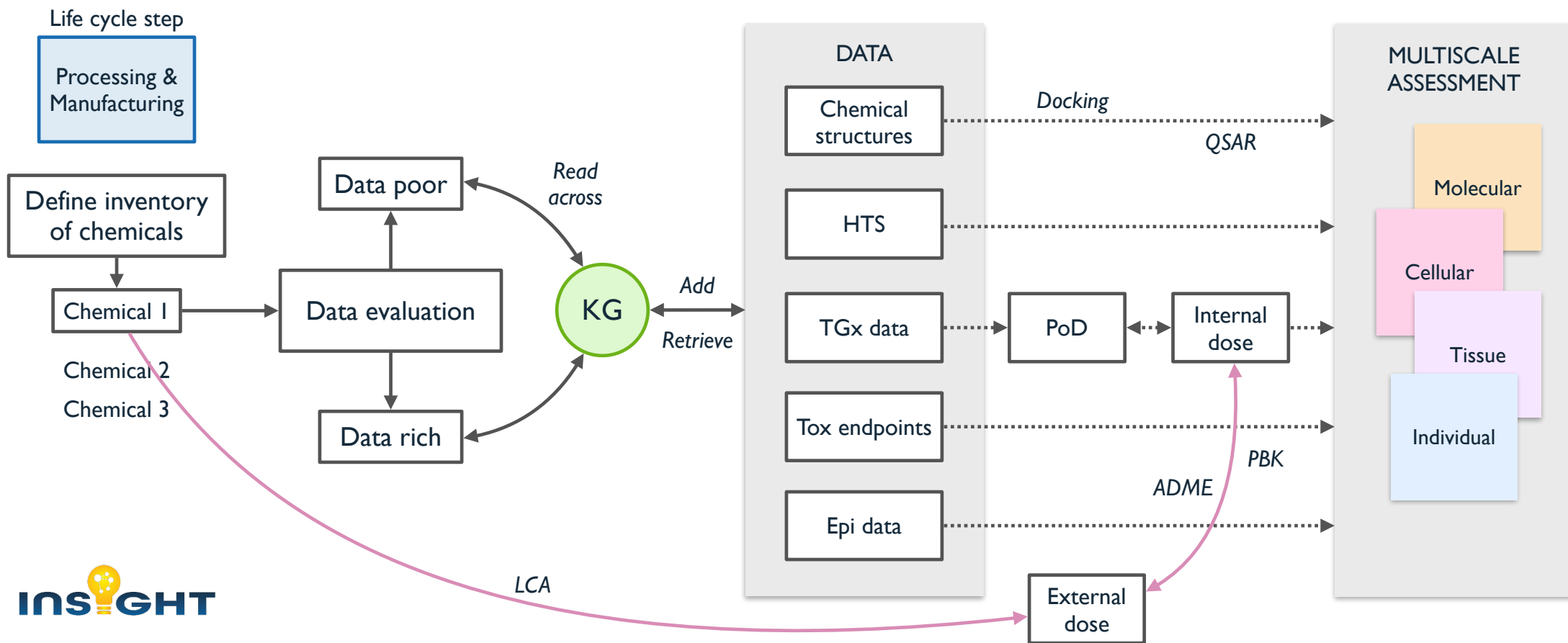


Linking IOP to the chemical life cycle



Multi-scale integrated assessment

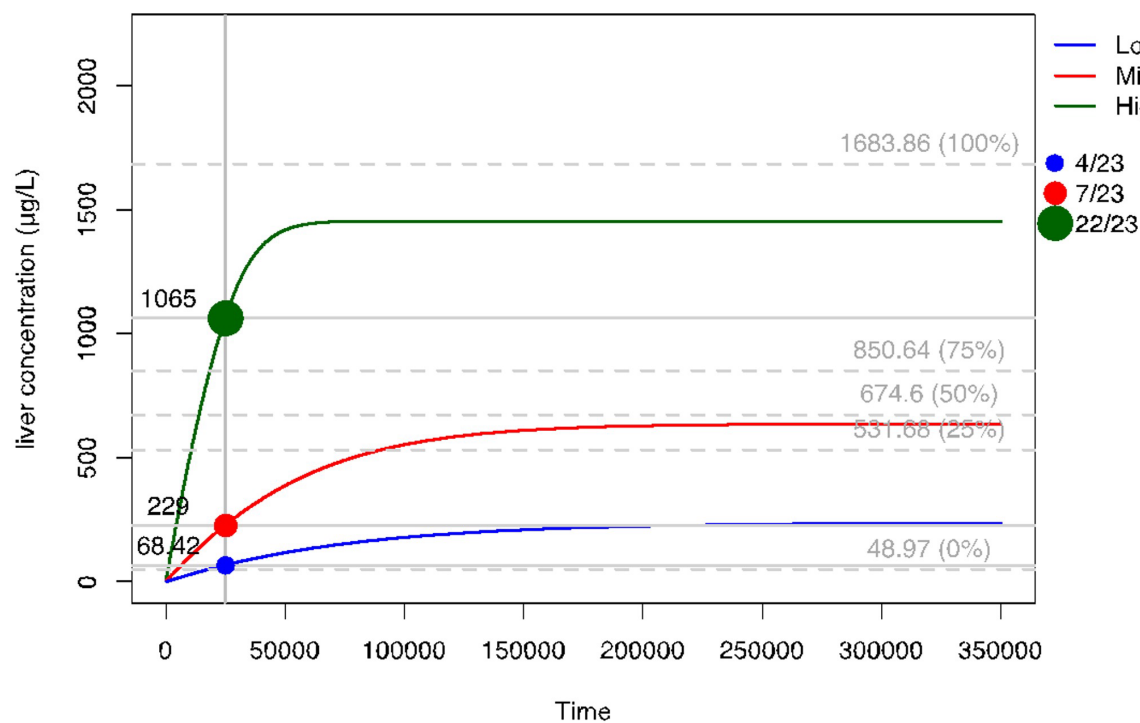
Example for health



PFOS

PFOS molecular weight = 500.13

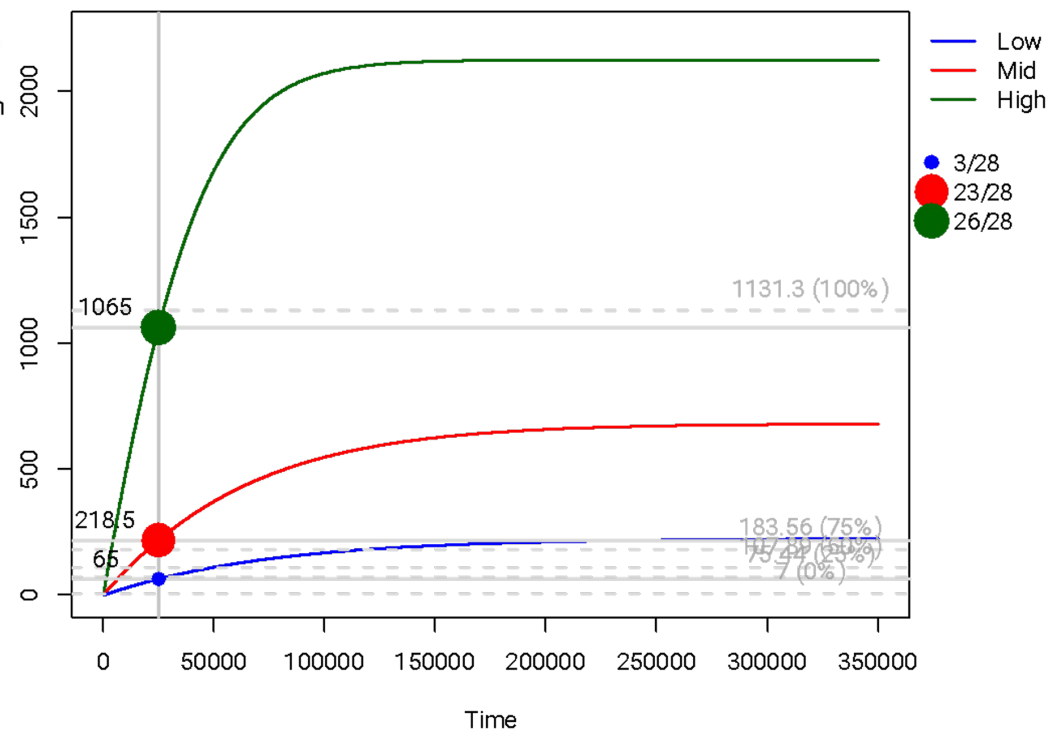
in vitro time point: 1 day/s



PFOA

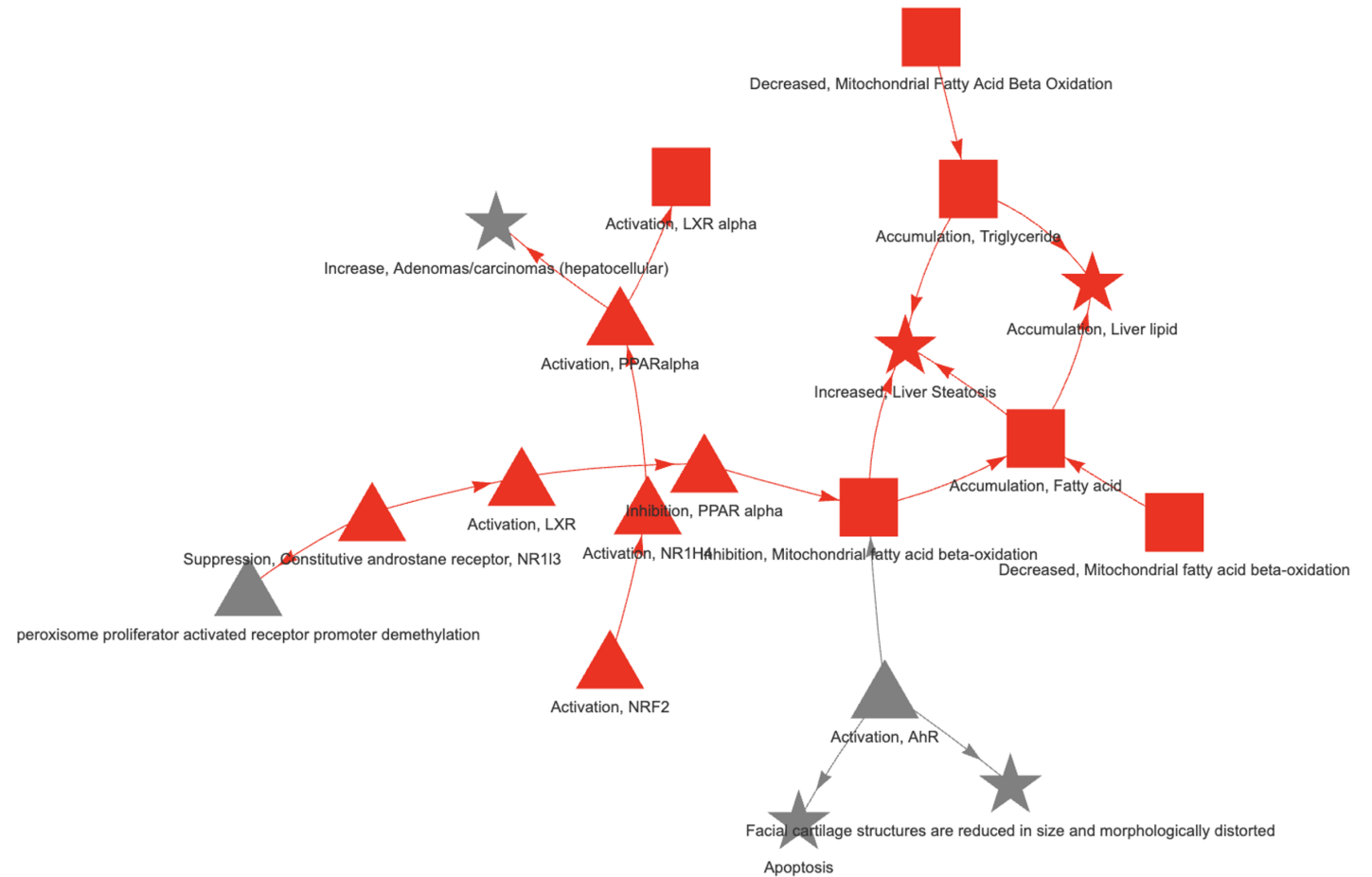
PFOA molecular weight = 414.07

in vitro time point: 1 day/s



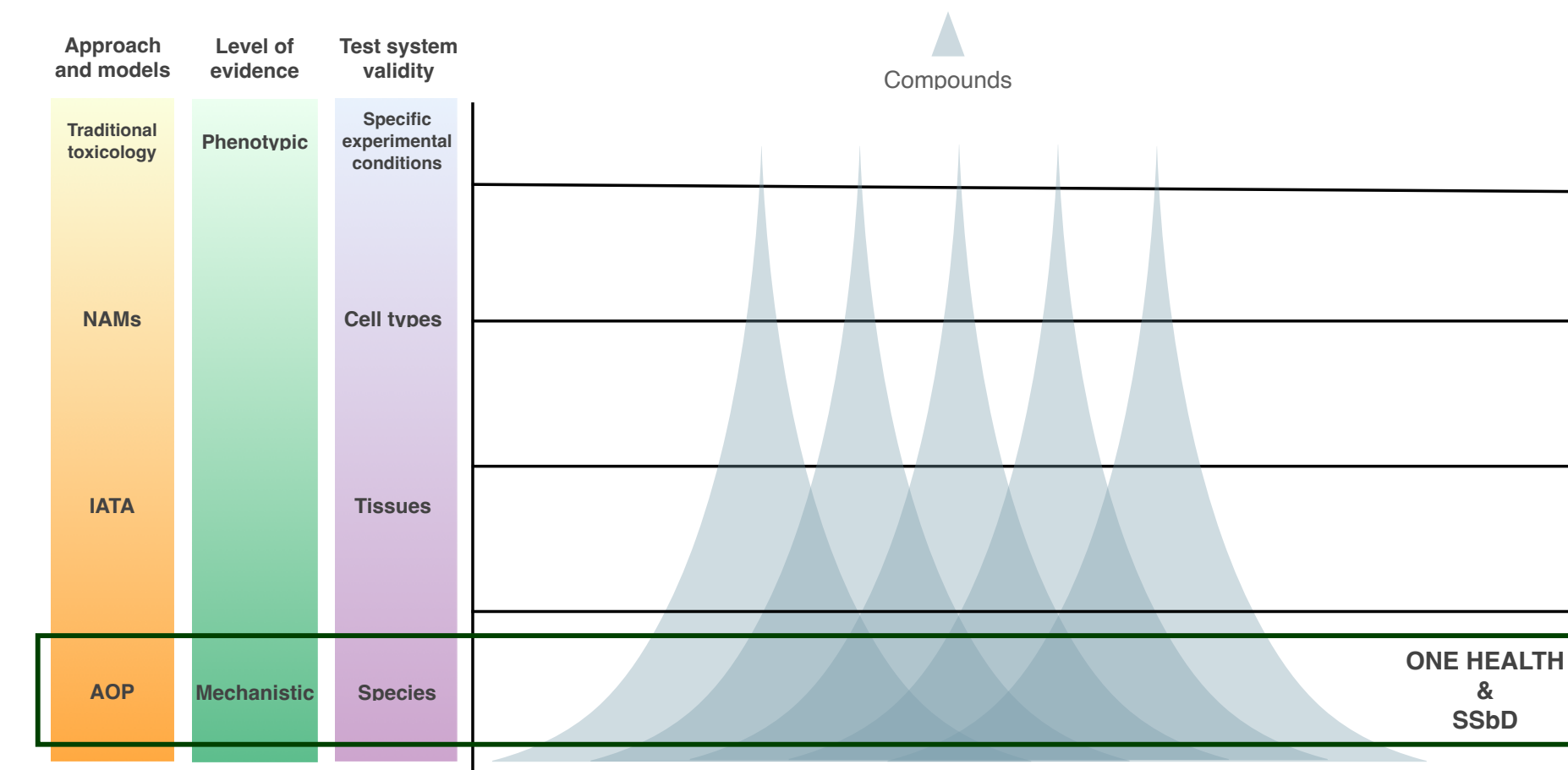
Serra et al., *in prep.*

PFOS-PFOA Common KE subnetwork



Serra et al., *in prep.*

toxicoEPIgenomics for one health models and SSbD



Saarimäki *et al.* Front. Tox. 2024

