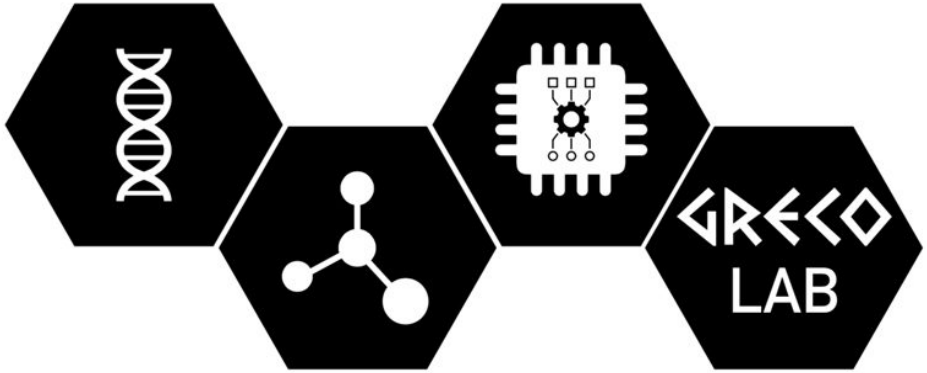
Tampereen yliopisto
Tampere University

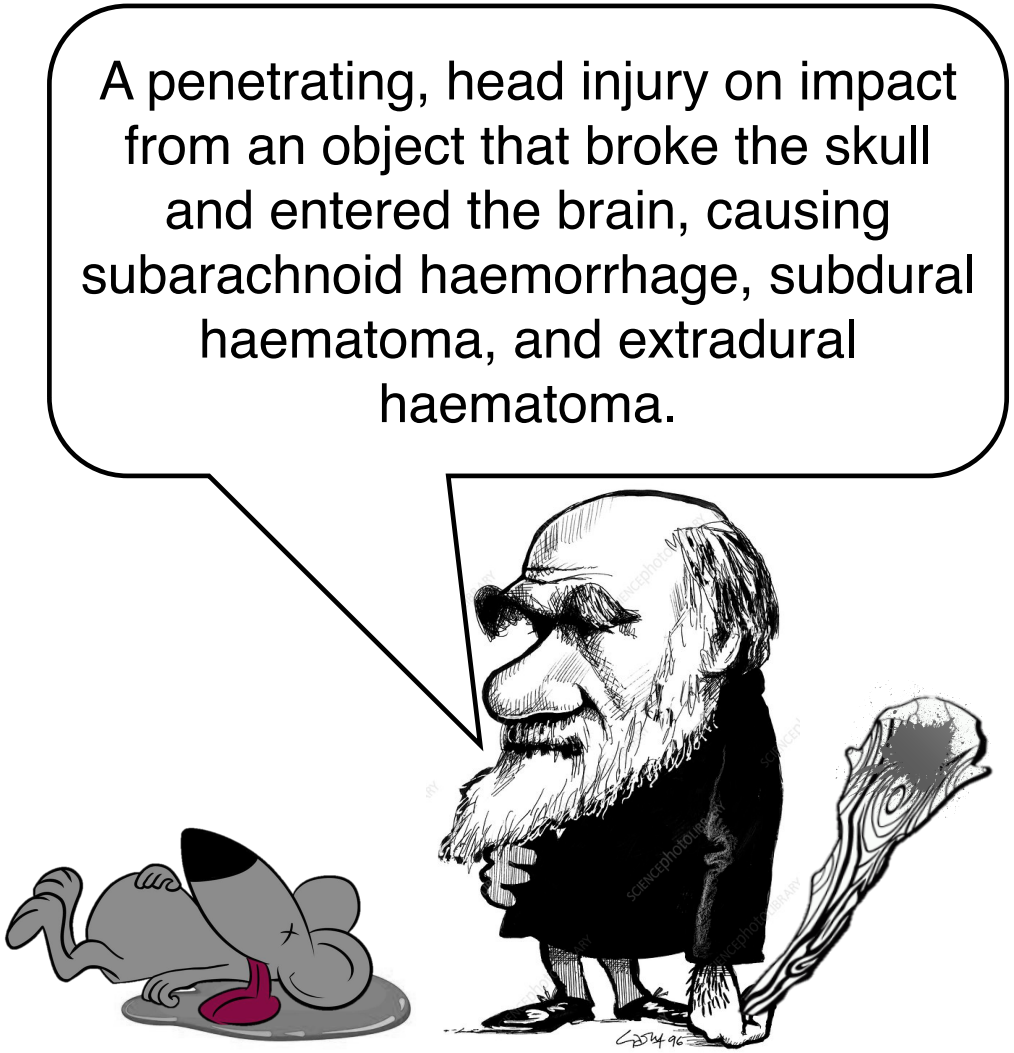


Beyond chemocentric models:
from toxicogenomics to integrated approaches for IATA development

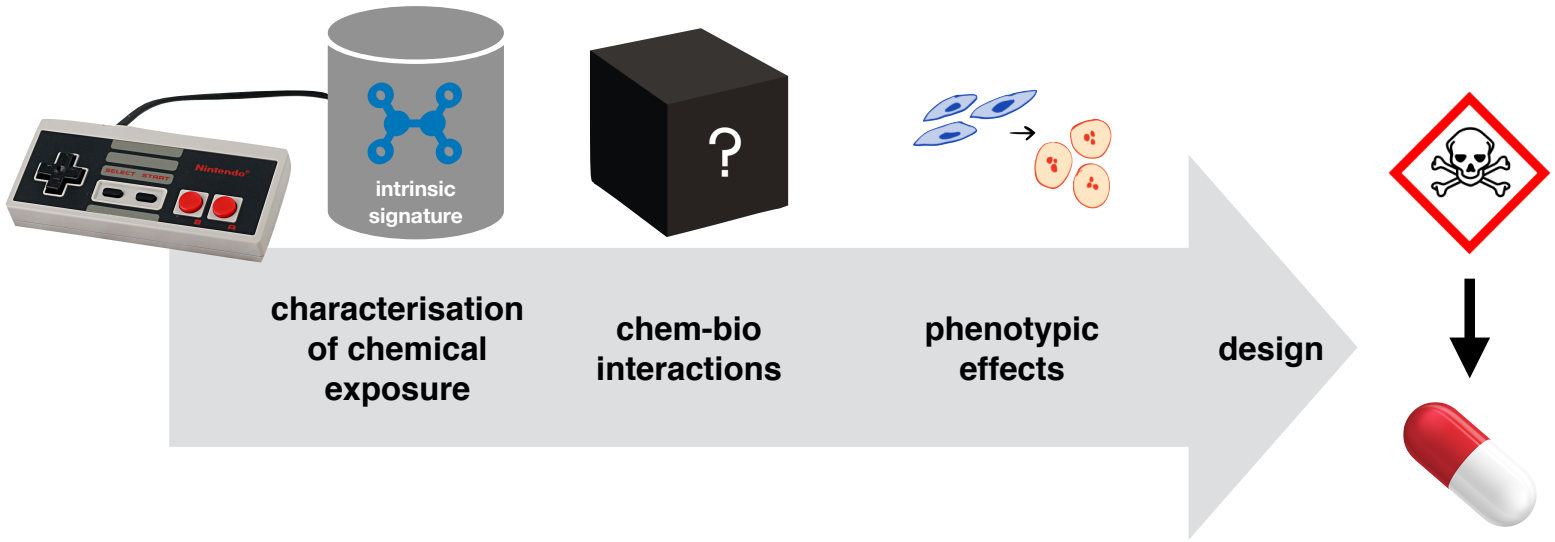
Dario Greco
PhD, professor

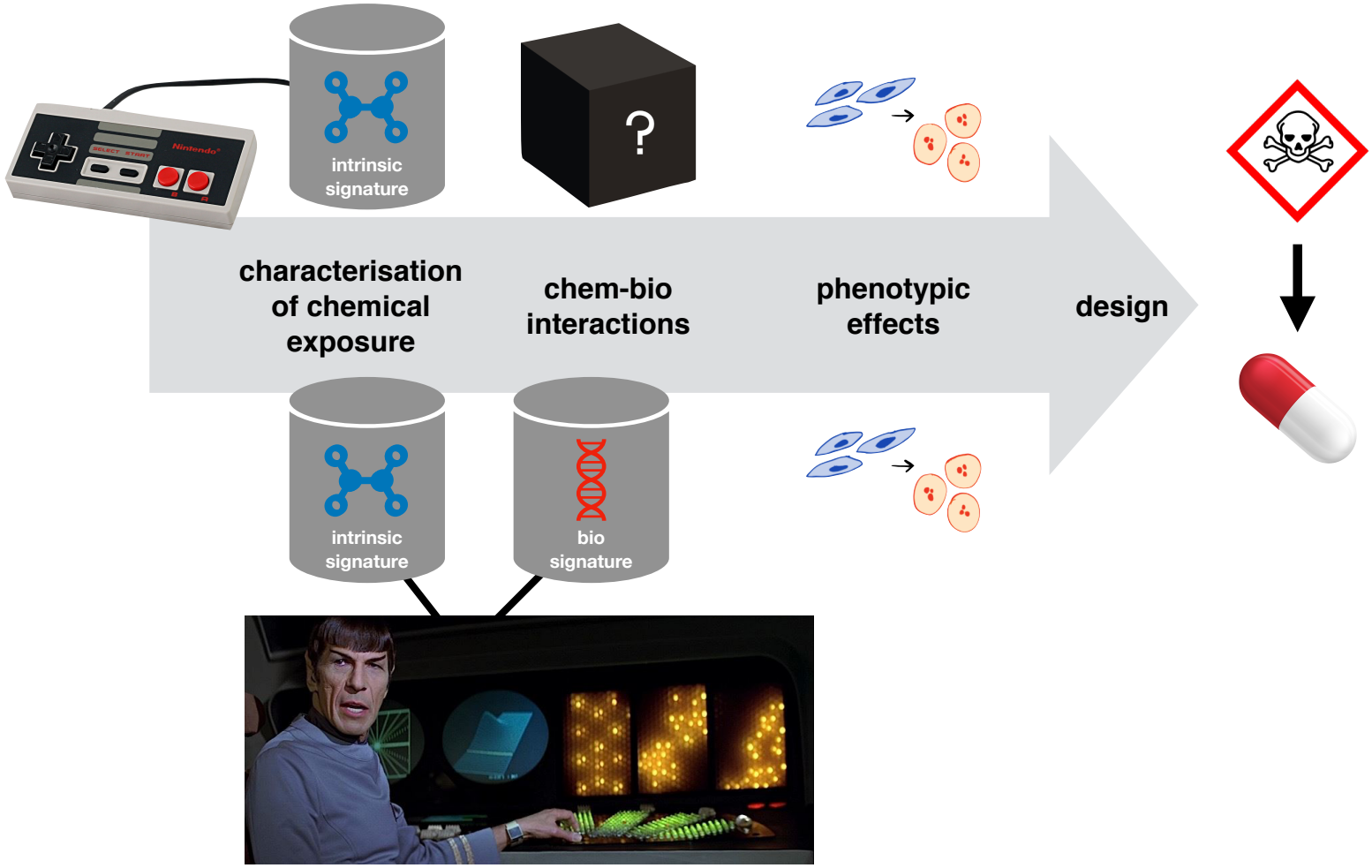
Tampere University
Finland

Traditional toxicology



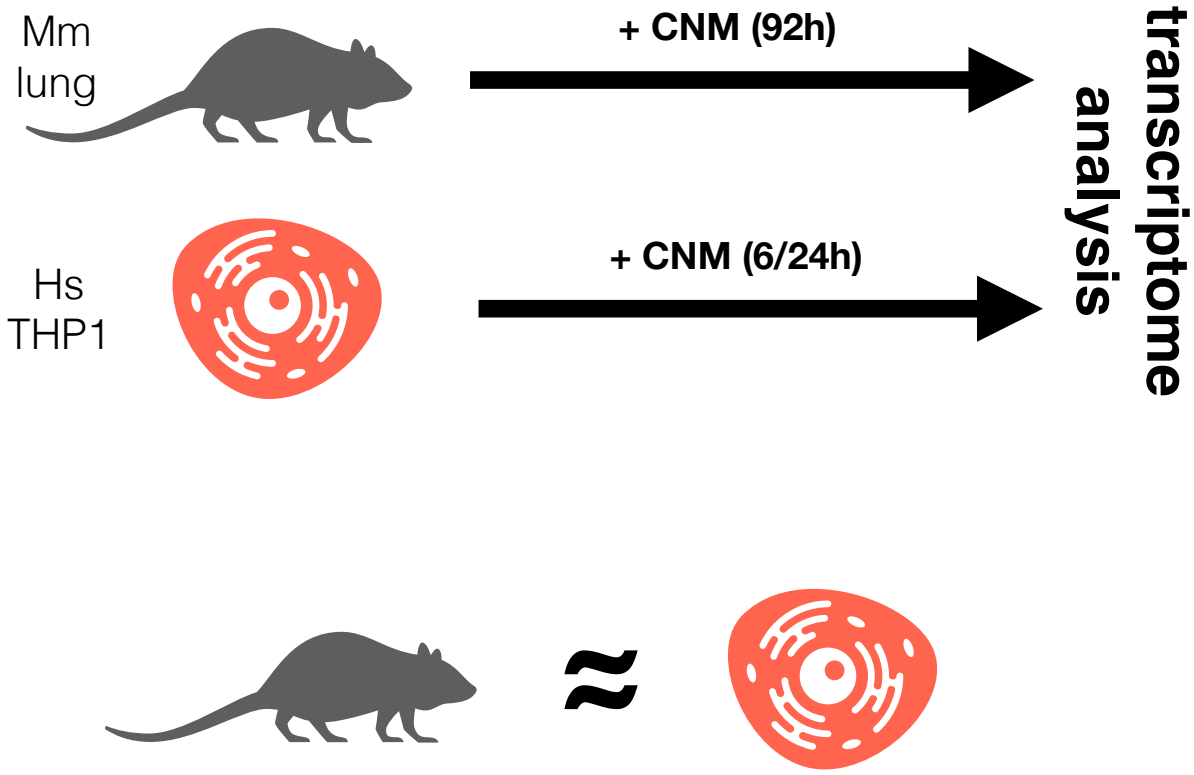
Toxicogenomics


intrinsic
signature
?
characterisation
of chemical
exposure
chem-bio
interactions
phenotypic
effects
design

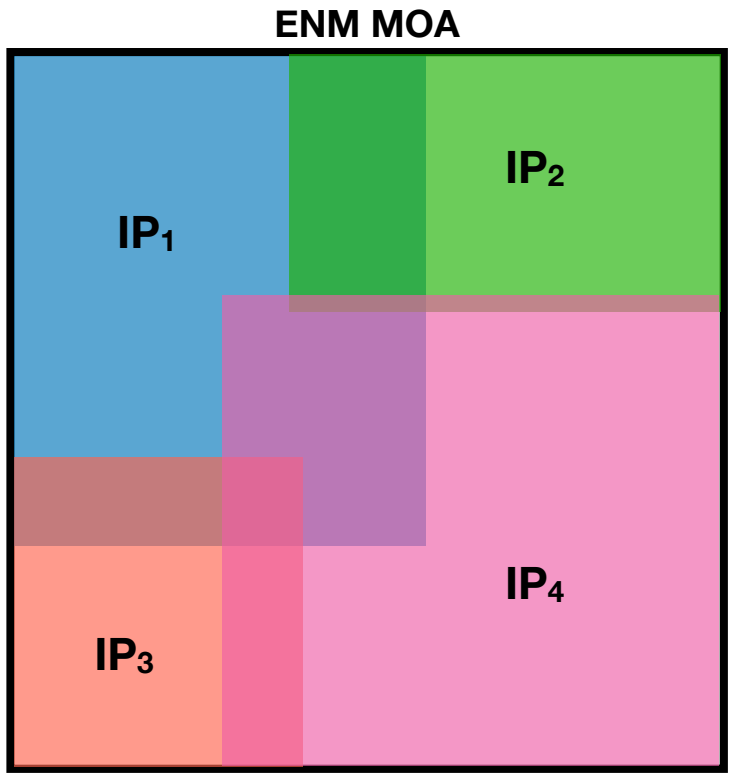

intrinsic signature
?
characterisation of chemical exposure
chem-bio interactions
phenotypic effects
design
intrinsic signature
bio signature

from *in vivo* to *in vitro*

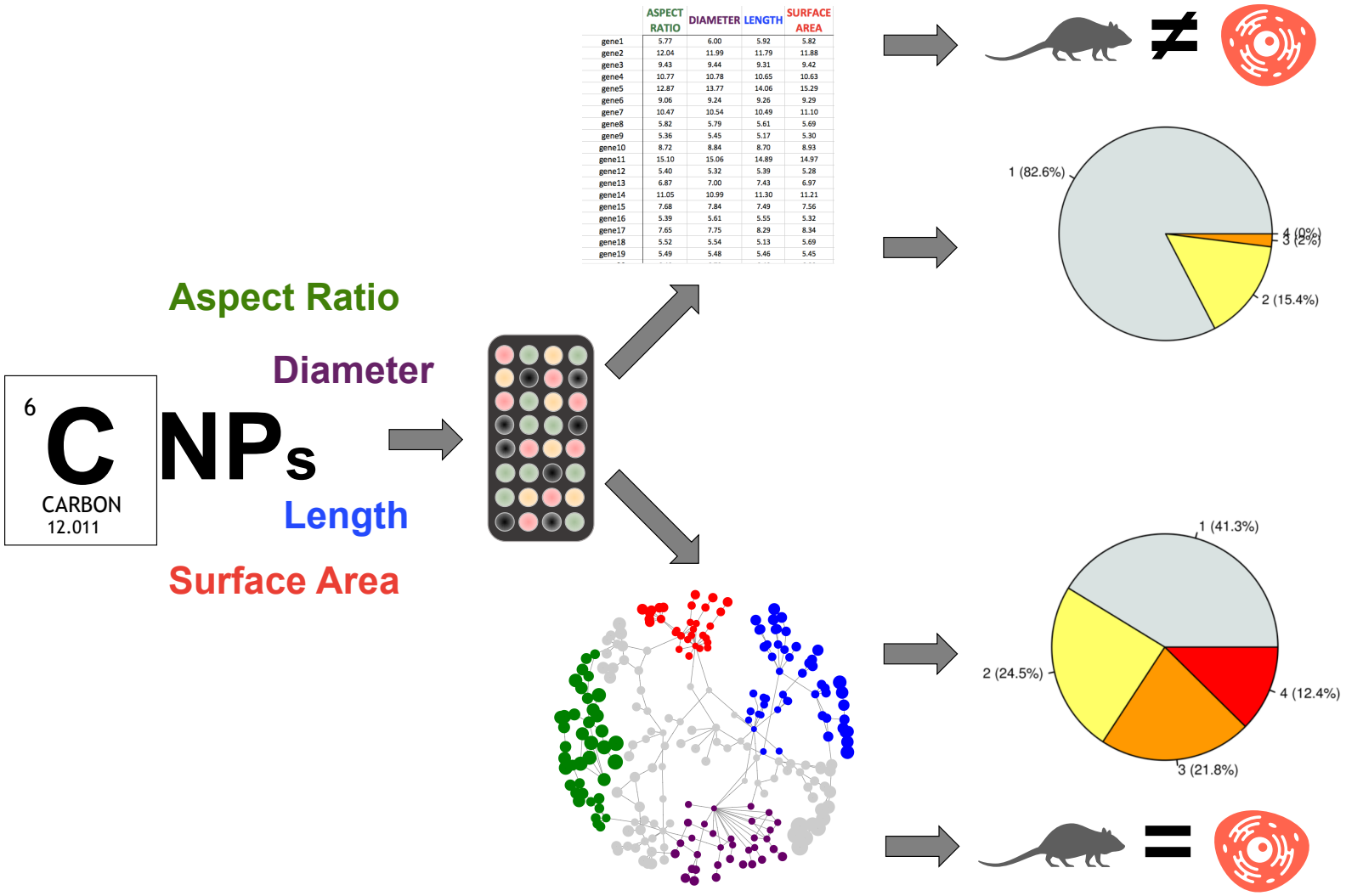
6 CNM of different geometry



Kinaret *et al.* ACS Nano 2017



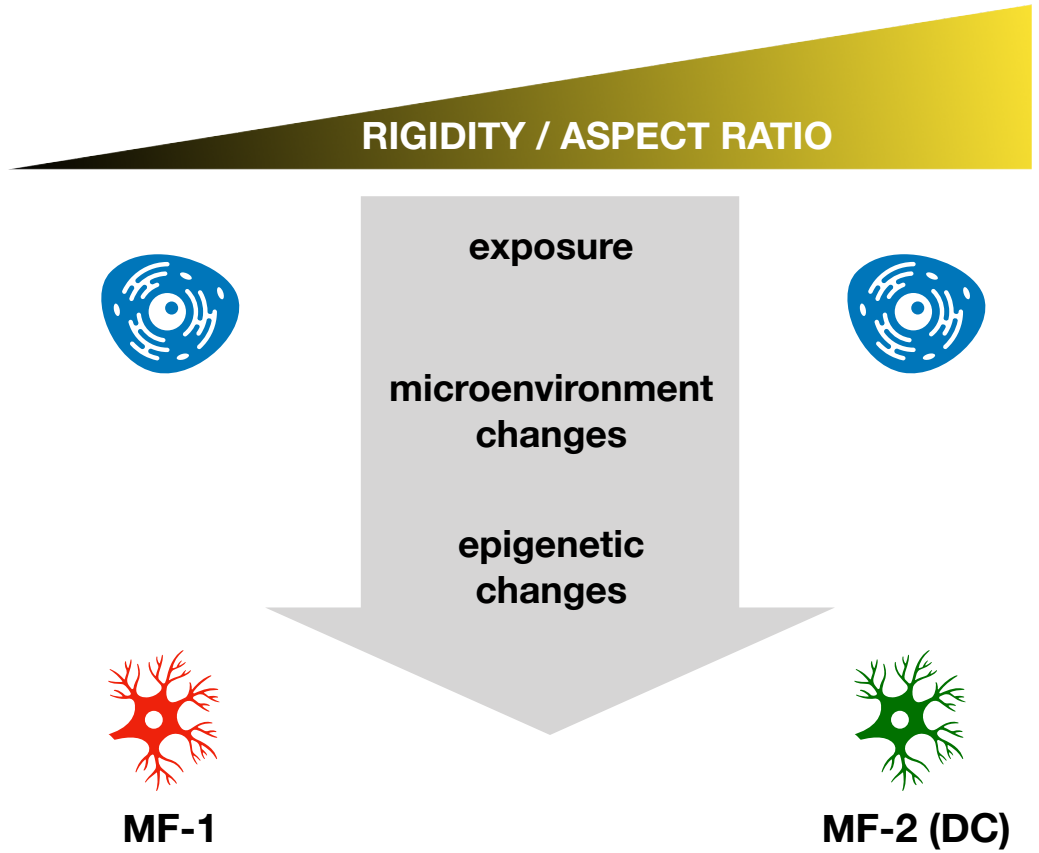
$$MOA_{(ENM)} = MOA_{(IP_1)} \;\&\; MOA_{(IP_2)} \;\&\; MOA_{(IP_3)} \;\&\; MOA_{(IP_4)}$$



Kinaret *et al.* ACS Nano 2017

macrophage polarisation

DNA-met
mRNA
miR
secretome

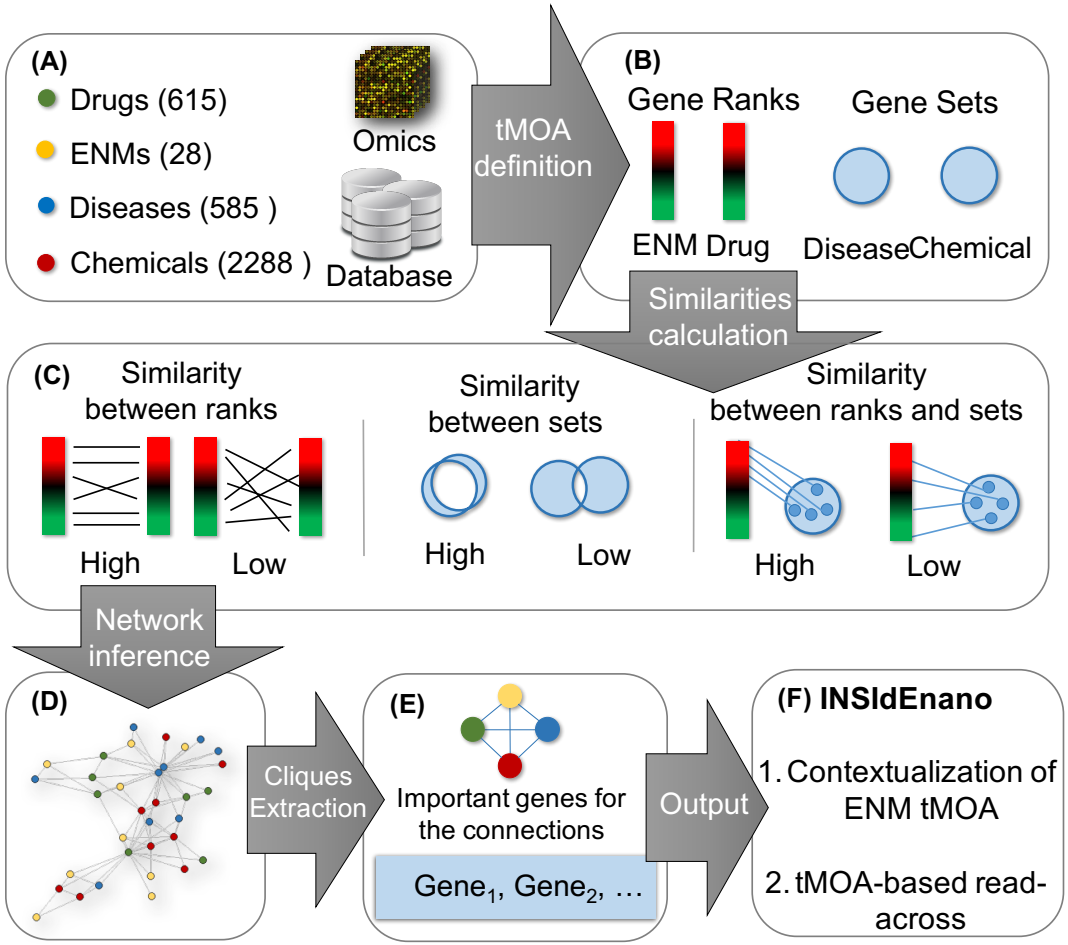


Kinaret *et al.* SMALL, 2020

beyond
toxicity endpoints

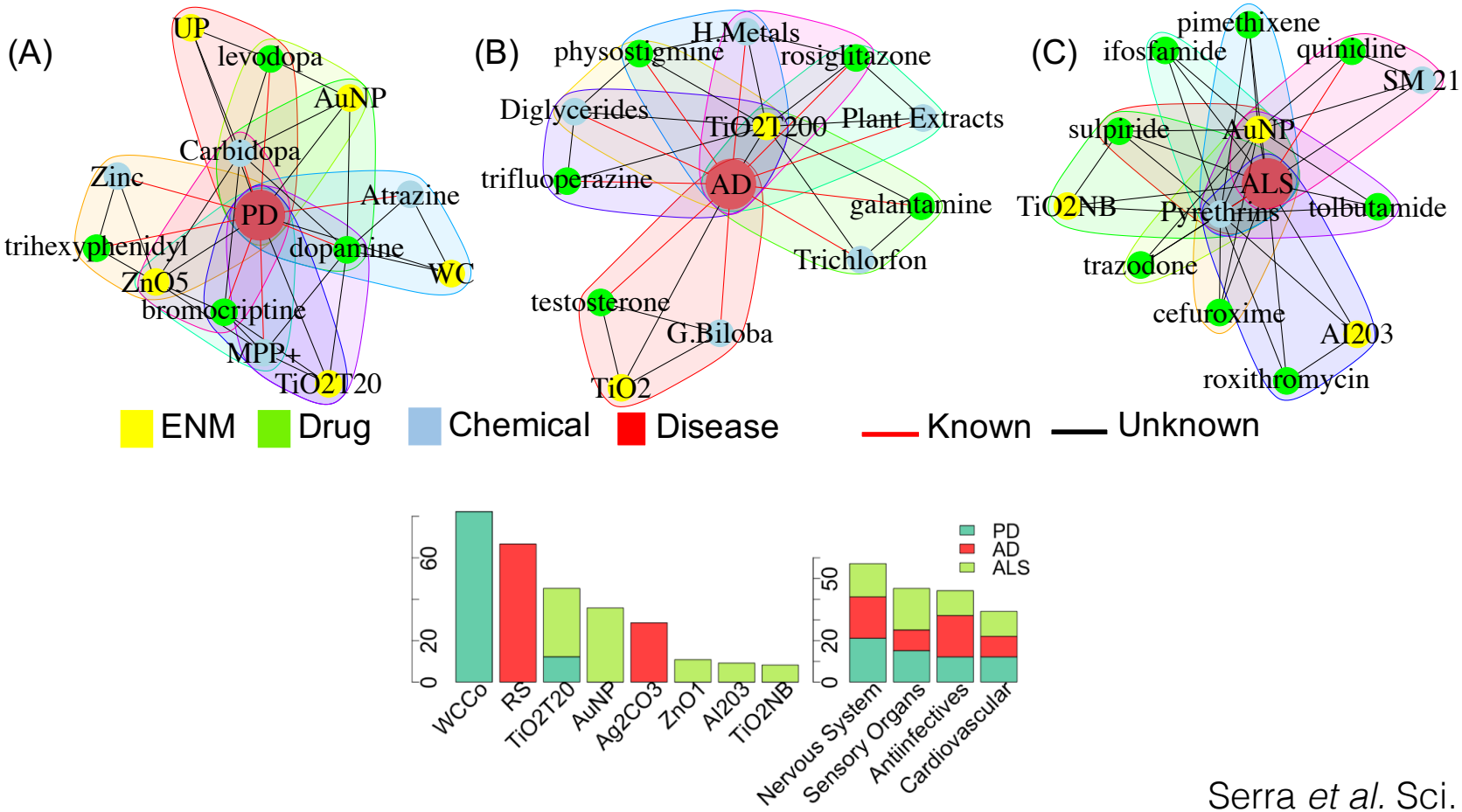
from exposure to human diseases

INSIdE NANO: schematic view

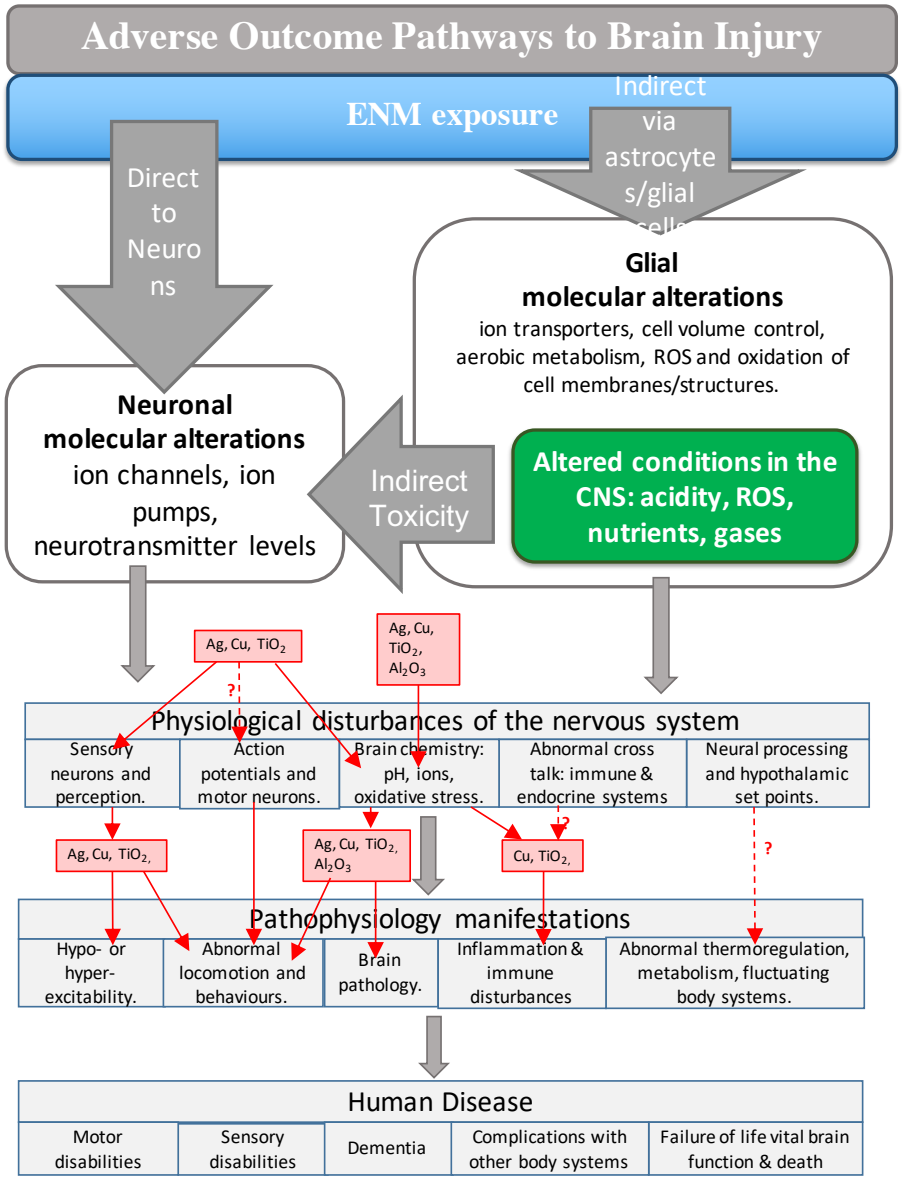


Serra *et al.* Sci. Rep. 2019

metal NPs and neurodegeneration

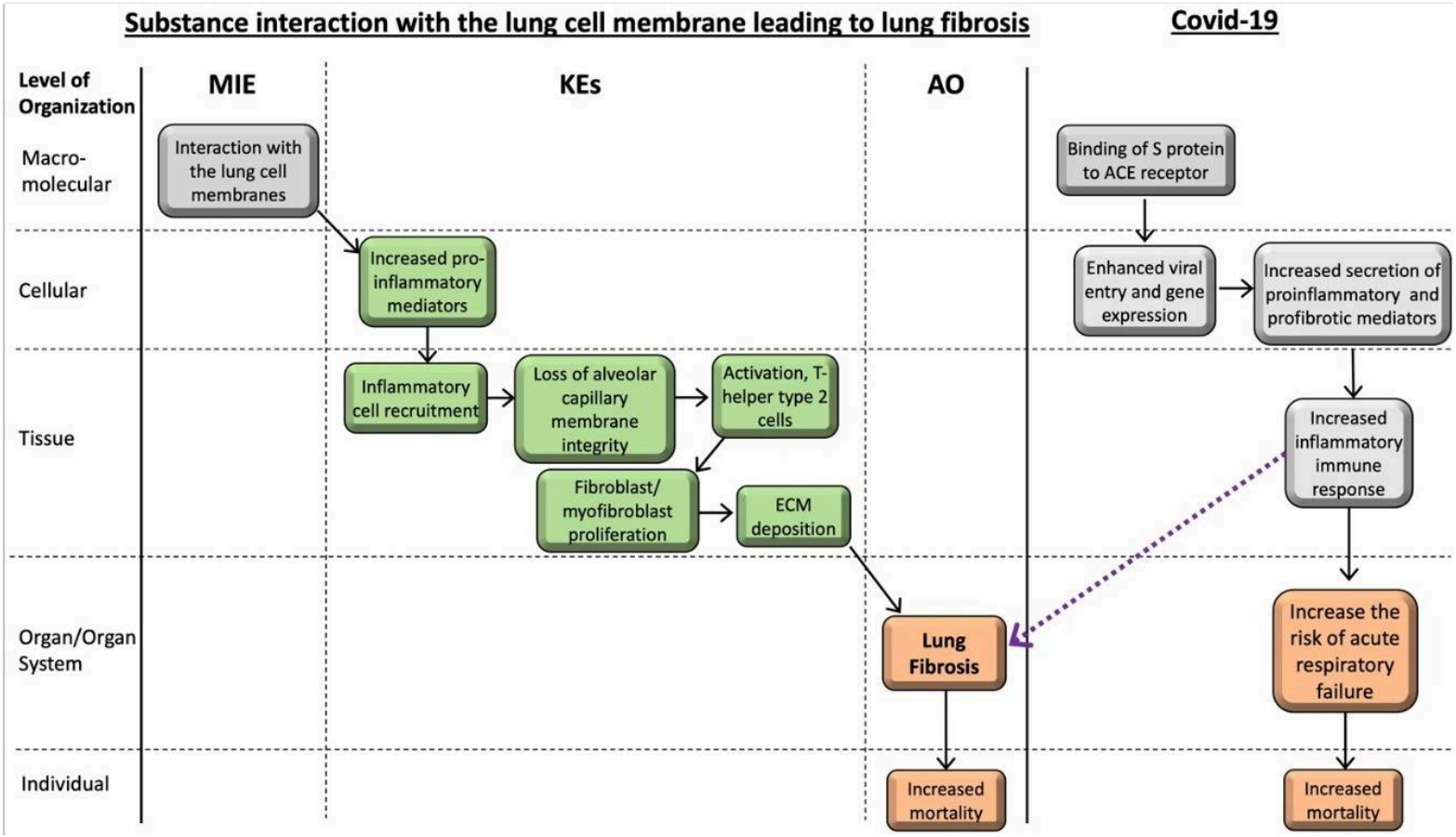


Serra *et al.* Sci. Rep. 2019



Serra *et al.* Sci. Rep. 2019

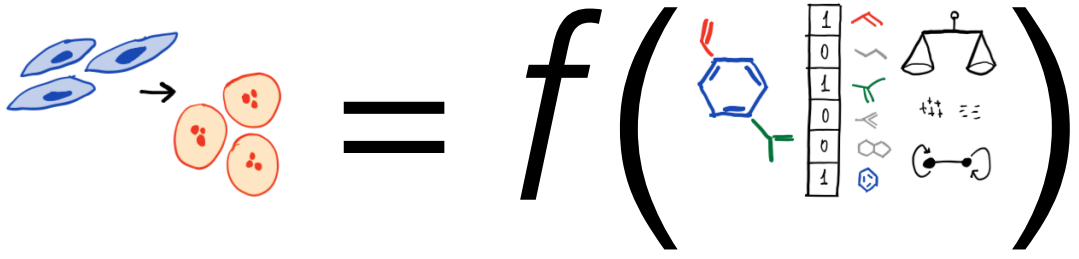
COVID AOP & Lung Fibrosis



Kinaret et al. Nano Today 2020

next generation predictive toxicology

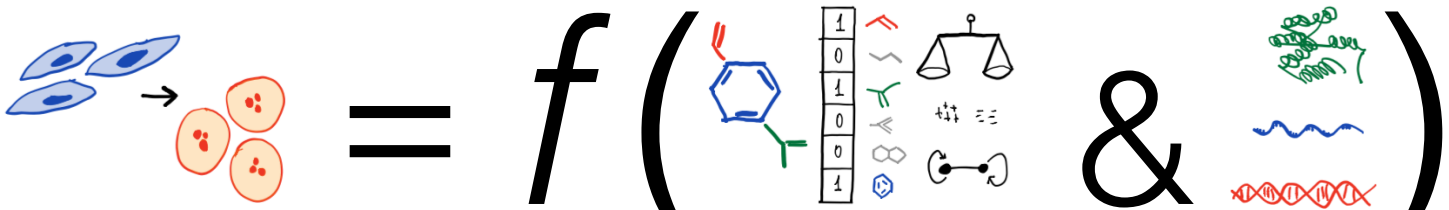
QSAR



toxicity effects

intrinsic properties

QSMART



toxicity effects

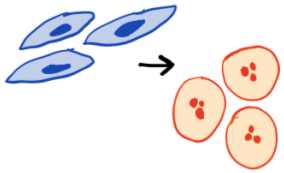
intrinsic properties

mode of action

Fortino *et al*, in revision

DATA OVERVIEW

biological effects



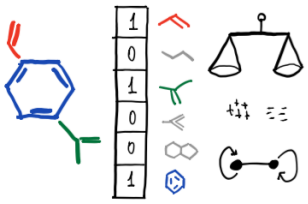
LT	HT		
	■	Apoptosis	CYTOTOX
	■	CTG	
■		DAPI	
■		Hoechst	
■		Viability	
	■	DNA dam (pH)	GENOTOX
	■	CHR dam 80H	
	■	DoublePos	
■		Comet	
■		Micronucleus	
	■	Cytok/Chemok	IMMUNO
■		BAL	

H

M

L

intrinsic properties



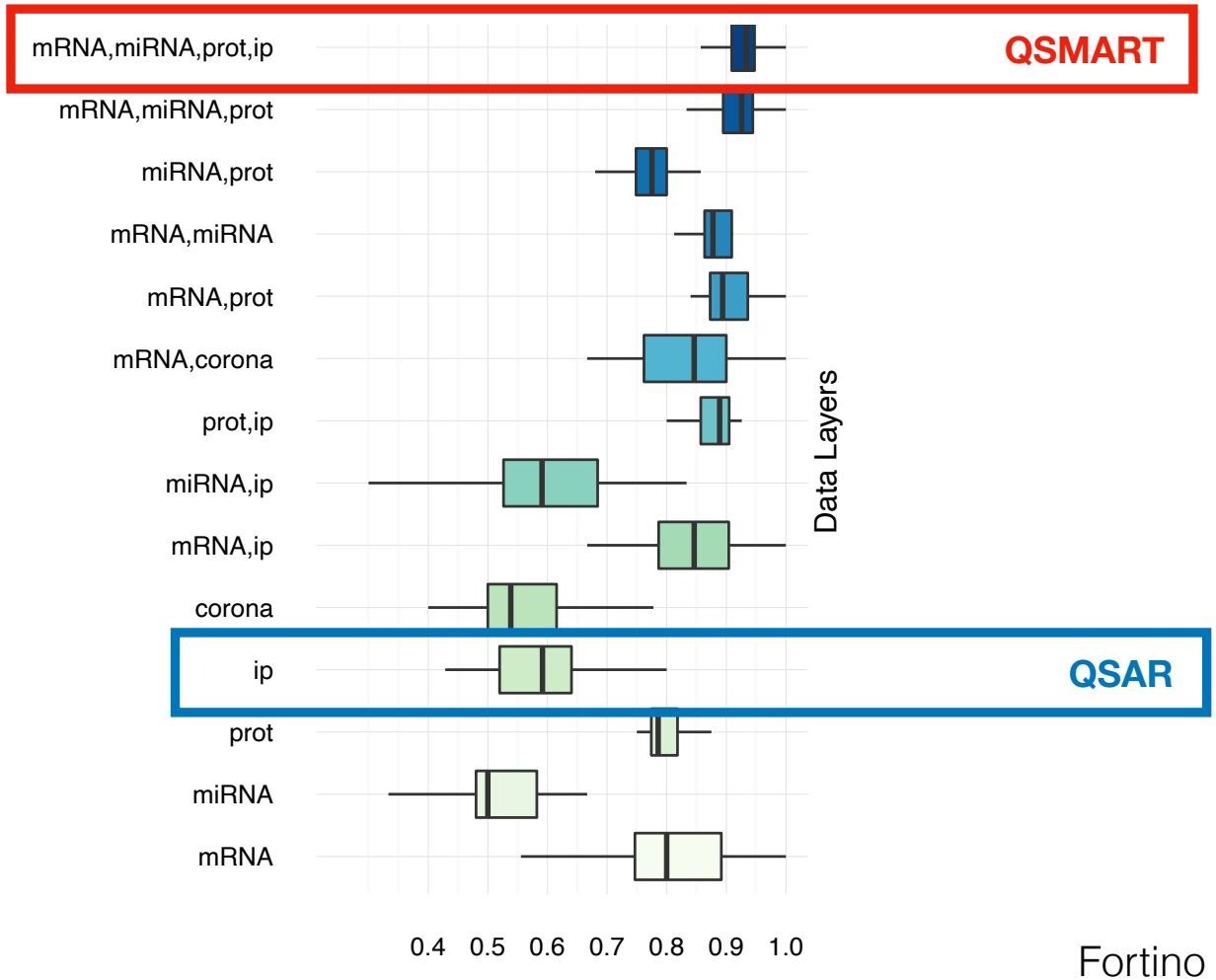
intrinsic properties

mode of action

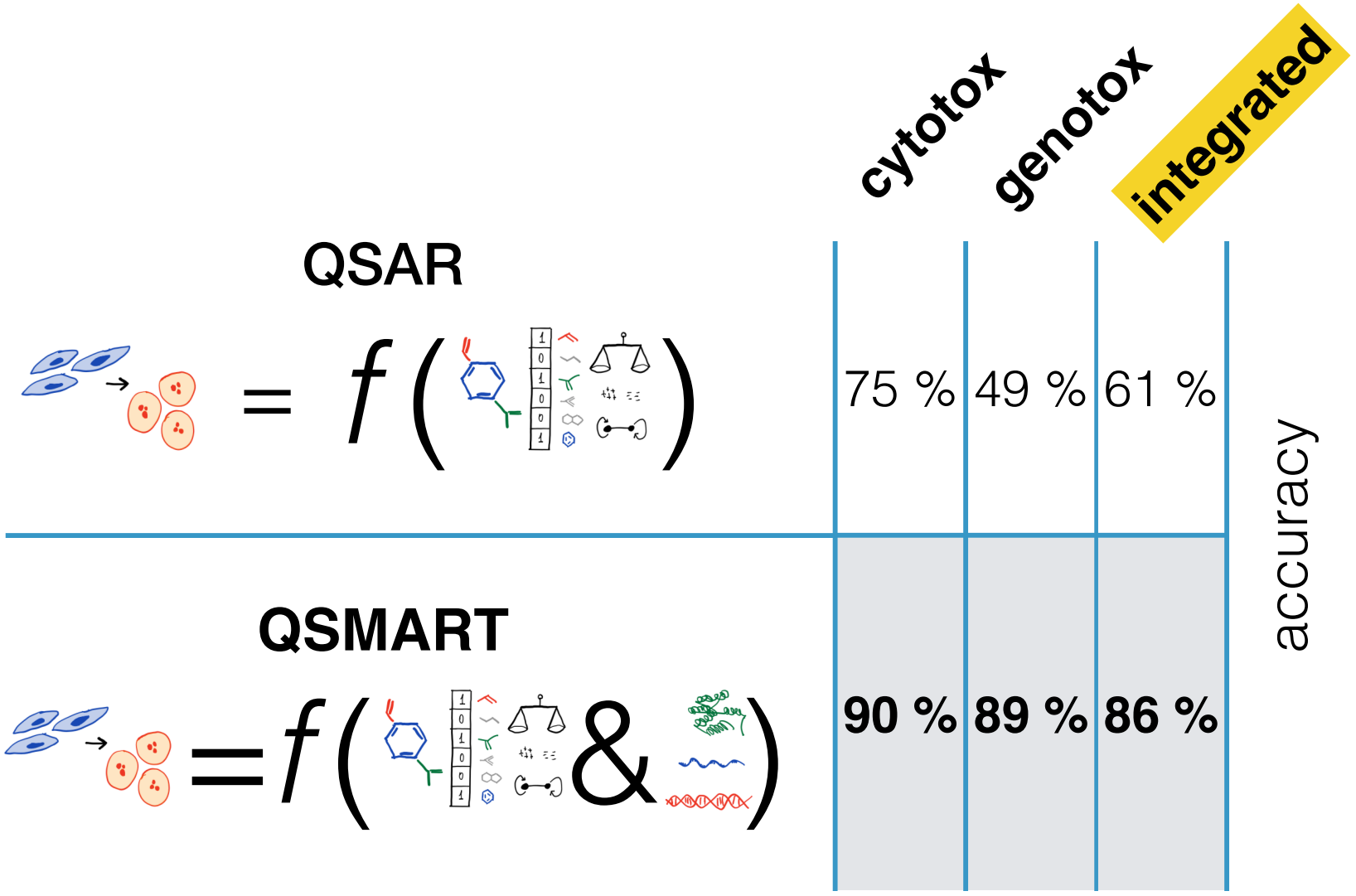
Mm (in vivo) | mRNA (seq) | lung

Hs (in vitro) | mRNA (array) | mRNA (seq) | Proteomics | miR (seq) | Corona | BEAS2B | THP1

hybrid models are better

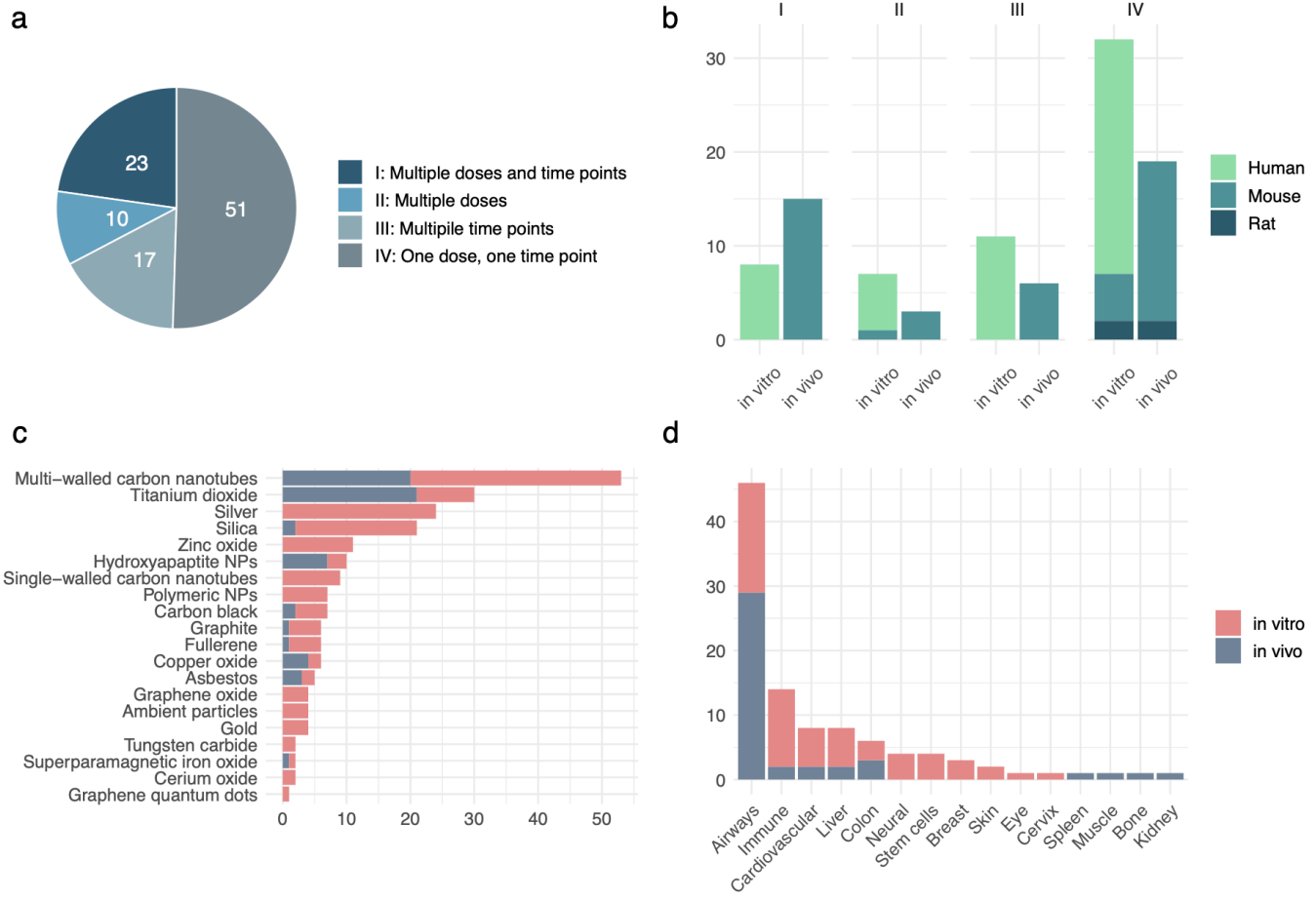


Fortino *et al*, in revision.



Fortino *et al*, in revision.

Good modelling depends on good data



Reason to discard	Number of entries
Lack of replicates	26
Non-commercial or marginally represented platform	5
Two-color setup with no dye swapping	4
No raw data available	2
Incomplete metadata	2
Lack of control samples	1
Total entries discarded	**40**

Saarimäki *et al*, in revision.

SUMMARY

- inference of molecular networks highlights similarities between *in vivo* and *in vitro* exposure
- Contextualisation of ENM MOA allows to find direct implications to human pathogenesis
- hybrid predictive models including ENM MOA and IP outperform traditional QSAR approaches

Thanks to

GrecoLab

Pia Kinaret
Angela Serra
Tonino Federico
Michele Fratello
Laura Saarimäki
Luca Cattelani
Alisa Pavel
Giusy Del Giudice
Troy Faithfull

Vittorio Fortino
Giovanni Scala
Veer Marwah
Veera Hautanen

Collaborators

Antreas Afantitis
Iseult Lynch
Harri Alenius
Kai Savolainen
Bengt Fadeel
Ulla Vogel
Sabina Halappanavar
Roland Grafström
Harry Sarimveis
Tomasz Puzin
Giuseppe Balistreri
Olivier Joubert
Henrik Wolff

NEXTCAST
Innovate wise.
BUSINESS FINLAND

Biomap

nanoinformaTIX

NanoSolveIT

caLIBRAte
nano risk governance

ACADEMY OF FINLAND