

My view on Good Quality Data

Costanza Rovida

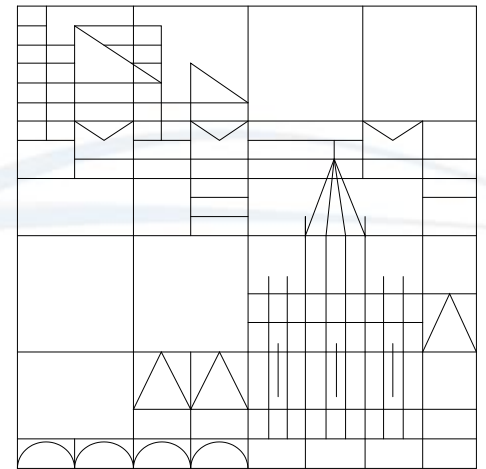
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The primary aim of *ecopa* is to promote "the three Rs" (Replacement, Reduction and Refinement) in the use of animals in research, testing, education and training in Europe. *ecopa* strives for consensus between all four stakeholders in attempting to achieve its goals:

1. Government and regulatory authorities
2. Academia
3. Industry
4. Animal protection and welfare organisations

ecopa supports the establishment of National Consensus Platforms which promote the three Rs and include representatives of all four stakeholders in their governing body.



Are we happy with the actual model?

Research Article

Analysis of Draize Eye Irritation Testing and its Prediction by Mining Publicly Available 2008-2014

Thomas Luechtefeld¹, Alexandra M. and Thomas Hartung^{1,4}

¹Center for Alternatives to Animal Testing (C. Health Sciences, Baltimore, MD, USA; ²The Camden, NJ, USA; ³Department of Chemistry Konstanz, Konstanz, Germany

Tab. 3: Conditional probability of Draize evaluations given a previous test result

Substances filtered to those with at least two Draize studies and extractable eye irritation category in REACH registrations 2008-2014 (491 substances).

Prior Type	1	2A	2B	Non	Total
1	73%	16.1%	0.4%	10.4%	46
2A	4.2%	32.9%	3.5%	59.4%	138
2B	0.2%	4%	15.5%	80.2%	86
Non	1.1%	3.5%	1.5%	93.9%	400

Cancer bioassay results

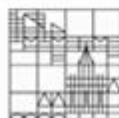
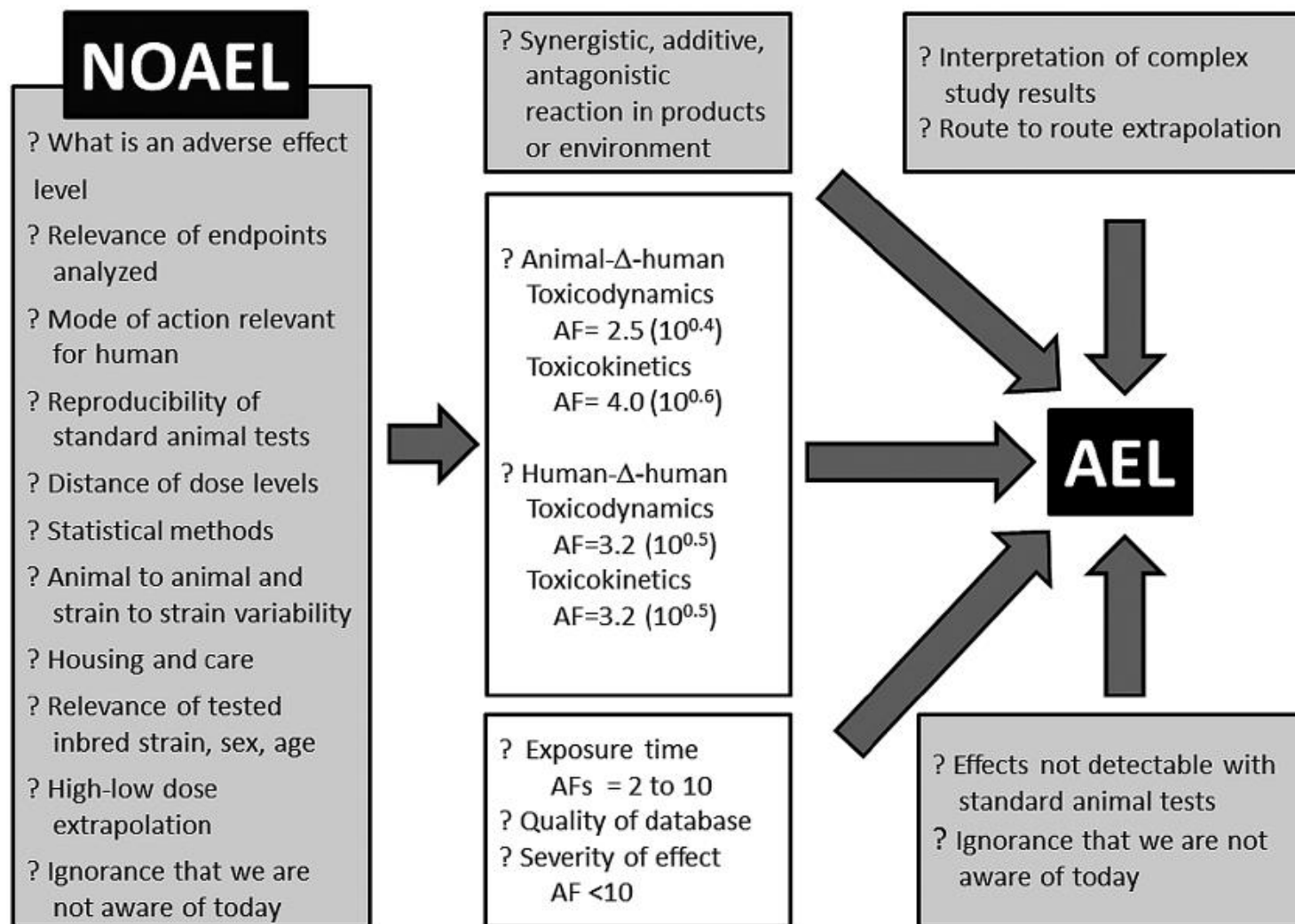
[Ames & Gold 2000]



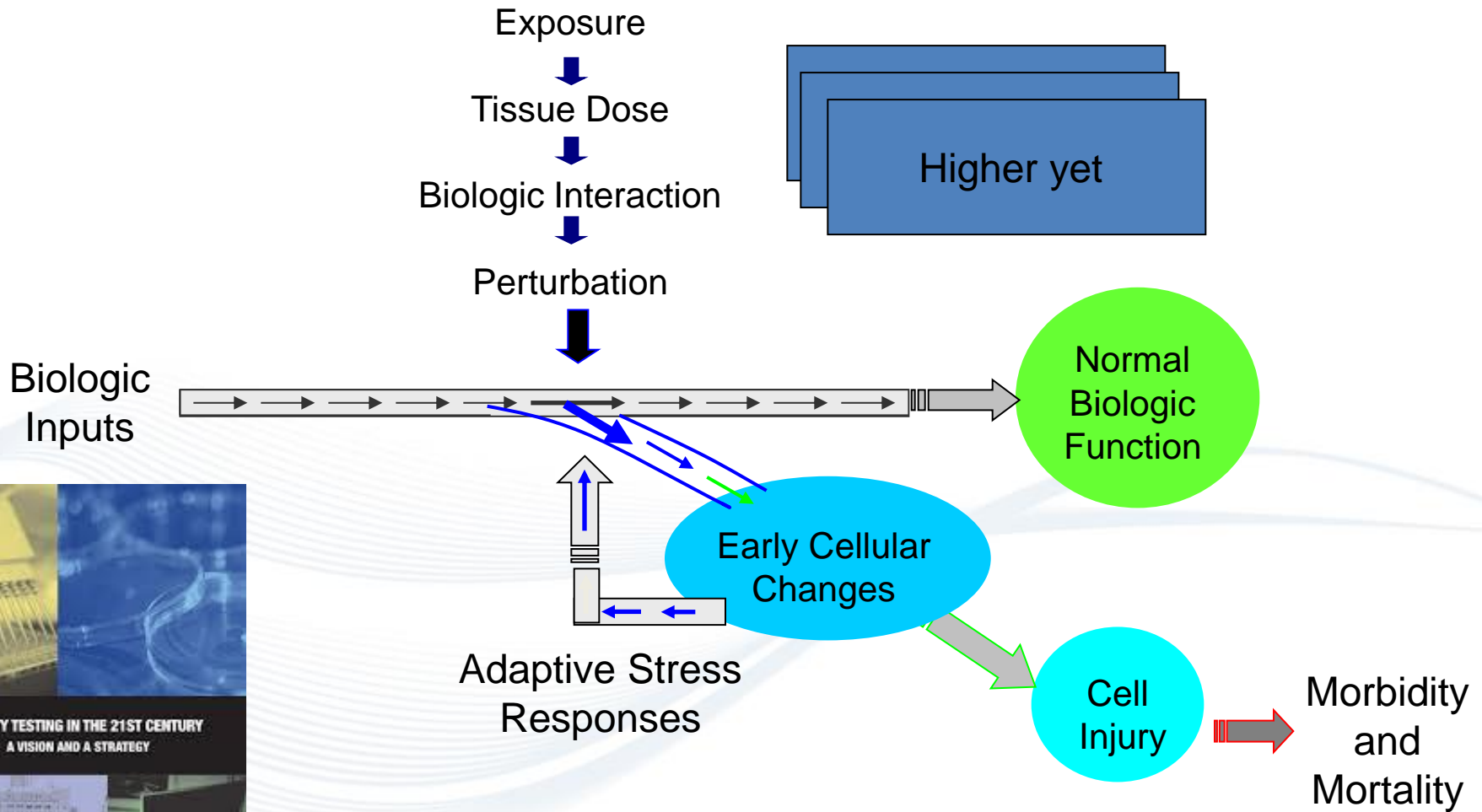
	Proportion	%
Chem. tested in rats and mice	350 / 590	59 %
- natural	79 / 139	57 %
- synthetic	271 / 451	60 %
Chem. tested in rat or mice	702 / 1348	52 %
- Natural pesticides	37 / 71	52 %
- Chem. in coffee	21 / 30	70 %
- Mold toxins	14 / 23	61 %
Drugs (PDR)	117 / 241	49 %
Drugs (FDA)	125 / 282	44 %



Are we happy with the actual model?



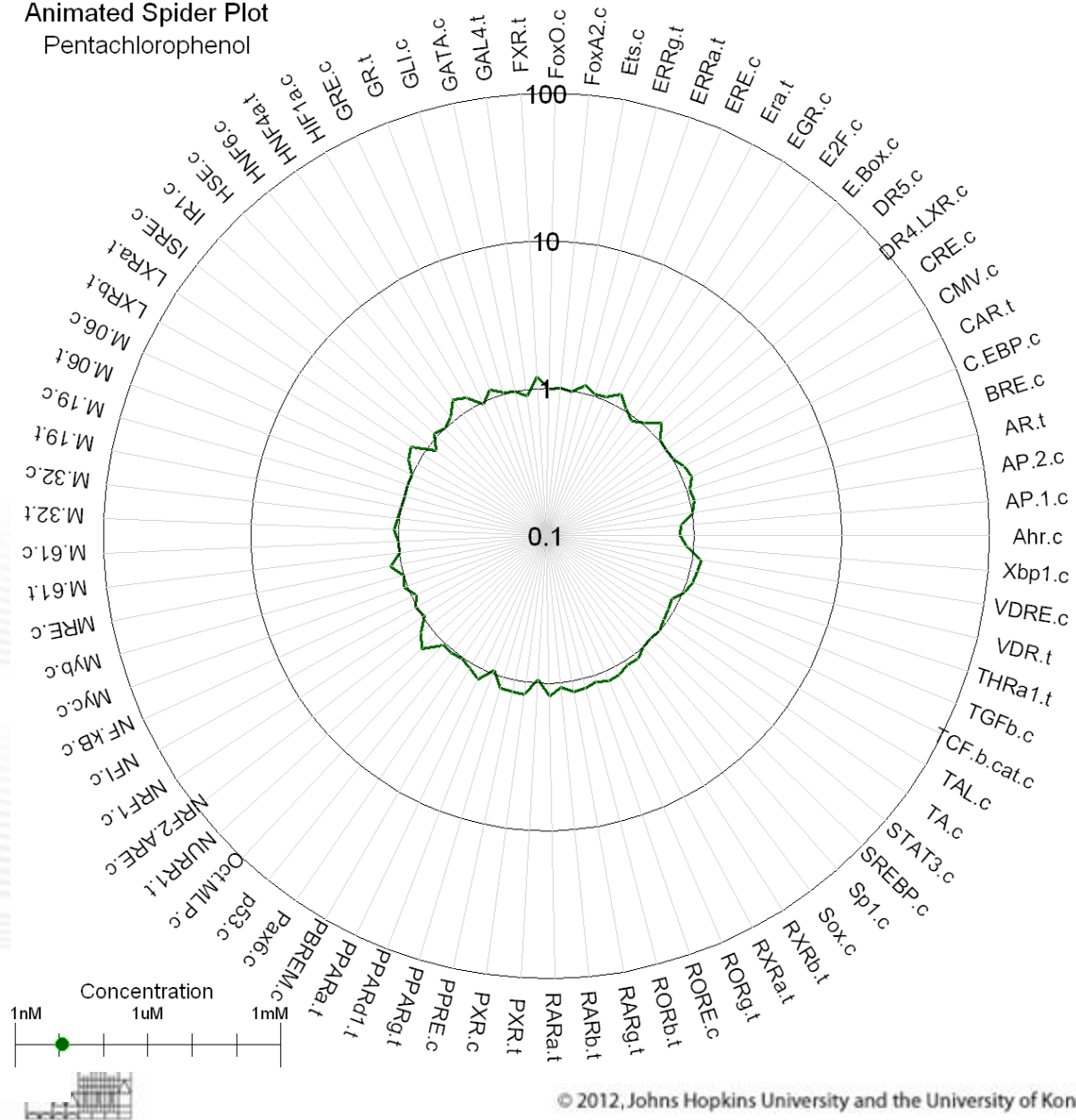
A new paradigm shift: Activation of toxicity pathways in human cells



Google: "Toxicity Testing in the 21st Century"

Pentachlorophenol

Animated Spider Plot
Pentachlorophenol



ADVERSE OUTCOME PATHWAY

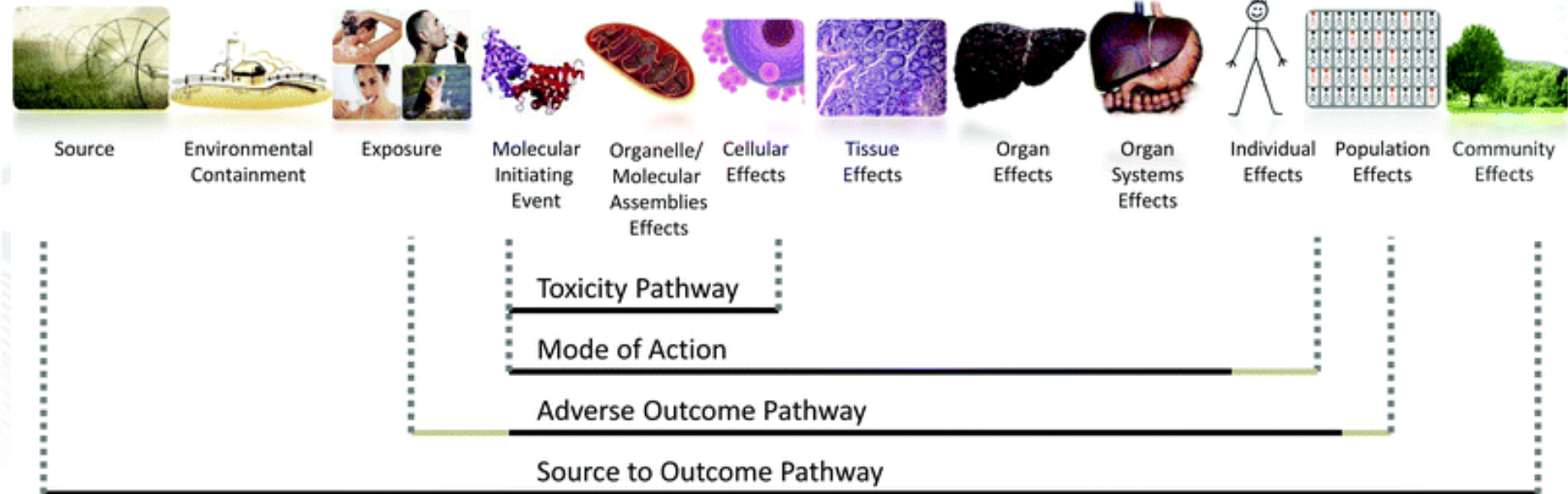
Molecular properties

Molecular initiating events

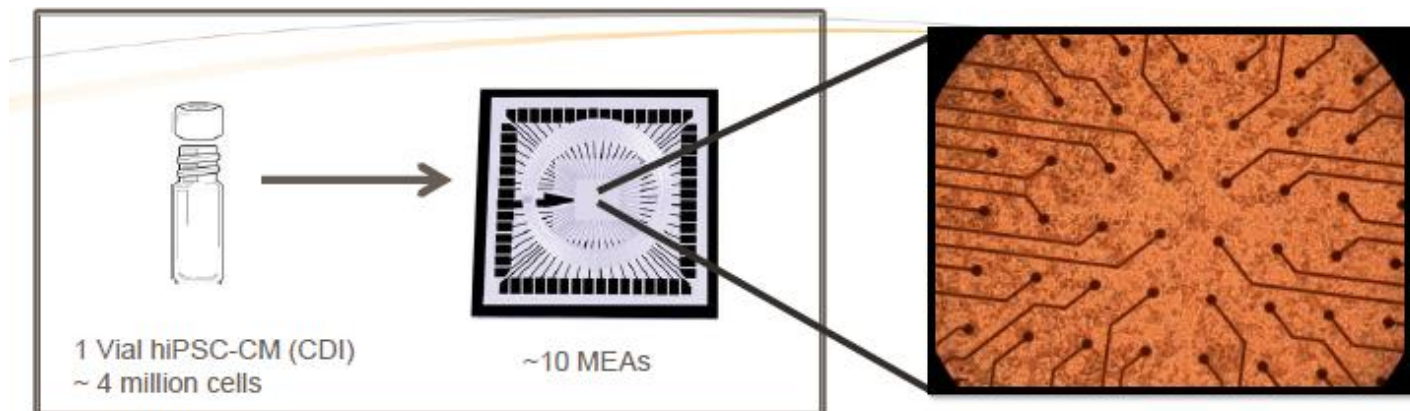
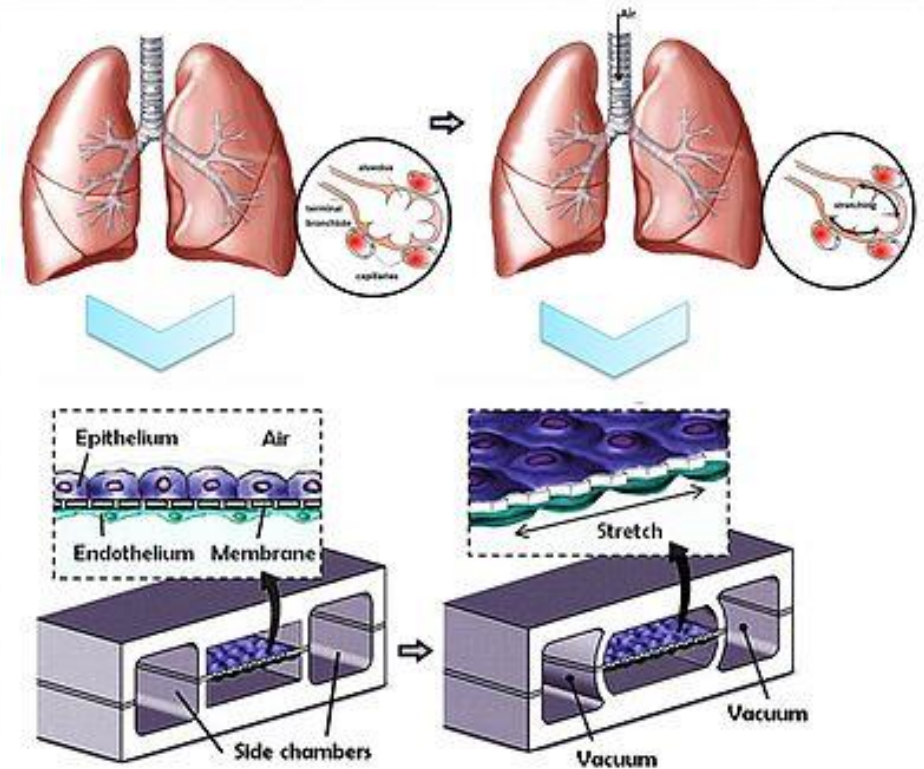
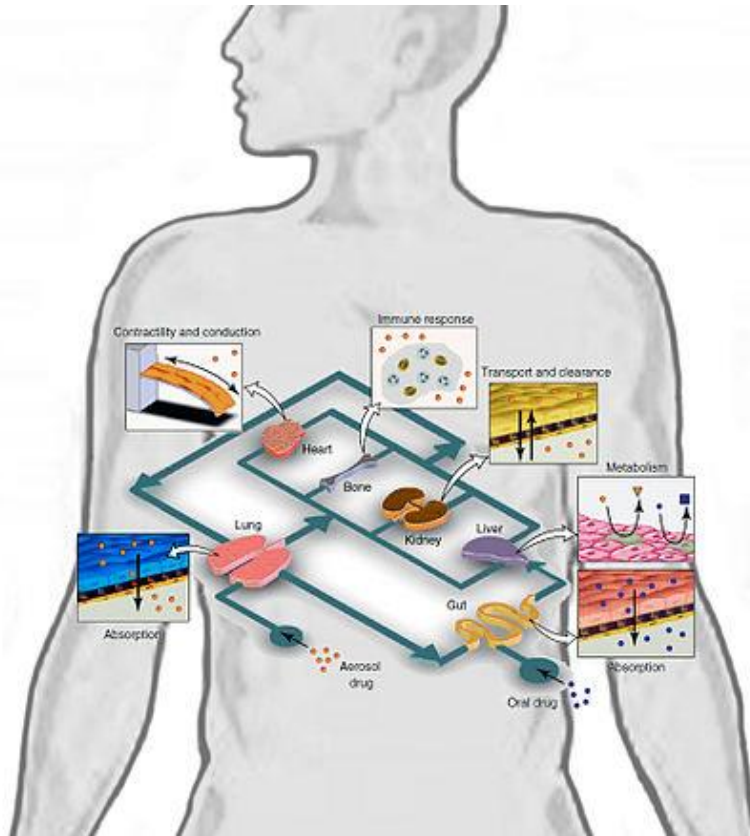
Cellular responses

Organ response

Organism response



Human-on-a-chip project



Limitations of in vitro models

- Mycoplasma
- Dedifferentiation conditions

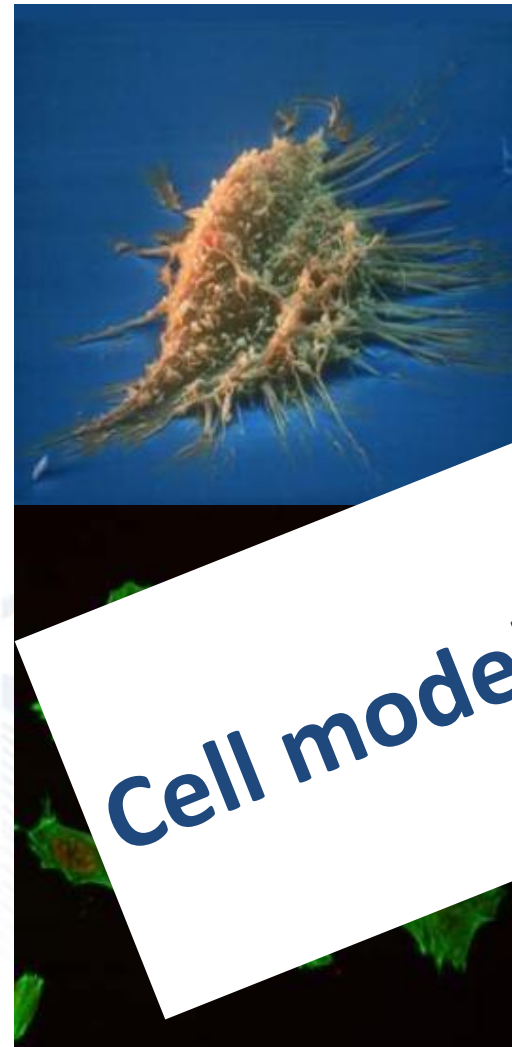


Cell models have not less limitations

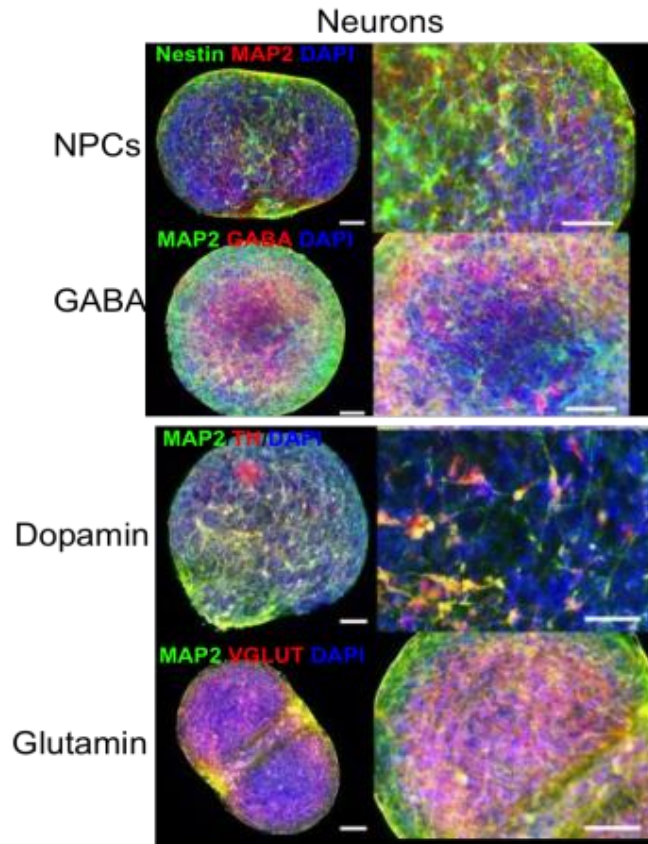
and defense
rate of test compounds in

are

- Tumor origin of many cells
- Cell identity



Human “mini-brain” developing from iPSC



- All cell types but micro-glia
- 350um diameter
- 800 per batch
- Reproducible
- Electrophysiological active
- From patient cells:
gene/environment interactions

Method development and validation process at FICAM

- Research model: scientifically solid model.
Deliverable: publication
↓
- Optimised model: all conditions optimised, method tested with the chemical substances it will be used by end users. **Deliverable:** SOP
↓
- Validated model: validation according to relevant guidelines. **Deliverable:** intra-laboratory validated method.

***Please, always
consider that rats are
not lab reagents!!!***

Questions?

