

# 25 years of research within in vitro methodologies

**3R Center DK 16<sup>th</sup> Nov 2021**

Rie Vinggaard

National Food Institute, Technical University of Denmark

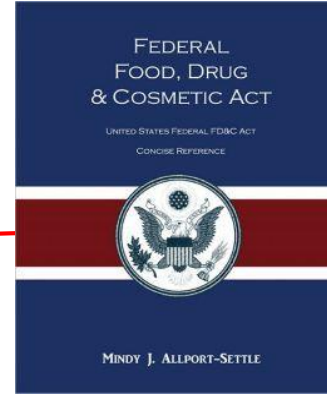
# Evolution of test strategies



Shen Nung **2695 BC**;  
Tested 265 herbs on  
himself and died from it



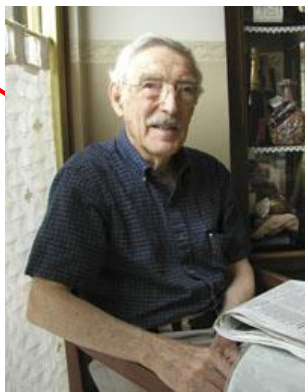
Cleopatra, **30 BC**;  
tested on prisoners



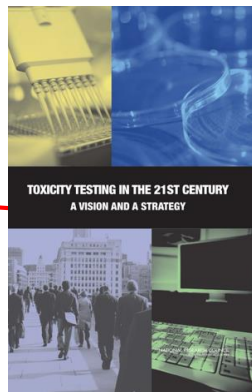
US FDC, **1938** starts  
animal testing of drugs,  
foods, cosmetics



Russell & Burch, **1959**;  
the 3R principles



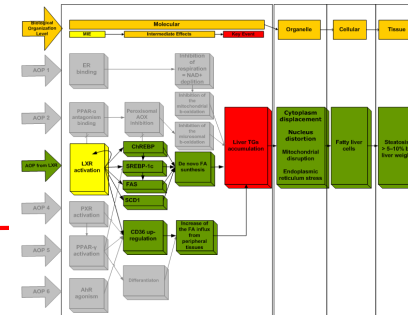
Bruce Ames, **1971**;  
the Ames test



Tox21c & ToxCast,  
**2007**; Toxicity pathways



EU Cosmetic Directive,  
**2013**; only in vitro testing



AOP, IATA, NAM **2017**;  
Network analysis

# EU-Parlamentet presser på for at afskaffe dyreforsøg i forskning

Der er forskningsområder, hvor vi kan undgå at bruge dyr til forsøg, siger ekspert.



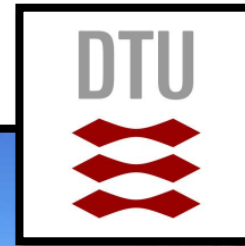
DR Nyheder 17. Sept 2021

I dag er dyreforsøg ikke tilladt, hvis forskningen handler om at teste kosmetik.









# My research fields

- Endocrine disrupting effects of chemicals
- Predictive toxicology (e.g. stem cells)
- Chemical mixture effects



# ***In vitro* assays for endocrine activity and their impact**

- **Androgen Receptor assay**
- Estrogen Receptor assay
- Ah Receptor assay
- PPAR $\alpha$ / PPAR $\gamma$  Receptor assay
- Thyroid Screen
- **H295R Steroidogenesis assay**
- The Embryonic Stem Cell Test
- 3T3-L1 Adipogenesis Assay
- **PluriLum: hIPSC-based assay for embryotoxicity**



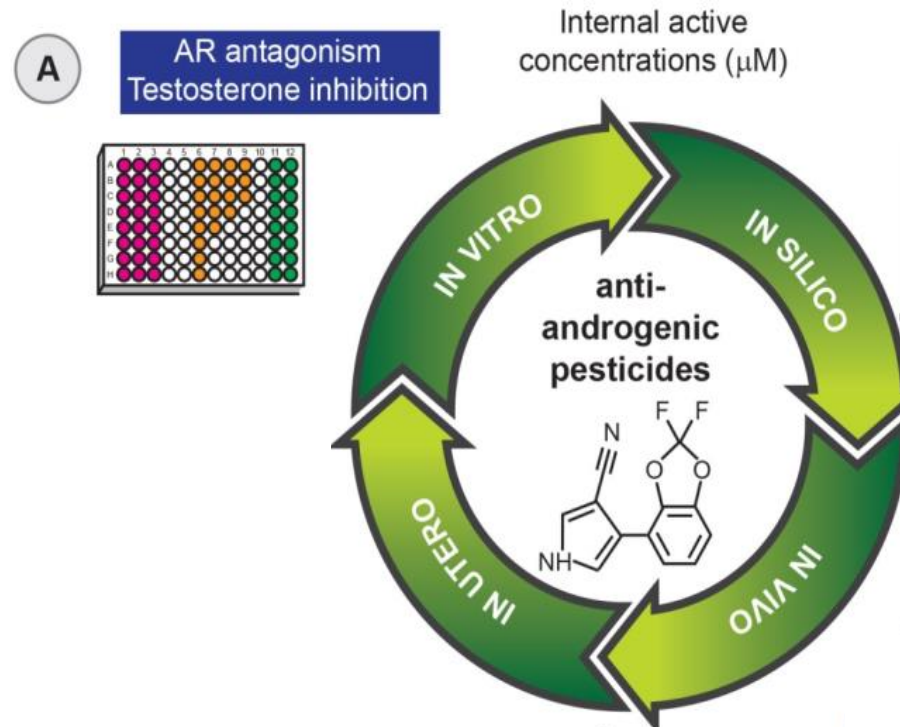


	AR ↑	AR ↓	ER	AhR	PPAR $\gamma$	RAR	Nrf2	p53	Ames
Sandwich wrapper	Red	Red	Grey	Red	Red	Grey	Red	Grey	Grey
Muffin forms	Grey	Red	Grey	Red	Red	Grey	Red	Grey	Grey
Baking paper	Grey	Grey	Grey	Red	Red	Grey	Grey	Grey	Grey
Flour bag	Grey	Grey	Red	Red	Red	Grey	Red	Red	Grey
Pizza box	Grey	Grey	Red	Red	Red	Grey	Red	Red	Grey
White pizza box	Grey	Red	Grey	Red	Red	Grey	Red	Grey	Grey
Microwave pizza box	Red	Grey	Grey	Red	Red	Grey	Grey	Grey	Red
Popcorn bag 1	Grey	Grey	Grey	Red	Red	Red	Grey	Grey	Grey
Popcorn bag 2	Grey	Grey	Grey	Red	Red	Red	Grey	Grey	Red
Sausage tray	Grey	Grey	Red	Red	Red	Grey	Red	Red	Grey
Fish tray	Grey	Grey	Red	Red	Red	Grey	Red	Grey	Grey
Tomato tray	Grey	Grey	Red	Red	Red	Red	Red	Grey	Grey
Cereal box	Grey	Grey	Grey	Red	Red	Red	Red	Red	Grey
Nordic paper	Red	Red	Grey	Red	Red	Grey	Red	Grey	Grey
Basis paper	Red	Red	Grey	Red	Red	Grey	Red	Grey	Grey
Chinese paper 1	Red	Grey	Red	Red	Red	Red	Red	Red	Grey
Chinese paper 2	Red	Red	Red	Red	Red	Grey	Red	Grey	Grey
Board w UV print	Grey	Grey	Red	Red	Red	Grey	Red	Red	Grey
Board w watersol print	Grey	Grey	Red	Red	Red	Grey	Red	Red	Grey
Board w offset print	Grey	Grey	Grey	Red	Red	Grey	Red	Red	Grey

# In vitro data demonstrate similar hazard profiles of structural analogues to bisphenol A

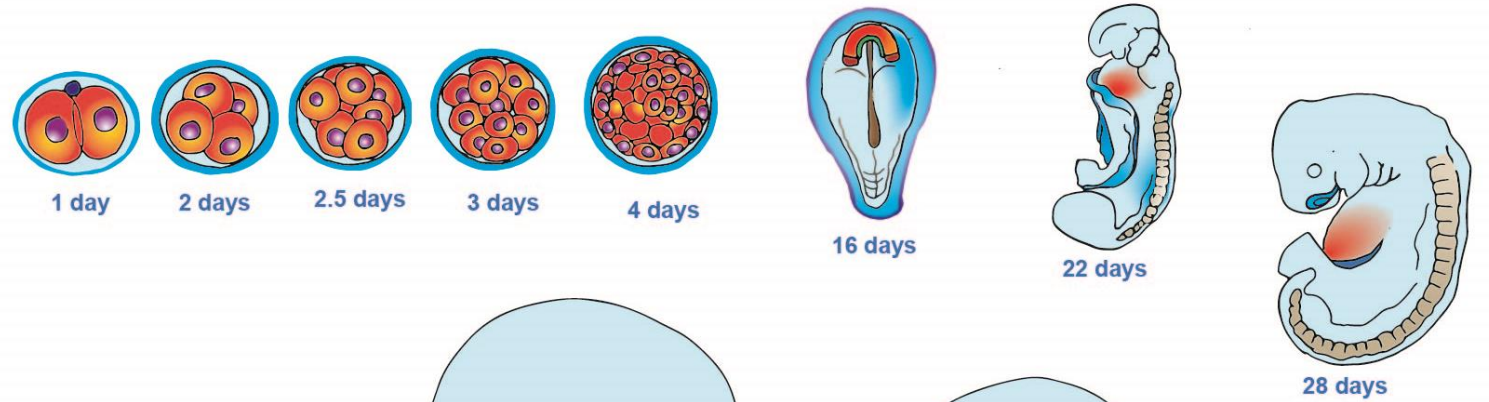
	ER	AR	Steroid hormone synthesis				AhR	PPAR $\alpha$	PPAR $\gamma$	RAR	Nrf2	p53	Lipid accumulation
			Prog	Corticoids	Androgens	Estrogens							
BPA	↑	↓	↑	↓	↓	↑	↑				↑	↑	
BPB	↑	↓	↑	↓	↓	↑	↑				↑	↑	
BPE	↑	↓	↑	↑	↓	↑	↑		↑		↑	↑	
BPF	↑	↓	↑	↑	↓	↑	↑		↑	↑		↑	
BPS	↑	↓	↑	↓	↓				↑			↑	
CP	↑	↓	↑	↓	↓	↑						↑	

# A novel approach for predicting male reproductive health disorders



# Developmental toxicity

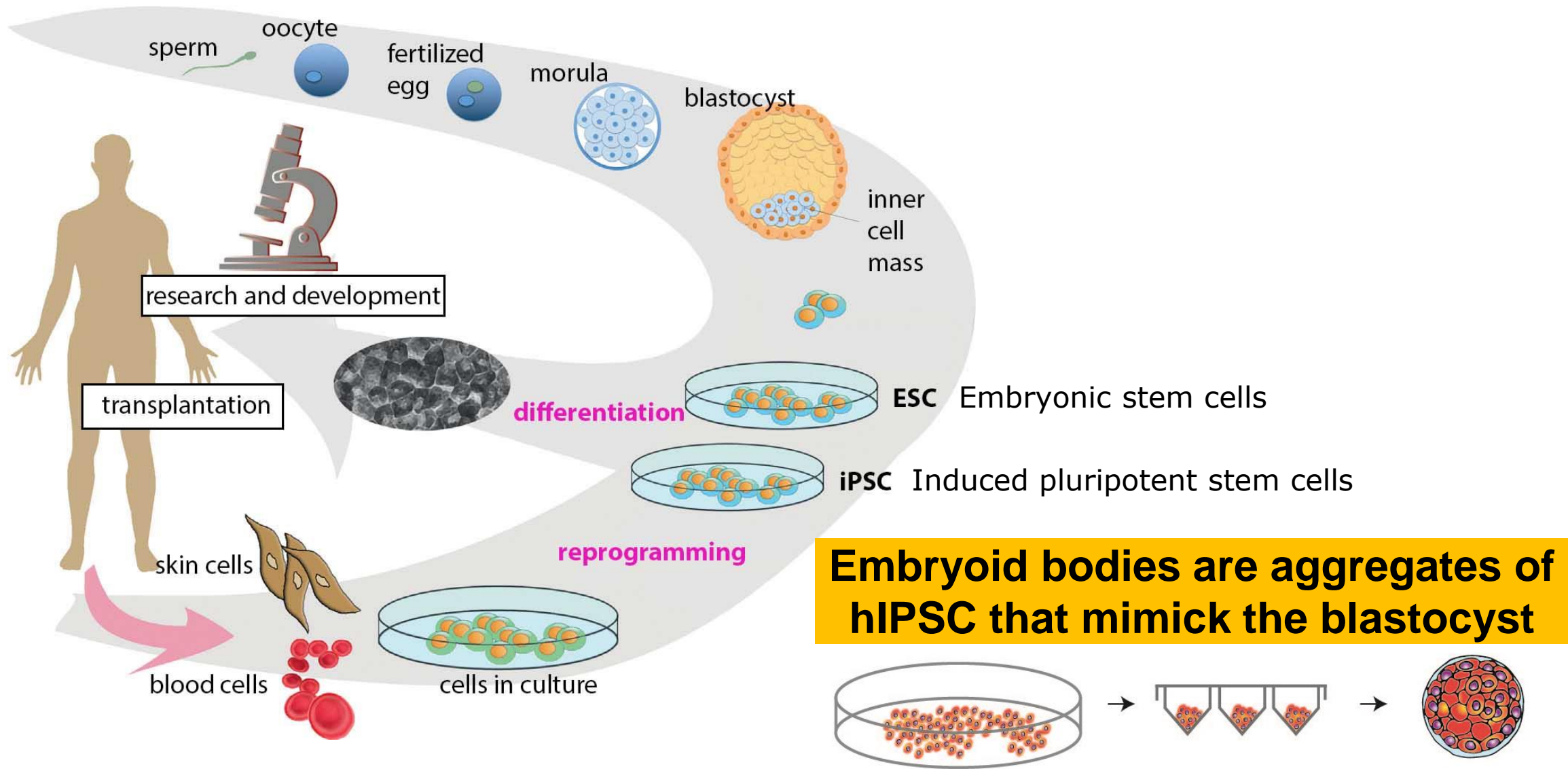
## Human prenatal development:



Best example of developmental toxicity: Thalidomide (1960s)

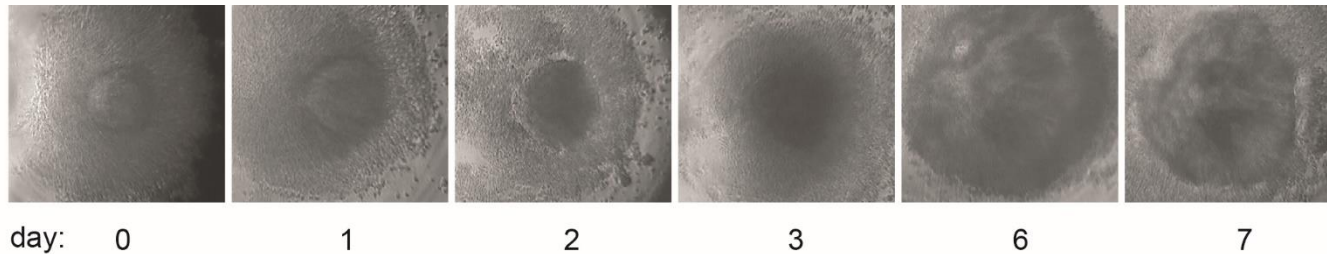
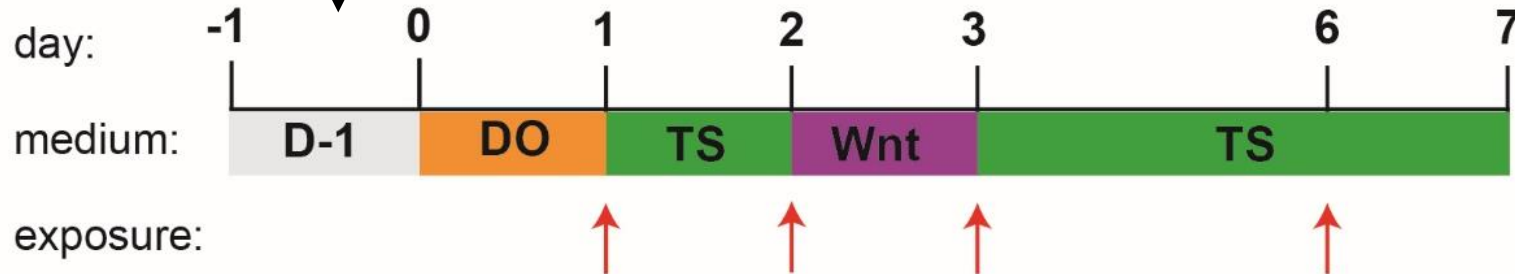
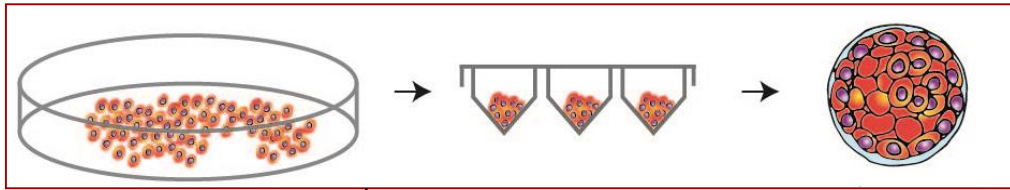


# Human-induced pluripotent stem cells have no ethical issues





# Development of the PluriLum assay – hiPSC as a model of embryonic development



LAUSCHKE K ET AL. *A novel human pluripotent stem cell based assay to predict developmental toxicity.* Arch.Toxicol 94(11), 3831, 2020

LAUSCHKE K, TRESCHOW AF ET AL. *Creating a human NKX2.5 reporter stem cell line for developmental toxicity testing.* Arch Toxicol 95, 1659, 2021



Topic ID:LC-GD-8-2-2020  
Technical annex – section 1-3

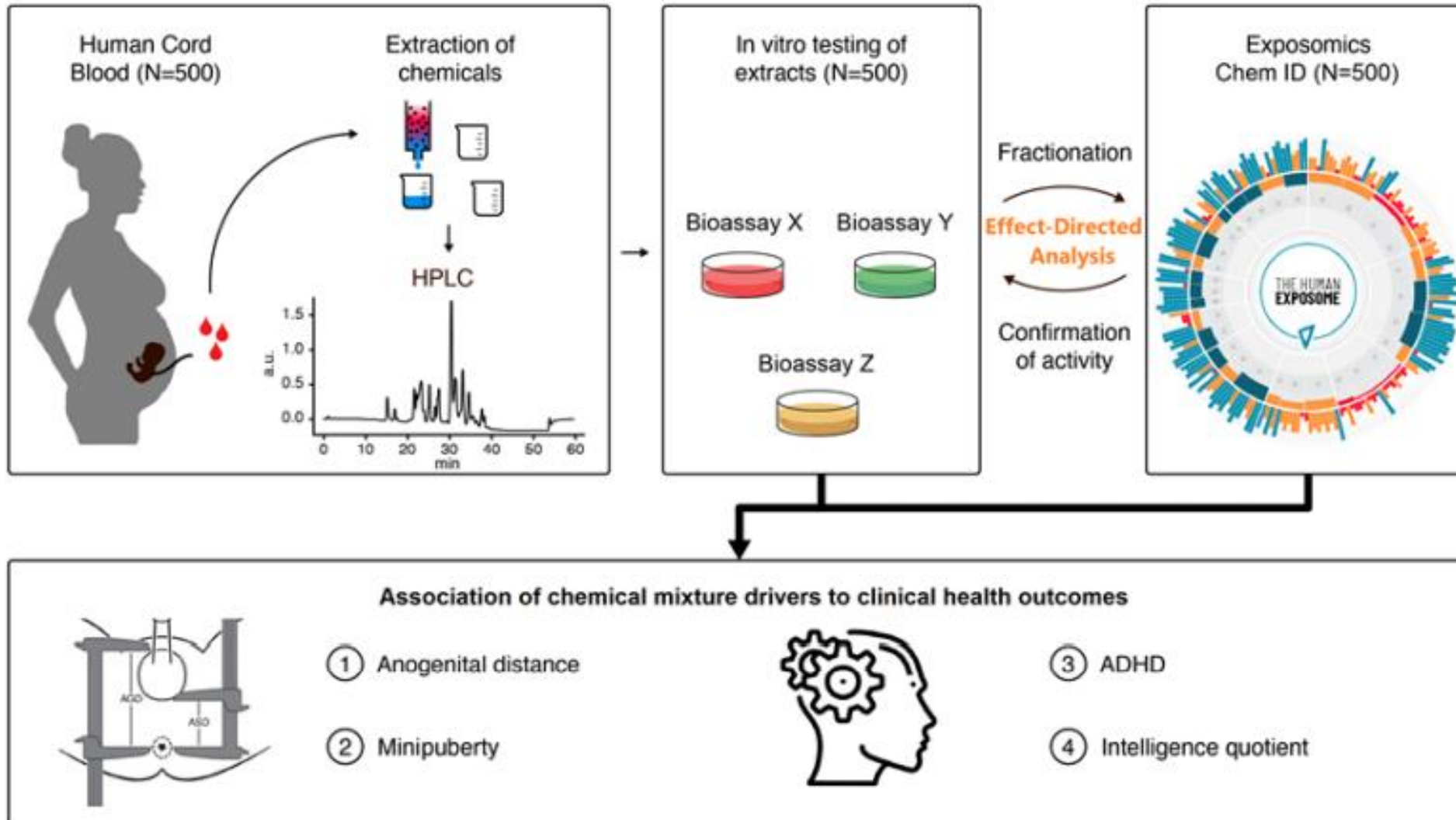
# PANORAMIX

**H2020 GreenDeal  
project  
Nov 2021 – 2025  
4.5 mill €**

*Providing risk assessments of complex real-life mixtures for the protection of Europe's citizens and the environment*



# The link of unknown chemicals in newborn's blood with adverse health effects – using in vitro methods to guide the identification



# Cell Toxicology team



Rie Vinggaard  
Prof.



Tina Alstrup Hansen  
Post doc



Maria João Valente  
Post doc



Yanying Ma  
PhD student



Andreas Treschow  
PhD student

## Projects

**PANORAMIX (2021-2025)**

PARC (2022-2029)

SafeWater (2021-2024)

Pyrethroid project (PYT) (2021-2023)

**H2020 GreenDeal project on chemical mixtures**

H2020 Joint program on chemical risk assessment

Independent Research Fund Denmark

DEPA Pesticide Research program



Horizon 2020  
European Union Funding  
for Research & Innovation



**DET FRIE FORSKNINGSRÅD**  
DANISH COUNCIL FOR  
INDEPENDENT RESEARCH



**Ministry of Environment  
and Food of Denmark**  
Environmental  
Protection Agency

