



# Investigating the Health Impact of Pollutants (HORIZON-HLTH-2025)

July, 3<sup>rd</sup>, 2025

KIST Europe, Saarbrücken, Germany

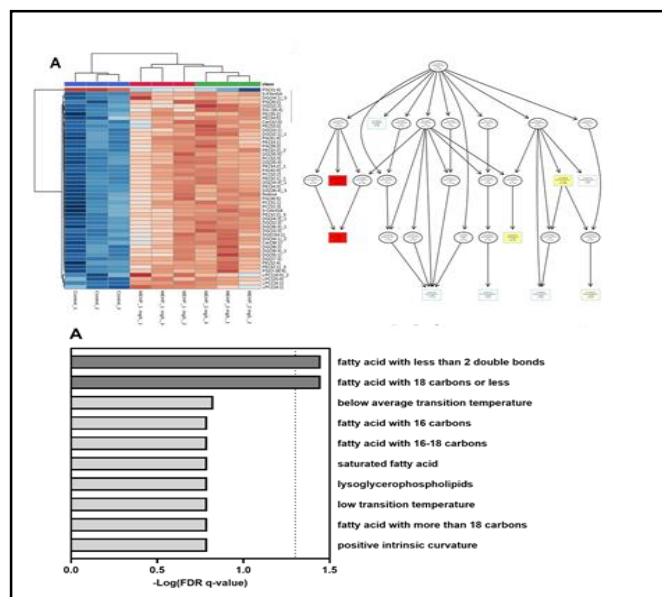
Kim, Young Jun



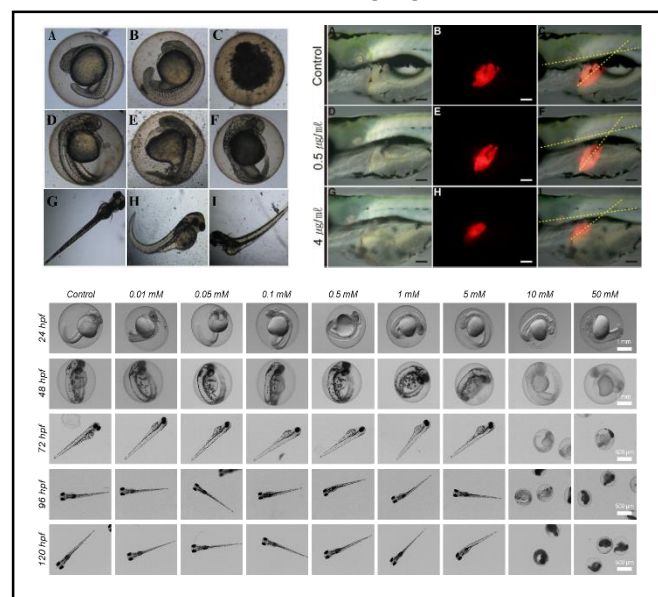
# Cutting Edge technologies

- Report gene assay for receptor and ligand interaction
- Molecular simulation/docking
- Predicting toxicity using QSAR
- Molecular imaging
- 3D In vitro organoid models
- Next-generation sequencing for pathway enrichment

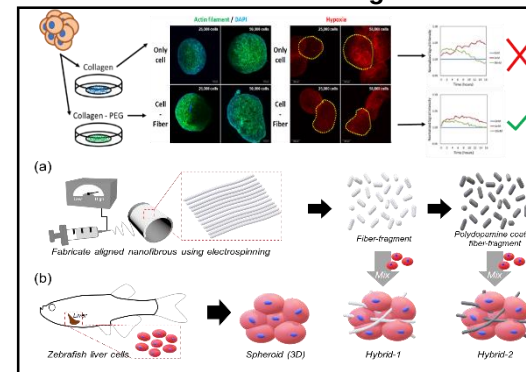
## Non target metabolomics



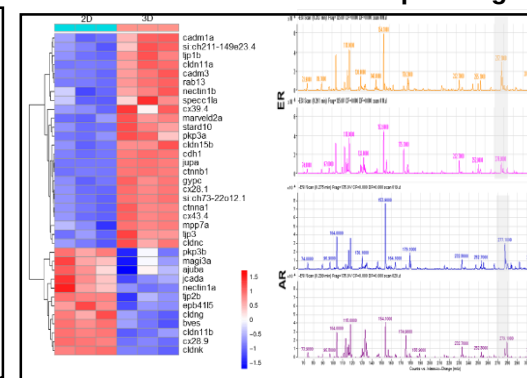
## In vivo imaging



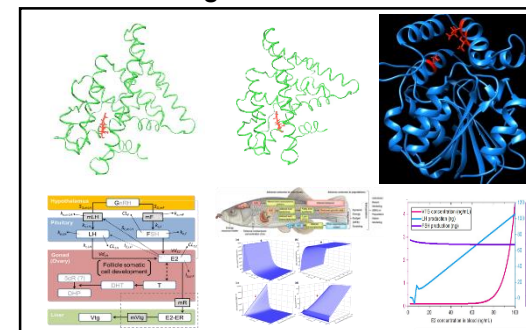
## 3D Cell technologies



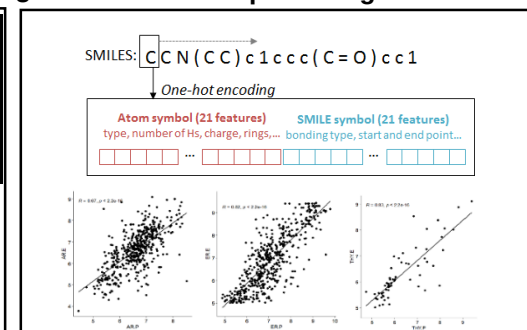
## Genomics/metabolomics profiling



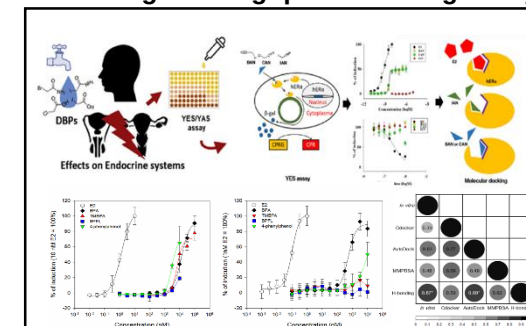
## Molecular docking and Mathematical modeling



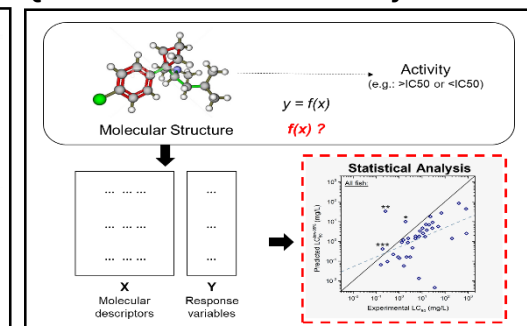
## Best Deep learning selection



## In vitro High-throughput screening assay

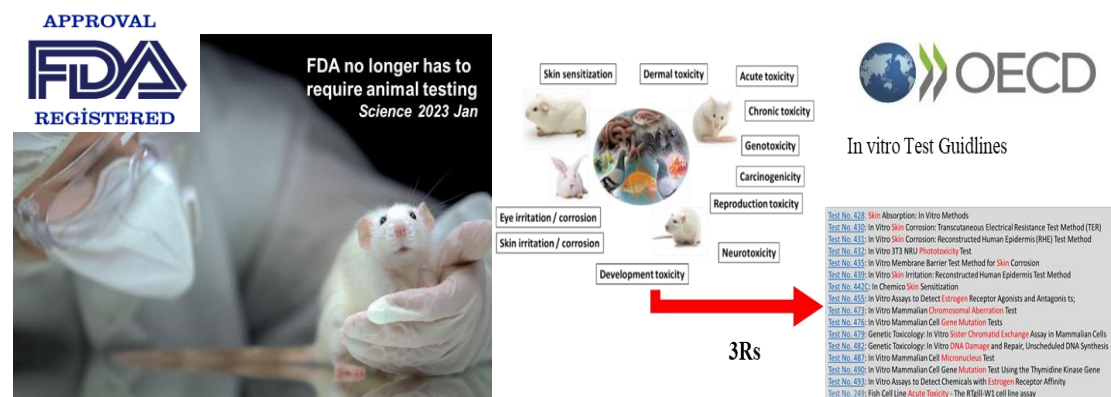


## Quantitative structure-activity relationship



# Demands on Alternative Animal Testing

## FDA and OECD TG focus on 3Rs

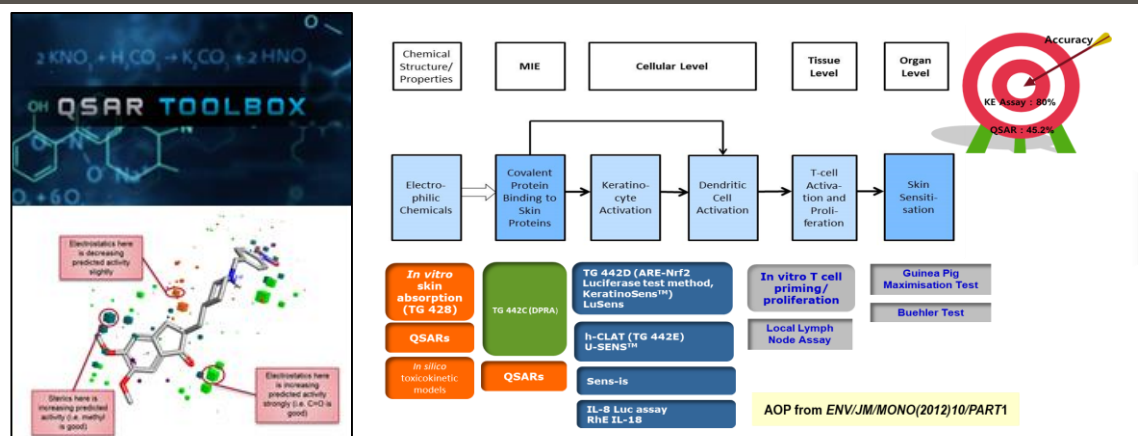


## Over 5000 regulatory decisions annually

“... The US will reduce its requests for, and our funding of, mammal studies by 30 % until 2025 and eliminate all mammal study requests and funding by 2035.”



## Improve QSAR prediction accuracy



## Non-tariff barriers to trade

*Promoting the use of non-animal methods BY AVOIDING ANIMAL TESTING FOR INDUSTRY AND NON-TARIFF TRADE BARRIERS:*

**AT LEAST € 150 MILLION / YEAR**

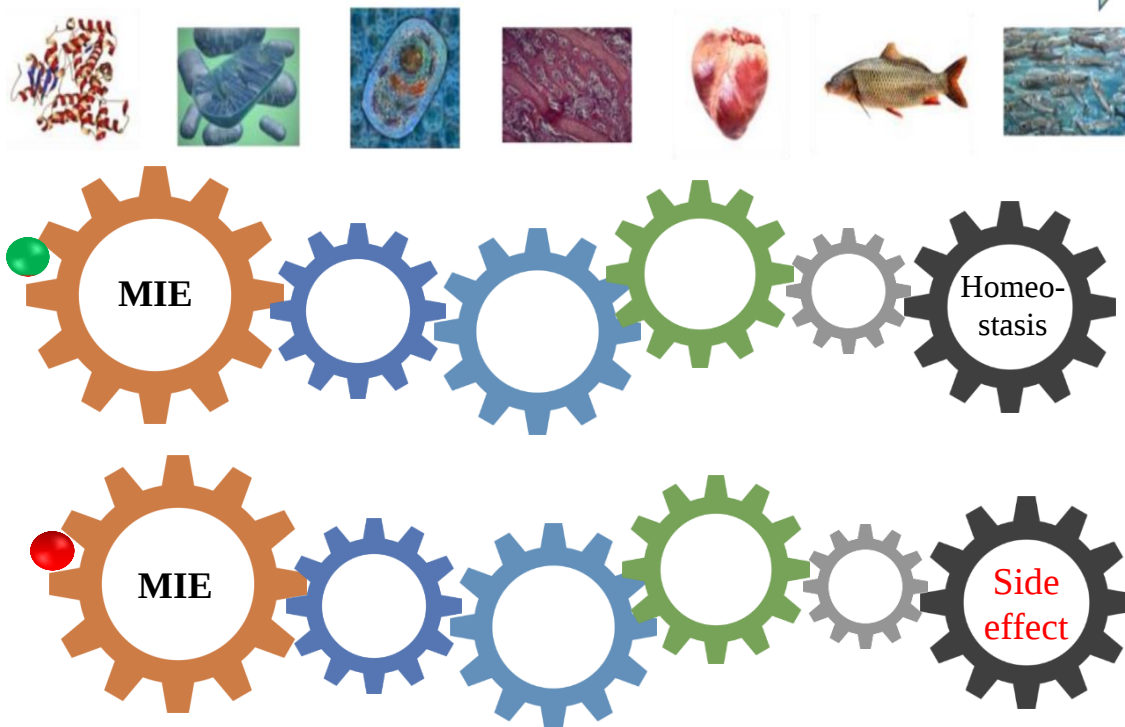


**Advancements in REGULATION have led to the development of various in vitro assays that aim to enhance functionality and reduce reliance on animal testing!**

# Brief definition of AOP under OECD

## Adverse Outcome Pathway (AOP)

Chemical Stressor | MIE Subcellular | KE1 Cellular | KE2 Tissue | KE3 Organ | AO Individual/Population



**Finally approved and endorsed by OECD**

## AOP Development Process

TGs/GDs published by OECD  
i.e. First skin sensitization AOP implemented into OECD Toolbox

### Regulatory conclusion

Once an AOP is endorsed by the WNT/TFHA it is considered adopted by the OECD for development of **Guidance Document**

### WoE assessment

Once the AOP has successfully passed the EAGMST\* review, it is handed over for **external review** to experts nominated by the WNT and the TFHA.

### Generate information

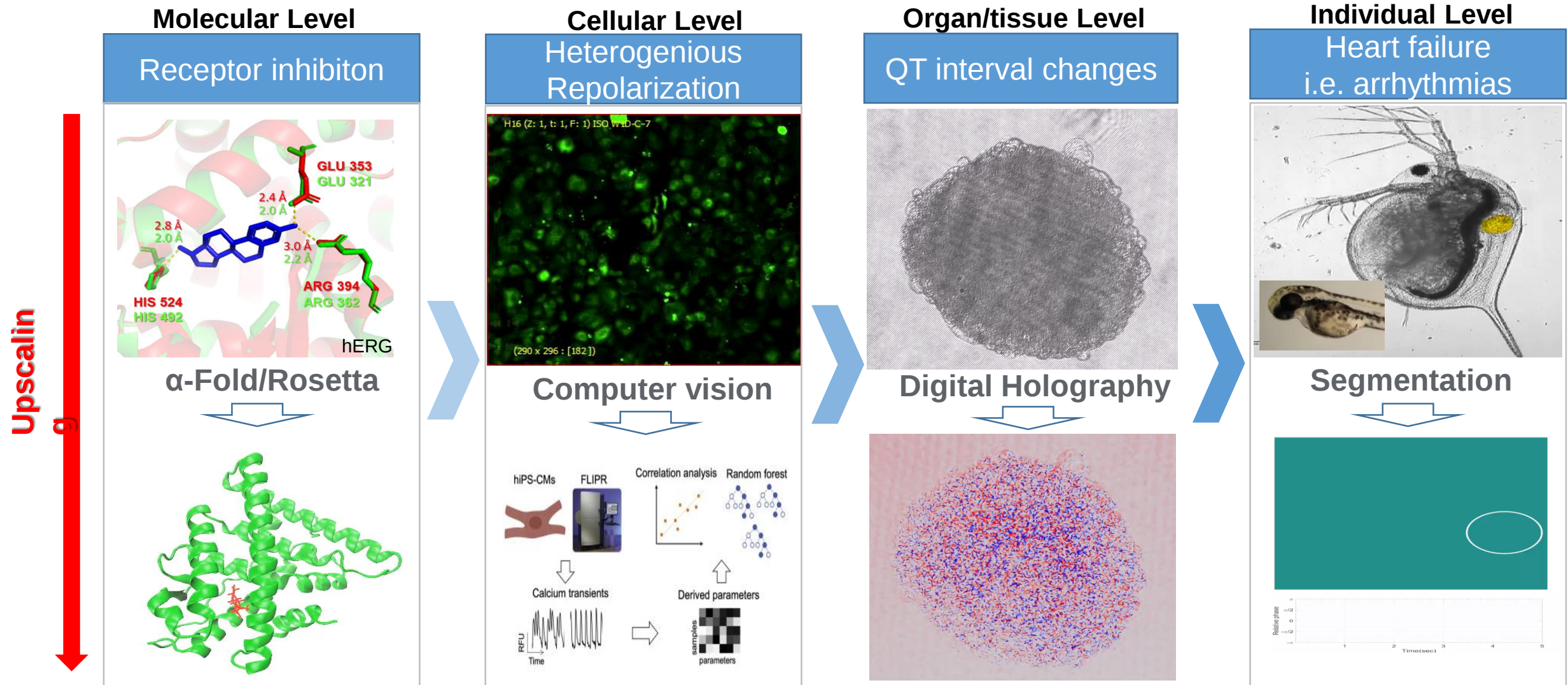
Once an AOP is considered mature enough by its authors, it can undergo an **internal review** by members of the EAGMST.\*

### Problem formulation

AOPs in the lowest tier can, but do not have to go through the EAGMST\* procedure to get onto the **OECD work program**.

\* EAGMST: Extended Advisory Group on Molecular Screening and Toxicogenomic

# AOP 433: hERG channel blockade leading to sudden cardiac death



# AOP Toolbox development

## Test System Selection

Select appropriate test model and exposure system (conditions)

## Reference Pollutants selection

Well-characterized compounds with known modes of action were selected as reference MNPs for toolbox development and validation testing

## Assay Optimization

Standardize and optimize NAMs for different 3D organoid models. Ensure assays are specific, sensitive and reproducible for diseases

## Mechanistic Studies (MoA Anchoring)

Conduct mechanistic studies to elucidate how NMPs impact in vitro at the molecular level, employing qPCR and/or transcriptomic approaches to identify biomarker genes linked to key events (KEs) across distinct modes of action (MoA).

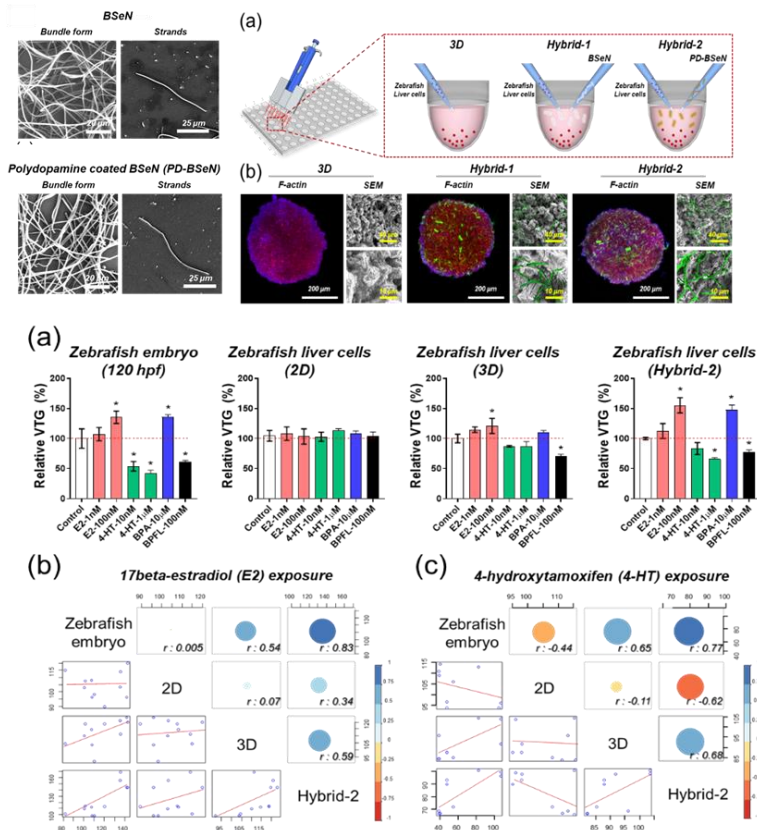
## AOP Integration, SOP standardization

Integrate mechanistic data into AOP frameworks. Develop and refine AOPs through Weight Of Evidence (WOE) assessments

# OECD TG-based Alternative Toxicity Research

## OECD Test No. 234: Fish Sexual Development Test

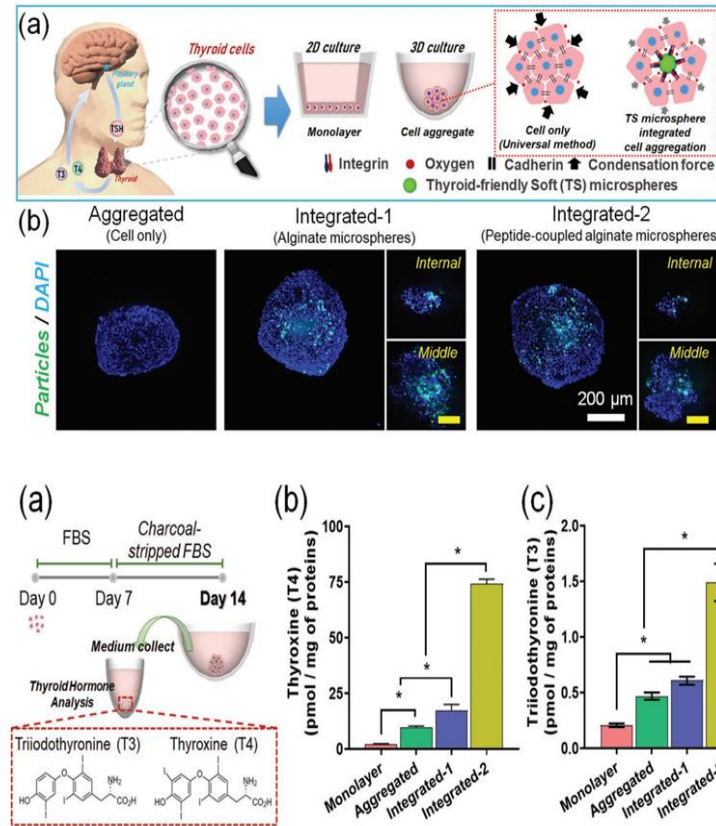
### Quantitative Analysis of Vtg in Fish 3D Cells



Small 2022

## OECD Test No. 248: Xenopus Thyroid Assay

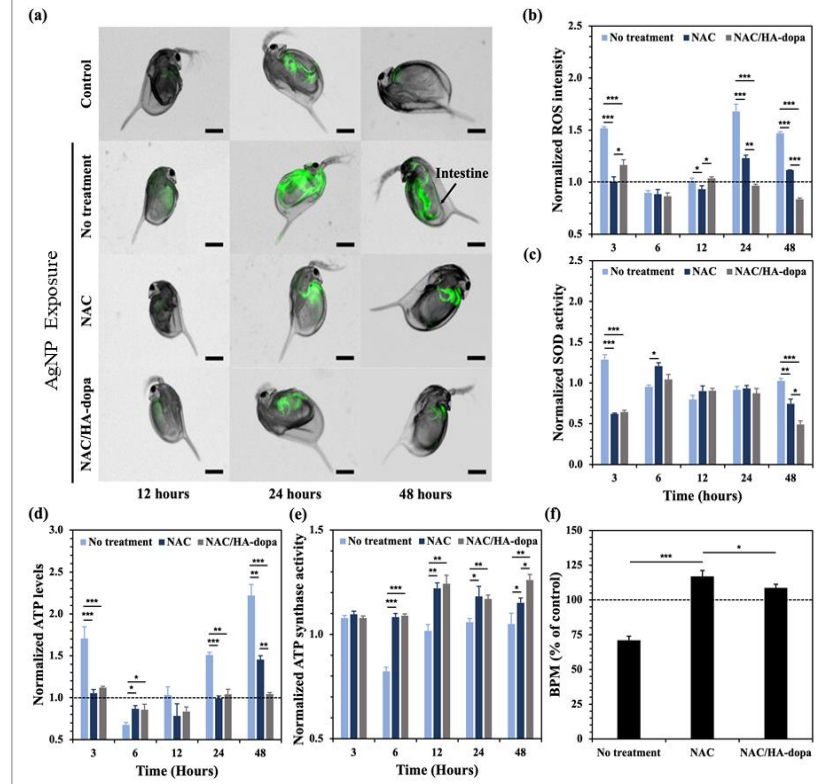
### Human-derived 3D cell-based thyroid hormone assay



Small 2023

## OECD Test No. 202: Daphnia. Acute Immobilisation

### Reproductive toxicity with water fleas



ACS Appl. Mater. Interfaces 2023



# Participation in Horizon Project



## CHIAsMA - ACCESSIBLE INNOVATIVE METHODS FOR THE SAFETY & SUSTAINABILITY ASSESSMENT OF CHEMICALS & MATERIALS

- Call: HORIZON-CL4-2023-RESILIENCE-01
- Period: 2025. 01- 2028. 01 ( total 4years)
- Total budget : EUR 213 million

| No.           | Organisation Name                                                                        | Country        |
|---------------|------------------------------------------------------------------------------------------|----------------|
| 1<br>(Coord.) | LIST – Luxembourg Institute of Technology                                                | Luxembourg     |
| 2             | UoB – University of Birmingham                                                           | United Kingdom |
| 3             | TAU – University of Tampere                                                              | Finland        |
| 4             | 7P9-SI – Seven Past Nine                                                                 | Slovenia       |
| 5             | RIVM – Rijksinstituut voor Volksgezondheid en Milieu                                     | Netherlands    |
| 6             | MUI – Medical University Innsbruck                                                       | Austria        |
| 7             | AIST – AcumenIST SPRL                                                                    | Belgium        |
| 8             | SU – Swansea University                                                                  | United Kingdom |
| 9             | NMBU – Norwegian University of Life Sciences                                             | Norway         |
| 10            | NovaM – NovaMechanics                                                                    | Cyprus         |
| 11            | NTUA – National Technical University of Athens                                           | Greece         |
| 12            | AIT - Austrian Institute of Technology                                                   | Austria        |
| 13            | IUF – Leibniz Institute für Umweltmedizinische Forschung GmbH                            | Germany        |
| 14            | BASF – BASF SE                                                                           | Germany        |
| 15            | IOM – Institute for Occupational Medicine                                                | United Kingdom |
| 16            | UniTOV - University of Rome Tor Vergata                                                  | Italy          |
| 17            | UV – University of Amsterdam                                                             | Netherlands    |
| 18            | ECETOC                                                                                   | Belgium        |
| 19            | HU – Hanyang University                                                                  | South Korea    |
| 20            | EMPA – Eidgenössische Materialprüfungs- und Forschungsanstalt                            | Switzerland    |
| 21            | <a href="#">KIST Europe-Korea Institute of Science and Technology Europe South Korea</a> | Germany        |
| 22            | <a href="#">KRISS-Korea Research Institute of Standards and Science South Korea</a>      | South Korea    |

## Evolution in RISK assessments



New approach methodologies (NAMs)  
 Alternatives to animal testing  
 In vitro and in silico alternatives  
 Focus on human-relevant models  
 (IVIVE)  
 Get mechanistic outputs (AOPs)  
 3Rs  
 Refinement  
 Reduction  
 Replacement



## PARC-PARTNERSHIP FOR THE ASSESSMENT OF RISKS FROM CHEMICALS

- Call: HORIZON-HLTH-2021-ENVHLTH-03-01
- Period: 2022. 05 - 2029. 04 (total 7 years)
- Total budget : € 400 million (EU Funding €200 million+)
- Matching €200 million)

| 번호 | 기관 이름                                                                           | 국가          |
|----|---------------------------------------------------------------------------------|-------------|
| 1  | Norwegian Institute of Public Health (NIPH)                                     | Norway      |
| 2  | National Institute of Health Doutor Ricardo Jorge (INSA)                        | Portugal    |
| 3  | <a href="#">Korean Institute of Science and Technology Europe (KIST Europe)</a> | Germany     |
| 4  | ANSES                                                                           | France      |
| 5  | University of Utrecht (UU)                                                      | Netherlands |
| 6  | Institute of Environmental Protection - National Research Institute (IEP – NRI) | Poland      |
| 7  | University of Aveiro (UAVER)                                                    | Portugal    |
| 8  | National Institute of Biology (NIB)                                             | Slovenia    |
| 9  | Institut National de Recherche et de Sécurité (INRS)                            | France      |
| 10 | Norwegian Institute for Water Research (NIVA)                                   | Norway      |
| 11 | University of Wageningen (WU)                                                   | Netherlands |
| 12 | Benaki Phytopathological Institute (BPI)                                        | Greece      |

# Tasks : Mechanistic understanding of Health Risk using Adverse Outcome Pathway (AOP)-informed pollutant Exposures

**Policy** : Scientific basis for regulatory action(e.g.EMA,ECHA), vulnerability protection

**Technology** :Standardized OECD AOP-based test methods (NAMs)

**Society** :Citizen-facing health risk prediction services

**Industry** :Entry into integrated toxicology-healthcare-digital platforms market

# Target Call Selection

## [Risks of pollutants in the vulnerable : Emerging Concerns for Human Health]

- **HORIZON-HLTH-2025-03-ENVHLTH-01-two-stage: The impact of pollution on the development and progression of brain diseases and disorders**
- **HORIZON-HLTH-2025-03-ENVHLTH-02-two-stage: Research on the Health Impact of Micro and Nanoplastics on Human Health**

| Topic ↑                                                                                          | Budget (EUR) -<br>Year : 2025 ↓↑ | Stages ↓↑ | Opening date ↓↑ | Deadline ↓↑              | Contributions ↓↑   | Indicative number<br>of grants ↓↑ |
|--------------------------------------------------------------------------------------------------|----------------------------------|-----------|-----------------|--------------------------|--------------------|-----------------------------------|
| HORIZON-HLTH-2025-03-DISEASE-02-two-stage - HORIZON-RIA HORIZON Research and Innovation Actions  | 50 000 000                       | two-stage | 2025-05-22      | 2025-09-16<br>2026-04-16 | 6000000 to 8000000 | 7                                 |
| HORIZON-HLTH-2025-03-ENVHLTH-01-two-stage - HORIZON-RIA HORIZON Research and Innovation Actions  | 40 000 000                       | two-stage | 2025-05-22      | 2025-09-16<br>2026-04-16 | 6000000 to 7000000 | 6                                 |
| HORIZON-HLTH-2025-03-ENVHLTH-02-two-stage - HORIZON-RIA HORIZON Research and Innovation Actions  | 40 000 000                       | two-stage | 2025-05-22      | 2025-09-16<br>2026-04-16 | 7000000 to 8000000 | 5                                 |
| HORIZON-HLTH-2025-03-IND-03-two-stage - HORIZON-RIA HORIZON Research and Innovation Actions      | 40 000 000                       | two-stage | 2025-05-22      | 2025-09-16<br>2026-04-16 | 6000000 to 8000000 | 5                                 |
| HORIZON-HLTH-2025-03-STAYHLTH-01-two-stage - HORIZON-RIA HORIZON Research and Innovation Actions | 40 000 000                       | two-stage | 2025-05-22      | 2025-09-16<br>2026-04-16 | 6000000 to 8000000 | 5                                 |



**Thank you for your attention**

