

# Future outlook for Omics including AI

David Rouquié  
Bayer

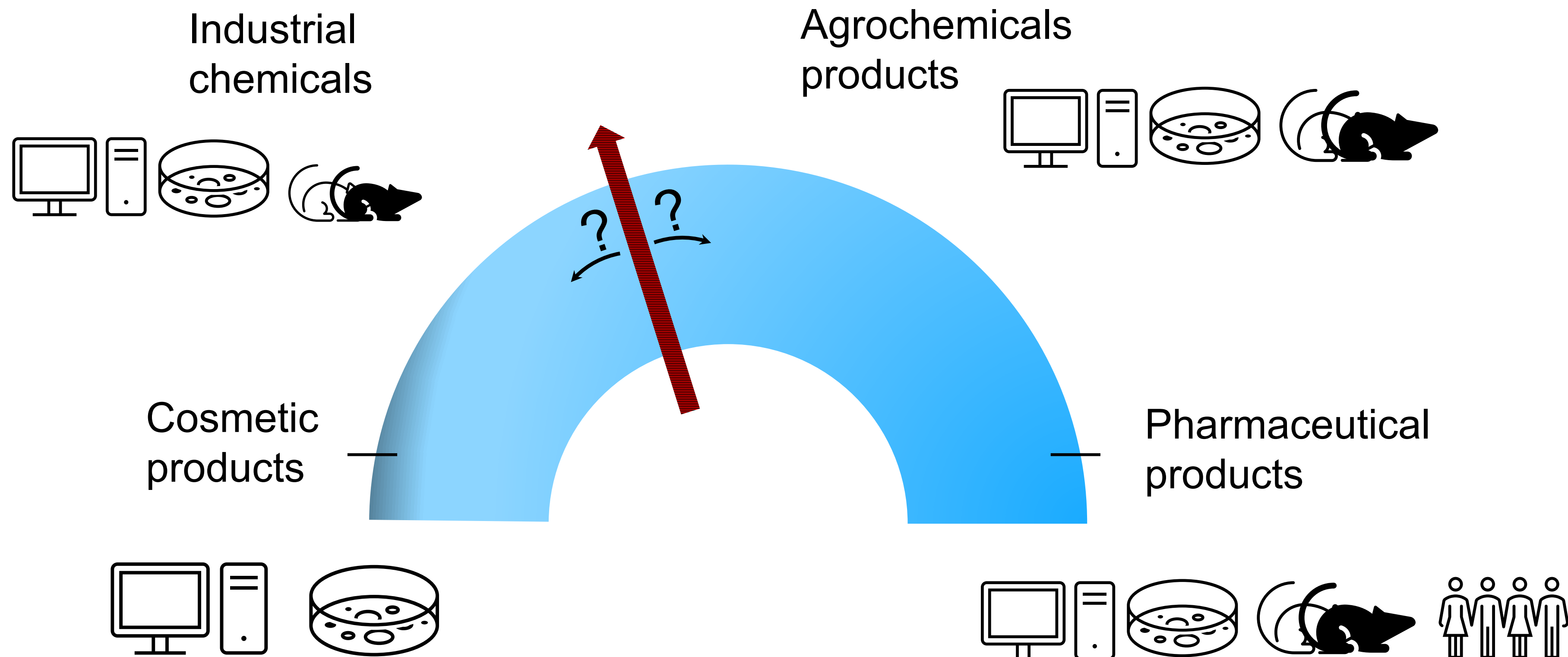
September 22, 2025

# Agenda

- Omics in the context of NGRA
- Few challenges
- Opportunities
- On-going ECETOC activities

# Few words about Next Generation Risk Assessment

Spectrum of evaluations in chemical risk assessment

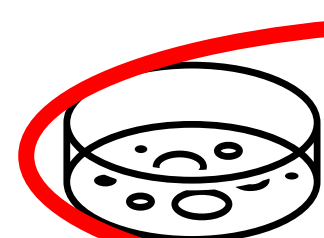
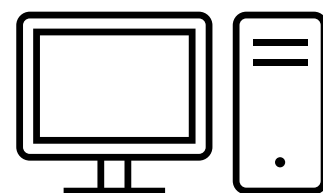


# Few words about Next Generation Risk Assessment

Spectrum of evaluations in chemical risk assessment

Industrial  
chemicals

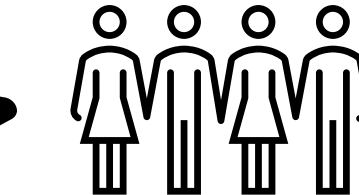
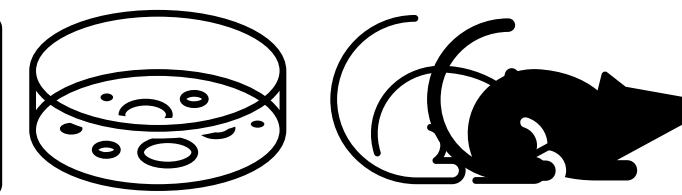
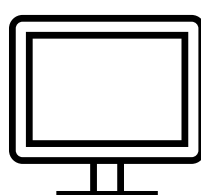
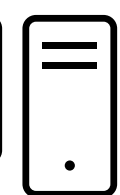
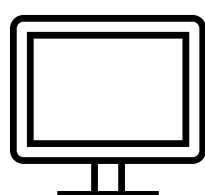
Agrochemicals  
& products



Short term in vivo studies  
enriched with omics endpoints

Cosmetic  
products

Pharmaceutical  
products



SOT | Society of  
Toxicology  
academic.oup.com/toxsci

Toxicological Sciences, 2025, 1–6  
<https://doi.org/10.1093/toxsci/kfaf120>  
Advance Access Publication Date: August 25, 2025  
Forum

## Navigating complexity in modern toxicology: the role of omics in short-term in vivo studies

Constance A. Mitchell <sup>1,\*</sup>, Leah Wehmas <sup>2</sup>, David Rouquié <sup>3</sup>, Florian Caiment <sup>4</sup>, Richard A. Currie <sup>5</sup>, Christine E. Crute <sup>1</sup>

<sup>1</sup>Health and Environmental Sciences Institute, Washington, DC 20005, United States

<sup>2</sup>Chemical Characterization and Exposure Division, Center for Computational Toxicology and Exposure, U.S. Environmental Protection Agency, Research Triangle Park, NC 27711, United States

<sup>3</sup>Toxicology Data Science, Bayer SAS Crop Science Division, Cedex, Sophia Antipolis 06906, France

<sup>4</sup>Department of Translational Genomics, GROW Research Institute for Oncology and Reproduction, Maastricht University, 6229 ER Maastricht, The Netherlands

<sup>5</sup>Jealott's Hill International Research Centre, Syngenta, Bracknell, Berkshire RG42 6EY, United Kingdom



**Omic's high  
content  
biological  
assays**

# Opportunities

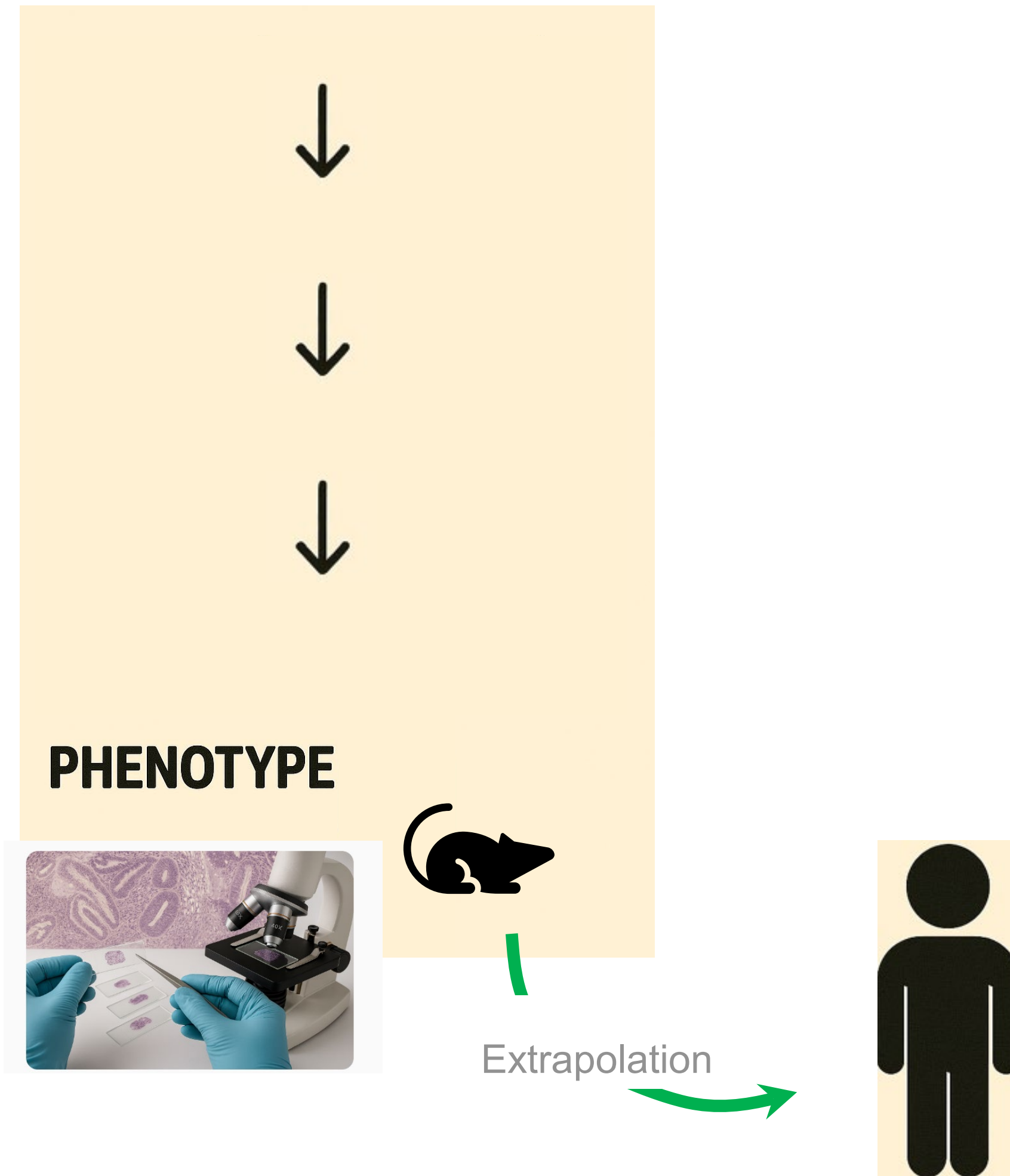
## They provide several advantages

- They generate rich, multiparametric data on cellular and molecular responses from wide range of cell cultures (2D, 3D) or tissues.
- They enable chemical grouping based on bioactivity patterns.
- They support the identification of benchmark concentrations for biological activities.
- They provide insights into mechanistic understanding.

From ...

chemical exposure

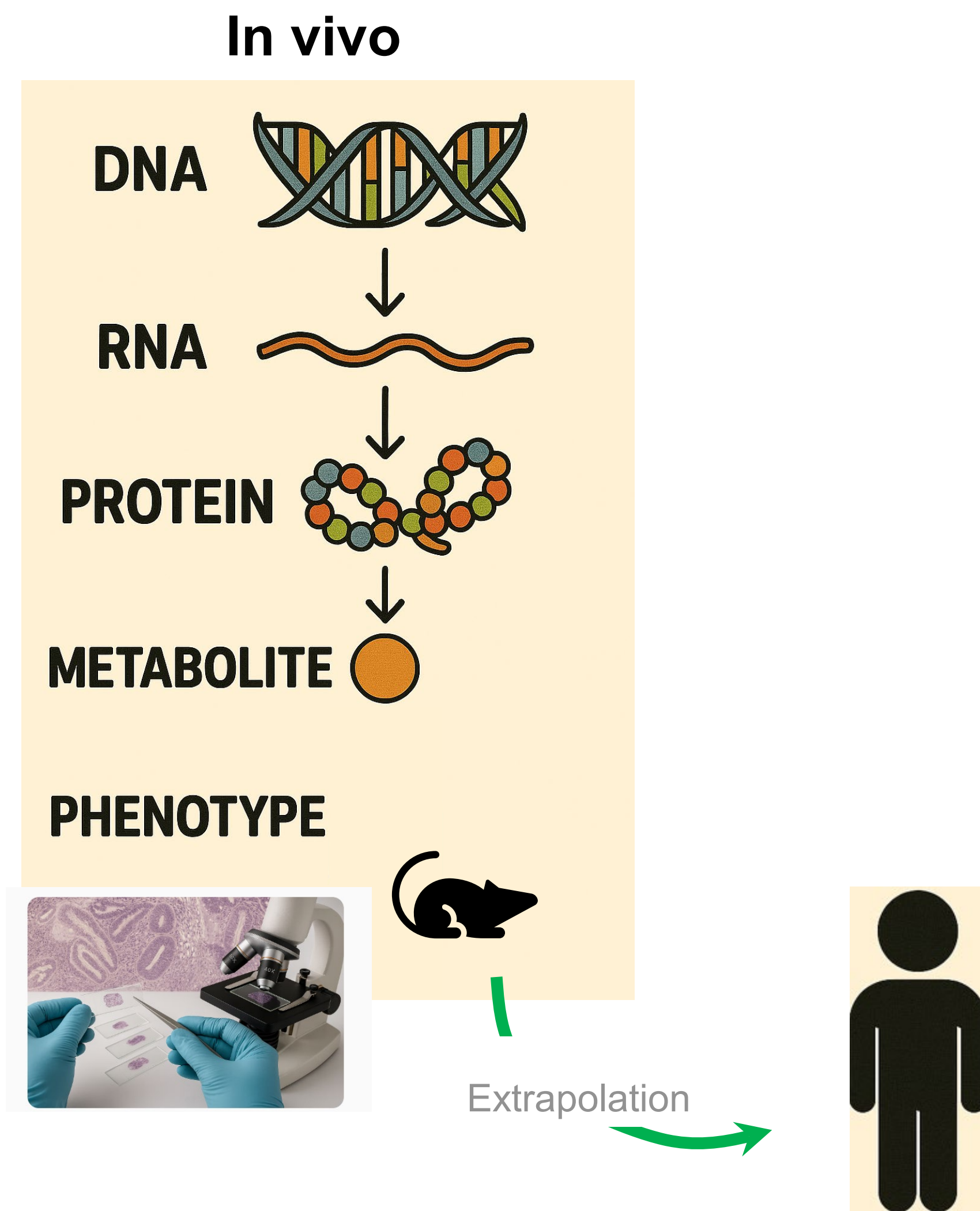
In vivo



to adverse outcome

From ...

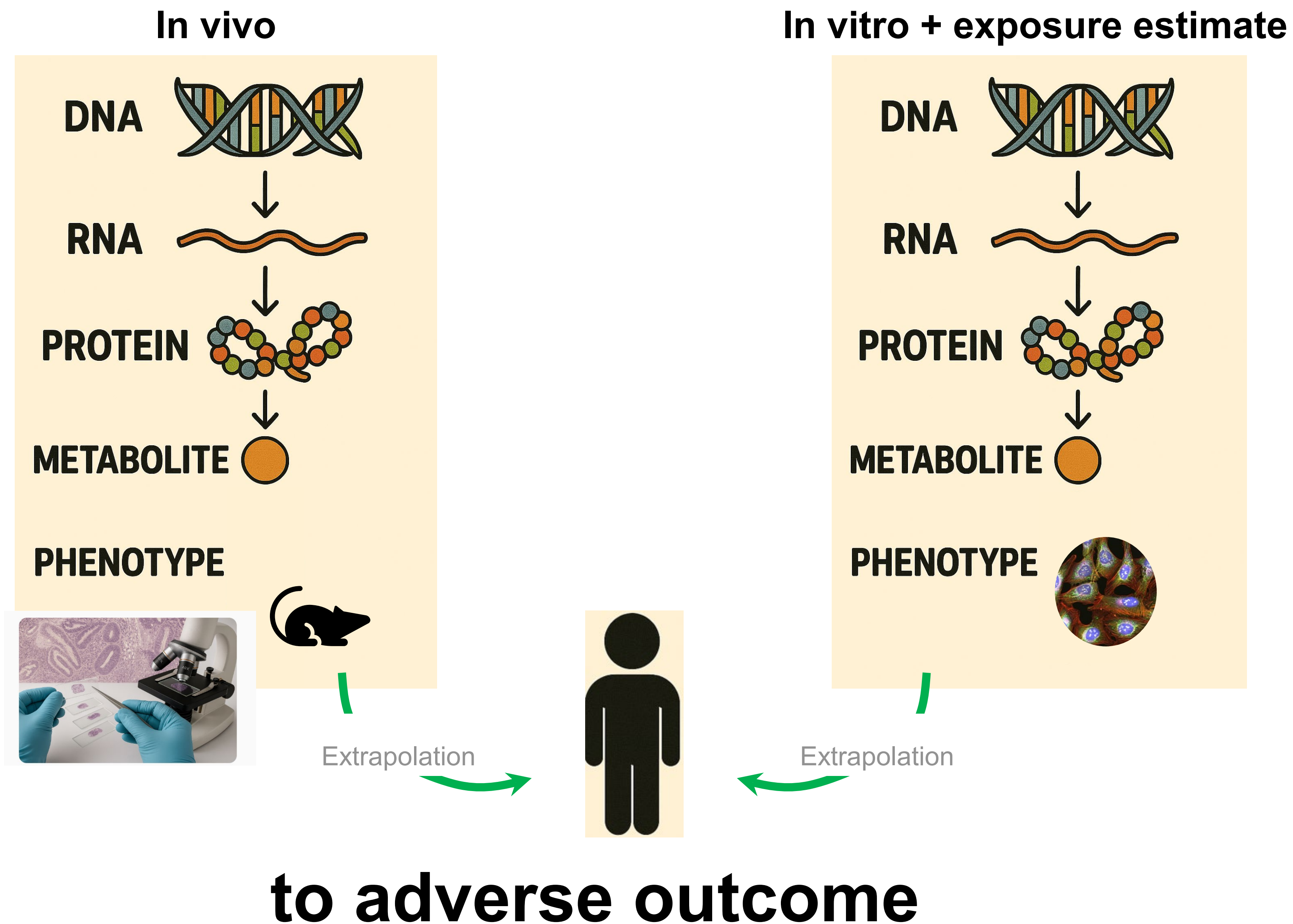
chemical exposure



to adverse outcome

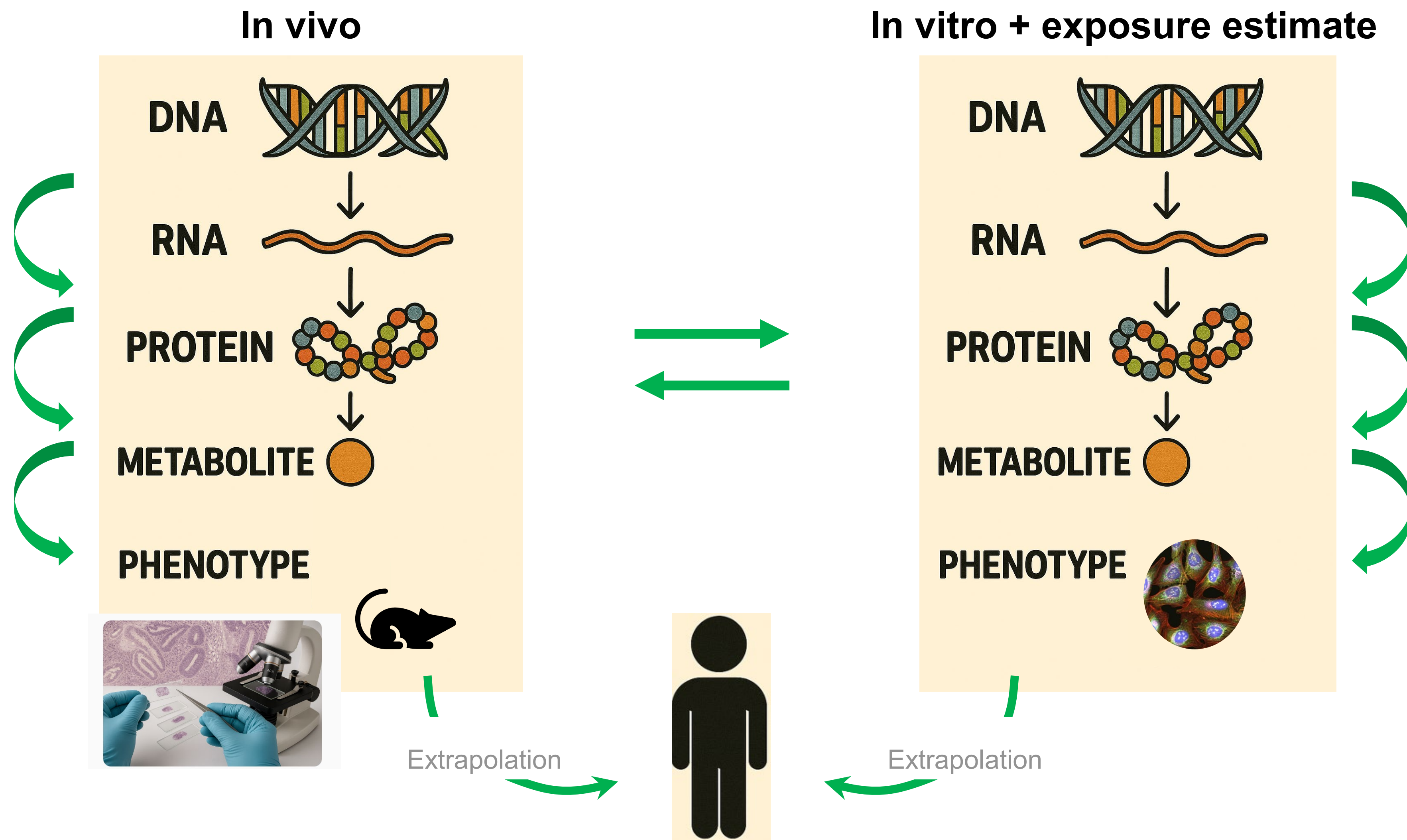
From ...

# chemical exposure



From ...

# chemical exposure



to adverse outcome

# Big Challenge

- The various omics technologies describe specific layers of the **universe of chemical induced effects**
- **For each layer in their corresponding test system**, we need to better understand
  - the **natural variability** of the individual descriptors (transcripts, set of transcripts, proteins, metabolites, morphological features, ...)
  - their corresponding **dynamic and dynamic ranges**
  - the proportion of the **biological knowledge** they provide with regards to **adverse outcomes**

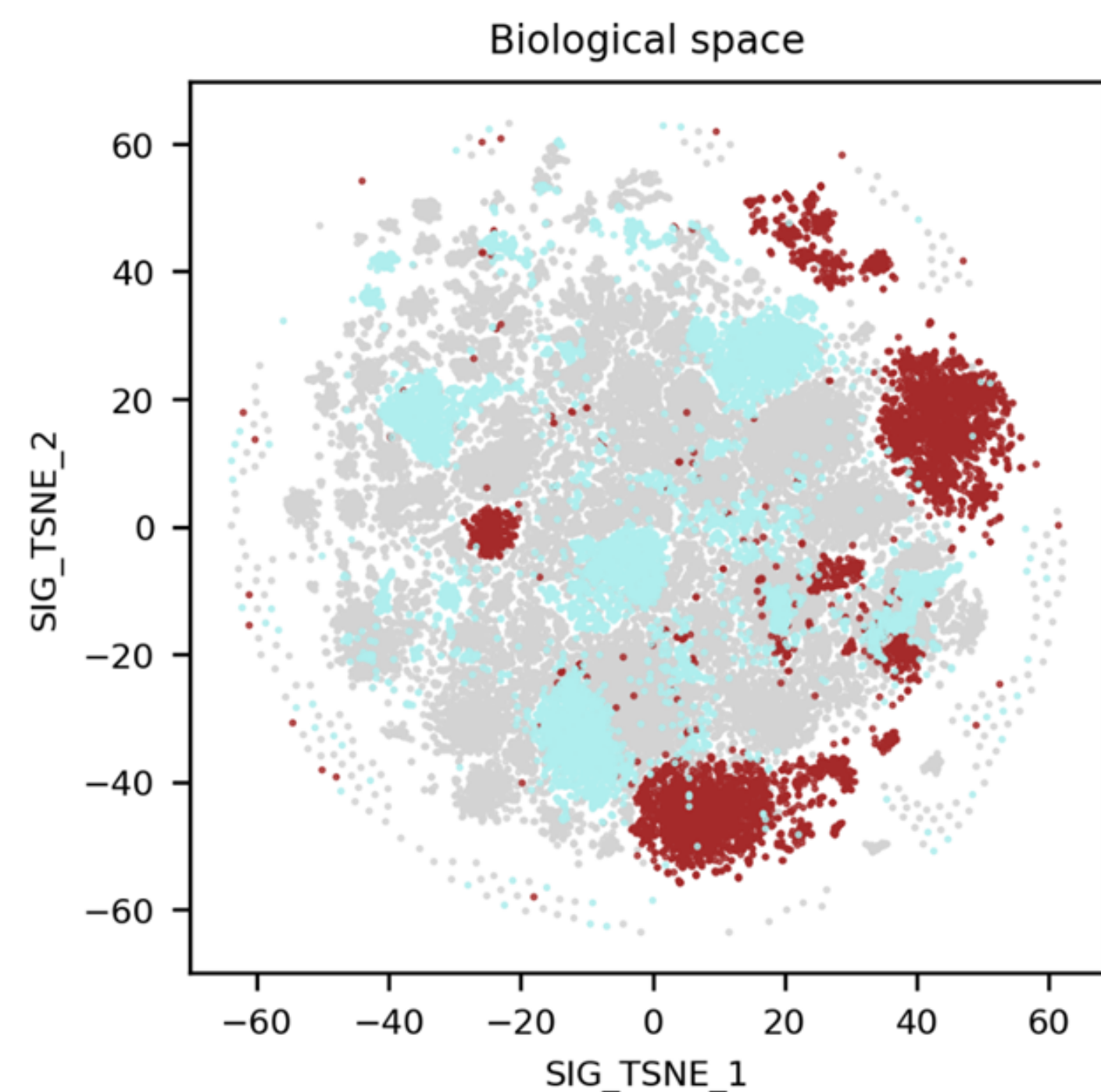
Big challenge : not to get lost in all those translations 😊

# Biological coverage translational challenge

Physiological relevance considerations

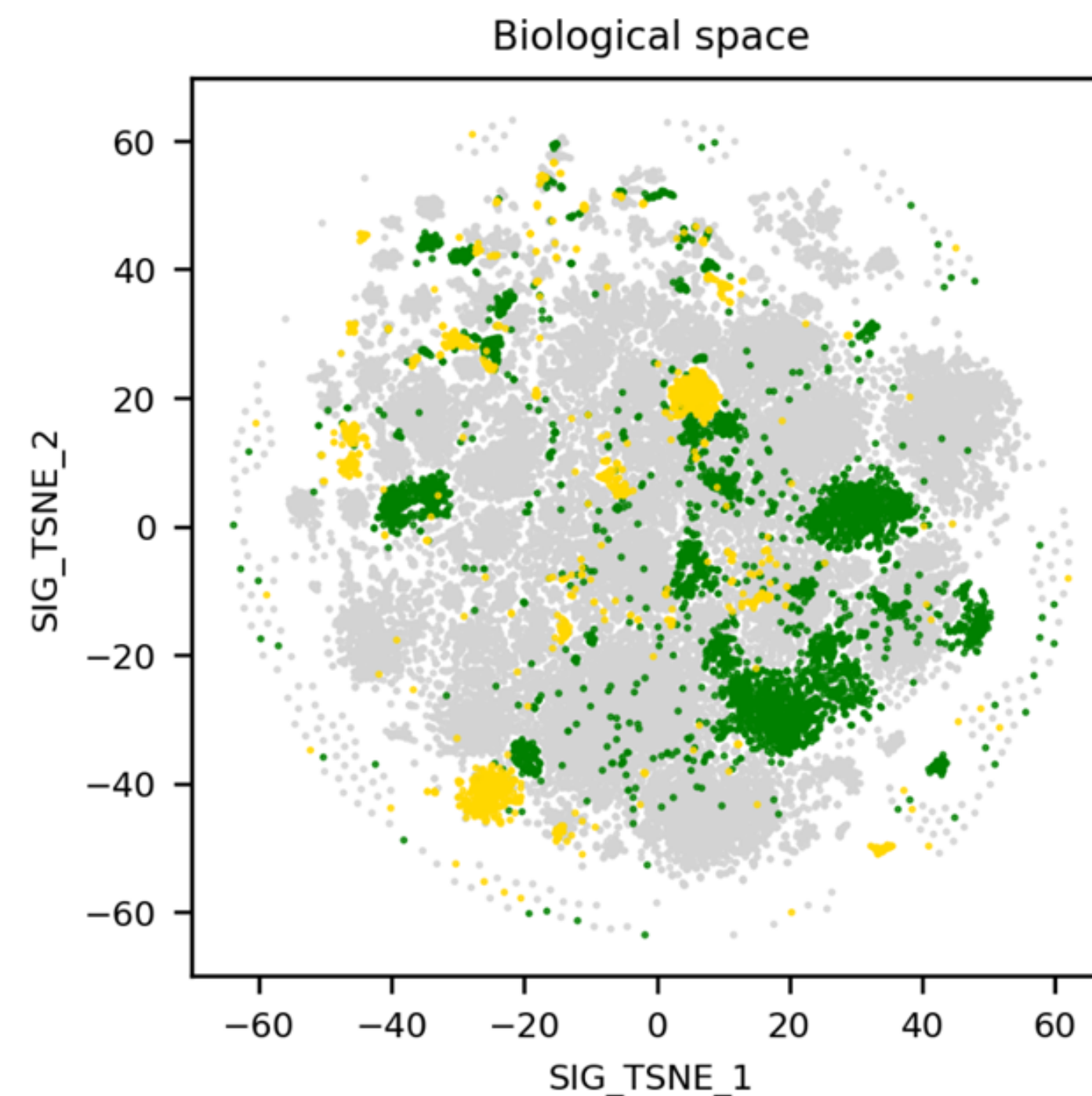
dataset:  
8 000  
compounds  
4 cell lines

## Prostate cancer cell lines



Brown = VCAP  
Blue = PC3

## Lung cancer cell lines



Yellow = HCC515  
Green = A549



Exploring the Use of  
Compound-Induced Transcriptomic  
Data Generated From Cell Lines to  
Predict Compound Activity Toward  
Molecular Targets

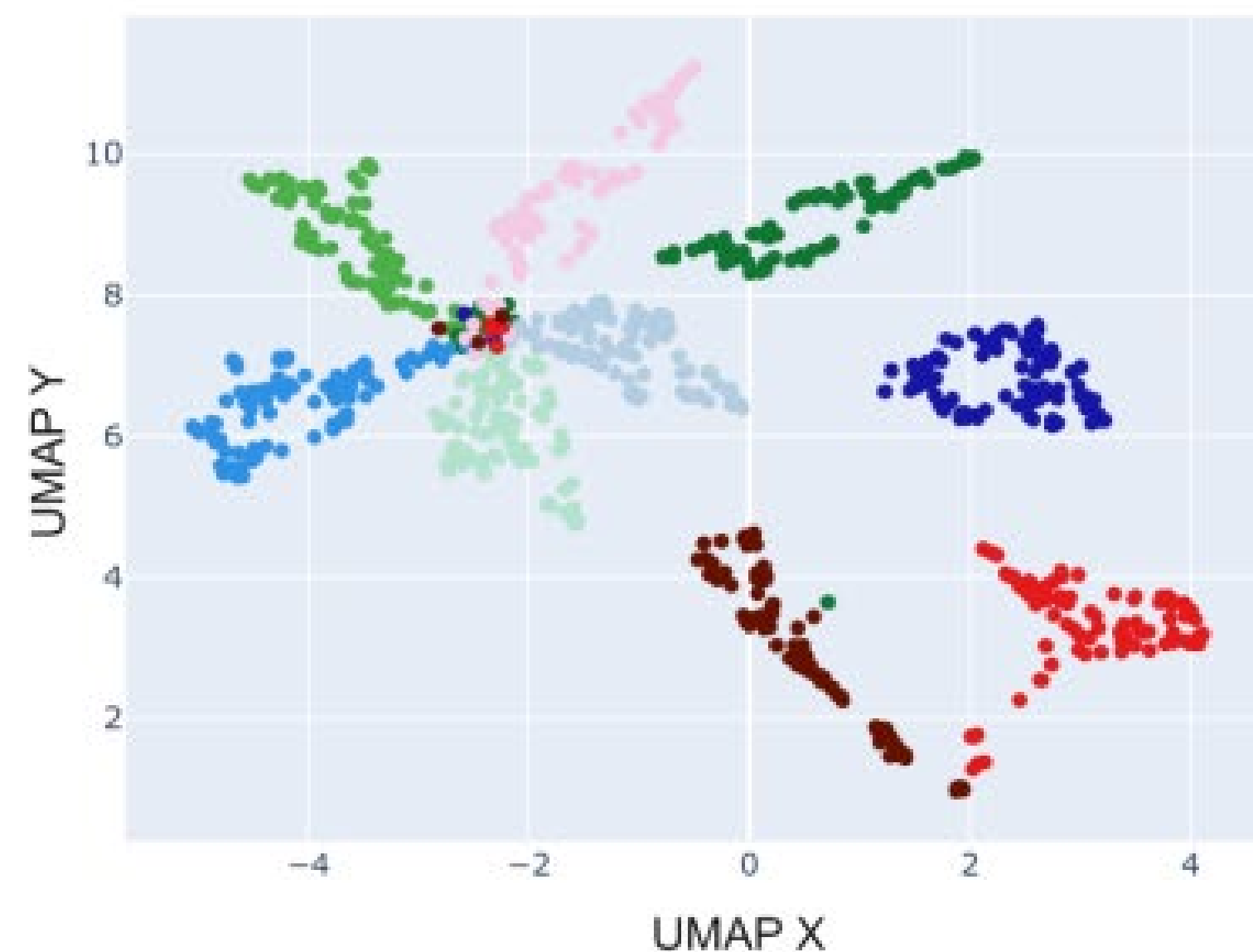
Benoît Baillif<sup>1</sup>, Joerg Wichard<sup>2</sup>, Oscar Méndez-Lucio<sup>1,3†</sup> and David Rouquié<sup>1\*†</sup>

<sup>1</sup> Bayer SAS, Bayer CropScience, Sophia Antipolis, France, <sup>2</sup> Department of Genetic Toxicology, Bayer AG, Berlin, Germany,  
<sup>3</sup> Bloomoon, Villeurbanne, France

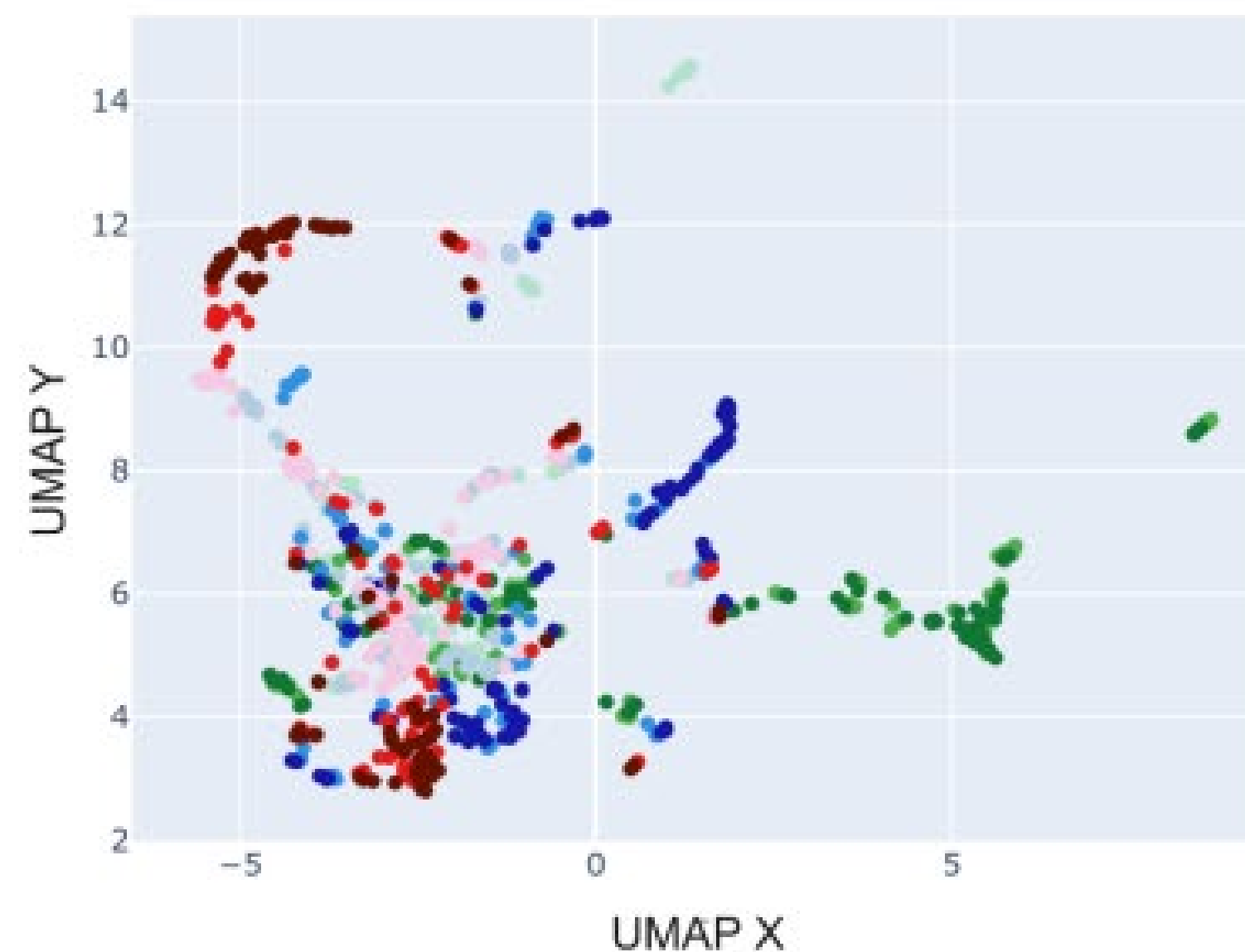
# Time translation challenge

**dataset:**  
110 chemicals  
3 cells lines  
3 time points  
2 readouts

A. UMAP - Cell Painting



B. UMAP - L1000



Cell Line - Time Point

- U2OS - 6H
- U2OS - 24H
- U2OS - 48H
- A549 - 6H
- A549 - 24H
- A549 - 48H
- MCF7 - 6H
- MCF7 - 24H
- MCF7 - 48H

Toxicology and Applied Pharmacology

Cell morphology and gene expression: tracking changes and complementarity across time and cell lines

Vanille Lejal<sup>a</sup>, David Rouquié<sup>b</sup>, Olivier Taboureau<sup>a,\*</sup>

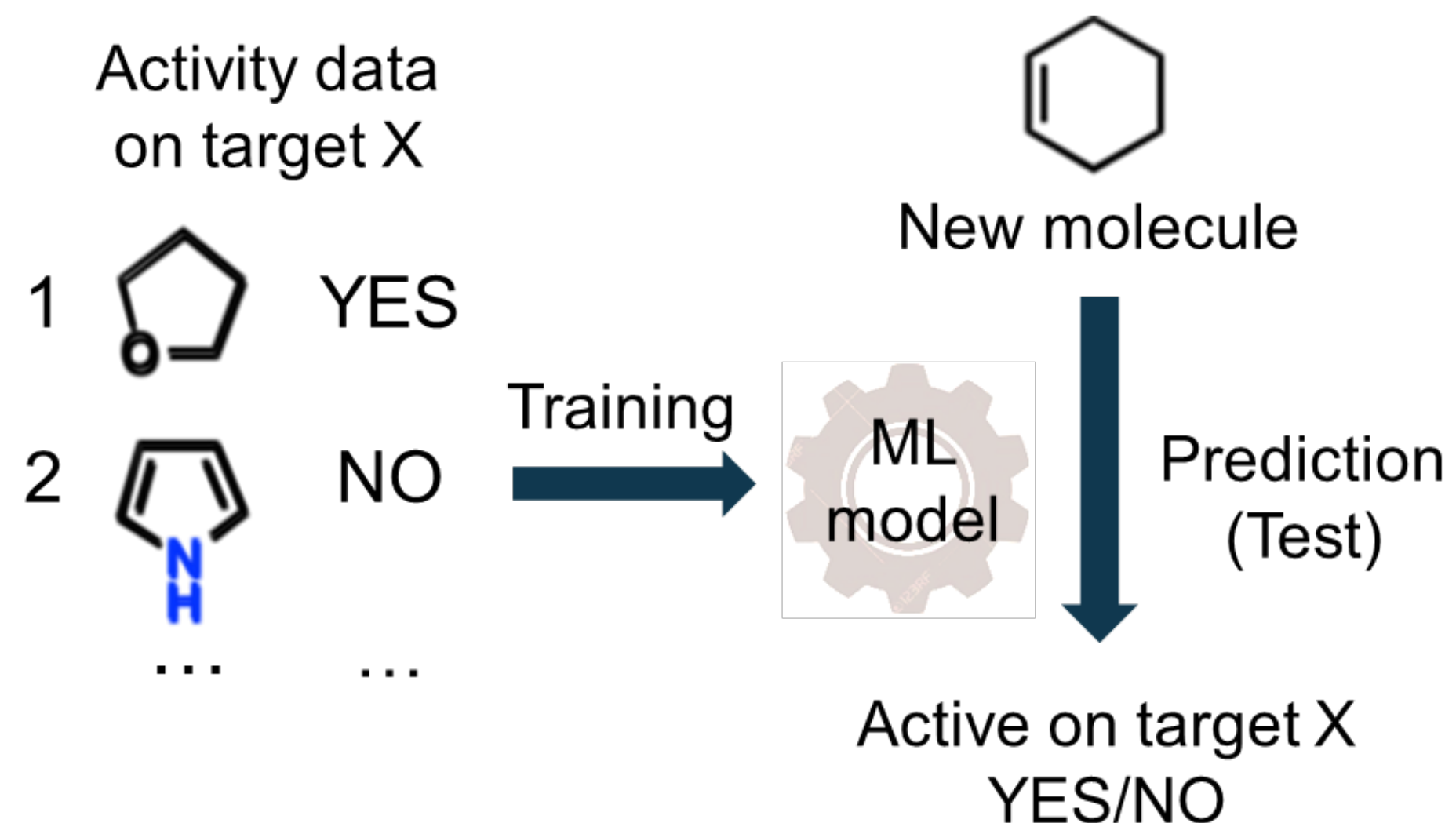
<sup>a</sup> Université Paris Cité, Inserm U1133, CNRS UMR 8251, Paris, France

<sup>b</sup> Bayer SAS, Bayer Crop Science, 355 rue Dostoïevski, CS 90153, 06906, Valbonne Sophia-Antipolis, France

# Opportunity Predictive AI

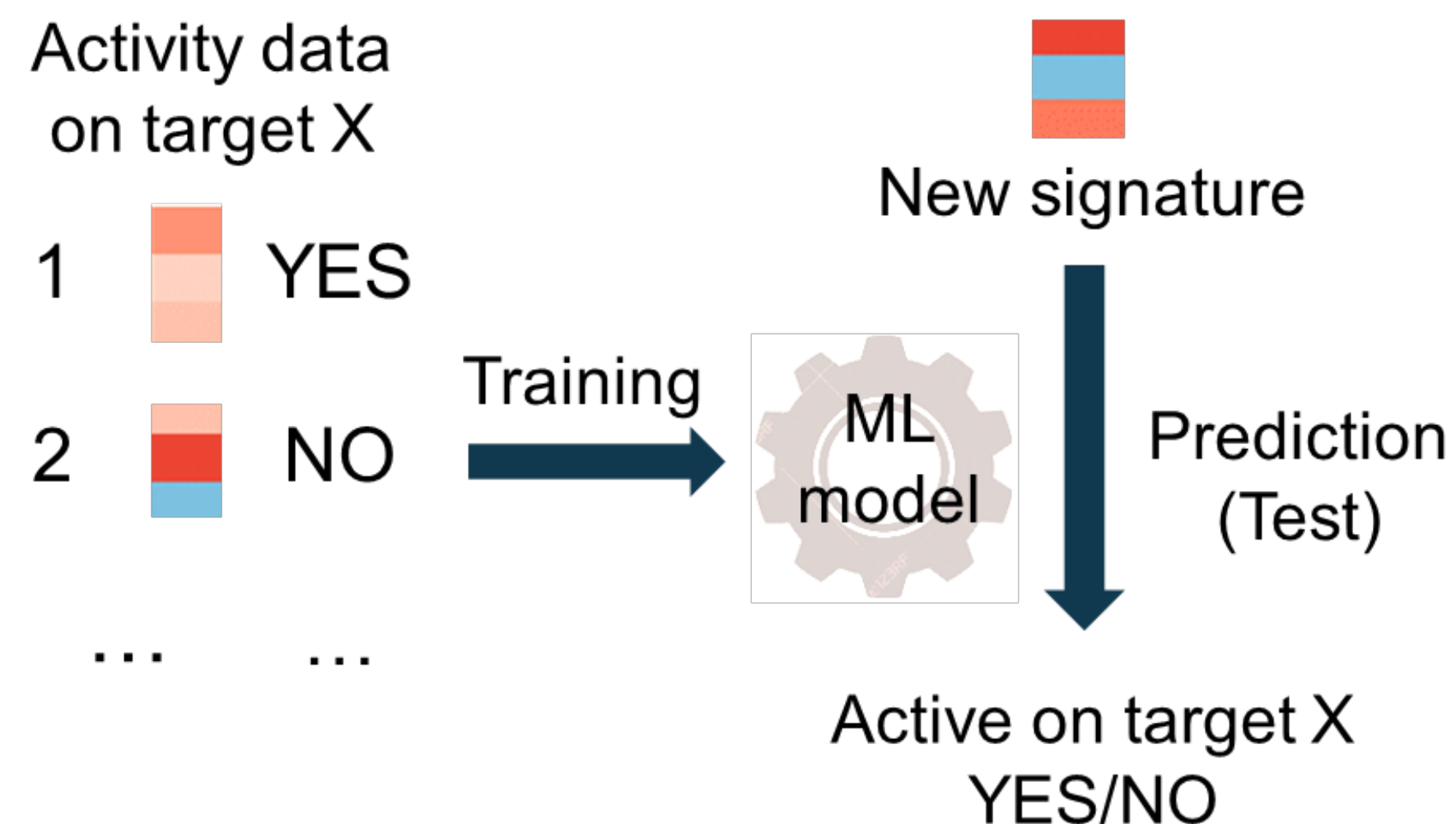
Example MIE prediction

## Structure models Morgan FP (QSAR)



## Signature models

For each cell line :



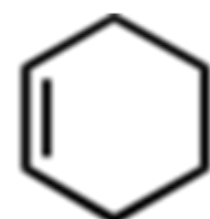
Exploring the Use of  
Compound-Induced Transcriptomic  
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Predict Compound Activity Toward  
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Benoît Baillif<sup>1</sup>, Joerg Wichard<sup>2</sup>, Oscar Méndez-Lucio<sup>1,3†</sup> and David Rouquié<sup>1\*†</sup>

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# Opportunity Predictive AI

Example MIE prediction



## Morgan FP models

**NR3C1** activity prediction:

- Compounds tested in **A549**: BA = **96 %**
- Compounds tested in **MCF7**: BA = **93 %**

**TUBB** activity prediction:

- Compounds tested in **A549**: BA = **80 %**
- Compounds tested in **MCF7**: BA = **82 %**



## Signature models

**NR3C1** activity prediction:

- **A549** signatures: BA = **77 %**
- **MCF7** signatures: BA = **60 %**

**TUBB** activity prediction:

- **A549** signatures: BA = **81 %**
- **MCF7** signatures: BA = **88 %**

## Global results:

On a set of 69 targets, for **25 %** of the target prediction tasks, models using signatures performed **similarly or better** than their counterpart Morgan FP models



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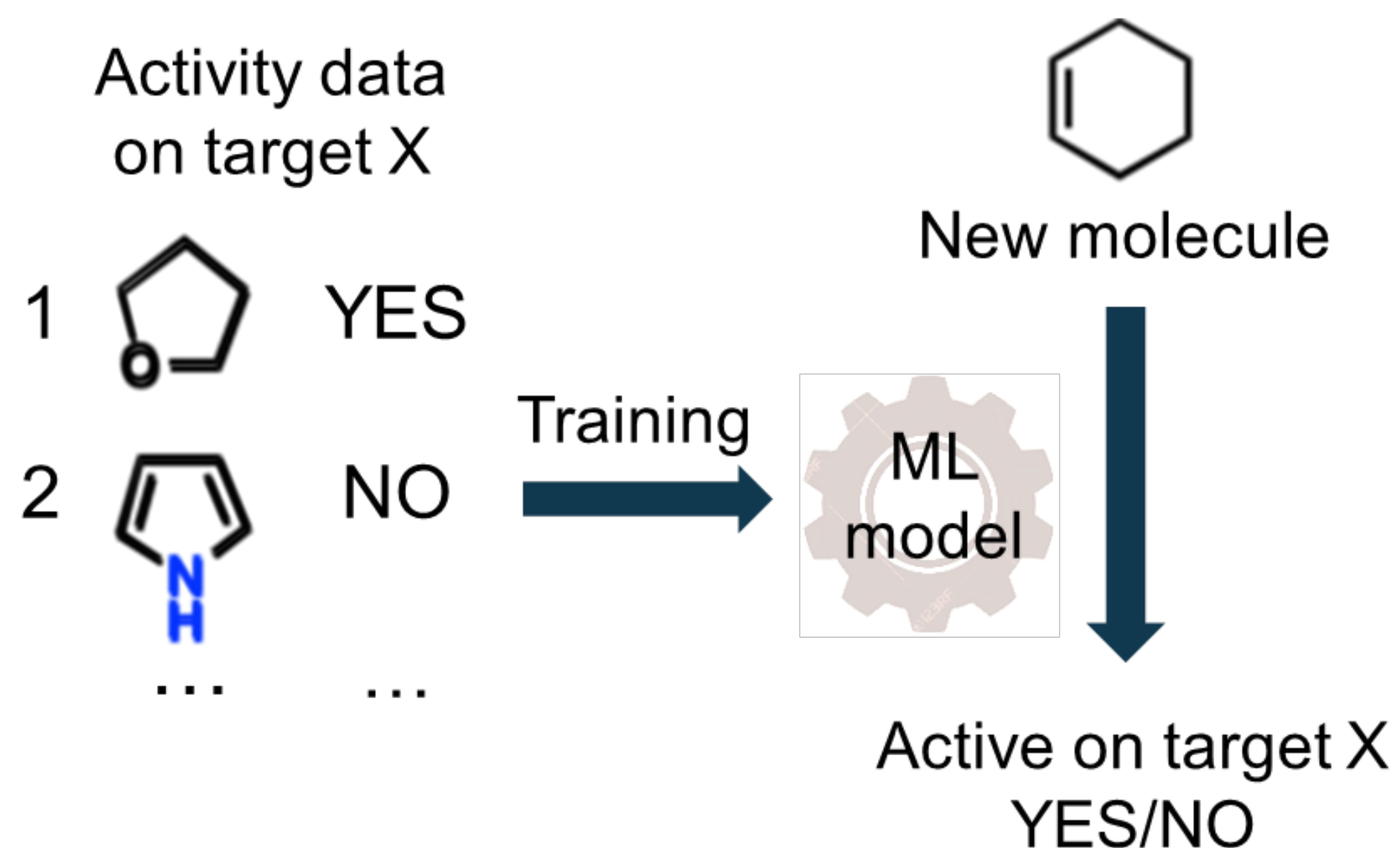
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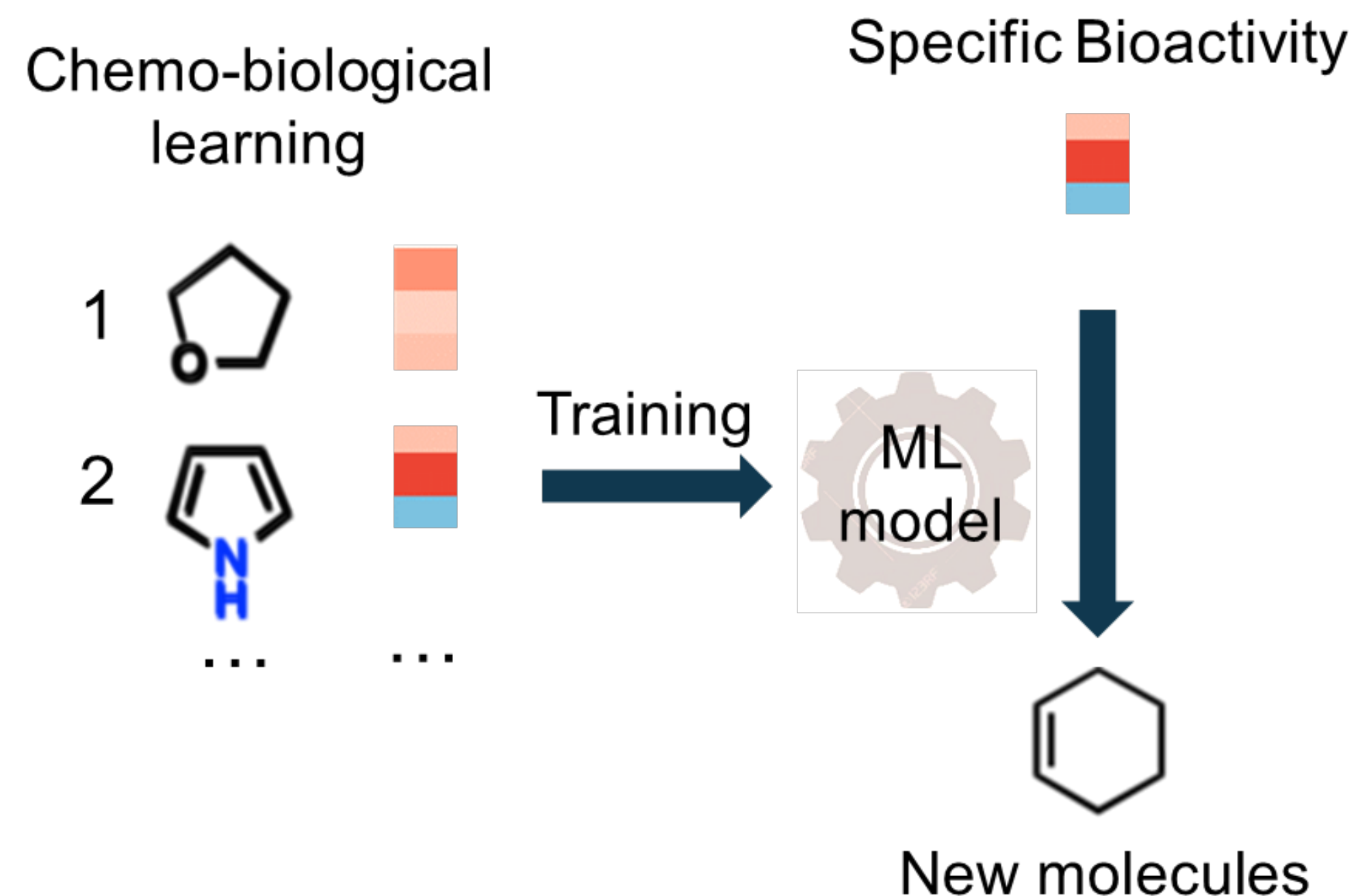
# Opportunity Generative AI

Example: de novo design of compounds

## Predictive AI (QSAR)



## Generative AI

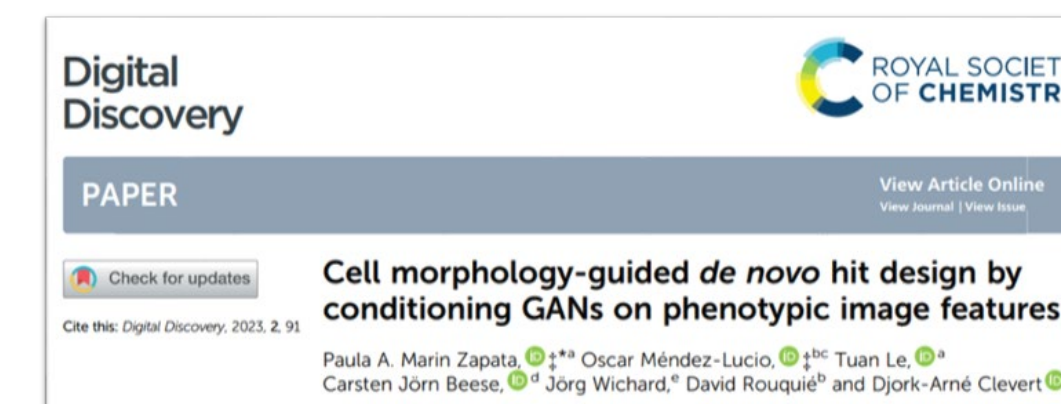


ARTICLE

<https://doi.org/10.1038/s41467-019-13807-w> OPEN

De novo generation of hit-like molecules from gene expression signatures using artificial intelligence

Oscar Méndez-Lucio<sup>1,2\*</sup>, Benoit Baillif<sup>1</sup>, Djork-Arné Clevert<sup>3</sup>, David Rouquié<sup>1,5\*</sup> & Joerg Wichard<sup>4,5\*</sup>



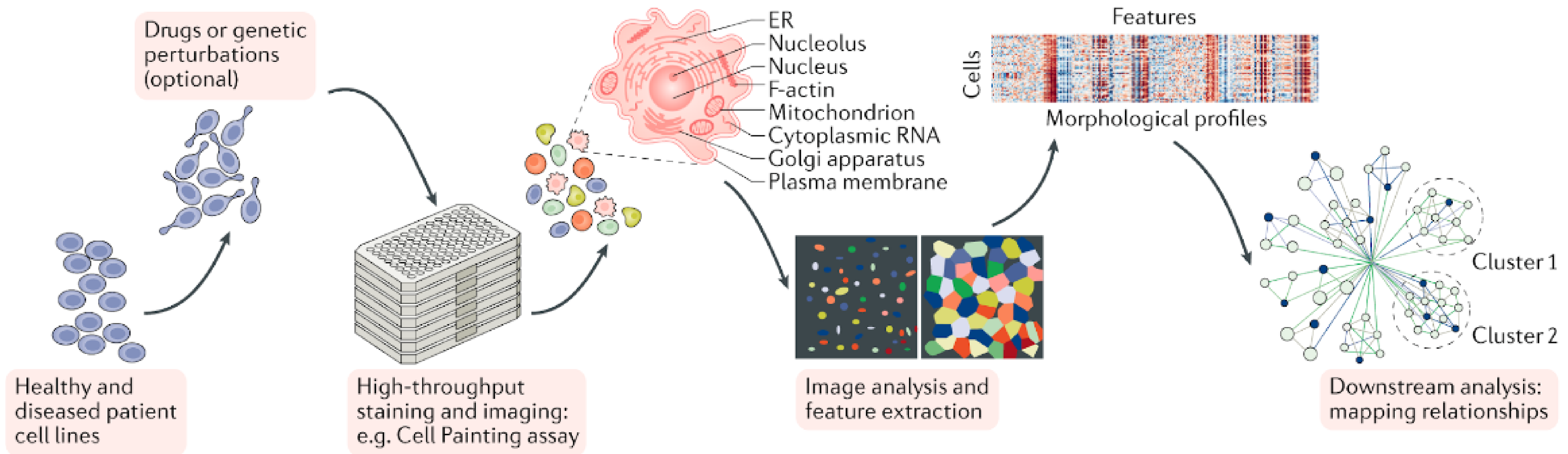
# Experimental valuation of *de novo* chemistry design

- We provide experimental evidence of the cGAN performance in designing chemical compounds with desired biological activity.
- Compounds designed on TP53 target showed measurable morphological activity, transcriptional changes and biological activity.

**88%**  
of the *de novo*  
compounds had an  
impact on overall  
cellular morphology

**37%**  
of the compounds  
significantly affected  
transcriptomic pathways  
associated with the  
intended target

# Emergence of Cell Painting



## Applications:

Prediction of various toxicity endpoints (e.g. acute, mitochondrial toxicity, developmental toxicity, liver toxicity, etc)

# On going Task Forces

ecetoc



## Ongoing Task Force

**Smart studies: Examine how in vivo studies could provide more information encompassing novel studies (and endpoints)**

Why

"Smart" or exten

They fall into 2 c

- those that follc

- those that follc



ecetoc

Ecetoc recently launched calls for nominations for three new Task Forces that are scheduled to kick off their activities in Q2:

➤ **New TF on 'Omics data interpretation framework'**

The aim of the TF is to explore and agree an Omics Data Interpretation Framework for regulatory application (ODIFRA) and to develop suitable accessible educational materials for outreach and training that can aid uptake of the use of omics data for regulatory purposes.



# Thank you.

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# Thank you.

Date

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2022 / 05

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for science to be at the centre of  
policy making.

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