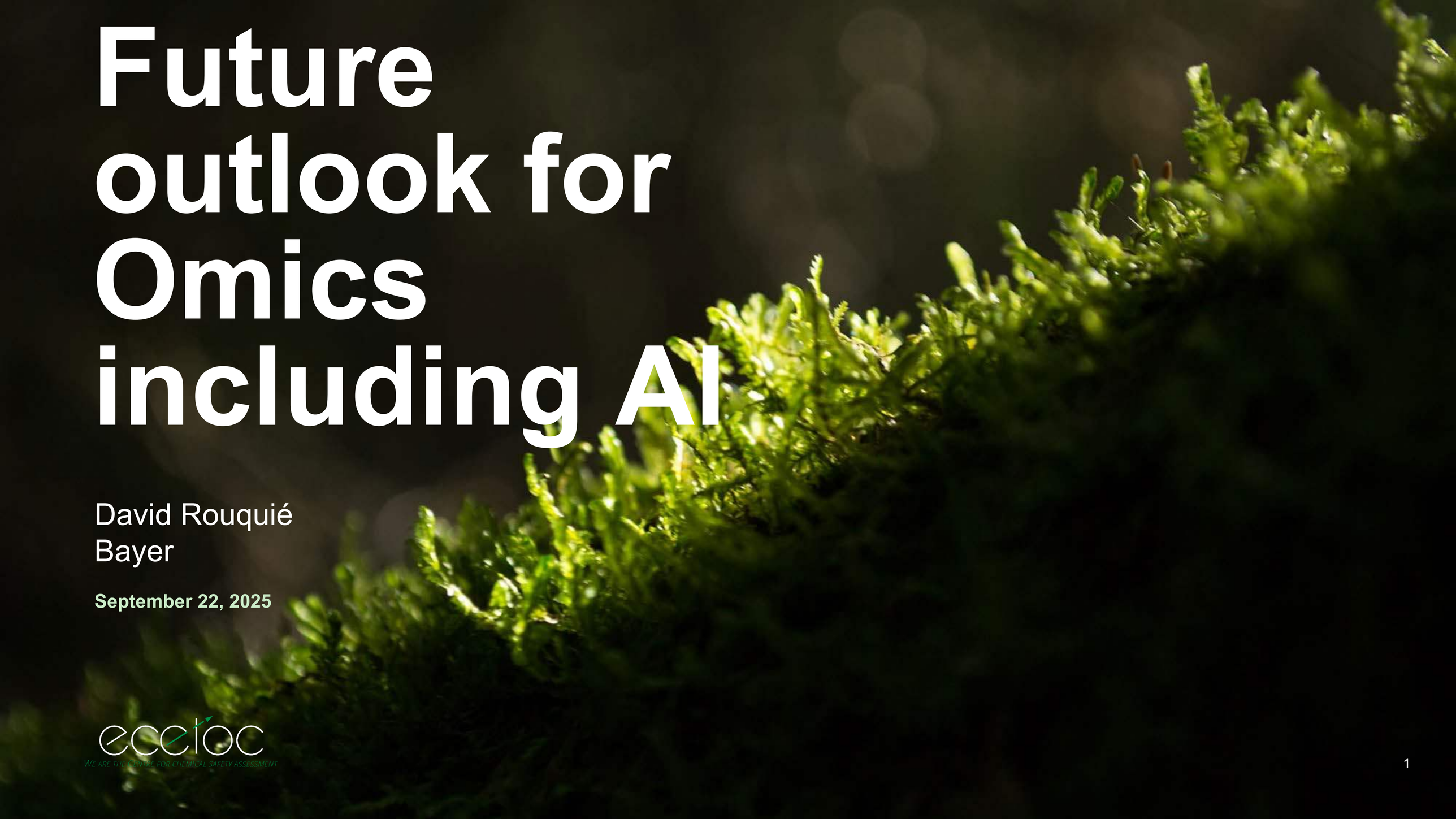
Future outlook for Omics including AI

David Rouquié
Bayer

September 22, 2025



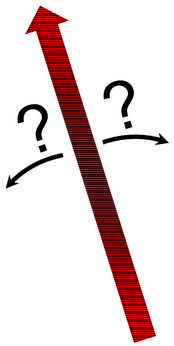
Agenda

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

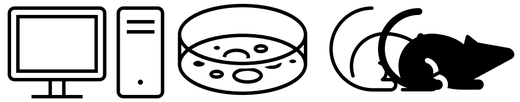
Few words about Next Generation Risk Assessment

Spectrum of evaluations in chemical risk assessment

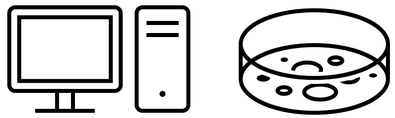
Industrial chemicals



Agrochemicals products



Cosmetic products



Pharmaceutical products

Few words about Next Generation Risk Assessment

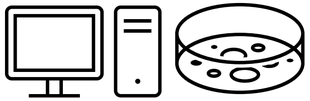
Spectrum of evaluations in chemical risk assessment

Industrial chemicals & Agrochemicals products

Short-term in vivo studies enriched with omics endpoints

Cosmetic products

Pharmaceutical products



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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 [1,*], Leah Wehmas [2], David Rouquié [3], Florian Caiment [4], Richard A. Currie [5], Christine E. Crute [1]

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[2]Chemical Characterization and Exposure Division, Center for Computational Toxicology and Exposure, U.S. Environmental Protection Agency, Research Triangle Park, NC 27711, United States
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[4]Department of Translational Genomics, GROW Research Institute for Oncology and Reproduction, Maastricht University, 6229 ER Maastricht, The Netherlands
[5]Jealott's Hill International Research Centre, Syngenta, Bracknell, Berkshire RG42 6EY, United Kingdom

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Omic’s high content biological assays

Opportunities

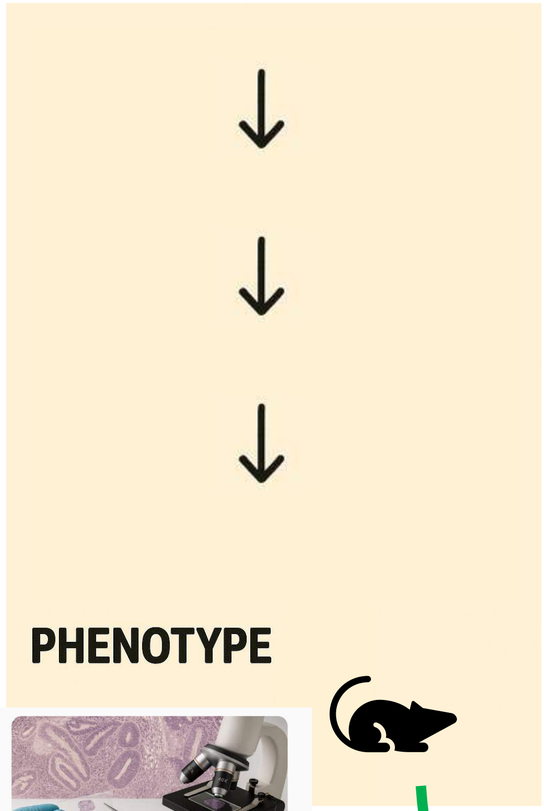
They provide several advantages

- 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

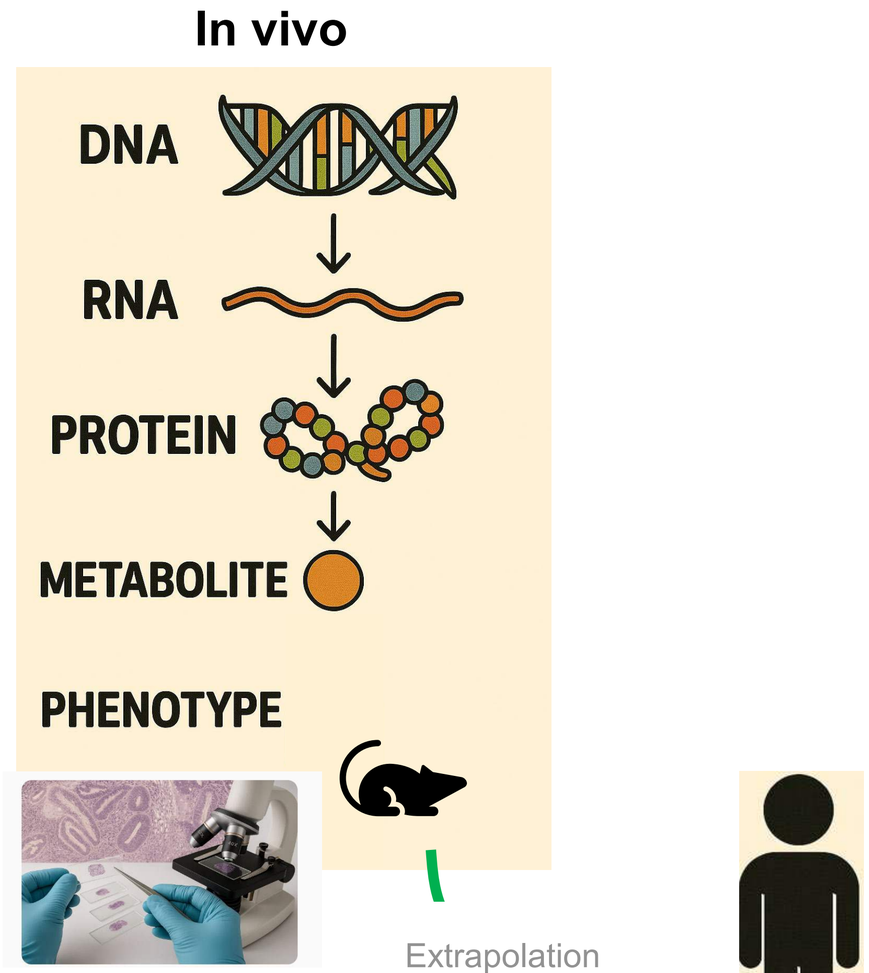
In vivo



to adverse outcome

From …

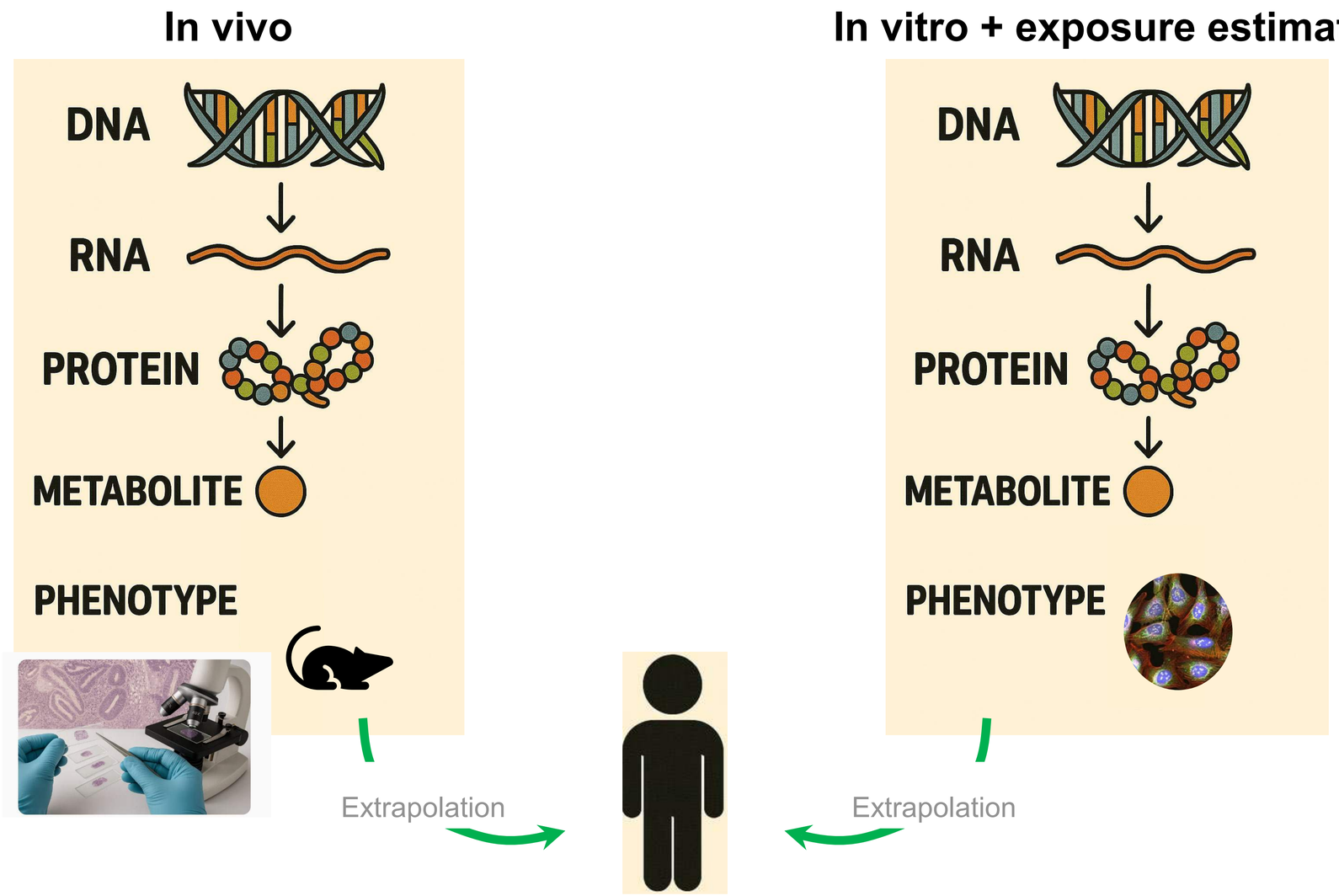
chemical exposure



to adverse outcome

From …

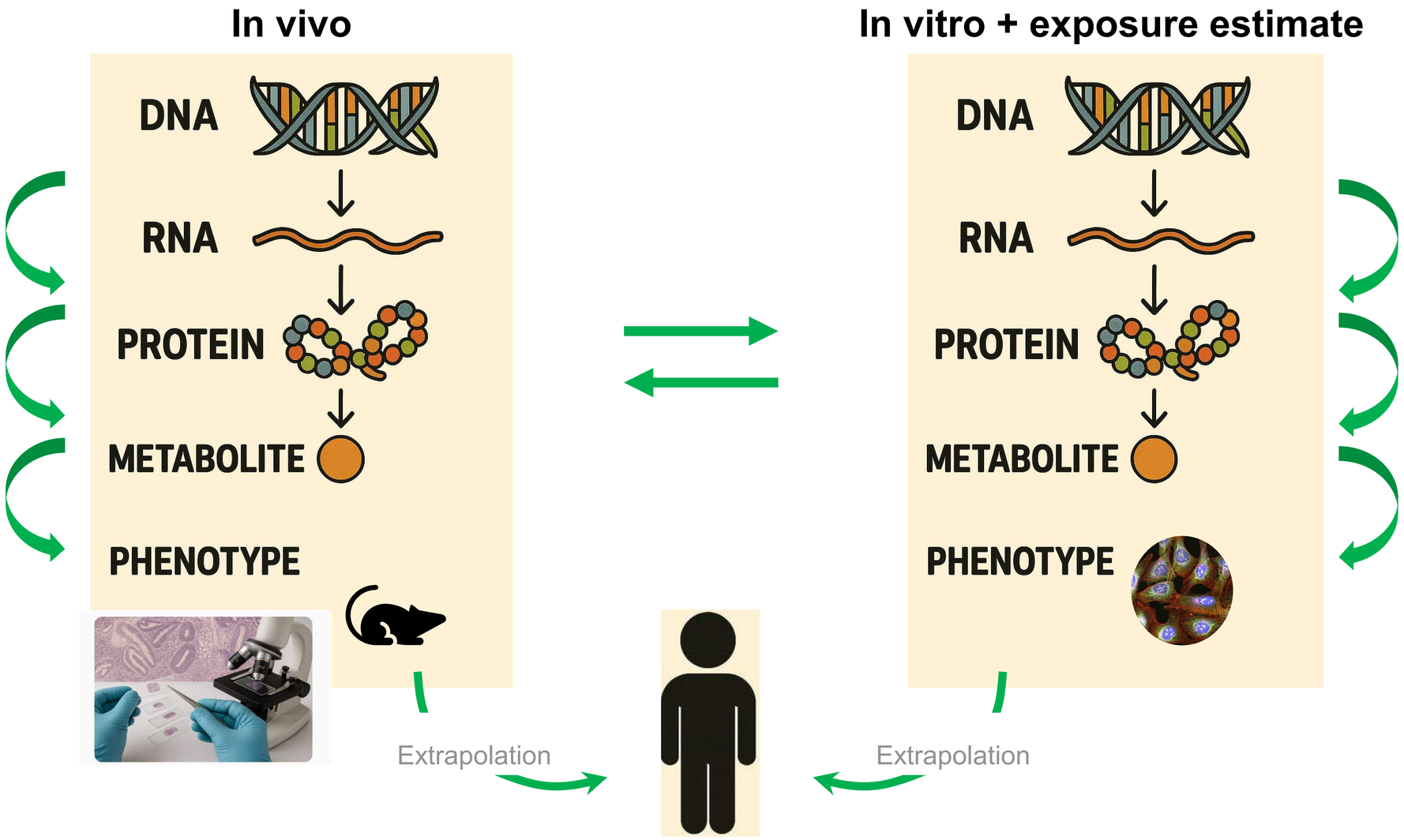
chemical exposure



to adverse outcome

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**

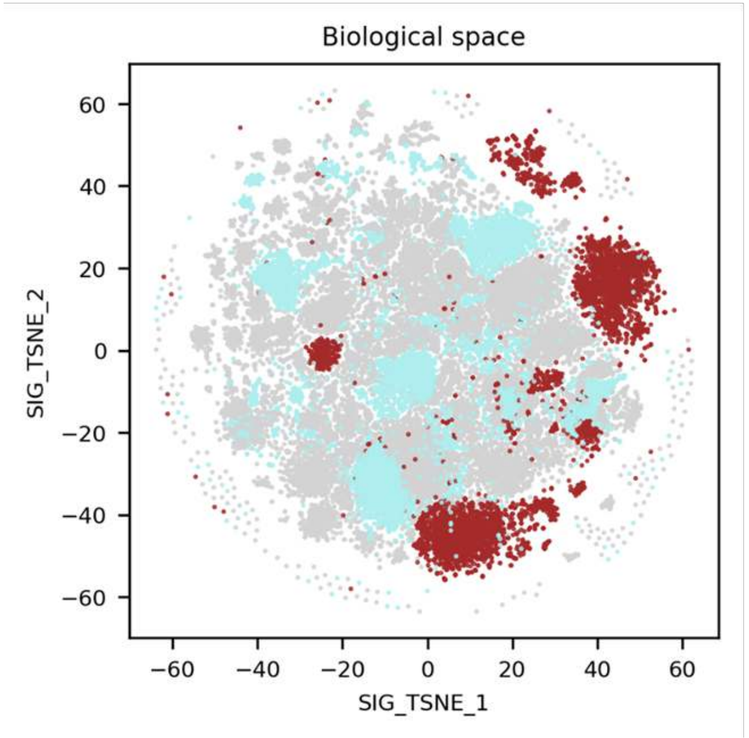
Big challenge : not to get lost in all those translations ☺

Biological coverage translational challenge

Physiological relevance considerations

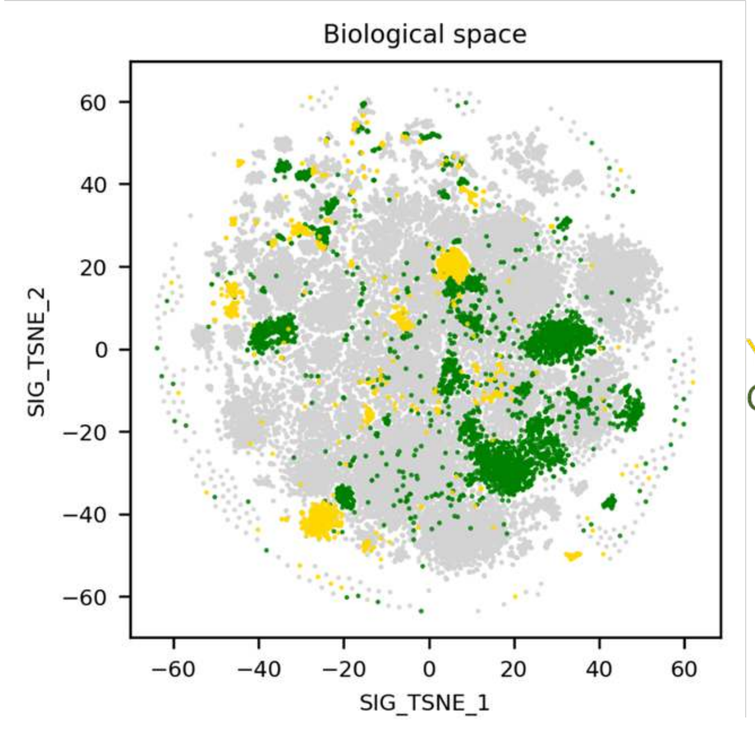
dataset:
8 000 compounds
4 cell lines

Prostate cancer cell lines



Brown = VCAP
Blue = PC3

Lung cancer cell lines



Yellow = HCC515
Green = A549

frontiers in Chemistry

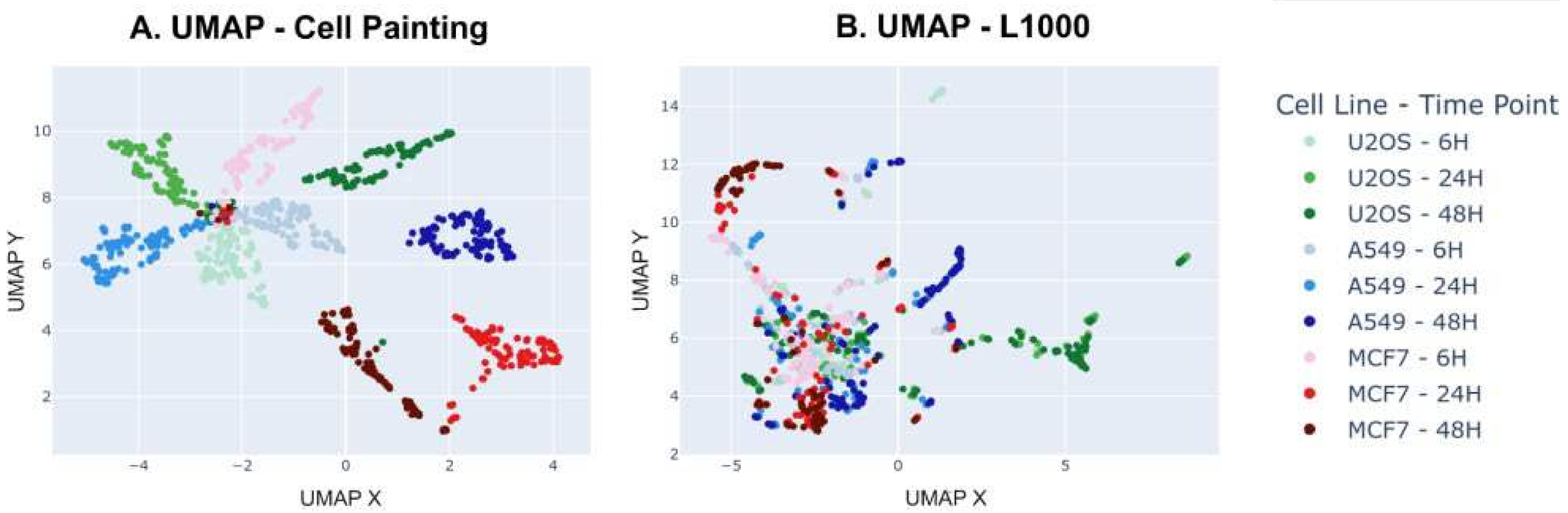
Exploring the Use of Compound-Induced Transcriptomic Data Generated From Cell Lines to Predict Compound Activity Toward Molecular Targets

Benoît Baillif[1], Joerg Wichard[2], Oscar Méndez-Lucio[1,3†] and David Rouquié[1†]*

[1] Bayer SAS, Bayer CropScience, Sophia Antipolis, France, [2] Department of Genetic Toxicology, Bayer AG, Berlin, Germany, [3] Bloomoon, Villeurbanne, France

Time translation challenge

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



Toxicology and Applied Pharmacology

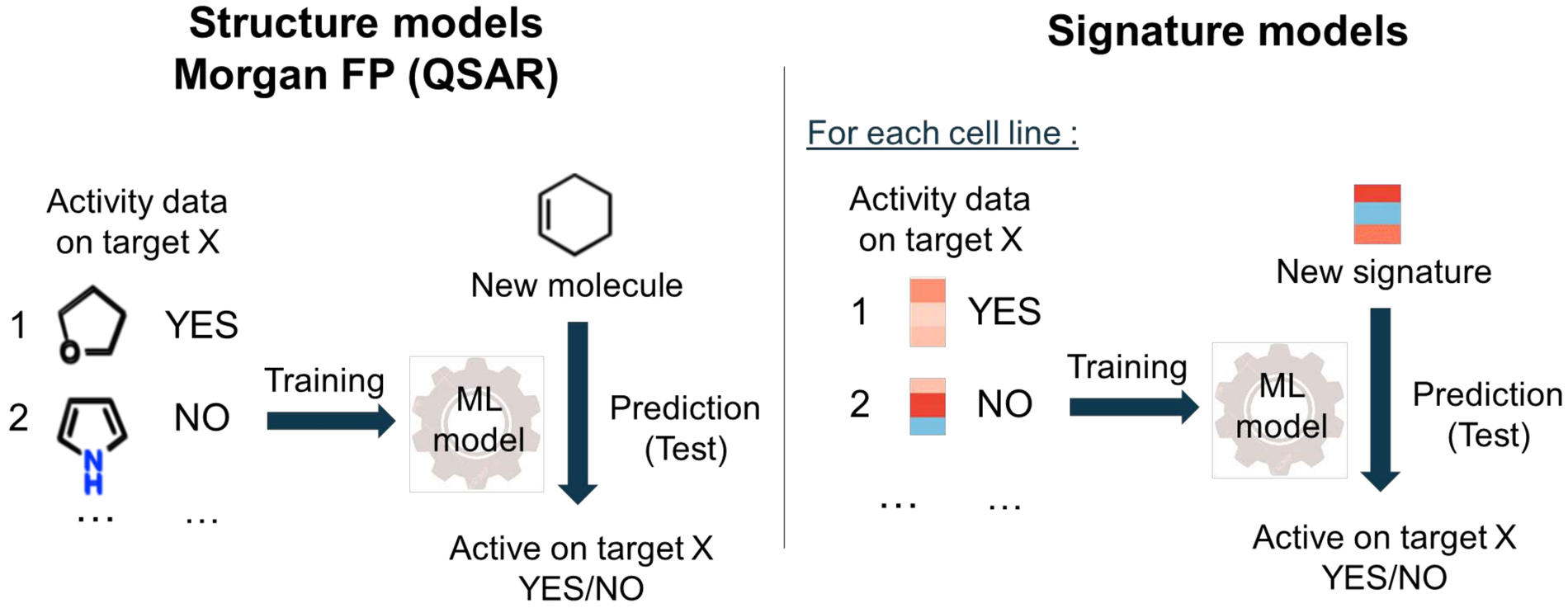
Cell morphology and gene expression: tracking changes and complementarity across time and cell lines

Vanille Lejal [a], David Rouquié [b], Olivier Taboureau [a,*]

[a] Université Paris Cité, Inserm U1133, CNRS UMR 8251, Paris, France
[b] Bayer SAS, Bayer Crop Science, 355 rue Dostoïevski, CS 90153, 06906, Valbonne Sophia-Antipolis, France

Opportunity Predictive AI

Example MIE prediction



frontiers in Chemistry

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Balanced Accuracy (BA) to assess model performances : between 0 and 100 % (50 % = flip a coin).

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

frontiers in Chemistry

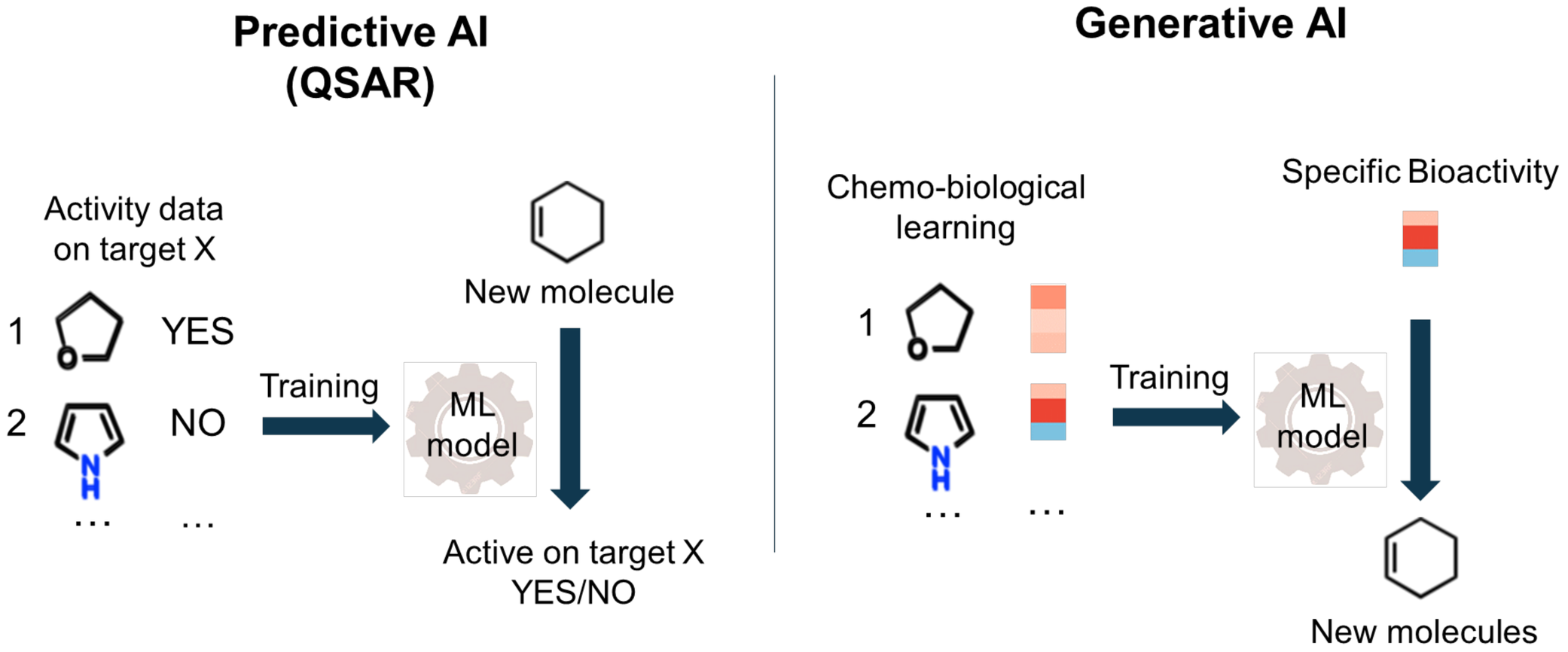
Exploring the Use of Compound-Induced Transcriptomic Data Generated From Cell Lines to Predict Compound Activity Toward Molecular Targets

Benoît Baillif[1], Joerg Wichard[2], Oscar Méndez-Lucio[1,3†] and David Rouquié[1†]*

[1] Bayer SAS, Bayer CropScience, Sophia Antipolis, France, [2] Department of Genetic Toxicology, Bayer AG, Berlin, Germany, [3] Bloomoon, Villeurbanne, France

Opportunity Generative AI

Example: de novo design of compounds



nature COMMUNICATIONS

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[1,2*], Benoit Baillif[1], Djork-Arné Clevert[3], David Rouquié[1,5*] & Joerg Wichard[4,5*]

Digital Discovery

ROYAL SOCIETY OF CHEMISTRY

PAPER

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Cite this: Digital Discovery, 2023, 2, 91

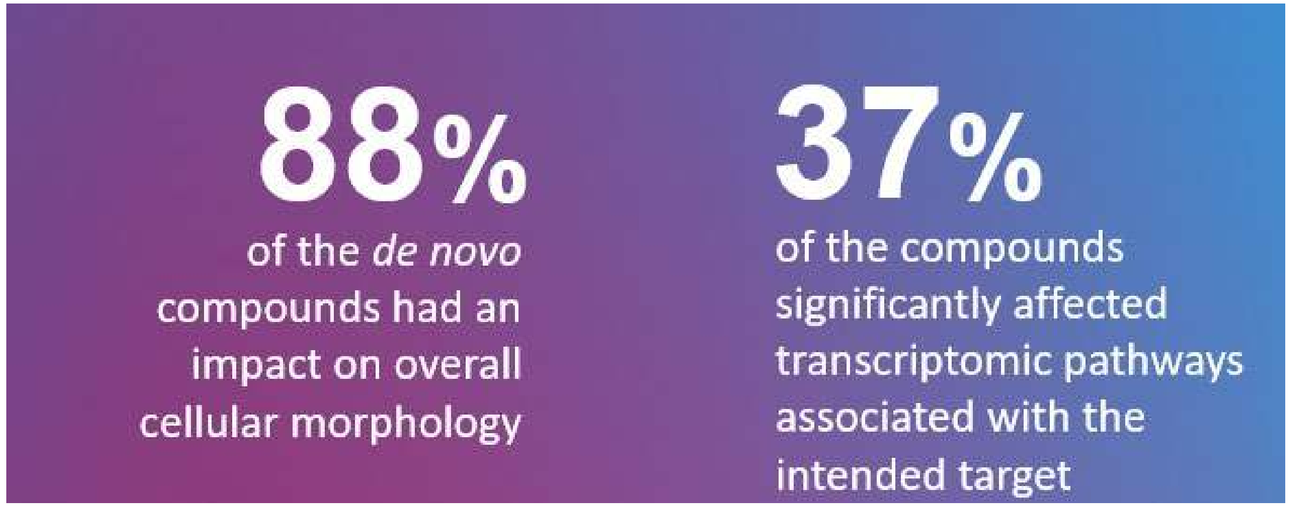
Cell morphology-guided *de novo* hit design by conditioning GANs on phenotypic image features†

Paula A. Marin Zapata, Oscar Méndez-Lucio, Tuan Le, Carsten Jörn Beese, Jörg Wichard, David Rouquié and Djork-Arné Clevert

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.



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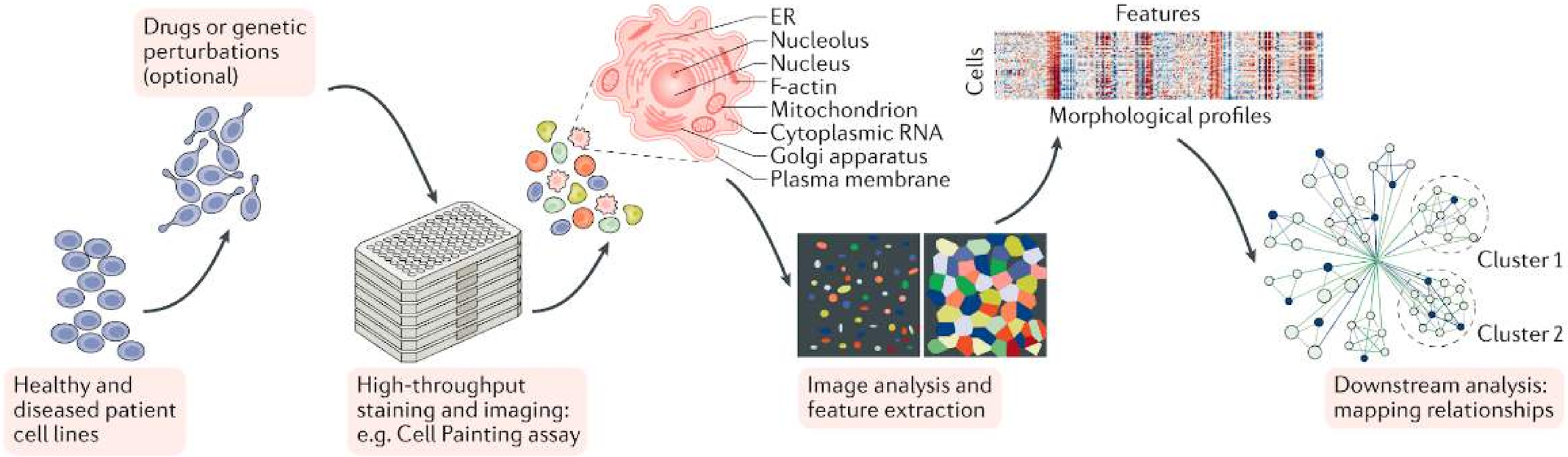
Large-scale experimental validation of phenotype-guided generative AI for de novo drug discovery

Jure Fabjan, Joanna M. Wenda, Claire Pecoraro-Mercier, Paula Andrea Marin Zapata, Joerg Wichard, Djork-Arné Clevert, Oscar Méndez-Lucio, David Rouquié

doi: https://doi.org/10.1101/2025.09.13.676062

Emergence of Cell Painting



Applications:

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

On going Task Forces

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 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.

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Date

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2022 / 05

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To lead the debate on the need for science to be at the centre of policy making.

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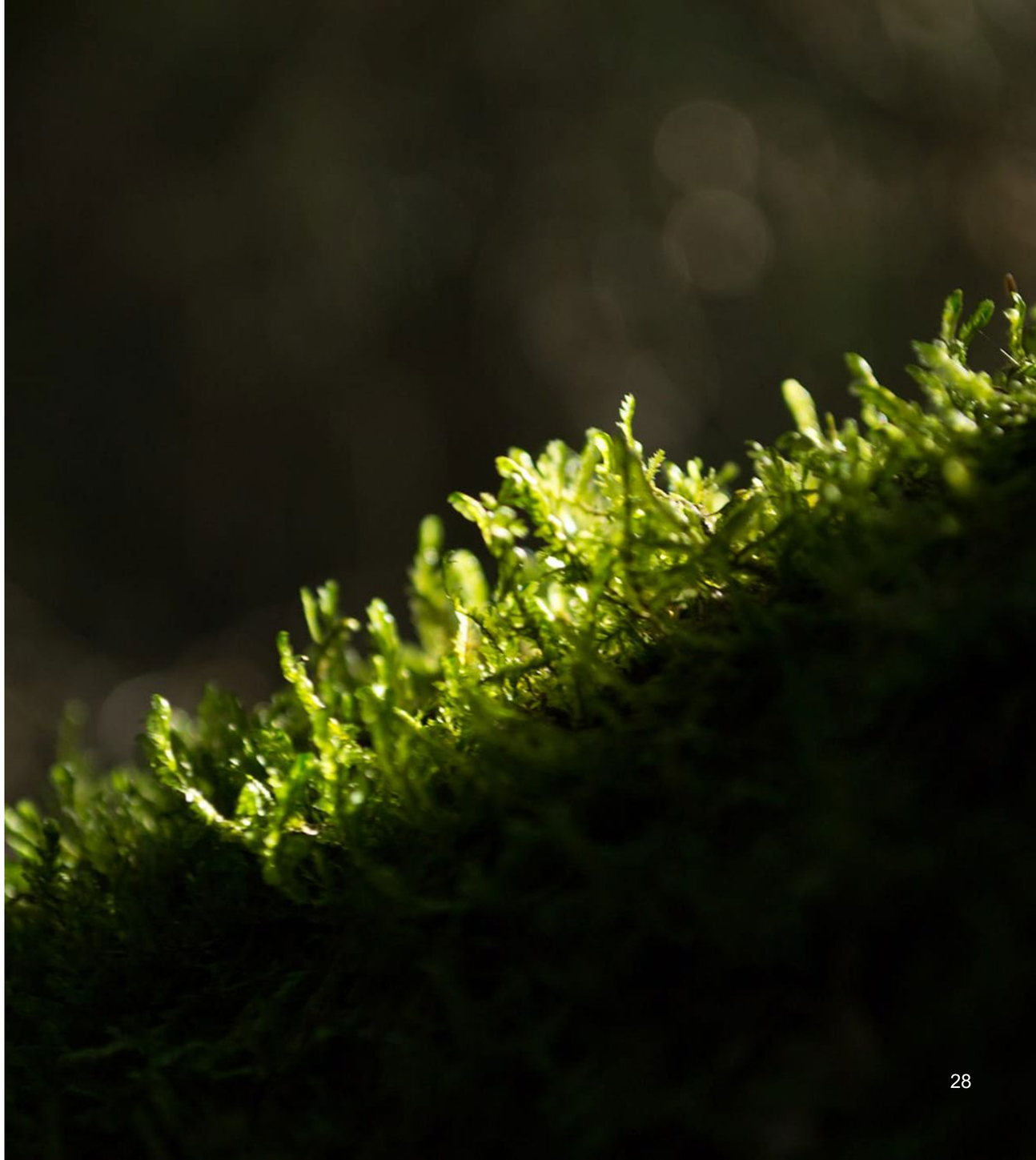

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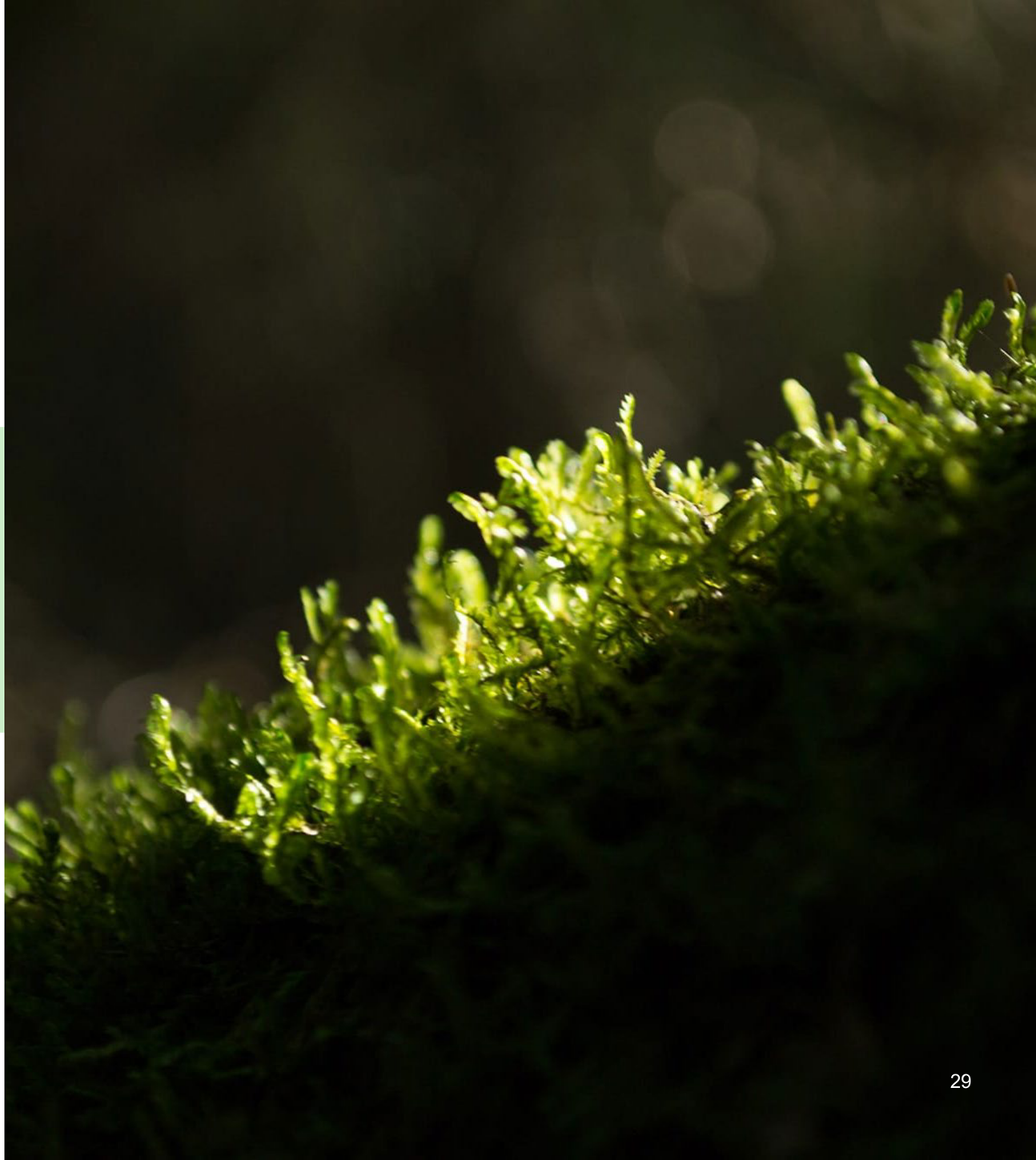

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