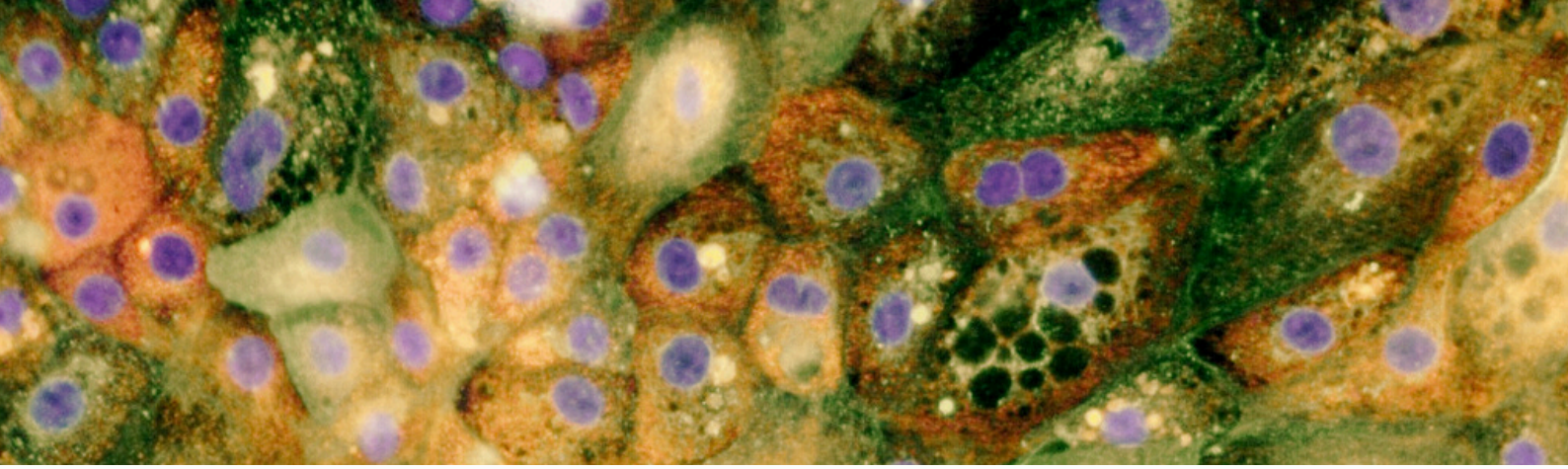
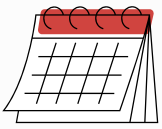


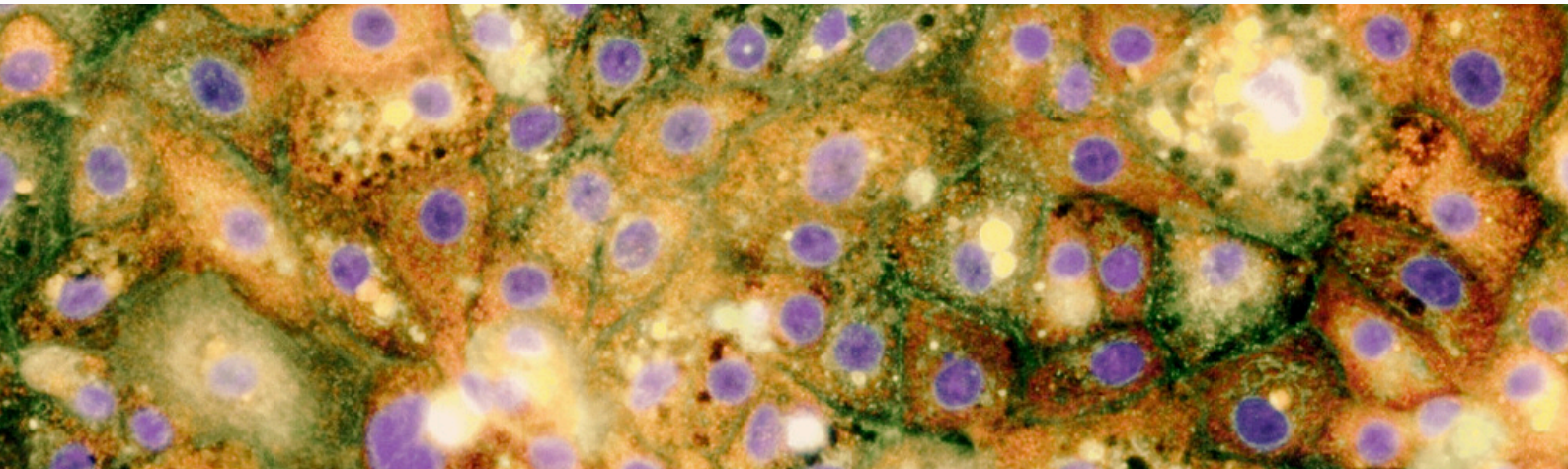
SOCIETY OF BIOMOLECULAR IMAGING AND INFORMATICS

Premier European meeting of Society of Biomolecular Imaging and Informatics



July 7-8, 2026

The Discovery Centre,
Biomedical Campus,
1 Francis Crick Ave,
Cambridge, UK



Welcome from the President of the SBI² Board of Directors

Dear Colleagues, Friends, and Members of the SBI² Community,

On behalf of the Board of Directors of the Society for Biomolecular Imaging and Informatics (SBI²), it is my great pleasure to welcome you to the inaugural SBI² European Regional Meeting.

This gathering marks an exciting milestone in the evolution of our society. Since its founding, SBI² has served as a global community united by a common belief: that imaging and informatics are transformative technologies capable of revealing new biological insights, accelerating scientific discovery, and advancing human health. Today, that vision is more relevant than ever.

As the pace of innovation continues to accelerate, our field stands at the intersection of biology, engineering, computation, and artificial intelligence. The themes of this meeting reflect the remarkable breadth of our community—from virtual cell models and AI-driven image analysis to next-generation high-content technologies, translational screening applications, and emerging 3D biological systems. Together, these advances are reshaping how we understand biology and discover new therapies.

What makes SBI² unique, however, is not only the science. It is the people. Our society thrives because of the collaborative spirit, intellectual curiosity, and willingness to share knowledge that define our members. Whether you are a student attending your first SBI² meeting, an early-career scientist building new connections, or an established leader helping shape the future of the field, your participation strengthens this community.

This first European Regional Meeting represents an important step in expanding opportunities for engagement across our global membership. By bringing together scientists from academia, biotechnology, pharmaceutical research, and technology development, we create new avenues for collaboration, learning, and innovation that extend far beyond this event.

I would like to express my sincere gratitude to the European Regional Organizing Committee, our speakers, sponsors, volunteers, and our hosts at AstraZeneca for their dedication and support in making this meeting possible. Their efforts have created a program that showcases both scientific excellence and the collaborative spirit that has always been at the heart of SBI².

I encourage you to take full advantage of the opportunities this meeting offers: engage in discussions, challenge assumptions, exchange ideas, and build new relationships. The conversations that begin here will help shape the future of biomolecular imaging and informatics for years to come.

Thank you for being part of the SBI² community. I wish you an inspiring, productive, and enjoyable meeting.

Warm regards,

Kristin Halfpenny, Ph.D.

President, Board of Directors
Society for Biomolecular Imaging and Informatics (SBI²)

Welcome to SBI^2 Regional - The Premier European Meeting

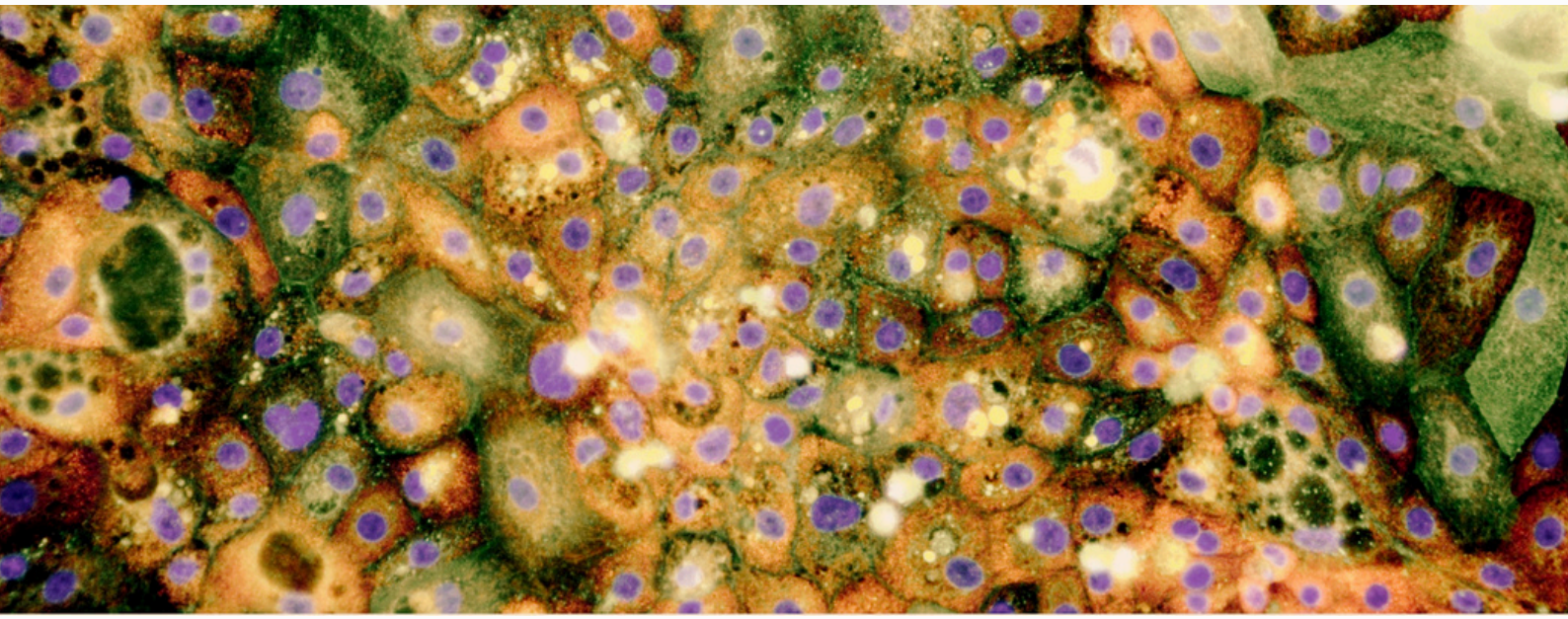
Dear Colleagues,

The Society for Biomolecular Imaging and Informatics was born out of passion, dedication, and curiosity. The strong belief that imaging and informatics are essential to both basic research and drug discovery has always driven this society, inspiring its members to pursue constant innovation. Just as importantly, SBI^2 is built on the pillar of education, ensuring these advancements remain inclusive and accessible to all.

We aim to continue this legacy with the European SBI^2 meetings: pushing scientific boundaries while sharing knowledge openly with the broader community.

This mission has guided our regional organising committee. To our volunteers: thank you so much for your hard work and for taking on this challenge!
I hope you all have a wonderful and productive conference.

Magdalena Otrocka
SBI2 Regional Committee Chair



Organising Committee

Anusuya Banerjee
(GSK)

Bolek Zapiec
(Merck KGaA)

Christopher Trummer
(Pixlbio)

David Egan
(Tréan)

Magdalena Otrocka
(Ardigen)

Michael Munson
(AstraZeneca)

Morag Rose Hunter
(AstraZeneca)

Neil Carragher
(University of Edinburgh)

Peter Horvath
(HUN-REN Biological Research Centre)

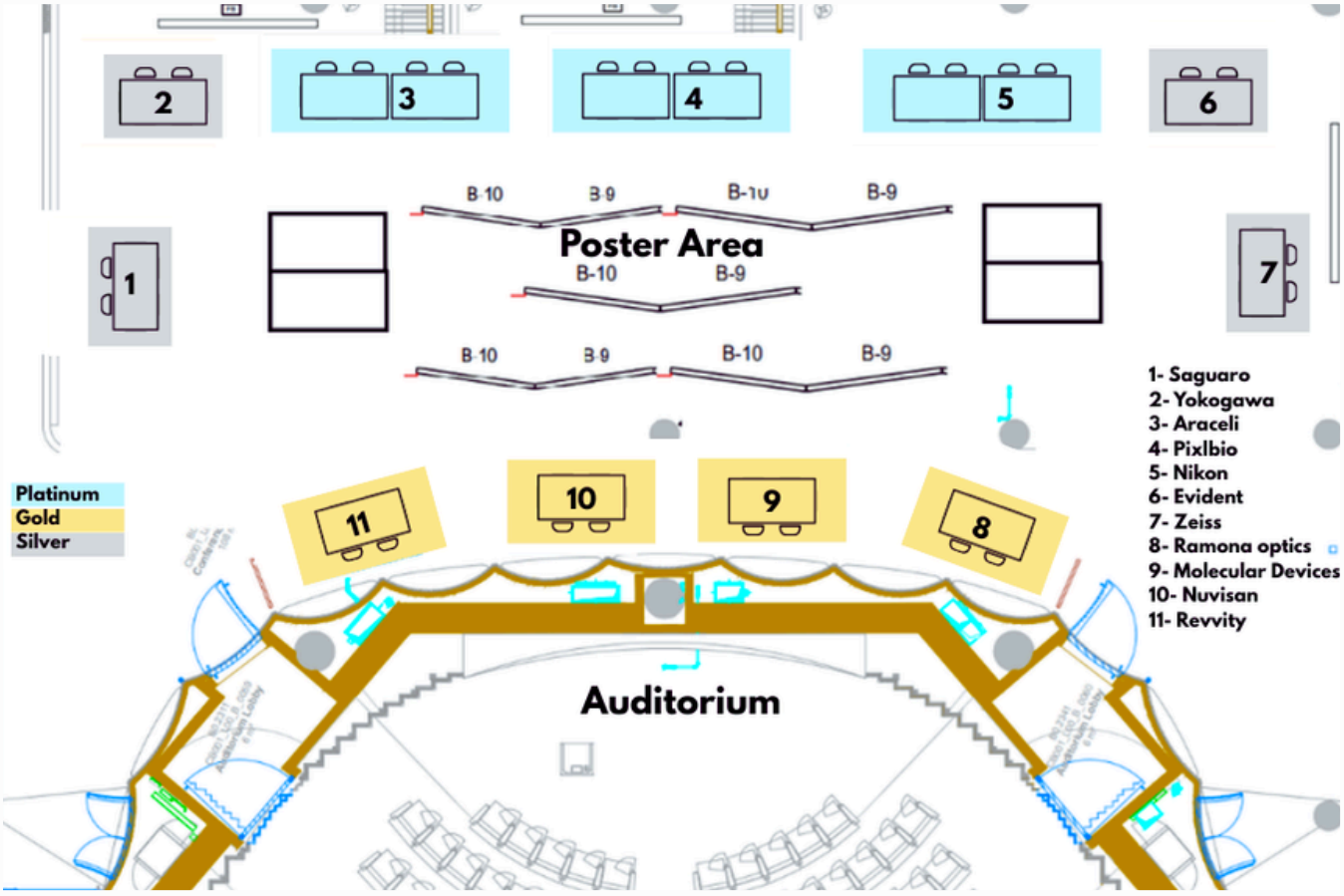
With thanks to our sponsors:

We are grateful to **EU-OPENSCREEN** for sponsoring the poster session and awards, and to the **Royal Microscopical Society (RMS) Life Sciences Section** for funding the Early Career Researcher Prize for excellence in imaging.

Exhibition and poster area

We are delighted to host several vendors offering excellent solutions for high-content imaging and informatics and highly encourage you to discuss with them during the conference.

Vendors will be present in the break out area beside the auditorium during all coffee and lunch breaks throughout the conference - see below for a map of vendor locations.



Education and Scientific Program

Education session

The education session led by expert speakers provides a practical roadmap for high-content screening, from foundational assay design to advanced AI-driven discovery. Attendees will gain the strategic insights needed to bridge the gap between wet-lab execution and complex computational modeling.

Session 1: Simulating Life: The Virtual Cell Revolution

The virtual cell is no longer science fiction: this session presents three complementary advances towards in silico biology — predicting how perturbations propagate from single cells to spatial tissue contexts, measuring thousands of proteins per cell at scale, and fusing morphological imaging with proteomics to capture the full phenotypic fingerprint of a cell.

Session 2: Silicon Meets Cell: AI Seeing What We Can’t

Images of cells encode far more biological information than the eye can see, this session demonstrates how deep learning and AI-powered image analysis are decoding that hidden language, from single-cell phenotyping and microenvironment-aware classification to mechanism-of-action inference and drug discovery.

Session 3:The Future is Now: Next-Wave High Content Technologies

This session showcases the cutting edge of high-content screening hardware, software, and methodology — opening with the HCS-3DX platform, which brings light-sheet fluorescence microscopy and AI-driven single-cell analysis to 3D cell cultures including spheroids and organoids, unlocking a dimension of biological information inaccessible to conventional 2D screening systems.

Session 4: Image to Impact: High-Content Screening Delivered

This session explores how high-content screening converts images into actionable insights that drive decision-making in real-world projects.

Session 5: Dimension Matters: Revolutionizing Drug Discovery in 3D

This session will encompass presentations describing cutting-edge high content imaging applications to map spatial interactions between cells with their 3-dimensional microenvironment. Presentations will describe new tools which combine with high content imaging to optimally exploit and scale complex human in vitro 3D models of disease incorporating human iPSC-derived co-culture and organoid models.

Agenda

Day 1: Tuesday July 7th 2026

8:30-9:00	**Registration**	
	Education session	
9:00- 10:00	**Jordi Carreras-Puigvert** *Pixl Bio*	From Pixels to Profiles: A Practical Guide to High-Content Screening in Drug Discovery
10:00-11:00	**Adriana Borowa** *Ardigen*	Navigating Deep Learning for High Content Image Analysis
11:00-11:30	**Coffee Break**	
11:30-12:30	**Steffen Jaensch** *Johnson & Johnson*	From Features to Decisions: Practical Downstream Analysis Strategies for High Content Imaging
12:30-13:30	**Lunch break**	
Session 1	**Simulating Life: The Virtual Cell Revolution**	
	Chair: Peter Hovath, *Biological Research Centre, Szegad*	
13:30-14:30	**Keynote: Fabian Theis,** *Helmholtz Munich* Closing the loop: from single-cell perturbations to spatial interventions	
14:30-14:40	**Platinum Spotlight**	**Nikon**
14:14- 15:10	**Coffee Break**	
15:10-15:40	**Tami Geiger** *Weizmann Institute of Science*	Elucidation of Cancer Heterogeneity through Deep Visual Proteomics
15:40-16:10	**Bolek Zapiec** *Merck Healthcare*	Painting a Better Picture: Multimodal Approaches with Cell Painting and Proteomics
16:10-16:20	**Daniel Alpern** *Alithea Genomics*	Integrating Imaging and Transcriptomics for Scalable Drug Screening and Virtual Cells
16:20-16:25	**Spotlight**	Glencoe Software
16:25 +	**Poster Session and Evening Networking** **Light refreshments and canapés**	

Day 2: Wednesday July 8th 2026

Session 2	**Silicon Meets Cell: AI Seeing What We Can't**	
	Chair: Bolek Zapiec, *Merck Healthcare*	
9:00-10:00	**Keynote: Andreas Bender,** *Khalifa University* From Cellular Imaging to Decision Making - Approaches and Pitfalls	
10:00-10:30	**Peter Horvath** *HUN-REN Biological Research Centre*	Life beyond the pixels: single-cell analysis using deep learning and image analysis methods
10:30-10:40	Platinum Spotlight	**Pixl Bio**
10:40-10:50	**Jessica Ewald** *EMBL-EBI*	Evaluating Cell Painting for In Vivo Hepatotoxicity Prediction from In Vitro Exposures
10:50-11:15	**Coffee Break**	
Session 3	**The Future is Now: Next-Wave High Content Technologies**	
	Chair: Anusuya Banerjee, *GlaxoSmithKline*	
11:15-11:45	**Akos Diosdi** *HUN-REN Biological Research Centre*	HCS-3DX: imaging platform for 3-dimensional cell cultures using light-sheet microscopy
11:45-12:15	**Britt Vervoort** *Princess Máxima Center for Pediatric Oncology*	BEHAV3D-HIGH THROUGHPUT: A 3D high-content life imaging immuno-oncology assay for immunotherapy screening
12:15-12:20	Spotlight Talk	**Saguaro Biosciences**
12:20-12:30	**Shoma Kataoka** *University of Würzburg*	Multiplexed Fourier Ptychographic Microscopy for High-Throughput Cellular Phenotyping
10:50-11:15	**Lunch Break & Poster session**	
Session 4	**Image to Impact: High-Content Screening Delivered**	
	Chair: Morag Rose Hunter, *AstraZeneca*	
13:30-14:00	**Guido Zagnoli** *AstraZeneca*	Seeing Decisions: Embedding Imaging Across the DMTA cascade
14:00-14:30	**Melanie Sakatis** *GlaxoSmithKline*	Use of High Content Imaging in DILIsym QST modelling for regulatory submission
14:30-14:40	Platinum Spotlight Talk	**Araceli Biosciences**
14:40-14:50	**Martina Zowada** *DKFZ Heidelberg*	A high-throughput screening platform for the identification of WNT signaling inhibitors in CRC
14:30-15:15	**Coffee Break**	

Session 5	Dimension Matters: Revolutionising Drug Discovery in 3D	
	Chair: Neil Carragher, *University of Edinburgh*	
15:15-15:45	**Ilya Lukonin** *IHB Basel*	A toolbox for phenotypic discovery in complex in vitro model systems
15:45-16:15	Davide Danovi *Migration Biotherapeutics, Hoya Consulting*	A human iPSC-based neural spheroid platform for modelling glioblastoma infiltration using high-content imaging
16:15-16:20	Spotlight Talk	**Zeiss**
16:20-16:30	**Michele Zagnoni** *ScreenIn3D*	Upscaling 3D complex drug combination and PK-PD assays
16:30	**Closing Remarks**	

Venue information

Venue Address:
The Discovery Centre (DISC),
1 Francis Crick Avenue,
Cambridge,
CB2 0AA, UK

Getting There:

We strongly advise attendees to take public transport or taxi to the venue where possible due to limited car parking capacity (priority blue badge spaces are available).

The closest rail station is **Cambridge South** (due to open June 28th 2026).
The closest bus stop is **Royal Papworth Hospital.**

Limited car parking is available at Addenbrooke's Hospital (Car Park 2).

Speakers

Education Session:
Jordi Carreras-Puigvert
Pixl Bio

Bio:
Jordi Carreras-Puigvert, PhD is Chief Scientific Officer and co-founder of Pixl Bio, a biotechnology company combining automated phenomics, iPSC-derived human cell models, and artificial intelligence for predictive biology. Jordi holds a MSc in Biotechnology by the Universtiat Autònoma de Barcelona, Catalonia, and a PhD in Life Sciences by Leiden University, Leiden, the Netherlands. With a prolific scientific publication record, and over a decade of experience in high-content imaging and cell-based phenotypic screening, Jordi has been leading the application of Cell Painting and morphological profiling for drug discovery and toxicity assessment. In parallel, Jordi holds an Associate Professor and Senior Lecturer position at Uppsala University, Uppsala, Sweden, affiliated with the Pharmaceutical Bioinformatics group. Prior to this position, Jordi gained a solid scientific background during two postdoctoral periods at the Leiden University Medical Center, Leiden, the Netherlands, and Karolinska Institutet, Stockholm, Sweden, where he was also Assistant Professor. His research sits at the intersection of quantitative imaging, chemical biology, and machine learning, with a strong focus on translating phenotypic data into actionable insights for early drug development and safety prediction.

From Pixels to Profiles: A Practical Guide to High-Content Screening in Drug Discovery

Abstract:
High-content screening (HCS) has evolved from a niche imaging technology into a cornerstone of modern phenotypic drug discovery. By combining automated fluorescence microscopy with quantitative image analysis, HCS enables the simultaneous measurement of multiple cellular parameters at scale, bridging the gap between simple biochemical assays and complex biological reality.
This lecture provides a practical overview of HCS, from foundational principles to advanced applications. We begin with the core technology: how automated microscopes, fluorescent probes, and multi-parametric readouts work together to capture rich cellular information across thousands of samples. We then discuss critical experimental considerations, including assay design, cell model selection, staining protocols, and quality control, which determine whether a screen succeeds or fails.
A central focus is image analysis: from segmentation and feature extraction to the statistical frameworks needed to derive robust, reproducible readouts. We explore how single-parameter HCS assays can be extended into morphological profiling approaches such as Cell Painting, which captures hundreds of features per cell to generate unbiased phenotypic fingerprints of compound activity.
Finally, we address the practical and strategic challenges of building and operating a high-throughput HCS facility, covering instrumentation choices, workflow automation, data management, and team expertise.
Whether you are setting up your first HCS experiment or scaling toward industrial phenomics, this lecture aims to provide both the conceptual grounding and the practical insights to advance your work.

Education Session:
Adriana Borowa
Ardigen

Bio:
Adriana is a Lead Data Scientist at Ardigen responsible for the development of Ardigen phenAID platform that enables the identification of small molecule candidates. Her diverse experience includes work in digital pathology and neuron imaging with commitment to making meaningful contributions in various domains of life sciences. Adriana earned PhD in Technical Computer Science from Jagiellonian University and her research interests are focused on advancing the field of biomedical imaging by leveraging AI models. Her scientific work on cutting-edge deep learning algorithms aims to automate the analysis of High Content Screening images as well as microscopy images of bacteria.

Navigating Deep Learning for High Content Image Analysis

Abstract:
The landscape of image analysis is undergoing a fundamental shift as deep learning (DL) moves from a niche research interest to a core component of high-content screening. This session provides a comprehensive overview of the transition from "traditional" computer vision to modern AI-driven architectures, such as Convolutional Neural Networks (CNNs) and Transformers.
We will begin by evaluating the pros and cons of traditional vs. DL-based analysis. While classical methods offer high interpretability and lower computational costs, DL provides unmatched feature extraction capabilities for complex phenotypes. Understanding when to use which, and the trade-offs involved in transparency versus performance, is critical for any robust analytical pipeline.
Presentation will cover essential, yet often overlooked, stages of image processing and normalization, because a model is only as good as the data it consumes. We will discuss: strategies to mitigate experimental variation that can lead to false discoveries, ensuring data consistency across diverse datasets, and defining the requirements that make a dataset truly "AI-ready" for reproducible science.
Finally, we will explore the training of AI models specifically for downstream analysis. Beyond simple classification, we will examine how to generate and interpret features that drive biological discovery. Attendees will leave with a clear conceptual roadmap for integrating deep learning into their workflows, focused on achieving high-quality, reliable results in large-scale screening environments.

Education Session:
Steffen Jaensch
Johnson & Johnson

Bio:
Dr. Steffen Jaensch is a Senior Principal Scientist at Johnson & Johnson in Beerse, Belgium. He leverages AI/ML approaches on high-content imaging and transcriptomics data to drive early drug discovery efforts in disease biology modeling, target identification and compound mechanism/safety understanding. He earned his Ph.D. through a joint program at the Max Planck Institute of Molecular Cell Biology and Genetics (Dresden, Germany) and HHMI Janelia Research Campus (Ashburn, USA), where he developed image analysis algorithms to study centrosome dynamics in C. elegans embryos.

From Features to Decisions: Practical Downstream Analysis Strategies for High Content Imaging

Abstract:
High-content imaging produces vast, multidimensional datasets, but the true value emerges only when these features are translated into meaningful decisions. This session delivers a practical, end to end overview of downstream HCI analytics, anchored by multiple real world use cases from a large pharma environment. We'll begin with effective data management and visualization in Phaedra, enabling intuitive navigation of imaging data. We'll then cover key concepts in morphological profiling to detect phenotypes, score similarities, and generate mechanism or target hypotheses. Finally, we'll highlight assay activity modelling, showing how deep learning models built on imaging features can predict compound activity in safety and project assays. Together, these approaches illustrate how downstream analytics turn complex imaging data into actionable insights to accelerate decision-making in drug discovery.

Session 1
Simulating Life: The Virtual Cell Revolution

Chair: Peter Horvath

HUN-REN Biological Research Centre, Szegad

Bio:

Peter Horvath is an institute director at the Hungarian Research Network (HUN-REN), a group leader at the AI4Health Institute in Helmholtz Center Munich, and a visiting scientist as well as a Finland Distinguished Professor Fellow at the University of Helsinki (FIMM-EMBL). With over 20 years of experience in image analysis and machine learning, he has conducted research at leading institutions, including ETH Zürich and INRIA Sophia Antipolis, where he earned his PhD in 2008.

His research groups focus on developing computational solutions to biological problems, integrating wet-lab techniques and light microscopy with AI-driven image analysis. His innovations in computational microscopy have contributed to the discovery of genes with essential roles in cancer, bacterial and viral infections, and diabetes. He has also introduced groundbreaking methods in single-cell research. Horvath's scientific contributions have been published in top-tier journals, including Science, Cell, and over 20 different Nature journals, totaling 150+ peer-reviewed publications. He has secured numerous international and national grants, including funding from CZI, NIH, and EU-Horizon programs.

Currently, his research focuses on integrating AI-driven algorithms with molecular measurements to develop personalized, targeted cancer treatments and translate these advancements into real-world clinical applications. His vision is to harness single-cell manipulation technologies to improve cancer diagnostics and patient outcomes.

Peter Horvath has submitted 11 patent applications and is committed to translating scientific discoveries into practical solutions. He is the founder and CEO of Single-Cell Technologies Ltd. and the founder of mAIskin AB, a company dedicated to bringing cutting-edge research into clinical practice

Session 1, keynote speaker

Fabian Theis

Helmholtz Munich

Bio:

Prof. Dr. Dr. Fabian Theis is a leading scientist in biomedical AI and computational life sciences. He heads the Helmholtz Munich Computational Health Center and holds the Chair for Mathematical Models of Biological Systems at the Technical University of Munich. His research pioneers machine-learning frameworks, scalable inference methods, and foundation models that integrate multimodal single-cell and spatial omics data, enabling a deeper understanding of cellular decision-making, tissue organization, and disease mechanisms. A core contributor to the Human Cell Atlas, he develops AI-powered approaches that have become widely adopted standards in the global single-cell community.

Fabian Theis has established a highly recognized center for AI driven biomedicine, supporting the translation of advanced computational methods into biomedical discovery and precision medicine. His group's tools, including widely used analysis platforms and deep generative models, shape how high dimensional biological data are integrated, interpreted and applied across research and industry.

In addition to his academic leadership, he is deeply involved in entrepreneurship. He co-founded RN.AI Therapeutics and Instant Solutions and advises a portfolio of biotech and AI companies, including Phylo, Valinor Industries, GenBio.AI, BioTuring, Cytoreason, Immunai, and Cellarity, linking frontier machine learning with real-world biomedical innovation.

His scientific impact has been recognized with major international distinctions, including the Gottfried Wilhelm Leibniz Prize (2023), the Hamburg Science Award (2021), the Erwin Schrödinger Prize (2017), the SIB Bioinformatics Innovative Resource Award for scverse (2025), and multiple ERC grants (Starting, Advanced, Proof of Concept). He regularly delivers keynotes at leading international conferences and advises governments and major scientific institutions on AI strategy.

Closing the loop: from single-cell perturbations to spatial interventions

Abstract:

The integration of automated high-content imaging with complex human in vitro models provides a robust framework for phenotypic drug discovery. However, translating these models from exploratory work to industry-scale execution requires a toolbox with seamless integration of assay development, lab automation, imaging and large-scale data analysis.

In this talk, I will present how the Institute of Human Biology's (IHB) uses this toolbox for scaling complex human biology. We deploy a modular automation environment not merely for throughput, but as a ""standardization engine"" for biological assays. This investment yields a versatile toolbox that supports a diverse portfolio of model systems. To manage 100s of TBs of resulting data, we deploy a centralized, high-performance image processing framework, empowering biologists to independently analyze terabyte-scale datasets and leverage machine learning.

I will showcase this integrated toolbox across diverse complex model systems and readouts. I will highlight how we used automated multiplexed whole-mount imaging in pancreatic ductal adenocarcinoma (PDAC) tumoroids, to map spatial interactions within the microenvironment through unsupervised machine learning. I will showcase screens in patient-derived colorectal cancer liver metastasis (CRCLM) tumoroids investigating treatment-dependent cellular states at the single-cell level. Furthermore, our applications extend to high-throughput live-cell imaging screens in arrayed reporter organoids, and automated functional assays quantifying predictive toxicity across diverse donor-derived intestinal epithelium models.

Ultimately, this ecosystem enables the systematic quantification of compound effects across human physiological contexts, priming the next generation of drug discovery approaches.

Session 1:
Tami Geiger
Weizmann Institute of Science

Bio:
Tami Geiger studied biology at the Hebrew University of Jerusalem, Israel, where she also completed her master's and doctoral degrees in biochemistry. In 2008 she moved to the laboratory of Prof. Matthias Mann at the Max Planck Institute of Biochemistry to specialize in proteomics technology and to apply it to cancer research. In October 2011, Tami moved back to Israel and opened her own research laboratory at the Sackler Faculty of Medicine at the Tel Aviv University. In 2021 Tami moved to the Weizmann institute of Science, Rehovot, Israel. She is proceeding with clinical proteomic research of breast cancer, melanoma, ovarian and Ewing sarcoma with emphasis on the interactions with the immune system, metabolic changes that occur during cancer progression, and integration with genomic analyses and imaging. Additionally, Tami works on development of single cell proteomic technologies. She studies questions related to cancer progression, drug response, and tumor heterogeneity.

Elucidation of Cancer Heterogeneity through Deep Visual Proteomics

Abstract:
Intratumoral heterogeneity represents a fundamental barrier to effective cancer therapy and a primary driver of acquired drug resistance. We have previously demonstrated that this heterogeneity is critically governed by interactions between malignant cells and neighboring populations within the tumor microenvironment (TME), rather than being solely a cell-intrinsic property.
To resolve this heterogeneity at the proteomic level, we implemented Deep Visual Proteomics (DVP) workflow integrating spatially resolved multiplexed imaging with high-sensitivity mass spectrometry. Multiplexed imaging is performed on the PhenoCycler-Fusion platform, enabling simultaneous visualization and phenotypic classification of distinct cell populations within their native tissue architecture. Individual cell types are subsequently isolated by laser microdissection according to their cellular neighborhoods and subjected to ultra-sensitive mass spectrometric analysis, yielding proteomic profiles encompassing thousands of proteins at single cell-type resolution.
Applying this approach to patient-derived tumor specimens, we can identify discrete proteomic phenotypes in cancer cells that are spatially dependent on their microenvironmental context, demonstrating that cellular neighborhood composition drives divergent molecular states. These neighborhood-specific proteomic signatures illuminate previously unresolved mechanisms underlying drug resistance.

Session 1:
Bolek Zapiec
Merck Healthcare

Bio:
Bolek Zapiec is Head of Digital & Data Science in Discovery Development Technologies in R&D at Merck Healthcare, working at the intersection of imaging informatics, knowledge management, and AI-enabled drug discovery. He played a central role in establishing Cell Painting at Merck — building the data infrastructure, image analysis pipelines, and phenotypic profiling workflows that brought this technology into routine use for pharmacological characterisation.
Bolek's scientific background is rooted in advanced bioimaging. He began his career in neuroscience at Columbia University before earning his PhD from Heidelberg University, with subsequent research at the Max Planck Institute of Biophysics and the Max Planck Research Unit for Neurogenetics. His experimental work spanned neurodegeneration and axon biology, underpinned by extensive hands-on experience with whole-brain two-photon fluorescent tomography, STED super-resolution microscopy, automated slide staining, and deep learning-based image analysis — a foundation that continues to inform his computational work today.
Since joining Merck in 2021, Bolek has extended this imaging expertise into the broader data and AI landscape of drug discovery. He now leads efforts in knowledge graph architecture and data strategy, integrating multi-omics, imaging, and biomedical data streams to build AI-driven platforms for evidence synthesis and target assessment. This includes the development of multi-agent AI systems and integrated knowledge infrastructures that connect phenotypic, molecular, and clinical evidence to support drug discovery decisions.
His work sits at the convergence of bioimaging informatics, multi-omics data integration, and knowledge graph-powered AI — making him well placed to both chair and contribute to sessions on the evolving role of AI in biomolecular imaging and drug discovery.

Painting a Better Picture: Multimodal Approaches with Cell painting and Proteomics

Abstract:
Understanding the full pharmacological footprint of a small molecule — on-target engagement, off-target liabilities, and phenotypic consequence — is a central challenge in early drug discovery. High-content OMICS profiling assays offer powerful, unbiased windows into compound biology, yet each technology illuminates only a partial landscape of drug action.
Cell Painting captures cell-wide morphological perturbations across thousands of image-derived features, detecting downstream phenotypic consequences of compound activity — including those arising from mechanisms invisible to target-centric approaches — but remains agnostic to the underlying molecular machinery. Mass spectrometry-based proteomics, by contrast, delivers direct target deconvolution and mechanistic resolution at the protein level, yet is often blind to how the cell integrates those perturbations as a system.
Using a curated, mechanistically diverse reference set of 2,805 late-stage compounds with matched Cell Painting profiles and quantitative proteomics readouts, we explore the complementarity and blind spots of both modalities — where they converge on compound mechanism, where they diverge, and what those divergences reveal about off-target biology and polypharmacology that neither method captures alone. We further examine which aspects of the proteome are predictable from morphological profiles alone using AI models, probing the degree to which phenotypic space encodes molecular-level information and where the two modalities remain fundamentally orthogonal. We discuss practical frameworks for deploying multimodal profiling in a discovery pharmacology setting and the broader case for multimodal phenotypic fingerprinting as a cornerstone of translational early discovery.

Session 1:
Daniel Alpern
Alithea Genomics

Bio:
Daniel Alpern, PhD, is Co-founder and Chief Scientific Officer at Alithea Genomics, a company advancing high-throughput RNA sequencing technologies for drug discovery and biomarker research. Previously a researcher at the École Polytechnique Fédérale de Lausanne (EPFL), he developed BRB-seq, the technology underpinning Alithea's platform, and now leads the company's scientific strategy in scalable transcriptomics and AI-ready biological data generation.

Integrating Imaging and Transcriptomics for Scalable Drug Screening and Virtual Cells

Abstract:
High-content imaging has become a cornerstone of modern drug screening, providing scalable and information-rich views of cellular morphology. Cell Painting is particularly powerful for surveying biological responses across large compound libraries. However, imaging alone does not directly reveal molecular mechanisms, which becomes a key limitation as the field moves toward predictive modelling and virtual cell simulations.
Transcriptomics provides this missing mechanistic layer, but single-cell approaches are difficult to scale sufficiently to systematically explore large chemical spaces. Bulk transcriptomics uniquely addresses this bottleneck. By pooling cells while preserving perturbation resolution, bulk assays enable orders-of-magnitude more compounds, doses, and conditions to be profiled than single-cell methods. In an integrated screening framework, imaging provides phenotypic breadth, single-cell assays offer molecular precision, and bulk transcriptomics supplies the scale required to navigate vast chemical perturbation space.
Alithea's DRUG-seq, a low-cost, ultra-high-throughput bulk transcriptomics platform designed as a data-generation engine for large-scale chemical perturbation screening. We used DRUG-seq in combination with Cell Painting to profile annotated JUMP MOA and DILI–labelled compounds. While imaging sensitively detected diverse phenotypic responses and early points of departure, DRUG-seq provided stronger resolution for MoA classification. Integrating both modalities improved clustering consistency, highlighting their functional complementarity.
Our results reinforce a central lesson from recent foundation model efforts: better models require more data and more diverse perturbations. Integrating imaging with bulk scale and targeted single cell transcriptomics is therefore required for generating the datasets needed to build scalable, mechanistically grounded virtual cell models.

Session 2
Silicon Meets Cell: AI Seeing What We Can’t

Chair: Bolek Zapiec
Merck Healthcare

Bio:
Bolek Zapiec is Head of Digital & Data Science in Discovery Development Technologies in R&D at Merck Healthcare, working at the intersection of imaging informatics, knowledge management, and AI-enabled drug discovery. He played a central role in establishing Cell Painting at Merck — building the data infrastructure, image analysis pipelines, and phenotypic profiling workflows that brought this technology into routine use for pharmacological characterisation.
Bolek's scientific background is rooted in advanced bioimaging. He began his career in neuroscience at Columbia University before earning his PhD from Heidelberg University, with subsequent research at the Max Planck Institute of Biophysics and the Max Planck Research Unit for Neurogenetics. His experimental work spanned neurodegeneration and axon biology, underpinned by extensive hands-on experience with whole-brain two-photon fluorescent tomography, STED super-resolution microscopy, automated slide staining, and deep learning-based image analysis — a foundation that continues to inform his computational work today.
Since joining Merck in 2021, Bolek has extended this imaging expertise into the broader data and AI landscape of drug discovery. He now leads efforts in knowledge graph architecture and data strategy, integrating multi-omics, imaging, and biomedical data streams to build AI-driven platforms for evidence synthesis and target assessment. This includes the development of multi-agent AI systems and integrated knowledge infrastructures that connect phenotypic, molecular, and clinical evidence to support drug discovery decisions.
His work sits at the convergence of bioimaging informatics, multi-omics data integration, and knowledge graph-powered AI — making him well placed to both chair and contribute to sessions on the evolving role of AI in biomolecular imaging and drug discovery.

Session 2 keynote speaker:
Andreas Bender
Khalifa University

Bio:
Dr Andreas Bender is a Professor for Machine Learning in Medicine at the Department of Medicine at Khalifa University, Abu Dhabi, analyzing heterogenous chemical, biological and medical data. Before this post, he has been Professor for Molecular Informatics at Cambridge University and a Director for Digital Life Sciences at Nuvisan/Berlin, as well as Associate Director for Data Science and AI in the Clinical Pharmacology & Safety Sciences group at AstraZeneca/Cambridge, UK. In his work, Andreas is involved with the integration and analysis of chemical and biological data from different sources, such as structural and bioactivity data, gene expression readouts, cellular imaging data, pathway information, electronic health records, etc., for clinically relevant decision making. On the entrepreneurial side, Andreas was founding CTO of Healx Ltd. for data-driven drug repurposing, and scientific co-founder of PharmEnable Ltd., for designing novel chemistry for targets that are difficult to drug conventionally, both based in Cambridge/UK. More recently, he was CITO of Pangea Bio, a clinical stage company located in London/UK as well as Berlin/Germany, working on CNS drug discovery supported by historical use information. The companies helped establish currently have several drugs in clinical phase 2 trials He received his PhD from the University of Cambridge and worked in the Lead Discovery Informatics group at Novartis in Cambridge/MA as well as at Leiden University in the Netherlands before his current post.

From Cellular Imaging to Decision Making - Approaches and Pitfalls

Abstract:
Cellular imaging, in implementations such as Cell Painting[1], allows for the multi-dimensional characterization of compound effects (and those of other interventions), in both generic cell lines, and more disease-relevant systems. However, next ‘data’ needs to be transformed into ‘insight’, and then form the basis for decision making in a concrete use case. In this presentation we will discuss fundamental aspects that need to be fulfilled for such processes to work in practice, and present concrete applications related to predicting the mitochondrial toxicity of small molecules[2] as well as PROTACs[3]. However, we will also show that one needs to be careful with conclusions drawn from benchmark studies (and, more generally, performance metrics) that aim to utilize cellular morphology data for predicting e.g. the on-target activity of small molecules[4]. The same caution needs to be applied also to other types of data, and endpoints in general – data, model, performance metric, and use case need to be aligned to impact decision making in a positive way.

[1] Seal, S. et al. (2025). Cell Painting: a decade of discovery and innovation in cellular imaging. Nat. Meth. 22(2), 254–268. https://doi.org/10.1038/s41592-024-02528-8
[2] Seal, S. et al. (2022). Integrating cell morphology with gene expression and chemical structure to aid mitochondrial toxicity detection. Comm. Biol. 5(1), 858. https://doi.org/10.1038/s42003-022-03763-5
[3] Trapotsi, M. A. et al. (2022). Cell Morphological Profiling Enables High-Throughput Screening for PROteolysis TArgeting Chimera (PROTAC) Phenotypic Signature. ACS Chem. Biol. 17(7), 1733–1744. https://doi.org/10.1021/acschembio.2c00076
[4] Seal, S. et al. (2026). Counting cells can accurately predict small-molecule bioactivity benchmarks. Nat. Comm. Advance online publication. https://doi.org/10.1038/s41467-026-68725-5

Session 2:
Peter Horvath
HUN-REN Biological Research Centre, Szegad

Bio:
Peter Horvath is an institute director at the Hungarian Research Network (HUN-REN), a group leader at the AI4Health Institute in Helmholtz Center Munich, and a visiting scientist as well as a Finland Distinguished Professor Fellow at the University of Helsinki (FIMM-EMBL). With over 20 years of experience in image analysis and machine learning, he has conducted research at leading institutions, including ETH Zürich and INRIA Sophia Antipolis, where he earned his PhD in 2008.
His research groups focus on developing computational solutions to biological problems, integrating wet-lab techniques and light microscopy with AI-driven image analysis. His innovations in computational microscopy have contributed to the discovery of genes with essential roles in cancer, bacterial and viral infections, and diabetes. He has also introduced groundbreaking methods in single-cell research. Horvath's scientific contributions have been published in top-tier journals, including Science, Cell, and over 20 different Nature journals, totaling 150+ peer-reviewed publications. He has secured numerous international and national grants, including funding from CZI, NIH, and EU-Horizon programs.
Currently, his research focuses on integrating AI-driven algorithms with molecular measurements to develop personalized, targeted cancer treatments and translate these advancements into real-world clinical applications. His vision is to harness single-cell manipulation technologies to improve cancer diagnostics and patient outcomes.

Peter Horvath has submitted 11 patent applications and is committed to translating scientific discoveries into practical solutions. He is the founder and CEO of Single-Cell Technologies Ltd. and the founder of mAIskin AB, a company dedicated to bringing cutting-edge research into clinical practice.

Life beyond the pixels: single-cell analysis using deep learning and image analysis methods

Abstract:
In this talk I will give an overview of the computational steps in the analysis of single cell-based large-scale microscopy experiments. First, I will present a novel microscopic image correction method designed to eliminate illumination and uneven background effects which left uncorrected, corrupt intensity-based measurements. New single-cell image segmentation methods will be presented using differential geometry, energy minimization and deep learning methods. I will discuss machine learning software tools capable of identifying cellular phenotypes based on features extracted from the image. To improve the learning speed and accuracy, we propose an active learning scheme that selects the most informative cell samples. Our recently developed Deep Visual Proteomics method for single-cell isolation methods, based on laser-microcapturing and patch clamping, utilizes the selection and extraction of specific cell(s) using the above machine learning models. I will show that we successfully performed DNA and RNA sequencing, proteomics, lipidomics and targeted electrophysiology measurements on the selected cells and their usage in personalized precision cancer therapies.

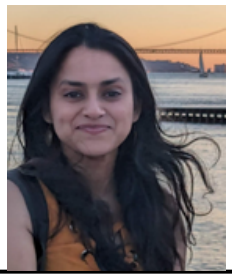
Session 2 short podium presentation
Jessica D. Ewald
EMBL-EBI

Bio:
Jess joined EMBL-EBI as a Group Leader in June 2025. The focus of her lab is on using cell profiling to investigate the impact of environmental chemical exposures on human health. Prior to joining the EBI, she was a postdoc with Anne Carpenter and Shantanu Singh at the Broad Institute where she learned how to use machine learning (including deep learning) to extract biological insights from high-content imaging datasets. She earned a PhD in Bioinformatics from McGill University, where she worked with Niladri Basu and Jianguo Xia to develop web-based tools, algorithms, and databases for incorporating omics data into chemical risk assessments conducted by regulatory agencies around the world.

Evaluating Cell Painting for In Vivo Hepatotoxicity Prediction from In Vitro Exposures

Abstract:
Reliable in vitro approaches for predicting in vivo hepatotoxicity are critical to improve the scalability and human relevance of compound safety assessments. We exposed five cell lines with varying relevance to human liver (U2OS, HepG2, HepaRG, rat primary hepatocytes, human primary hepatocytes) to 8 concentrations of ~1500 compounds with in vivo rat or human liver toxicity data and profiled responses using the Cell Painting assay (data available in the Cell Painting Gallery at accession cpg0037-oasis). Image-based features were extracted with CellProfiler. Dose-response analysis was used to quantify bioactivity and derive points-of-departure (PODs). In vivo liver toxicity endpoints were curated from ToxValDB, TG-GATES, DrugMatrix, DILIrank, and LiverTox, and standardised into ~60 tissue- and cell-type–resolved endpoints using LLMs and expert review. Each compound–endpoint pair was encoded as binary (0/1) with associated effect or no-effect concentrations. In vitro to in vivo extrapolation was applied to convert PODs to equivalent oral doses. We report bioactivity rates, potency, AUROC for toxicity prediction, and concordance between in vitro and in vivo PODs. These results support the potential of Cell Painting as a scalable approach for hepatotoxicity prediction in modern safety assessment.

Session 3
The Future is Now: Next-Wave High Content Technologies



Chair: Anusuya Banerjee
GlaxoSmithKline

Bio:
Anusuya Banerjee is a Principal Investigator in the Cellular Imaging and Dynamics group within Bioimaging at GSK. During her doctoral research at ESPCI-Paris, and postdoctoral Research at the University of Oxford, she focused on developing broad-spectrum fluorescent probes derived from synthetic and biological nanoparticles, for various diagnostic and biosensing applications. Prior to joining GSK, she worked in microscopy start-ups to develop diagnostic platforms for early-stage dementia, viral diseases, and respiratory disorders.
At GSK, the group applies diverse microscopy assays and techniques to validate, characterise, and study the mechanisms of various drug targets. She leads the development of localization microscopy-based platforms to profile and validate pre-clinical assets. Additionally, she partners with various academic groups and start-ups to co-develop and internalise novel imaging techniques within the organisation.

Session 3:
Akos Diosdi
HUN-REN Biological Research Centre, Szegad

Bio:
Ákos Diósdi studied Cell and Molecular Biology at the University of Szeged, Hungary. After earning his BSc, he joined the Biological Image Analysis and Machine Learning Group (BIOMAG) at the Biological Research Centre, where he completed his MSc in Bioinformatics. He received the Discipuli pro Universitate Award in 2019 for academic excellence, followed by the Straub Young Researcher Award for his scientific achievements. During his PhD research, he was awarded the Straub Young Researcher Award. Since 2021, he has also been employed part-time as an application specialist at the company Single-cell Technologies. Currently pursuing his postdoctoral research under Prof. Péter Horváth, Ákos focuses on advanced imaging technologies, including light-sheet microscopy, in vitro 3D models, tissue clearing protocols, and computational biology. His interdisciplinary work combines experimental biology, microscopy engineering, and algorithmic development to address challenges in 3D imaging and analysis. He is co-inventor of a PCT patent and a registered utility model protecting a novel plate assembly for rapid, high-penetration-depth imaging with light-sheet microscopy. In 2024, he received the HUNRENTECH grant, awarded to support the product-level development of his patented concepts and in recognition of the underlying innovative idea. This patented innovation directly enabled the development of the HCS-3DX platform, which integrates custom hardware and AI-driven automation for next-generation 3D high-content screening, and served as the technological foundation for a publication in Nature Communications.

HCS-3DX: imaging platform for 3-dimensional cell cultures using light-sheet microscopy

Abstract:
Three-dimensional (3D) cell culture models, known collectively as “-oids” (including spheroids, organoids, tumouroids and assembloids), have recently attracted considerable interest because they offer an in vivo-like environment for cell–cell interactions in 3D. Systematically assessing these models is essential for developing the next generation of high-content screening (HCS) platforms for patient-specific drug testing and cancer research. However, standardising workflows for 3D-oids remains challenging and is still not widely implemented.
In this study, we introduce HCS 3DX, a next generation platform designed for 3D imaging based HCS and advanced image analysis. HCS 3DX integrates three core components: an automated AI driven micromanipulator for selecting 3D oids, an optimised HCS foil based multiwell plate for improved imaging, and image analysis AI software for single-cell data analysis.
We validated HCS-3DX using 3D tumour models, including tumour–stroma co-cultures, and demonstrated that it overcomes key limitations of current systems by enabling reliable, efficient, single-cell-level 3D high-content screening. HCS-3DX represents a major advance in 3D HCS by integrating AI-driven micromanipulation with state-of-the-art imaging technologies such as LSFM, alongside powerful image-analysis software. The system was tested across multiple experiments, showing strong potential for personalised medicine and drug-screening pipelines. Overall, the robustness and flexibility of HCS-3DX make it a valuable tool for both academic and clinical research, opening new avenues for detailed investigation of cellular behaviour within complex 3D environments.

Session 3:
Britt Vervoort
Princess Máxima Center, Utrecht

Bio:
Dr. Britt Vervoort is a postdoctoral researcher in the group of Anne Rios, where she develops high-throughput 3D live imaging approaches to advance T-cell immunotherapies against cancer. She developed the high-throughput version of the BEHAV3D platform, enabling large-scale, real-time profiling of T cell–tumor interactions in 3D organoid co-cultures. This technology captures the dynamic behavior of engineered T cells as they engage with tumor organoids, providing unprecedented insight into what drives immunotherapy response and resistance.

Dr. Vervoort obtained her MSc working with Sara Courtneidge (OHSU, USA) on breast cancer biology. During her PhD at the Princess Máxima Center, she uncovered genetic drivers of chemotherapy resistance in B-cell acute lymphoblastic leukemia. She joined the Rios group to merge her functional genomics expertise with advanced 3D live imaging, tackling immunotherapy improvement from both sides: overcoming tumor heterogeneity and enhancing the T cells themselves using cutting edge imaging technologies.

BEHAV3D-HIGH THROUGHPUT:
A 3D high-content life imaging immuno-oncology assay for immunotherapy screening

Abstract:
Conventional drug screens rely on endpoint readouts — a single snapshot of cell viability or tumor size — which is well suited for static compounds. However, immunotherapies are fundamentally different: they are a living drug. T cells navigate complex tumor microenvironments, form dynamic contacts, and adapt their behavior over time. Capturing this complexity requires a readout that matches it.
Here, I present BEHAV3D-High Throughput, a 3D high-content live imaging platform designed to capture the dynamic behavior of engineered T cells engaging with cancer organoids at scale. Building on the original BEHAV3D framework (Dekkers et al., Nature Biotechnology), I developed an imaging workflow that scales the platform from 8 to up to 96 conditions in a single experiment, enabling its use as a true screening tool. This required optimizing co-culture conditions, imaging parameters, and acquisition strategies to maintain high-quality 3D live imaging across large numbers of conditions without compromising temporal or spatial resolution. The platform simultaneously records two complementary layers of information in real time: organoid death dynamics, tracking how and when individual organoids are killed over the course of an experiment, and T cell behavior, capturing how T cells migrate, engage, and interact with their targets. By generating this rich, time-resolved imaging data across many conditions at once, BEHAV3D-High Throughput lays the foundation for a new type of immunotherapy screen — one that treats the T cell as a dynamic, behaviorally diverse living drug, and is designed to reveal not just whether a therapy works, but how and why.

Session 3:

Shoma Kataoka

University of Würzburg

Bio:

Shoma Kataoka is a Postdoctoral Researcher in the Machine Biophotonics Lab (AG Zimmer) at the Rudolf Virchow Center, University of Würzburg, Germany. He received his Ph.D. in Engineering from The University of Osaka, Japan. His research interests are in computational imaging. After working on deep-learning-based single-pixel imaging during his doctoral studies, he is now developing high-throughput imaging methods based on Fourier ptychographic microscopy for biological imaging applications.

Multiplexed Fourier Ptychographic Microscopy for High-Throughput Cellular Phenotyping

Abstract:

Image-based phenotypic screening plays an increasing role in drug discovery thanks to its ability to characterize cellular responses to chemical and genetic perturbations in great detail. AI-based analysis can extract subtle perturbation-dependent image features from large-scale datasets, but is also particularly sensitive to subtle technical biases, which can degrade model performance. Image-based phenotyping generally uses high-magnification objectives to image multi-well plates. However, this results in small fields of view (FOV), thus requiring the sequential acquisition of many images by scanning the plate under the objective. This time-consuming process limits throughput, and also increases time-dependent biases associated e.g. with fluorescence decay, cellular growth, detachment, or movement. To address these limitations, we employ Fourier ptychographic microscopy (FPM), a technique allowing to reconstruct high-resolution images with large FOVs from low-resolution images acquired under oblique illumination without scanning. However, conventional FPM requires many images taken at different illumination angles, limiting throughput. To reduce acquisition time, we adopt a multiplexed illumination scheme that activates multiple LEDs per exposure. Whereas conventional multiplexed approaches improve the synthetic numerical aperture relative to the objective by 3-4 fold, our system achieves a 10-fold improvement, thanks to larger illumination angles and a larger number of simultaneously activated LEDs. Our simulations show sub-300 nm resolution over a centimeter-scale FOV with fewer than 100 exposures, and early experimental data support feasibility. These results suggest that the proposed method will enable cellular-scale imaging over a large fraction of a multi-well plate within minutes, enabling high-throughput, low-bias data acquisition for AI-powered phenotypic drug screening.

Session 4
Image to Impact: High-Content Screening Delivered

Chair: Morag Rose Hunter
AstraZeneca

Bio:
Morag Rose Hunter is a cell biologist with a special interest in high throughput, high content imaging assays. After her PhD in Pharmacology at the University of Auckland (New Zealand) and a postdoctoral position at the University of Cambridge (UK), Morag joined AstraZeneca in 2018 as a postdoctoral fellow. Now she is an Associate Principal Scientist in Functional Genomics, running target identification screens with complex imaging and machine learning / artificial intelligence-based analysis techniques. Her long-term interest is in cellular membrane trafficking and it's influence on the efficacy of RNA therapeutics.

Session 4:
Guido Zagnoli
AstraZeneca

Bio:
Dr. Zagnoli Vieira holds a PhD in Genome Stability from the University of Sussex and completed postdoctoral training at the University of Cambridge. He is an Associate Principal Scientist in Discovery Sciences at AstraZeneca, where he partners with project teams to deliver imaging-enabled profiling across the DMTA cascade, from efficacy characterization to early safety, to inform mechanism-of-action and decision-making. He supports oncology programs spanning small molecules, PROTACs, molecular glues, and ADCs, and brings deep expertise in DNA Damage Response (DDR) and oncology biology. Dr. Zagnoli Vieira also leads the department's imaging strategy, advancing high-content and advanced cellular imaging to accelerate discovery.

Seeing Decisions: Embedding Imaging Across the DMTA cascade

Abstract:
A well-designed Design–Make–Test–Analyze (DMTA) cascade is essential for efficient project progression, and imaging-driven assays are increasingly central to its success. This session will showcase how high-content imaging and advanced cellular imaging translate cellular phenotypes into actionable decisions from early hit identification through lead optimization and mechanism-of-action (MoA) elucidation, culminating in the selection of robust clinical candidates. We will discuss assay strategies that balance physiological relevance with throughput, and how standardized image acquisition, AI-enabled analysis, and rigorous quality controls ensure reproducibility across the cascade. We will highlight how image-derived multiparametric profiles accelerate triage, reveal off-target liabilities, and integrate with complementary readouts to refine SAR and increase confidence in progression.

Session 4:
Melanie Sakatis
GlaxoSmithKline

Bio:
Melanie Sakatis is the Non-Clinical Hepatotoxicity Lead at GSK, and an Associate Director in the Cellular Tox group in Non-Clinical Safety. She is responsible for the Non-Clinical Hepatotoxicity strategy for predicting and assessing clinical risk, and the Non-Clinical Lead within the GSK clinical Hepatic Safety Panel. As part of this role she advises project teams on clinical risk based on the non-clinical data, integrating data from in silico, in vitro and in vivo studies, as well as co-ordinating the development and assessment of new capabilities in this space. Externally Melanie co-chairs the Non-Clinical Working Group of the IQ DILI cross-pharma consortium, which serves to give an industry-wide perspective on non-clinical hepatotoxicity approaches. Melanie has over 20 years of experience in the pharmaceutical industry, with over 16 years in DMPK, before transitioning to Non-Clinical Safety at GSK approximately 7 years ago. She has numerous publications describing her work, and is a deep expert in reactive metabolite formation, as well as other in vitro and in silico approaches for evaluating clinical hepatotoxicity risk.

Use of High Content Imaging data in DILIsym QST modelling to predict hepatotoxicity as part of regulatory submission

Abstract:
The non-clinical hepatotoxicity strategy at GSK includes early in silico and in vitro screening assays, later followed by DILIsym QST modelling as appropriate, shortly before a compound is candidate selected for development. This QST modelling integrates high content imaging data and other in vitro data (transporter and mitochondrial data) with a PBPK model to simulate and predict hepatotoxicity in non-clinical species and human. This simulation is considered alongside other hepatotoxicity data (in vitro and in vivo) to give an integrated risk assessment as part of regulatory submission for FTIH clinical studies and beyond. This approach has impacted progression decisions, aided in understanding mechanism, and impacted clinical study design. Future developments are on-going to maximise this data to apply both earlier on in discovery, and later on post-FTIH at GSK.

Session 4:
Martina K. Zowada
DKFZ Heidelberg

Bio:
Martina K. Zowada is a postdoctoral researcher from Heidelberg, Germany. Her research focus is the targeting of stem cell activity in colorectal cancer (CRC). She obtained her BSc and MSc in Molecular Biotechnology from the University of Heidelberg gaining research experience at the German Cancer Research Center (DKFZ) Heidelberg and the Dana-Farber Cancer Institute in Boston. In 2016, she joined the National Center for Tumor Diseases (NCT) Heidelberg, where she started working with patient-derived 3D models to gain understanding of stem cell activity in CRC. In 2021, she obtained her PhD in Biology from the University of Heidelberg and continued her work at NCT in an academia-industry collaboration. In 2023, she joined the Division of Signaling and Functional Genomics at the DKFZ Heidelberg headed by Prof. Michael Boutros. As an experimental scientist, she is establishing a high-throughput drug discovery platform for the identification of WNT signaling inhibitors in CRC.

A high-throughput screening platform for the identification of WNT signaling inhibitors in CRC

Abstract:
The WNT signaling pathway is a main regulator of stemness in colorectal cancer (CRC). Secretion of WNT ligands is regulated by the protein EVI/WLS, which thus represents a highly interesting target for the development of stemness-targeting drugs against CRC. To identify inhibitors of EVI/WLS, we have developed a targeted assay reporting endogenous EVI/WLS levels upon perturbation. This assay can be used for high-throughput drug screening approaches in 2D cell lines as well as 3D organoids. Furthermore, combination with viability readout as well as phenotypic profiling allows for in-depth characterization of perturbation effects in high-throughput.
In an initial screening campaign, we have screened a diversity oriented screening library of 105k compounds using our targeted EVI/WLS reporter assay. In this screen, 430 compounds showed inhibition of reporter activity higher than 70%. Applying an additional threshold for viability, we selected 83 compounds for further analysis.
Next, compounds targeting the assay instead of EVI/WLS were identified in a counterscreen. Furthermore, the candidate compounds were re-screened for their effect in patient-derived 3D models with heterogeneous mutation and expression profiles. Phenotypic profiling upon perturbation with the candidate compounds gains further insights into potential mode-of-actions. To achieve this, candidate treatment-induced phenotypes will be integrated into a unique atlas of thousands of drug-induced phenotypes obtained by phenotypic screening of cell lines (n = 19) as well as patient-derived organoid lines (n = 9).
Taken together, we here present a novel high-throughput drug discovery platform for the identification of WNT signaling inhibitors in 2D and 3D models of CRC.

Session 5
Dimension Matters: Revolutionizing Drug Discovery in 3D

Chair: Neil Carragher

University of Edinburgh

Bio:

Neil Carragher graduated from the University of Aberdeen, Scotland in 1992 with a BSc Honours degree in the subject of “Cell and Immunobiology”. He then took up a position within industry at the Yamanouchi Research Institute, Oxford, England where he also gained his PhD. He then held consecutive postdoctoral positions within the Department of Pathology, University of Washington, Seattle, USA and at the Beatson Institute for Cancer Research, Glasgow, Scotland. In 2004 Neil returned to the pharmaceutical industry as Principal Scientist with the Advanced Science and Technology Laboratory at AstraZeneca where he pioneered early multiparametric high-content phenotypic screening approaches. In 2010 he once again made the career switch from industry to academia and took up the post of Principal Investigator at the Institute of Genetics and Cancer within the University of Edinburgh where he leads a research group and is currently Director of Innovation and Professor of Drug Discovery. He is also an Associate Director of the joint Glasgow-Edinburgh Cancer Research UK Scotland Centre.

Session 5:
Ilya Lukonin
Roche Institute of Human Biology

Bio:
Ilya leads the Automation and Advanced Assay development group at the Roche Institute of Human Biology (IHB). Ilya's work is focused on enabling reproducible, high-impact science at scale by developing and implementing robust automation solutions and end-to-end pipelines for high-content screening in complex in vitro models. The group's ultimate goal is to provide the support and self-service infrastructure that allows IHB scientists to reliably execute complex experiments, such as phenotypic screens in organoids, at scale.
Ilya's professional journey began in Berlin, where he earned his Bachelor's and Master's degrees in Biochemistry. He then obtained his PhD degree in 2019 from the University of Basel for the work in the lab of Prisca Liberali at the Friedrich Miescher Institute (FMI). There, his research pioneered the use of large-scale, image-based screening to map the phenotypic landscape of intestinal organoid regeneration. He developed a high-throughput pipeline to generate multivariate phenotypic fingerprints from hundreds of thousands of organoids, pioneering use of organoids for large-scale imaging screens. At IHB, Ilya leverages this foundational expertise to enable high-content screening across diverse model systems and spearheads the development of the analytical tools to solve the bioimage analysis bottleneck inherent to large-scale imaging.
His academic work has been published in high-impact journals, including a first-author and co-authorships in Nature and Cell Stem Cell. His contributions have been recognised with multiple honors, including the 2021 Bruno Speck Award and the 2020 Chiquet Originality Prize.

A toolbox for phenotypic discovery in complex in vitro model systems

Abstract:
The integration of automated high-content imaging with complex human in vitro models provides a robust framework for phenotypic drug discovery. However, translating these models from exploratory work to industry-scale execution requires a toolbox with seamless integration of assay development, lab automation, imaging and large-scale data analysis.
In this talk, I will present how the Institute of Human Biology's (IHB) uses this toolbox for scaling complex human biology. We deploy a modular automation environment not merely for throughput, but as a "standardization engine" for biological assays. This investment yields a versatile toolbox that supports a diverse portfolio of model systems. To manage 100s of TBs of resulting data, we deploy a centralized, high-performance image processing framework, empowering biologists to independently analyze terabyte-scale datasets and leverage machine learning.
I will showcase this integrated toolbox across diverse complex model systems and readouts. I will highlight how we used automated multiplexed whole-mount imaging in pancreatic ductal adenocarcinoma (PDAC) tumoroids, to map spatial interactions within the microenvironment through unsupervised machine learning. I will showcase screens in patient-derived colorectal cancer liver metastasis (CRCLM) tumoroids investigating treatment-dependent cellular states at the single-cell level. Furthermore, our applications extend to high-throughput live-cell imaging screens in arrayed reporter organoids, and automated functional assays quantifying predictive toxicity across diverse donor-derived intestinal epithelium models.
Ultimately, this ecosystem enables the systematic quantification of compound effects across human physiological contexts, priming the next generation of drug discovery approaches.

Session 5:
Davide Danovi
Migration Biotherapeutics + Hoya Consulting

Bio:
Davide Danovi is Co Founder and CSO of Migration Biotherapeutics. The company develops a decoy conduit technology targeting migrating glioblastoma cells to address tumour recurrence. He also works as an independent partner with Hoya Consulting, based in Stockholm.
Trained as an MD and PhD, he led research groups, facilities, and cross functional teams in academia and biotech after completing his postdoctoral research fellow work at University College London and the University of Cambridge.
Davide holds visiting positions at King's College London and the University of Cambridge, and is a FLIER Future Leader at the Academy of Medical Sciences.
He is a founding member of the London Stem Cell Network and serves on the organising committee of the UK Stem Cell Network.
Davide has extensive experience in human cell characterisation using high content imaging and artificial microenvironments platforms.

A human iPSC-based neural spheroid platform for modelling glioblastoma infiltration using high-content imaging

Abstract:
Glioblastoma is the most aggressive adult brain tumour, characterised by resistance to therapy and high recurrence due to diffuse infiltration. We have previously developed high-content based platforms for chemical screens in patient-derived cells using viability as a read out.
Here we developed a physiologically relevant co-culture model, combining patient-derived glioblastoma cell lines with cortical-like neural spheroids differentiated from human induced pluripotent stem cells. Using high-content imaging, we demonstrate that Glioblastoma patient-derived cells migrate directionally along axons toward neural spheroids in live imaging assays and infiltrate spheroids extensively in endpoint assays.
A proof-of-principle drug screen identified potent suppressors of infiltration in distinct patient-derived cell lines. Bulk RNA sequencing revealed gene expression profiles correlating with invasive behaviour and drug sensitivity.
This platform offers a valuable model for studying glioblastoma infiltration along axons and provides proof-of-principle that migration can serve as a measurable and actionable phenotype to screen therapeutic vulnerabilities in glioblastoma.
I will present work recently published here https://www.nature.com/articles/s41598-025-30914-5 and may touch upon broader use of imaging in different contexts such as
https://www.nature.com/articles/s41467-023-36634-6
https://link.springer.com/article/10.1007/s00204-024-03922-z

Session 5:
Michele Zagnoni
ScreenIn3D

Bio:
Michele Zagnoni is CEO of ScreenIn3D and a Professor at the University of Strathclyde. With an electronic and bioengineering background, he has more than 20 years' expertise in developing microsystem technologies for healthcare and multidisciplinary research. At ScreenIn3D he leads the development of New Approach Methodologies (NAMs) and the commercialization of the company's lab-on-a-chip technologies.

Upscaling 3D complex drug combination and PK-PD assays

Abstract:
The need for physiologically relevant, 3D, complex in vitro models of human disease is steadily increasing due to the emergence of drugs targeting the immune system and the tumour microenvironment (TME). Current in vivo and in vitro models are not sufficiently representative of the human TME and can fail to accurately predict clinical outcomes. With the FDA's guidelines to reduce reliance on animal testing for drug discovery and development, the focus now shifts to human-centric technologies that better predict drug efficacy and safety for improved clinical outcomes.
Our patented lab-on-a-chip technology, UpScale3D®, offers a versatile approach to screen at scale limited amounts of clinical samples, facilitating the screening of thousands of spheroid co-cultures, biopsy-derived organoids or immune-oncology 3D models in miniaturised and perfused conditions. The latter is particularly important to reproduce in vitro, and at scale, experiments typically performed in mouse models in low numbers.
UpScale3D® is engineered for self-generation of long lasting and stable drug concentration gradients (24-36 hours periods) without the need for syringe pumps, tubing or rocking plates, lending itself to automated, integration in existing robotic workflow, and cost-effective assays.
Multiple tumour indications were tested for their sensitivity to standard of care chemotherapeutic compounds, applied in isolation or combination, comparing results from freshly expanded and banked organoids. Results from these screening assays directly supports drug discovery and precision medicine applications with human relevance, offering reproducibility through standardization. This New Approach Methodology (NAM) workflow brings screening of translational disease models to earlier stages of drug discovery.

Sponsors

Platinum

Araceli Biosciences, based in Portland, Oregon, is on a mission to transform therapeutic discovery with technologies built for speed, precision, and impact. Our advanced High Content Imaging platforms deliver real-time analysis, providing researchers with immediate, actionable answers during experiments. This ability to respond at the pace of biology accelerates decision-making, improves candidate selection, and reduces costly downstream failures.
At the same time, our platforms generate high-quality, analysis-ready data that feed into AI-driven models and discovery pipelines. This dual advantage, instant insights today and predictive power tomorrow, positions Araceli as the catalyst for faster, more confident therapeutic breakthroughs. We believe in a future where patients gain access to the most effective treatments sooner, and Araceli Biosciences is forging that future.

At **Nikon**, we are focused on supporting researchers and laboratory specialists with a wide range of industry leading microscope-based imaging solutions and services, to support scientists in their pursuit to continuously improve the quality of human life. Our microscopy solutions harness the power of light to provide scientists with a wide range of cutting-edge microscopes, including confocals, super-resolution systems, digital imaging products and software. Alongside our product offering, the Nikon BioImaging Lab is a Contract Research Organization that provides imaging and analysis services to the biotech, pharma, and research communities, offering contract research services from the company that knows imaging.

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Pixl Bio (pixl.bio) is a biotechnology and AI company focused on turning complex cellular data into predictive insights for drug discovery. The company combines human iPSC-derived cell models, automated high-content imaging, and AI-driven phenomics to analyze how cells respond to drugs, disease mutations, and biological perturbations.

Through large-scale cellular imaging and machine learning, Pixl Bio converts millions of cellular pixels into quantitative phenotypic signatures that help researchers understand mechanisms of action, predict toxicity, and improve the success of therapeutic development.

The company operates at the intersection of biotechnology, automation, and artificial intelligence, providing platforms and services that enable pharmaceutical and biotech partners to design experiments, screen compounds, and generate reproducible, human-relevant biological data.

Pixl Bio was formed from the merger of DefiniGEN and Phenaros Pharmaceuticals, bringing together expertise from Cambridge (UK) and Uppsala (Sweden) to develop predictive biology technologies for the life-sciences industry.

Gold

Molecular Devices provides innovative bioanalytical solutions, including microplate readers, automation systems, software, and reagents, that support life science research and drug discovery.

A key focus of our portfolio is high-content imaging, led by the new ImageXpress® HCS.ai platform, which enables advanced cellular analysis and quantitative phenotyping in both 2D and 3D biology models. Complemented by IN Carta® AI analysis software, our imaging solutions help researchers extract meaningful insights from complex data, generate high-quality, reproducible results, and accelerate discovery.

Your partner of choice in bringing therapeutics to life

Nuvisan is a full-service contract research organisation (CRO) and development and manufacturing organisation (CDMO) with state-of-the-art laboratories in Germany and France.

Our pharmaceutical, biotechnology, venture capital and non-profit clients partner with us because our high-quality end-to-end solutions and scientific expertise enable us to streamline and accelerate drug discovery and development – from ensuring target understanding to helping bring therapeutics to life.

Founded over 40 years ago by a team of pharma industry innovators, Nuvisan has established a reputation for expertise and professionalism. Our team leaders have extensive experience in the biopharma industry, and our unique centres of excellence – for drug discovery in Berlin, formulation and GMP manufacturing in Sophia Antipolis, and our bioanalysis hub in Neu-Ulm – enable our experienced scientists to help guide and advance projects. We know how to discover, develop and bring the next generation of medicines to market. At the same time, we are committed to flexibility, transparency and collaboration in our approach, working closely with you to adapt to your individual needs, minimise risks and help deliver your project.

Gold

Ramona's Vireo™ is the world's fastest and most cost-effective live-cell imaging system, marrying live-cell imaging with high-throughput screening. It is a compact, benchtop 24-plex multi-camera array microscope (MCAM®) for rapid cellular assessment (brightfield and four-channel fluorescent imaging in 2 minutes per plate) and novel video assay functionalities in multiwell plates.

Industries we serve:

Life Sciences
Revvity offers comprehensive life science solutions, technologies, and services, covering workflows from discovery to cure. We revolutionize biomedical research with a focus on translational multi-omics, biomarker identification, imaging, prediction, screening, detection, diagnosis, informatics, and more.

Licensing and Contract Services
Collaborate with our skilled scientists and experts to reach your goals sooner. Our range of contract services supports preclinical oncology drug discovery, viral vector manufacture, omics discovery, the development of genetic disease treatments, and clinical genetic testing. We also provide novel licensable technologies for gene expression, editing, and delivery to help you bring safer, more effective treatments to patients.

Reproductive Health
Our innovative laboratory solutions enhance reproductive health across all stages. Our cutting-edge research solutions drive innovation in reproductive health science, while our advanced screening technologies enable early detection and timely interventions, ultimately empowering improved outcomes globally.

Immunodiagnostics
Our specialty portfolio delivers innovative, end-to-end solutions for identifying and investigating a broad range of immune system disorders. We integrate cutting-edge technologies, such as immunoassays, molecular assays, automation, and advanced software - to enable seamless workflow integration, ultimately expanding research and testing for these highly complex diseases.

Silver

Evident (formerly Olympus microscopy): Optical Technology that Illuminates the Unseen

Every discovery starts with uncovering the unknown. For over a century as Olympus, we advanced optical excellence, empowering the world's leading scientists, physicians, and engineers to see more, know more, and achieve more.

We have helped illuminate Nobel Prize-winning research, enable lifesaving medical advances, and ensure the integrity and safety of products and technologies that improve everyday life. We have supported groundbreaking research, advanced clinical insights, and driven precise industrial applications.

Today, as Evident, we're building on a century of optical superiority to create next-generation micro-imaging solutions—combining renowned optics with cutting-edge digital innovation to power scientific breakthroughs and help you move confidently from observation to insight.

Our life science portfolio supports research, clinical diagnostics, and education, offering a comprehensive range of imaging methods, from essential brightfield and darkfield microscopy to advanced fluorescence, 4D analysis, and digital pathology. In industrial microscopy, we deliver precision and flexibility through laser scanning, digital, and semiconductor microscopes designed for tasks ranging from routine inspection to intricate quality control and sophisticated manufacturing analysis.

Evident is headquartered in Tokyo and supported by R&D and manufacturing centers in Japan, the United States, Germany, and China, with operations and dedicated sales and service centers located around the world.

At Evident, we are paving a new path forward in microscopy. We are helping our customers advance into a new era of discovery. We are pushing the boundaries of optical technology to fuel discovery and bring the unseen into focus.

ZEISS Research Microscopy offer solutions for the Biotech & Pharma industry from Scientific Insights to Preventing, Treating and Curing Disease.
For every stage of the process; Early and Basic Research, drug discovery and drug development, ZEISS has the most powerful portfolio of advanced imaging systems and AI-assisted image analysis for life scientists, including specialized solutions for cell and cancer biologists, neuroscientists, and more.

Silver

Saguaro offers: innovative dyes, wet lab drug profiling services, and image analysis with cutting-edge ML tools.

Saguaro's non-toxic dyes set a new standard:
- Highest fidelity data. Preserves cell physiology to capture the most relevant and accurate biological data.
- One-step protocol for easy automation and screens.
- Perfect for 3D cell cultures with deep and uniform staining.

Non-Toxic Dyes Portfolio
- ChromaLIVE. The leading technology to profile drugs with images, surpassing the most cutting-edge gold standard cell painting assays to enrich hit detection and better elucidate drug mechanism.
- NucleoLIVE and MortaLIVE. Non-toxic nuclear and live-dead stain, allowing new cell health data (ex. viability, cytotoxic, cytostatic, stress) with simple assays.
- Others: LipoLIVE, ER-LIVE, and even more soon!

Drug Profiling Service
- The Leading Profiling Approach – Only by Saguaro. Leveraging our proprietary ChromaLIVE method, and using the most cutting-edge deep learning approaches.
- Reliable Data with State-of-the-Art Automation Facility.
- Live-Cell Assay Experts to Spare your Time.

About **Yokogawa Life Science:**

Yokogawa's life science business started in 1996 with the development of innovative instruments based on proprietary confocal microscopy technologies, and is dedicated to providing novel products employing microscopy and/or image analysis technology for the advancement of cell biology research and drug discovery. Our portfolio includes the Confocal Spinning Disk Unit (CSU), CellVoyager™ High Content Analysis Systems, and the Single Cellome™ portfolio for nano-point delivery and subcellular sampling. For more information, visit https://www.yokogawa.com/eu/solutions/products-platforms/life-science/#Overview

About **Yokogawa:**

Yokogawa provides advanced solutions in the areas of measurement, control, and information to customers across a broad range of industries, including energy, chemicals, materials, pharmaceuticals, and food. Yokogawa addresses customer issues regarding the optimization of production, assets, and the supply chain with the effective application of digital technologies, enabling the transition to autonomous operations. Founded in Tokyo in 1915, Yokogawa continues to work toward a sustainable society through its 17,000+ employees in a global network of 122 companies spanning 61 countries.

Coffee Breaks

Ardigen

Ardigen is a science-first, AI-native partner supporting biotech and pharmaceutical organizations across the entire drug discovery and development pipeline. We help life science teams navigate biological complexity by transforming fragmented biomedical data into governed, interoperable, and AI-ready foundations that drive confident, decision-ready insights.

With experience spanning over 700 discovery projects, we seamlessly connect data architecture, advanced analytics, and domain-specific biology and chemistry into a coherent framework to reduce pipeline risk and accelerate timelines.

Our Core Offerings:

- Data Strategy & Architecture: Feasibility consulting, multimodal data integration, harmonization, and building scalable, reproducible discovery infrastructure.
- Advanced Analytics & AI Products: Custom AI model development, biological interpretation, and lab-in-the-loop enablement to turn raw data into actionable assets.
- Phenomics & HCS Solutions: Scalable AI analytics for Cell Painting assays, phenotypic screening, and structural/phenotypic representation mapping.
- Target & Biomarker Discovery: Integrating genomics, multi-omics, and clinical signals to discover novel targets and predictive biomarkers.

Spotlight talk

Glencoe Software

Glencoe Software builds and delivers innovative, scalable, easy-to-use scientific imaging solutions for its clients and partners. Our proven image database technology makes the viewing, sharing, analysis and management of large sets of images and metadata easy and accessible to everyone in a group, team, project or organization.

Glencoe's products are installed and used in several world-leading academic labs, biotechs, pharmas and publishers, solving mission-critical problems in high-content screening, digital pathology, and many other modalities. Through our OEM licensing programme, our software tools are embedded in some of the world's most powerful and market-leading software data products. We combine world-beating technology and expertise with dedicated, reliable customer support

Poster session and awards

EU-OPENSCREEN is a not-for-profit European Research Infrastructure Consortium (ERIC) for chemical biology and early drug discovery.

We support all stages of a chemical tool development project, including assay adaptation, high-throughput screening and chemical optimisation of the resulting 'hit' compounds.

EU-OPENSCREEN operates an open-access database and a unique, common compound collection. Our main library, the European Chemical Biology Library (ECBL), consists of over 100,000 compounds.

EU-OPENSCREEN has over 30 affiliated high-throughput screening and chemistry facilities at partner sites in eight European countries. These partner facilities provide researchers with access to cutting-edge technologies to develop their own tool compounds.

EU-OPENSCREEN aims to support the global scientific and economic competitiveness of Europe by delivering public health benefits. In the future, we will act as an innovation accelerator for new start-ups.

RMS
Royal Microscopical Society

We are the only truly international microscopical society, drawing distinguished members from all over the world. We serve the needs of our company members who represent all the major manufacturers and suppliers of microscopes, equipment and services.

The Society provides a great community for microscope users, with a busy calendar of training courses and networking events each year. We also produce the Journal of Microscopy, infocus magazine exclusively for our members and a wide range of microscopy handbooks.

Our outreach activities are wide reaching, ranging from our free Microscope Activity Kits for primary schools, to our Facilities Database-the best resource for microscope and imaging facilities.

To ensure our activities remain up to date with the latest techniques and applications, the Society is advised and guided by its Scientific Section Committees, made up from those working at the forefront of their fields both in industry and academia.

The RMS is committed to providing equal opportunities and fair treatment for all, regardless of gender, age, marital status, sexual orientation, ethnic origin, religion, culture or disability.

The RMS is a not for profit organisation and is a registered Charity (number 241990~), under the Charities Act 2011.

Posters

All posters will be displayed during the whole meeting and can be viewed during any break.

Presenters are specifically requested to be by their posters for judging during:
Odd Numbers - Poster Session 1 - 7th July - Evening Networking (16:30-17:30)
Even Numbers - Poster Session 2 - 8th July - Lunch Time (12:35 -13:30)

Number	Session 1	Number	Session 2
#1		#2	
#3		#4	
#5		#6	
#7		#8	
#9		#10	
#11		#12	
#13		#14	
#15		#16	
#17		#18	
#19		#20	
#21		#22	
#23		#24	
#25		#26	
#27		#28	
#29		#30	
#31		#32	
#33		#34	
#35		#36	

Petter Byström (*PIXL Bio*)

AI-Powered Cell Painting in iPSC-Derived Hepatocytes for Liver Toxicity Profiling

Drug-induced liver injury (DILI) remains a major challenge in drug safety.Induced pluripotent stem cell (iPSC)-derived hepatocytes (pixHEP) closely resemble primary human hepatocyte function. At the same time, standard DILI-related endpoint assays (e.g., cell viability) often miss sub-lethal changes. Cell Painting (CP), a multiplexed assay staining several organelles, can detect morphological alterations linked to DILI risk and subtype. This study integrates pixHEP, CP, and AI-driven analysis for liver toxicity assessment.

Wild-type iPSCs were differentiated towards pixHEP using a three-step direct differentiation protocol. Upon differentiation, cells were matured for 14 days in 384-well plates and treated with 20 compounds, classified across all four DILIRank categories, at 2.5 µM and 10 µM for 48 hours. A fully automated CP protocol captured 9 fields per well across five channels.
DINOv2 extracted distinct morphological features per channel. Canonical correlation analysis found that joint channel variance exceeded permutations by 6–16%, though most variance per channel remained unique. Similarly, most compounds failed to elicit pronounced morphological alterations. However, treatment with the alkaloid drug Colchicine triggered significant ($p<0.05$) cellular clustering.
Colchicine induced pronounced morphological shifts without affecting cell count, illustrating the sensitivity of this approach. The phenotype likely reflects cytoskeletal stress, potentially impairing bile acid transport or vesicular repair. Low inter-channel shared variance implies DINOv3 captures non-redundant, complementary information, supporting analysis of all CP channels without early dimensionality reduction. These subtle alterations highlight the utility of combining pixHep, CP, and AI-driven image analysis for DILI risk detection.

Nils Dunlop (*Chalmers University of Technology*)

Explanations Grounded in Cell Painting for Interpretable Phenotypic Screening

Modern deep-learning models for high-content microscopy can accurately predict compound activity and mode of action, but they typically deliver these predictions as black-box scores. This creates a clear bottleneck for downstream users: pharmacologists and toxicologists need to verify predictions before acting on them. Without an interpretable bridge between image and decision, such models remain difficult to validate biologically and slow to gain the trust required for routine deployment.

We propose to ground explainability in the established Cell Painting analysis pipeline. Starting from the public RxRx3-core dataset, we apply an established sequence of segmentation, single-cell feature extraction, phenotypic profiling, and feature selection to obtain biologically interpretable morphological descriptors. These descriptors are used to train a tabular classifier of compound activity, from which exact per-well feature attributions are extracted and compared against plate-matched DMSO controls. The top-attributed features are then converted into structured natural-language explanations describing which morphological changes contributed to each active or inactive prediction. This ensures that explanations remain tied to measurable cellular phenotypes rather than free-form model rationales.

The resulting image-explanation pairs serve as training data for a vision-language model, enabling it to connect cell images with phenotypic activity and mode-of-action patterns. We evaluate predictive performance against established profiling baselines and assess explanation faithfulness through expert review and attribution-based validation. This pipeline positions explainability not as a post-hoc add-on, but as a foundation for building trustworthy multimodal models for image-based phenotypic screening.

Lili Li (*University of Turku*)

An ML-enabled HT framework for disease-relevant rare signaling events and synaptic dynamics

Understanding disease-relevant neuronal phenotypes requires capturing dynamic processes across multiple spatial and temporal scales, from intracellular signaling to synaptic organization.

We have developed a modular, high-throughput framework that permits low-level, long-term and non-toxic viral expression of cell signalling reporters and/or labelled forms of abundant endogenous proteins in rodent or human neurons in 384 –1536 well plates. On the one hand, multiplexed reporter panels are validated for specificity and reveal signaling network trajectories, at both single cell level and spatiotemporally across interacting multicellular circuits. On the other, delivery of labelled forms of abundant endogenous proteins such as SynGAP1, the second most abundant protein in the postsynaptic density, faithfully labels the expected compartments, neuronal synapses, and reports endogenous behaviours such as activity-dependent translocation that underlies the function of the protein. In both cases, cells can be followed dynamically in response to pharmacological or optogenetic stimulation, and longitudinally over days to weeks, for example before and after acoustic dispenser-delivered candidate drug libraries.

In all cases, machine learning strategies assist in segmentation and extraction of biologically interpretable features, unsupervised learning to identify heterogeneity and similarities across samples and supervised learning to establish disease signatures and identify hit compounds reducing disease phenotypes.

Using this framework, we identified off target effects of clinically used drugs, identified common perturbations between pathogenic variants and variants of uncertain significance of SynGAP1 that could contribute to rare disease diagnoses, and identified candidate hit compounds for follow-up. In summary, the framework enables potentially actionable disease- and treatment-relevant insights.

Łukasz Janisiów (*Jagiellonian University*)

Evaluating prototype-based frameworks for explainable cell phenotyping in Cell Painting data

High-content imaging assays such as Cell Painting capture rich and complex cellular phenotypes. Although deep learning models classify these phenotypes with high accuracy, their black-box nature limits biological interpretability and obscures features driving predictions. Prototype-based interpretable models aim to address this limitation by explaining predictions through representative image regions. One such approach is PIP-Net (Nauta et al., 2023), an interpretable classifier that learns prototypical image patches and explains predictions as a sparse scoring system based on prototype presence. PIP-Net achieved state-of-the-art performance among prototype-based models and demonstrated meaningful explanations in medical imaging.

We adapted PIP-Net for explainable classification of endothelial cell phenotype in response to various pharmacological interventions using Cell Painting data and CLOOME's ResNet (Sanchez-Fernandez et al., 2023) as a backbone model. We hypothesized that the model would discover biologically meaningful prototypes corresponding to characteristic cellular phenotypic responses induced by various chemical compounds. However, several architectural choices did not correspond to microscopy data. PIP-Net's fixed-size rectangular patches poorly align with cellular morphology, making it difficult to determine whether predictions are driven by structure, texture, or intensity. Max-pooling reduces each prototype to one score per image, discarding spatial relations between organelles and structures. Sparsity is enforced at the classifier weights, which does not prevent prototypes from mixing unrelated cues from different channels. Although we adapted the framework to channel-wise prototypes, many highly activated prototypes still corresponded to imaging artifacts rather than true cellular phenotypes.

Our findings suggest that Cell Painting requires specifically designed, channel- and morphology-aware explainability frameworks tailored for highly heterogeneous high-content microscopy data.

Flavio Bonanini (*InSphero*)

Scalable Whole-Plate Calcium Imaging of Human iPSC-Derived Neural Spheroids for Drug Screening and Neurotoxicity Assessment

Three-dimensional neuronal spheroid models have emerged as physiologically relevant systems for studying human neural activity, yet standardized, reproducible 3D cellular models paired with scalable functional readouts remain a methodological challenge. Here we present a scalable calcium imaging workflow for the assessment of functional neuronal activity in human neuronal spheroids using InSphero's Akura™ 384-well spheroid microplate and the Ramona Optics Multi-Camera Array Microscope (MCAM®). The Akura™ platform produces highly reproducible spheroids in size and morphology and, with its imaging-compatible flat-bottom, black-walled well design, provides a standardized platform ideal for high-throughput culturing and functional assessment of 3D cell culture models. In parallel, the MCAM® enables simultaneous fluorescent time-lapse acquisition of 12 or 24 wells, allowing whole-plate imaging with minimal acquisition time and low photon exposure. Human iPSC-derived neuronal spheroids comprising a co-culture of astrocytes, glutamatergic, and GABAergic neurons were loaded with a calcium-sensitive fluorescent indicator and imaged in real time to capture spontaneous calcium oscillations, providing a direct readout of microtissue-level neuronal activity. Subsequent video analysis enabled extraction of fluorescence traces and the quantification of frequency, amplitude, and peak-to-peak duration across the plate, revealing consistent oscillatory patterns and well-to-well reproducibility, as well as compound-induced perturbations resulting in alterations of these activity parameters. Together, the Akura™ platform and MCAM® system establish a scalable, high-throughput calcium imaging workflow ideal for functional characterization of human neuronal spheroids with applications in drug screening and neurotoxicity assessment.

Floriane Odje (*Saarland University*)

Cell Painting Maximum Common Profiles Reveal Diverse Endocrine Receptor Signatures

High-dimensional morphological profiles derived from Cell Painting images capture cellular responses to chemical perturbations and are increasingly applied to mechanism-of-action (MOA) annotation. Within the BMBF-funded MORPHEUS (MORPHology-based Endocrine Disruptor Screening) project, we develop robust morphological signatures for hormone receptor activity and use them for MOA annotation.

Building on the Maximum Common Profile (MCP) framework introduced by Pahl et al., we introduce two advances. First, we complement Weight-of-Evidence (WoE) reference selection with a Data-Driven (DD) strategy integrating ToxCast bioactivity assay data, expanding chemical coverage beyond well-characterised compounds. Second, we challenge the assumption that a single MCP is sufficient to describe an MOA. We hypothesise that a single MOA can be represented by multiple MCPs and introduce clustering of reference profiles to capture this heterogeneity. For each cluster, an MCP is derived using a sign-based consensus: features are retained when 85% of references agree in sign and |feature’s value| > 1.
Using exemplarily ERα antagonists, one of the six hormone receptor activities studied, we observed both conserved and heterogeneous MCPs from WoE and DD references. Clustering of DD-derived references yielded seven MCPs with moderate overall similarity (mean Jaccard 0.46 ± 0.19; mean cosine 0.54 ± 0.36). One DD-derived MCP closely matched the WoE-derived antagonist signature (Jaccard 0.75; cosine 0.81), while others showed lower overlap and, in some cases, negative cosine similarity, suggesting distinct antagonist subclasses within the same MOA.
Active compound retrieval experiments demonstrate that cluster-specific MCPs recover complementary sets, highlighting the advantages of multiple MCPs over a single consensus pattern.

Felix Lavoie-Perusse (*Saguaro Bio*)

Boosting Hit ID and MoA Elucidation through High-Fidelity Profiling of Unperturbed Cell States

Profiling of perturbations with images is a powerful approach for understanding disease biology and drug mechanism at scale. However, a fundamental challenge remains: do traditional assays capture the true biological response?

Cell painting, the gold standard approach for image-based profiling, has been shown to provide both overlapping and unique insights compared to common omics like RNA or protein profiling approaches. Yet, cell painting protocols rely on fixation, extensive washing, and “live-cell” (but toxic) probes, all of which perturb the very image features used to build those powerful phenotypic profiles.

Here, we report applications of a high-fidelity live-cell profiling assay with real impact on drug discovery pipelines. ChromaLIVE™, a data-rich and non-toxic dye that provides information-dense profiles and preserves cell physiology, is the central piece of this assay. It has been applied to multiple cell models: from the simplest to the more complex 3D, iPSC or patient-derived cell cultures, with improved performance over cell painting panels. Specifically, we present applications in HTS for detecting a new valuable Hit compound at early timepoints in a rare neurodegenerative disorder; in separating cell responses in 3D cell systems; and in personalized medicine applications, where ChromaLIVETM image profiles correctly stratified patients into cohorts not discernible by standard clinical methods.

Together, these results establish the importance of unperturbed live-cell profiling as a scalable and widely applicable assay that can provide high-fidelity data to AI-model training, and that reveals new, actionable insights hidden in preserved biological states and in the temporal dimension.

Molly McQuilken (*Zeiss*)

Studying Fibrosis in 3D InSight™ MASH Spheroids Leveraging ZEISS Lattice Lightsheet 7 for 3D HCA

Fibrosis is a hallmark of Metabolic dysfunction-associated steatohepatitis (MASH), a progressive severe liver disease. We leverage the ZEISS Lattice Lightsheet 7 and arivis platforms as well as the InSphero 3D InSight™ Human MASH microtissue model to establish a plate-based 3D-High-Content-Imaging (HCI) assay for direct quantification of fibrosis based on whole-spheroid immunofluorescence staining. We show MASH progression and validate the assay using the known fibrosis modulator ALK5 inhibitor (ALK5i) and a novel investigational anti-fibrotic compound.

Boyd Butler (*Molecular Devices*)

AI-assisted automated compound screening for toxicity effects using human 3D liver microtissues

Three-dimensional (3D) human liver microtissues provide physiologically relevant models for assessing drug-induced toxicity but require advanced analytical approaches to fully extract phenotypic information. We developed a high-content imaging workflow combined with AI-driven image analysis to enable multiparametric evaluation of compound effects. Microtissues were treated with hepatotoxic and non-toxic compounds, stained with fluorescent markers, and imaged using automated confocal high-content imaging. Image analysis incorporated machine learning-based segmentation and classification to extract morphological and intensity-based features and quantify phenotypic responses. This approach enabled clear differentiation of toxic versus non-toxic compounds and supported concentration-dependent analysis. The results demonstrate that integrating high-content imaging with AI-based analysis provides a scalable and robust platform for phenotypic profiling in 3D models, improving the evaluation of drug-induced toxicity.

Ozlem Yavas Grining (*InSphero*)

Non-destructive multiplexed imaging of 3D liver microtissues for multi-modal DILI assessment

Drug-induced liver injury (DILI) remains a leading cause of drug attrition and post-marketing withdrawals. New Approach Methodologies (NAMs) such as InSphero's 3D human liver microtissues, composed of primary liver parenchymal and non-parenchymal cells, provide a non-animal model that, when combined with viability endpoints, has been shown to flag DILI-inducing compounds with improved sensitivity and selectivity over 2D hepatocyte assays.
To further enhance the mechanistic information content of the current assay, we are developing a multiparametric framework in which a non-destructive high-content imaging panel covering mitochondrial dysfunction (TMRM), oxidative stress (CellROX) and bile salt export pump (BSEP) inhibition (Cholyl-Lys-Fluorescein) is paired, on the same microtissues, with either a downstream biochemical or a transcriptomic readout. The central challenge is integrating these readouts without compromising technical or biological performance. We now present several extensions of the workflow:

• Optimized 3-plex live-dye staining on sequential timepoints.
• Repeated live-cell imaging does not impair microtissue function: day-2-imaged tissues match non-imaged controls at day 7 (ATP and imaging readouts), enabling longitudinal imaging followed by secretion-based (LDH) or terminal lysate (viability) assays.
• Building on the previously reported TMRM + Organoid DRUG-Seq integration, ongoing work extends transcriptomic multiplexing to the full 3-plex panel as an alternative terminal readout.
Together, these results support a scalable workflow that pairs non-destructive, longitudinal imaging with either a biochemical or a transcriptomic terminal endpoint, increasing both the information content and practical efficiency of in vitro DILI assessment and moving multiplexed NAMs closer to routine preclinical use.

Natalia Karczewska (*Institute of Bioorganic Chemistry, Poznan*)

Cell Painting in High-Content Screening: Results, Challenges & Applications

Phenotypic image-based profiling approaches enable the generation of complex, information-rich datasets from microscopy images, which are highly valuable in drug discovery research. Within this framework, Cell Painting is a key High Content Screening technique that uses a multiplexed combination of fluorescent dyes to label major cellular structures, producing detailed morphological profiles at the single-cell level. After staining, cells are imaged using automated high-throughput fluorescence microscopy, and the resulting images are computationally processed to obtain quantitative descriptors of cellular morphology.

These downstream analyses typically include cell segmentation, feature extraction, and normalization across experimental batches. However, the approach presents several challenges, including the accurate segmentation of densely packed or morphologically irregular cells, variability in staining quality, and batch effects arising between plates or experimental runs. To mitigate these challenges, robust image analysis with quality control, statistical correction, and alternative staining strategies are applied.

Here, we present applications of the Cell Painting assay implemented in our laboratory, whose development and deployment were made possible through our participation in the EU-OPENSCREEN consortium and support from the POL-OPENSCREEN 2.0 project. Cell Painting approach supports applications such as compound screening, mechanism-of-action studies, and toxicity prediction, and can be integrated with complementary datasets (e.g., transcriptomics or proteomics) for a more comprehensive view of cellular responses.

Gantugs Atarsaikhan (*University of Helsinki*)

Self-supervised learning enables unbiased patient characterization from multiplexed microscopy image

Multiplexed immunofluorescence microscopy provides detailed insights into the spatial architecture of cancer tissue. Classical analysis approaches focus on single-cell data but can be limited by segmentation accuracy and the representational power of extracted features, potentially overlooking crucial spatial interrelationships among cells. We developed a hierarchical self-supervised deep learning approach that learns feature representations from multiplexed microscopy images without expert annotations. The method encodes tissue samples at both the local (cellular) level and the global (tissue architecture) level. We applied our method to lung, prostate, and renal cancer tissue microarray cohorts to investigate whether self-supervised learning can recognize clinically meaningful marker patterns from multiplexed microscopy images. We observed that the learned features identified prognostically distinct patient groups, which show significant differences in survival outcomes. These patient groups matched earlier findings obtained with classical single-cell analysis using expert annotations. Moreover, attention maps extracted from these models highlighted crucial tissue regions that correlate with specific marker combinations. Overall, the approach effectively profiles complex multiplexed microscopy images, offering potential for improved biomarker discovery and more informed cancer treatment decisions.

Jiří Reiniš (CeMM)

Dataset: morphological profiling of 100,000 compounds with vpCells pool of 7

Morphological profiling captures complex cellular responses to perturbations through high-dimensional image-based signatures. Large-scale, publicly available profiling datasets are valuable resources for drug discovery, mechanism-of-action annotation, and development of computational methods including deep learning models.
Here, we publicly release a morphological profiling dataset generated with visual proteomics cells (vpCells), a platform based on multicolor endogenously tagged reporter cell lines and live-cell confocal microscopy. A pool of 7 clones (HAP1 cell line) expressing 14 tagged proteins and 8 fluorescent localization subcellular markers was screened against >100,000 chemical compounds, including structural diversity libraries, FDA-approved drugs, kinase inhibitors, epigenetic modifiers, and natural products. The screen yielded 615,547 images and over 83 million segmented single cells across 5 fluorescence channels, captured at 40x magnification 6 hours post-treatment. With more than 100,000 chemical perturbations, this dataset is comparable in scale to the JUMP-Cell Painting consortium and represents one of the largest publicly available morphological profiling resources. Importantly, it differs from Cell Painting datasets in its information content: rather than fluorescent dyes, it employs endogenously tagged proteins, providing readouts on specific protein localization alongside global morphological features.
The full dataset, including raw and processed images, CellProfiler-extracted features, and compound metadata, is freely available for download (https://github.com/Kubicek-Lab-at-CeMM/vpCells_100k_compounds_screen_dataset_download). We anticipate this resource will be valuable for benchmarking and training computational models for phenotypic drug discovery, compound mechanism-of-action prediction, and image-based representation learning.

Vanille Lejal (*University of Luxembourg*)

Integrative Genome-Scale Metabolic Modeling for Toxicological Applications: A rFASTCORMICS-Based Fra

Genome-Scale Metabolic Models (GEMs) are mathematical representations of the metabolism of an organism, an organ, or a cell linking genes, proteins, metabolites, and biochemical reactions within a single model, enabling the analysis of pathway activities, metabolite exchange, and essential metabolic genes. They are notably used to give mechanistic insights and explore cellular behavior under genetic or environmental perturbations.
To improve model predictivity, efficient large-scale data integration methods enable the reconstruction of context-specific molecular networks relevant to diseases, or individuals by integrating multi-omics, in vivo, or pharmacokinetic data into metabolic models. Among these approaches, (r)FASTCORMICS and its associated analysis pipeline, developed in our group, provide a framework for context-specific modeling through transcriptomic integration.
The pipeline integrates well-established methods such as Flux Balance Analysis, gene deletion, and sampling, while also performing an exploratory analysis of the high-dimensional output generated. By calculating differential reaction activity, metabolite turnover, and reaction presence in a given context, it guides users toward the metabolic pathways and individual reactions of interest.
Overall, these models provide sufficient biological complexity to describe metabolism across conditions. By integrating transcriptomic from primary hepatocytes from publicly available resources such as TG-GATEs within our reconstruction algorithms, we aim to identify key differences in the modes of action of chemicals, as well as in toxicity mechanisms, between animals and humans. In addition, within a quantitative in vitro to in vivo extrapolation (qIVIVE) perspective, determinant factors such as exposure duration and dose can be incorporated into the framework to capture their impact on metabolic responses.

Sandra Schulz (*Mannheim University of Applied Sciences*)

High-Content MALDI MSI for Single-Cell and 3D Spatial Metabolomics

MALDI mass spectrometry imaging (MALDI-MSI) enables label-free spatial metabolomics, but extracting biologically meaningful information from high-dimensional datasets across biological scales requires dedicated computational strategies. Here, we present a MALDI-MSI-based high-content analysis platform illustrated by two application scenarios: single-cell analysis [1] and volumetric 3D cell culture imaging [2].
For single-cell applications, a mass-guided workflow (PRISM-MS) enables high-throughput profiling of thousands of individual cells while preserving low-mass metabolites (<200 Da). A two-stage acquisition (PreScan/DeepScan) is combined with computational pipelines for cell detection, segmentation, and spectral extraction. Downstream analysis integrates normalization, MS/MS-supported metabolite annotation, and unsupervised methods such as Monte Carlo reference-based consensus clustering to identify metabolically distinct subpopulations and activation-dependent marker signatures obscured in bulk measurements.
For 3D cell culture models, the platform supports volumetric MALDI-MSI of spheroids and organoids using an integrated framework for cross-section registration and 3D reconstruction. Data processing in the in-house software M^{2}aia[3,4] enables efficient handling of large datasets, spatial segmentation, and multivariate analysis. Voxel-based approaches resolve molecular gradients and heterogeneous regions across intact 3D structures. The workflow is complemented by advanced visualization, including mixed reality, and demonstrated in a translational setting using patient-derived colon cancer organoids.
Together, these use cases highlight how a shared MALDI-MSI foundation, combined with tailored bioinformatics workflows, enables scalable high-content spatial metabolomics from single cells to complex 3D systems.

[1]: Cairns et al. (2024), Adv. Science, doi:10.1002/advs.202410506
[2]: Iakab et al. (2025) Adv. Science, doi:10.1002/advs.202516098
[3]: Cordes et al. (2021) GigaScience, doi:10.1093/gigascience/giab049
[4]: Cordes et al. (2024) bioinformatics, doi: 10.1093/bioinformatics/btae133

Patricia Ye (*University of Edinburgh*)

Capturing Morphological Variation in Esophageal Cancer Models Using Variational Autoencoders

Cell painting is a high-throughput image-based cellular profiling assay that is able to generate rich morphological data that spans multiple cell lines and treatment conditions using multiplexed fluorescent dyes. This method has been used to expedite the drug-discovery pipeline through large-scale drug screening experiments. Following image quantification using CellProfiler software, these high-dimensional datasets still pose significant challenges for analysis. Conventional dimensionality reduction techniques like Principal Component Analysis (PCA) often fail to capture the complex, nonlinear relationships inherent in cell morphology data. To overcome this limitation, we implemented a variational autoencoder (VAE), a generative deep learning model, to learn informative low-dimensional representations of cellular morphologies. The VAE was trained on batch-corrected, image-level morphological features derived from seven esophageal cell lines—five adenocarcinoma and two tissue-matched controls—treated with small molecule drug compounds from Prestwick and LOPAC drug libraries.
The learned latent space was then evaluated by encoding low-dimensional representations of aggregated well-level morphological features of cells. Our results show that the VAE's latent space effectively captures both cell line-specific morphologies and drug-induced variation. The low dimensional representations of cellular morphologies are then used to identify compounds that induce distinct phenotypes from controls as treatment candidates. Additional in vitro screening experiments are then performed to validate the efficacy of the identified candidates and elucidate their mechanisms of action. This approach offers a robust method for summarizing complex phenotypes of multiple drug-treated cell lines with a practical downstream use case to advance drug discovery efforts.

Antoine Martin-Tissier (*CytooScreen*)

High-content mitochondrial phenotyping in human myotubes using deep learning embeddings & MyoScreen™

Mitochondrial network architecture in skeletal muscle is a sensitive readout of metabolic health, with a pivotal role in primary mitochondrial myopathies, type 2 diabetes, and age-related decline. Yet quantifying these networks in mature human myotubes remains challenging: their dense, anisotropic morphology exceeds the capacity of standard segmentation tools, and biologically distinct perturbations can converge on morphologically similar phenotypes. Fragmentation driven by OPA1 loss and fragmentation driven by bioenergetic collapse appear nearly identical on outer-membrane stains despite reflecting distinct underlying biology.
MitoLatentProfiler combines CYTOO's MyoScreen™ micropatterned human myotubes with a topology-preserving U-Net (Dice = 0.82, clDice = 0.86) and a Classifier U-Net that jointly optimizes segmentation and phenotype classification. The encoder structures the latent space along two orthogonal axes: a morphological axis shared across markers (TOMM20, MitoTracker), and a marker-specific axis accessible only through MitoTracker that reflects the imaging signature of bioenergetic insult. A marker-adaptive hierarchical classifier reaches macro F1 = 0.93 across held-out donors, markers, and plates, outperforming classical morphological descriptors.
Validated against siRNA dose-responses (OPA1, DRP1) and chemical perturbations (oligomycin/antimycin, CCCP), Fragmentation, Hypertubulation, and Damaged phenotype-scores yield Z' factors of 0.54, 0.38, and 0.87 to 0.96 respectively, meeting NCATS thresholds for screening. Generalization to unseen time-courses holds without retraining, and the encoder serves as a fixed feature extractor, so new phenotypes can be added by retraining only the downstream classifier.

Eleni Charla (*AstraZeneca*)

From Pixels to Prediction: Early Detection of Hepatic Liabilities in Novel Modalities via High-Conte

The Mechanistic Biology and Profiling unit delivers early safety characterization across all therapy areas, addressing hepatotoxicity, a critical challenge in drug development. To mitigate the risk, our portfolio encompasses hepatic liability assessment and modality-specific toxicology evaluations, including emerging modalities such as PROTACs. Our cascade progresses from simple to complex assays, ensuring high-quality and predictive data generation. A key component of our approach is the LiverTox imaging assay, which leverages automation, high-content imaging combined with AI-driven image analytics to mechanistically assess phospholipidosis, a marker of lipid dysregulation and potential hepatotoxicity in HepG2 liver-derived cells. This platform exemplifies the integration of advanced imaging technologies with AI analytics to enable: mechanistic understanding of lipid metabolism disruption and organelle dysfunction, early hazard identification in discovery toxicology workflows and quantitative, high-throughput screening that supports data-driven decision-making.
By combining mechanistic insights with AI-powered analytics, our strategy accelerates compound prioritization and supports safer therapeutic development and drug induced liver injury (DILI) risk across diverse modalities.

Adrian Tschan (*Roche*)

Benchmarking Phenotypic Profiling Assay Conditions for Context-Specific Biological Discovery

High-content imaging is a cornerstone of target deconvolution and predictive toxicology, yet optimal assay parameters remain highly contextual. In this study, we systematically benchmark Cell Painting against a Multi-Organelle staining protocol across two distinct cellular models: U2OS and primary-like Macrophages. Cells were treated with a reference set of mechanistically annotated small molecules in a 7-point dose-response and imaged at early (24h) and late (72h) timepoints. We compare the capacity of each combination of cell type, staining protocol, and timepoint to resolve specific mechanisms of action (MoA) and identify compound-induced toxicity. By evaluating both classical analytical pipelines (CellProfiler) and emerging AI-based feature extraction methodologies, we delineate the phenotypic space captured by each approach. Our findings provide a data-driven framework for selecting optimal screening conditions, maximizing biological relevance, and improving early-stage pipeline decision-making.

Monika Pyc (*Institute of Bioorganic Chemistry, Poznan*)

POL-OPENSCREEN: Infrastructure Enabling Advanced High-Throughput Screening and High-Content Microscopy

High-content imaging and high-throughput screening (HTS) methodologies represent powerful platforms for studying biological systems and functional characterization of biochemical mechanism. The Laboratory of Molecular Assays and Imaging at Institute of Bioorganic Chemistry, Polish Academy of Sciences, implements advanced imaging-based workflows integrating automated microscopy, high-content acquisition and quantitative image analysis for phenotypic profiling.
The laboratory infrastructure supports a wide range of high-throughput imaging assays, enabling both hypothesis-driven and unbiased screening approaches. Through participation in the POL-OPENSCREEN and EU-OPENSCREEN infrastructures, access is provided to diverse chemical libraries, significantly enhancing the identification of bioactive compounds and molecular probes.
A key focus is the development, optimization, and adaptation of molecular imaging assays, including evaluation of fluorescent probes and implementation of commercial and in-house staining and imaging kits tailored for high-content applications. Experimental workflows include fluorescence in situ hybridization (FISH) for nucleic acid detection and spatial localization, as well as Cell Painting assays for multiparametric phenotypic profiling of cellular responses to chemical perturbations.
Integration of automated microscopy with computational image analysis enables scalable and reproducible screening of chemical libraries, supporting identification of biologically active compounds and functional annotation of cellular phenotypes.
Overall, the Laboratory provides a versatile platform bridging chemical biology, fluorescence imaging, and phenotypic analysis, supporting internal research and collaborative projects within the POL-OPENSCREEN and EU-OPENSCREEN network.

Simone Schicktanz (*Leica Microsystems*)

Live Organoid Screening with SCAPE: Scaling Throughput for Light-Sheet Imaging

Single-objective light-sheet microscopy (SCAPE) enables fast and gentle volumetric imaging of live samples in standard multiwell plates, overcoming traditional throughput limitations. This allows long-term, high-resolution imaging of organoids with minimal photodamage. We used SCAPE to image human organoids over several days for quantitative 3D morphological analysis, comparing patient-derived neuroendocrine tumor organoids (PDTOs) and healthy fetal airway organoids (FAOs) enriched in pulmonary neuroendocrine cells (PNECs). Healthy organoids formed organized lumen-containing epithelia, while PDTOs exhibited compact, mechanically rigid architectures with altered actin organization and epithelial structure. These results establish SCAPE microscopy as a scalable platform for longitudinal organoid imaging, enabling quantitative links between cellular behavior, tissue architecture, and malignancy, with applications in disease modeling and therapeutic screening.

Caroline Dahlstrom (*Uppsala University*)

AI pipeline for isPLA detection at the single cell level in cytology material

Oral cancer is increasing in frequency world-wide, creating a need for improved diagnostics. Cytology offers an inexpensive, minimally invasive alternative to a regular tissue biopsy. We aim to develop a machine learning based artificial intelligence (AI) pipeline to identify potentially malignant cells in cytology samples. Cells obtained from the oral cavity by brush biopsy were deposited on glass slides for protein analysis by in situ proximity ligation assay (isPLA), visualized by fluorescence microscopy. An image analysis pipeline was developed in Python to segment individual cells and detect antibody signals using Cellpose and Big-FISH software, respectively. The distances between reaction products from protein detection, nuclei, and cell borders were computed to quantify and characterize protein localization patterns. The image analysis pipeline successfully segmented individual cells and quantified the fluorescence signals. Based on the spatial distribution of the fluorescence signals, we observe that the interactions are localized mainly within the cytoplasm, predominantly near the cell periphery. Molecular profiling of cytology samples could potentially replace the conventional invasive histopathology approach. Our image analysis pipeline has been adapted to handle samples where keratinocytes are not homogeneously distributed, and we are now exploring protein patterns that can distinguish malignant and normal cells.

Jochen Sieber (*Leica Microsystems*)

Advancing Spatial Biology with SpectraPlex: High-Multiplex Imaging of Tumor and Immune Landscapes

SpectraPlex introduces a comprehensive workflow for high-multiplex 3D imaging. The workflow integrates panel design, acquisition, and advanced spectral unmixing algorithms to enable simultaneous identification of 15+
markers within a meaningful 3D context.
The novel approach to acquire reference data, which generates the complete spectral reference sets from a few samples, eliminates the need for single stains that demand significant
preparation time and sample quantities, while maintaining high data quality. We first validated SpectraPlex on thick sections from pancreatic tumor mouse-models, capturing immune cell subsets and structural components in a singleshot 3D acquisition, providing detailed insight into the tumor microenvironment.
We further applied this workflow to tumor-draining lymph nodes (LNs), which play a critical role in immune regulation.
Lymphatic endothelial cells (LECs) within LNs govern lymph flow, antigen presentation, and immune cell trafficking, yet
their spatial organization and molecular interactions with immune subsets remain poorly understood. Using syngeneic
melanoma models, we generated a 10-marker panel on LN cryosections representing naïve and tumor-draining conditions, run them with SpectraPlex and performed subsequent image analysis to map immune cell subsets, including myeloid populations such as macrophages, monocytes and granulocytes, in relation to LEC networks.
Our preliminary findings suggest the remodeling of LEC architecture and the emergence of immunosuppressive niches in checkpoint-resistant tumors.
We highlight the adaptability of SpectraPlex for interrogating both tumor and lymph node microenvironments. By combining robust algorithms with flexible panel design, SpectraPlex sets a new standard for high-plex imaging and provides a scalable platform for spatial biology and immunology research.

Dave Bunten (*University of Colorado Anschutz*)

OME-Arrow: Unifying Images, Metadata, and Morphology for High-Content Imaging

Modern bioimaging workflows integrate images, metadata, and derived measurements across many tools, but these components are often stored in incompatible formats and disconnected systems. This fragmentation makes it difficult to join data, reproduce analyses, and scale from small experiments to large, multi-sample studies.

OME-Arrow is a data model and toolkit for working with bioimaging data in modern analytical environments. It unifies images, metadata, and derived measurements into a single structure organized as linked tables, enabling direct querying, filtering, and analysis using familiar operations in Python, R, and SQL. By making relationships between data explicit and queryable, OME-Arrow eliminates the need to manually reconstruct connections across files and tools.

Built on Open Microscopy Environment (OME) conventions and Apache Arrow, OME-Arrow supports ingestion from TIFF, OME-Zarr, and NumPy, and export to Arrow-native formats (e.g., Parquet) as well as OME-TIFF and OME-Zarr. Data can be analyzed locally or scaled to warehouse-style systems with support for versioning and schema evolution, without restructuring.

Within the Alex's Lemonade Stand Foundation (ALSF) Pediatric Cancer Cell Morphology Atlas (PCCMA), OME-Arrow enables end-to-end image-based profiling workflows in which raw images, single-cell features, and experimental metadata are analyzed together without intermediate data reshaping. This supports integrated analysis of cell line screening experiments, linking morphological profiles to drug perturbations and experimental conditions, improving reproducibility, and enabling consistent, large-scale exploration of phenotype–treatment relationships in pediatric cancer datasets.

Dr James Hutt (Revvity)

AI Brightfield Segmentation and Advanced Organoid Detection for Physiologically Relevant Screening

High content imaging faces critical bottlenecks in analyzing complex biological models, particularly in brightfield applications and 3D organoid systems. We present AI solutions that significantly improves these analytical capabilities.
Our Phenologic.AI™ engine advances brightfield analysis through AI models achieving >95% detection accuracy for label-free nuclear and cytoplasm segmentation, reducing user-dependent parameter optimization and threshold-based method variability. Additionally, the Phenologic.AI module enables artifact-reduced digital phase contrast reconstruction providing alternative methods for robust cytoplasm detection while preserving fluorescent channels. Critically, our label-free approach reduces phototoxicity, enabling extended time-lapse studies previously that may have been compromised by fluorescent nuclear stains.
Complementing this advancement, our enhanced "Find Organoids" building block in Harmony™ software delivers up to 2-fold increase in organoid detection through advanced 2.5D segmentation. This module robustly handles brightfield organoid imaging challenges: overlapping objects in Maximum Intensity Projections as objects originate from different z-heights, variable morphologies (cyst-like, dark rim, mature), and complex 3D optical properties in extracellular matrix.
This enhanced detection capability significantly reduces false negatives in drug efficacy studies, helping prevent erroneous dismissal of therapeutic compounds due to incomplete organoid identification. This improvement is important for identifying subtle phenotypic changes and compounds with narrow therapeutic windows, where missing populations could lead to incorrect drug activity conclusions.
These integrated technologies help address growing demand for physiologically relevant screening models. Automated organoid analysis in brightfield conditions, with a 2-fold increase in detection compared to current methodologies supports phenotypic screens on 3D models that more closely recapitulate in vivo biology than traditional 2D cultures.

Bram Bosch (*UMC Utrecht*)

Unsupervised analysis of shape and texture for multi-scale phenotypic profiling in 2D microscopy

Microscopy is widely used for phenotypic analysis of cells. Typically, descriptive features such as size and intensity are used to determine phenotypic differences. However, the inherent heterogeneity of cells and the dominance of shape often mask subtle variations in cellular signal patterns, presenting a challenge for traditional and unsupervised analysis. We introduce an unsupervised explicit disentanglement approach to decouple shape features from texture and intensity at the single-object level in 2D images. By employing two sequential Variational Auto-Encoders on principal axis aligned objects, we explicitly separate binary shape from continuous intensity information into distinct, non-overlapping, and rotational invariant feature sets. Enabling the independent analysis of shape and complex intensity patterns regardless of shape. We validated this method across biological scales, from nuclei and single cells to 2D brightfield acquisitions of patient derived intestinal organoids, revealing insights previously hidden by morphological variance. Our method provides a robust and interpretable method for multi-scale 2D phenotypic profiling.

Suganya Sivagurunathan (*SciLifeLab*)

BioImage Informatics at SciLifeLab: Enabling life science discovery through advanced image analysis

The BioImage Informatics unit (BIIF) develops new computational technologies and provides access to expertise and state-of-the art software for processing and quantitative analysis of all kinds of microscopy image data, primarily for applications in the life sciences. BIIF is a SciLifelab unit, and part of the National Bioinformatics Infrastructure Sweden NBIS. We are active within the GloBIAS and EuroBioImaging networks. We offer - i) advice on best-practice and guidance on overall experimental design for research involving microscopy imaging and quantitative data analysis, ii) guidance on image analysis assay development, including image processing algorithm development and software engineering to address challenging project goal, iii) advice on best-practice and guidance on high throughput/large-scale image processing using computing clusters, including data transfer and storage during the activity of the project, iv) guidance on large-scale data analysis and visualization and dissemination of bioimage analysis knowledge in courses and workshops.

As a part of the image analysis unit, few of our current projects are in the lines of,
Integration of multimodal data from spatial proteomics, metabolomics (mass spectrometry imaging) and spatial transcriptomics (xenium, visium)
Development of AI-based computational pipeline for segmenting an ecotoxicological test species to understand the toxicological effects of the tested environmental samples or industrial chemicals
Implementation of LLM- accelerated automated text extraction from handwritten microscopy slides
High content screening of chromatin organization in live cells
Development of a scalable 3D screening platform using volumetric U-Nets for analysing human motor neuron disease (MND) models using high-content microscopy

Guillaume Ollitrault (*EMBL-EBI*)

Cell Painting Suggests Hepatotoxic Mechanisms of Botanical Extracts and Their Constituents

Botanical extracts are widely consumed as herbal remedies and plant-derived products, yet pose challenges for toxicological risk assessment because they are complex mixtures with poorly characterised composition and bioactivity. Hepatotoxicity associated with botanical use is well documented, but underlying mechanisms remain unclear.

In this study, Cell Painting morphological profiling was applied alongside two cytotoxicity assays assessing metabolic and membrane integrity to characterise the bioactivity of 13 botanical extracts (Aristolochia, Goldenseal, Asian ginseng, Ashwagandha, Blue cohosh, Comfrey, Ephedra, Green tea, Kava, Kratom, Milk thistle, Usnea, and Yohimbe) and 85 of their constituents in primary human hepatocytes across multiple concentrations. Cell Painting detected morphological perturbations at lower concentrations than cytotoxicity assays, demonstrating greater sensitivity. Phenotype altering concentration (PACs) identified Aristolochia and Goldenseal as the most potent botanicals (PAC < 1 µM), with activity driven by key constituents including aristolochic acid I, and berberine, coptisine, jatrorrhizine, and palmatine. Morphological clustering showed overlap between extracts and their constituents, confirming the ability of Cell Painting can meaningfully characterise complex mixtures.

To predict mechanisms of action, XGBoost models were trained on 1,085 chemicals against 90 ToxCast assays endpoints. Applied to the botanical dataset, these models predicted cytotoxicity across multiple cell types and flagged potential endocrine-disrupting activity for several botanicals and constituents.

Together, these findings demonstrate that Cell Painting combined with machine learning provides a robust framework to characterise hepatotoxicity and mechanisms of botanical extracts and their constituents.

Christopher Schmied (*EU-OPENSCREEN*)

Large-scale Cell Painting dataset enables prediction of chemical compound properties

Morphological profiling with the Cell Painting assay has emerged as a promising method in drug discovery. The assay captures morphological changes across various cellular compartments, enabling the rapid prediction of compound bioactivity. We present a comprehensive morphological profiling resource generated from more than 100,000 compounds of the EU-OPENSCREEN collection. The data were generated across four imaging sites in Europe using high-throughput confocal microscopes and both the HepG2 and U2OS cell lines. We employed an extensive assay optimization process to ensure high data quality across the different sites. An analysis of the extracted profiles validates the robustness of the generated data. We used this resource to compare the morphological features of the different cell lines. By correlating the profiles with overall activity, cellular toxicity, several specific mechanisms of action (MOAs), and protein targets, we demonstrate the dataset‘s potential for facilitating a more extensive exploration of biological mechanisms.

Patrick Steigemann (*Nuvisan*)

Identification of NUV-244 as a Small Molecule PNPLA3 I148M Degrader

The PNPLA3 I148M variant is a key genetic determinant of metabolic dysfunction-associated steatotic liver disease (MASLD) and related conditions, contributing to lipid metabolism dysregulation and disease progression. To identify small molecules that modulate PNPLA3 I148M, we conducted a high-content screen of over 820,000 compounds and identified NUV-244, a potent degrader of PNPLA3 I148M in liver-derived cells. NUV-244 reduces PNPLA3 I148M levels on lipid droplets via the ubiquitin-proteasome system, involving the E3 ligase BFAR, without affecting PNPLA2. It restores lipid droplet morphology and improves cellular fitness in PNPLA3 I148M-expressing cells. These findings provide a tool to investigate PNPLA3 I148M function and offer a potential strategy for developing targeted therapies for MASLD and related diseases. By enabling selective degradation of PNPLA3 I148M, this approach expands therapeutic possibilities beyond genetic manipulation, addressing a critical need in metabolic liver disease research.

Saber Saharkhiz (*University of Ottawa*)

VNC-Dist 2.0: Automated Sparse VNC Nuclei Positioning in C. elegans

Introduction: The C. elegans ventral nerve cord (VNC) is a tractable model for investigating neuronal positioning mechanisms, yet high-throughput analysis is bottlenecked by manual localization of neuron nuclei (6 DDs, 7 DBs, and 9 DAs). Our previous tool, VNC-Dist, semi-automated this process but required manual initialization. Transitioning to a fully automated pipeline (VNC-Dist 2.0) presents a unique challenge: VNC nuclei appear as sparse punctate objects against noisy backgrounds, with high autofluorescence (AF) in the green channel, creating severe class imbalance that causes standard segmentation methods to fail.

Methods: We benchmarked state-of-the-art instance segmentation models—Cellpose and StarDist—on L1-stage VNC micrographs. To handle class imbalance, we fine-tuned the Cellpose "nuclei" base model on a custom dataset using Focal Loss and weighted BCE applied to the cell probability head. StarDist was trained from scratch with analogous loss optimizations.

Results: Custom loss functions produced modest improvements for DD and DB nuclei detection. Fine-tuned Cellpose achieved ~45% mAP and ~75% recall. StarDist trained from scratch proved markedly superior, achieving ~70% average F1 and ~97% recall, suggesting architectural design is critical for sparse punctate nuclei—star-convex polygon representations significantly outperformed topological flow fields. DA nuclei detection remains limited by green-channel AF; we are integrating an AF subtraction preprocessing step (SAIBR) to enable accurate 2D segmentation for distinct nuclei and 3D segmentation for overlapping cases.

Conclusion: VNC-Dist 2.0 integrates these optimized models to eliminate manual annotation, presenting a robust, fully automated pipeline that accelerates high-throughput neuronal phenotyping.

Adriana Borowa (*Ardigen*)

Bridging the Phenotype-Proteome Gap: A Multi-Modal AI Framework for analysis of Cell Painting images

Cell Painting assay captures a vast range of morphological information. However, translating these visual phenotypes into biological insight remains a challenge. This study investigates the capacity of AI architectures to reconstruct proteomic profiles directly from morphological features.

We developed a multi-modal AI framework for proteomic profile prediction by integrating Cell Painting images with corresponding mass spectrometry data from cells treated with ~2000 reference compounds. We compared CellProfiler features against various Deep Learning embeddings: Masked Autoencoder (MAE), self-distillation with no labels (DINO), and CLOOME. We focused on MAE with a ViT-8/224 backbone and optimized the model for microscopic images through high masking ratios and Fourier domain reconstruction loss. Using a Multilayer Perceptron (MLP) and nested cross-validation, we evaluated the models on two primary tasks: the classification of protein up/down regulation and the regression of normalized protein abundance.

Our findings demonstrate that classifying protein expression regulation is more robust than direct abundance regression. A substantial fraction of investigated proteins was predicted with high accuracy, with performance scaling in response to compound-induced perturbations. In a focused analysis of chemical treatments, the system successfully identified a large proportion of regulated proteins, showing strong dose-dependency for top-performing markers.

Results suggest a latent but measurable correspondence between cellular morphology and proteomic states. While challenges remain in achieving high-resolution reconstruction for all protein classes, we show that phenotypic profiling can serve as a proxy for capturing broader biological shifts, offering a potential bridge between morphological changes and proteomics cell state to support drug discovery processes.

Télio Cropsal (*Chalmers University of Technology*)

Compressing Biology: Evaluating the Stable Diffusion VAE for Phenotypic Drug Discovery

High-throughput phenotypic screens generate vast microscopy image datasets that push the limits of generative models due to their large dimensionality. Despite the growing popularity of general-purpose models trained on natural images for microscopy data analysis, their suitability in this domain has not been quantitatively demonstrated. We present the first systematic evaluation of Stable Diffusion's variational autoencoder (SD-VAE) for reconstructing Cell Painting images, assessing performance across a large dataset with diverse molecular perturbations and cell types. We find that SD-VAE reconstructions preserve phenotypic signals with minimal loss, supporting its use in microscopy workflows. To benchmark reconstruction quality, we compare pixel-level, embedding-based, latent-space, and retrieval-based metrics for a biologically informed evaluation. We show that general-purpose feature extractors like InceptionV3 match or surpass publicly available bespoke models in retrieval tasks, simplifying future pipelines. Our findings offer practical guidelines for evaluating generative models on microscopy data and support the use of off-the-shelf models in phenotypic drug discovery.

Brian Feng *(Calico Labs)*

A better way to MOA: Directly comparing morphological profiles and bioactivity representations

Morphological profiling is commonly used to predict the mechanisms of action (MOAs) of chemical perturbations. However, the colloquial vocabulary used to describe MOAs is often not derived from a structured ontology, and is cumbersome when describing multiple simultaneous bioactivities (polypharmacology) or dose-dependent effects. Recently, multiple groups have derived rich, multidimensional descriptions of small molecule bioactivity by capturing features of the 2D chemical structures of molecules as well as public bioactivity data regarding the known biochemical interactions of each molecule. These descriptions can be represented as vectors in a high dimensional space, just as the content of cellular imaging data can be collected as morphological profiles. Through direct comparison of these high dimensional spaces, we can quantitatively resolve nuanced phenotypes that may be unique to polypharmacological interactions or dose-dependent effects. Furthermore, a systemic approach to making these comparisons can serve as an objective benchmark for evaluating the performance of chemical or imaging representation models.

Martin Theiss *(Aracelli bioscineces)*

Live single cell phenotyping at scale: time-resolved high throughput high content imaging interrogat

Live cell imaging assays provide a dynamic view of cellular state, growth, and phenotype, but conventional high content imaging (HCI) is often too slow to support multiparametric live-cell screening at scale. Here, we overcome this limitation, demonstrating a live cell HCI toolkit enabled by the Araceli Endeavor®: a high throughput assay with subcellular, single cell phenotyping over time. Using human endothelial cells (U2OS) treated with the G2/M phase-arresting compounds Nocodazole and RO3306, we imaged > 500,000 cells/timepoint in approximately three minutes across five channels at 0.27 µm/pixel digital resolution. Over 48 hours we captured changes in proliferation, cell death, nuclear DNA content, nuclear and cellular morphology, and mitochondrial phenotype in the same assay. Single-cell image analysis linked nuclei, cytosol, mitochondrial signal, and dead-cell staining, extracting more than 200 features per cell over 7 time points.

Quantification of total nuclear intensity enabled live cell assessment of ploidy, distinguishing 2N, 4N, and >4N populations, finding a dose-dependent shift in ploidy after 18 hours. Across treatments, later timepoints revealed significant accumulation of 4N and high-polyploid cells. By stratifying cells by ploidy, we further separated phenotypic changes associated with mitotic state from drug-specific effects. Many morphological differences were explained by cell cycle state, but ploidy-matched analysis revealed drug specific phenotypic fingerprints beyond cell cycle arrest. Correlating proliferation, death, ploidy, morphology, and mitochondrial dynamics at the single cell level over time, this assay provides a scalable framework for live cell screening and mechanistic phenotyping.

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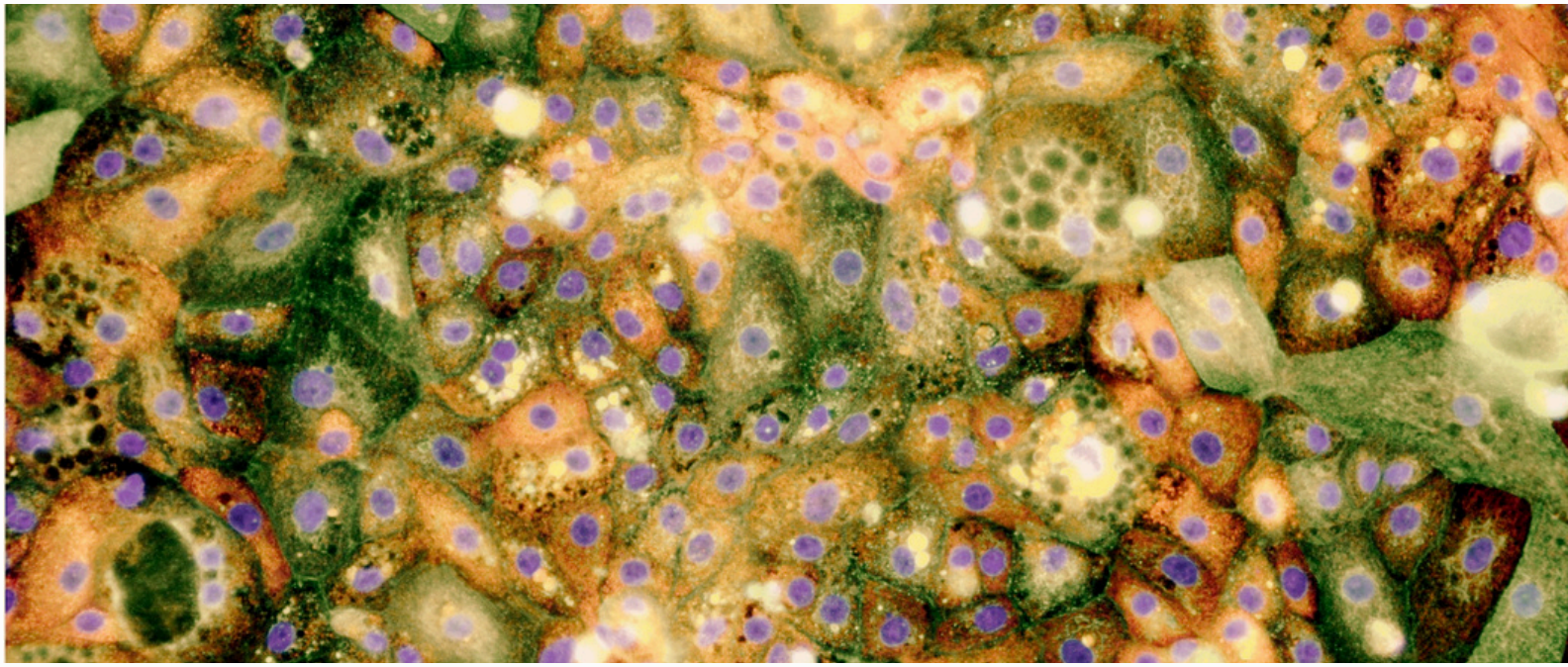

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