SIGNATURE
SInGle cells iN AuToimmUne inflammatoRy disEases

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NEWSLETTER

MSCA SIGNATURE

2026 marks the beginning of a new chapter for SIGNATURE. As an MSCA Doctoral Network dedicated to better understand chronic inflammatory and autoimmune diseases, our consortium continues to explore biological complexity at single cell resolution. In the year ahead, our researchers will advance innovative methodologies, strengthen interdisciplinary collaboration, and translate fundamental insights into meaningful scientific progress. This first SIGNATURE newsletter is designed to keep our community connected and informed across institutions, disciplines, and career stages.

In each edition, we will share research milestones, training and secondment opportunities, publications, conference participation, and consortium updates. We will also spotlight the people behind the science, introducing our doctoral candidates, supervisors, and partners, and highlighting the expertise that makes SIGNATURE a uniquely collaborative network.

A New Year of Learning, Discovery, and Impact

This issue highlights recent achievements, upcoming activities, and the teams driving our research forward. We hope it also serves as an invitation: to engage with one another, exchange ideas, and help shape the directions we pursue together in the months ahead.

Marta Alarcón-Riquelme
Scientific Director of GENyO Research Centre (FPS) and Scientific Coordinator of the 3TR and SIGNATURE projects

"SIGNATURE is a project with a vision where 10 students on their way towards attaining their doctoral degrees and comencing their scientific career encounter novel and innovative methods of single cell analysis in the context of autoimmune diseases such as systemic lupus erythematosus, rheumatoid arthritis or multiple sclerosis. The methods not only study cells from blood, but also from tissues and even bacteria, understanding that the interactions between the immune system with bacteria in the gut, may modulate the progression towards disease and the impact of treatments. Modifications across all cells in blood and tissues may lead to important discoveries of which these young scientists will be a part of."

Inside This Issue

From 3TR to SIGNATURE : Building the Next Generation of Translational Research

3TR is one of Europe's largest translational immunology research initiatives, created to improve understanding of why patients with immune-mediated, allergic and inflammatory diseases respond differently to treatment. The core mission is to identify the molecular pathways, biomarkers and disease mechanisms linked to response and non-response to therapy across seven diseases whic are **Multiple Sclerosis (MS), Systemic Lupus Erythematosus (SLE), Rheumatoid Arthritis (RA), Ulcerative Colitis (UC), Crohn's disease (CD), Asthma and Chronic Obstructive Pulmonary Disease (COPD).**

To do this, 3TR needs to combine clinical data, biosamples and advanced molecular profiling across large, longitudinal patient cohorts, supported by a structure of ten work packages covering data management, ethics, sample logistics, systems biology, cross-disease analysis and disease specific research clusters.

The strength of 3TR was again evident at the **6th 3TR Annual Project Meeting in Barcelona, held from 8 to 10 October 2025**, where more than **60 partners** from academia, industry, clinical sites and patient organisations gathered to review progress and prepare for the project's harvesting phase. The meeting highlighted the consortium's growing emphasis on cross-disease collaboration, translational impact and patient-centered research, while also reinforcing the importance of shared scientific language, integrated data interpretation and continued collaboration across sectors.

SIGNATURE builds directly on this foundation. According to its official research programme, SIGNATURE stems from the H2020 IMI2-funded 3TR project and uses the multidimensional molecular and clinical data generated in 3TR to go further in understanding autoimmune disease mechanisms. While 3TR established the broad cross-disease translational platform, SIGNATURE focuses this legacy through a doctoral network dedicated to systemic lupus erythematosus, rheumatoid arthritis and multiple sclerosis, using single-cell technologies and advanced bioinformatics to study the mechanisms of response and non-response to therapy. In this sense, SIGNATURE is both a continuation and an expansion of 3TR, it translates the consortium's scientific legacy into targeted research, innovation and training for the next generation of translational scientists.

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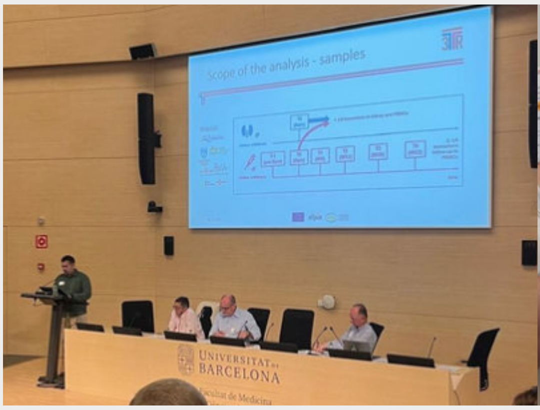
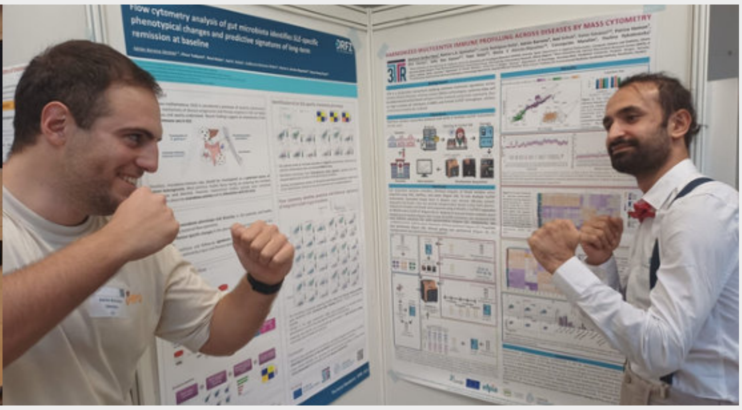
Together, the two meetings highlighted a common ambition: to connect molecular discovery, clinical relevance and interdisciplinary training in order to improve our understanding of disease mechanisms and treatment response.

Held on the same day as the 3TR Meeting, the SIGNATURE Annual Meeting naturally reflected the close connection between the two initiatives: 3TR provides the scientific platform, collaborative model and translational vision, while SIGNATURE advances that work through focused work packages, doctoral research and new analytical approaches.

Earlier this month, several SIGNATURE Doctoral Candidates took part in the annual 3TR meeting in Barcelona, where they had the opportunity not only to present their research, but also to connect more closely with the wider 3TR community.





The meeting offered an inspiring platform to exchange ideas, meet fellow researchers in person, and experience the collaborative spirit that lies at the heart of both 3TR and SIGNATURE. Among the highlights, Adrián Barreno (DC4) and Mehmet Serdar Koca (DC5) presented their work in the poster session, where their mass cytometry projects sparked lively discussion and even a friendly moment of "scientific face off" as they stood side by side with their posters. Meanwhile, Charisios Triantafyllou (DC1) delivered an oral presentation on his research using single cell RNA sequencing of kidney biopsies from lupus nephritis patients, showcasing the depth and translational relevance of the work being carried out within the network.

Beyond the scientific sessions, the meeting was also a valuable chance for the doctoral candidates to spend time together, strengthen their connections, and enjoy being part of an enthusiastic international research community.

The SIGNATURE research programme is organised into three complementary work packages. Work Package 1 focuses on the single-cell molecular characterisation of autoimmune disease tissues, generating high-resolution insights into affected organs and disease-specific cellular mechanisms. Work Package 2 addresses the identification of minimally invasive biomarkers using body fluids, following a liquid-biopsy strategy to develop clinically useful markers of tissue damage, treatment response, flares and relapse.

Work Package 3 centres on systems analysis and data modelling, integrating tissue, clinical and multiomic data to identify trajectories, clusters, shared mechanisms, biomarkers and potential therapeutic targets. Together, these work packages reflect SIGNATURE's role as the next step after 3TR: moving from large- scale collaborative discovery to deeper mechanistic understanding, data integration and translational application.

Progress in Focus : Perspectives from Work Package Leaders

WP 1 - Single cell molecular characterization or autoimmune disease tissues

"WP1 focuses on the single-cell molecular characterization of autoimmune tissues, analysing kidney and synovial biopsies using scRNA-seq, imaging mass cytometry and histology. Recruitment of kidney biopsies has been slower than expected due to delays in DC contracts and biopsy availability, and the timeline has therefore been extended to December 2025. Despite these challenges, important progress is being made. DC1 (Charisios) has already processed and analysed 29 kidney biopsies using scRNA-seq, moving forward the search for lupus nephritis biomarkers. DC2 (Hindol) has established and validated a 35-marker panel for renal biopsy analysis. DC3 (Emanuele CNAG) is progressing well, applying STAMP across different sample types while advancing spatial transcriptomics using VisiumHD, enabling higher-resolution analysis and supporting the translation of these approaches to clinical samples.

The project is also strengthening collaboration across the network: Giorgio Buzzanca, Íñigo Clemente and Luca Leomazzi are currently visiting CNAG, and Emanuele Pitino will soon undertake a research stay in Ghent, further promoting knowledge exchange and training within the consortium."

WP2 - Identification of minimally-invasive biomarkers of tissue damage using body fluids

"DCs uncovered multimodal immune activation patterns across systemic autoimmune diseases. TLR-stimulated transcriptomics identified interferon, cytokine, and neutrophil modules that stratify patients beyond clinical phenotypes. CyTOF revealed functional heterogeneity and differential signaling across immune subsets, aligning with transcriptomic modules to define mechanistic endotypes. A mucosal-focused CyTOF workflow distinguished activation states in active versus quiescent SLE. Machine-learning models accurately classified renal involvement, using urinary extracellular-vesicle miRNAs emerging as early non-invasive biomarkers of lupus nephritis. Together, these findings define immune endotypes, highlight translational biomarkers, and establish high-resolution assays for improved patient stratification."

WP3 - System analysis and data modelling

"Work Package 3 has successfully integrated multiple distinct projects to advance precision medicine for autoimmune diseases like SLE and MS. We began by identifying the critical biological pathways, specifically interferon overactivation, that drive treatment resistance and non-responsiveness. These insights fueled the development of sophisticated agent-based models that simulate individual immune dynamics within a virtual laboratory setting. To bridge the gap between simulation and clinic, we designed a deep-learning companion test that predicts therapy efficacy by integrating multi-omic data. Simultaneously, a new spatial analysis pipeline was established to transform complex tissue architecture into quantitative network motifs, revealing how immune cells interact. We then consolidated these breakthroughs into standardized virtual patient libraries, providing a robust, FAIR-compliant resource for testing personalized strategies in silico. Finally, the engineering of a hybrid multi-scale simulation system now allows us to model both systemic trends and discrete tissue events in a single framework. Together, these separate yet synergistic efforts provide a complete digital toolkit for predicting patient outcomes and optimizing future therapeutic interventions."

Where Scientific Breakthroughs Begin

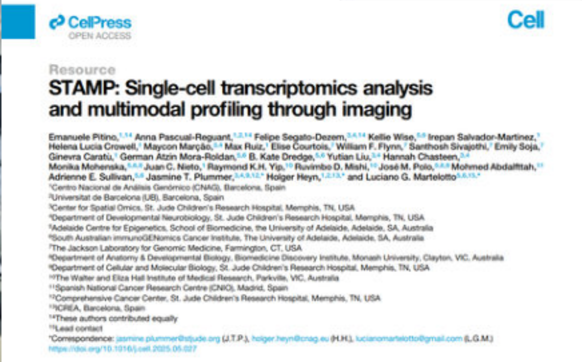
STAMP : Single-cell Transcriptomics Analysis and Multimodal Profiling through imaging

Understanding how individual cells behave is essential for studying health and disease. Over the past decade, single-cell RNA sequencing has transformed biomedical research by allowing scientists to measure gene expression at the level of individual cells. However, these technologies remain expensive, difficult to scale, and limited when very large numbers of cells are required – for example in population studies, drug screening, or clinical research. In our recent work we introduced STAMP (Pitino et al, Cell 2025), a new approach that enables large-scale single-cell profiling using imaging instead of sequencing. STAMP works by immobilizing cells from suspension onto glass slides and reading out RNA and protein molecules directly through high-resolution imaging platforms.

This strategy makes it possible to analyze hundreds of thousands to millions of individual cells in a single experiment, at a fraction of the cost of conventional sequencing-based methods. Importantly, STAMP preserves cellular structure and morphology, allowing molecular information to be linked to visual features of the cell. Using STAMP, we demonstrated accurate identification of immune cell populations in blood, reconstruction of cell state dynamics during stem cell differentiation, detection of extremely rare cell types such as circulating tumor cell mimics, and integration of RNA and protein measurements within the same cells. Across multiple platforms and experimental conditions, the method showed strong reproducibility and high sensitivity for biologically meaningful signals. The expected impact of STAMP is broad. By drastically reducing cost and increasing scalability, STAMP opens the door to large-cohort studies, high-throughput perturbation screens, and translational applications that were previously impractical. The approach is particularly well suited for collaborations between academia and industry, where scalability, flexibility, and cost efficiency are critical. Overall, STAMP represents a step toward making single-cell technologies more accessible, scalable, and applicable to real-world biomedical and clinical research.

Researchers are stamping cells to revolutionize health studies

The creation of the technique, called STAMP, has been co-led by the National Center for Genomic Analysis (CNAG) and has the potential to multiply and accelerate the collection of data obtained in cell biology laboratories.



Resource

STAMP: Single-cell transcriptomics analysis and multimodal profiling through imaging

Emanuele Pitino,[1,14] Anna Pascual-Reguant,[1,2,14] Felipe Segato-Dezem,[3,4,14] Kellie Wise,[5,6] Irepan Salvador-Martinez,[1] Helena Lucia Crowell,[1] Maycon Marção,[3,4] Max Ruiz,[1] Elise Courtois,[7] William F. Flynn,[7] Santhosh Sivajothi,[7] Emily Soja,[7] Ginevra Caratù,[1] German Atzin Mora-Roldan,[5,6] B. Kate Dredge,[5,6] Yutian Liu,[3,4] Hannah Chasteen,[3,4] Monika Mohenska,[5,6,8] Juan C. Nieto,[1] Raymond K.H. Yip,[10] Ruvimbo D. Mishi,[10] José M. Polo,[5,6,8] Mohmed Abdalfttah,[11] Adrienne E. Sullivan,[5,6] Jasmine T. Plummer,[3,4,9,12,*] Holger Heyn,[1,2,13,*] and Luciano G. Martelotto[5,6,15,*]

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[8] Department of Anatomy & Developmental Biology, Biomedicine Discovery Institute, Monash University, Clayton, VIC, Australia
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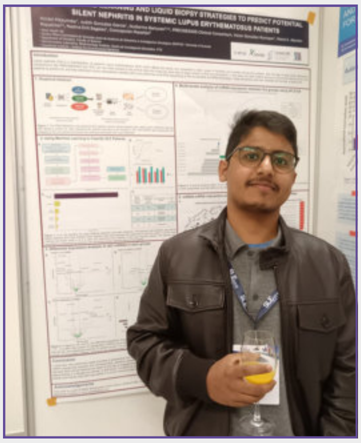
https://doi.org/10.1016/j.cell.2025.05.027

Science may be forged in the laboratory, but its first spark can appear anywhere in a passing idea, a conversation between sessions, or an unexpected exchange over coffee. Scientific congresses create exactly this kind of environment: places where the right people meet, ideas collide, and new collaborations begin.

One such moment took place at AGBT, one of the leading international meetings in biotechnology, where researchers gather each year to share the latest advances in genomics and molecular science. It was there that a conversation between Jasmine Plummer, Luciano Martelotto and Holger Heyn gave rise to a new idea that could significantly expand how scientists study individual cells.

Behind the Research : Meet the Doctoral Candidates

DC2 - Hindol Mazumdar

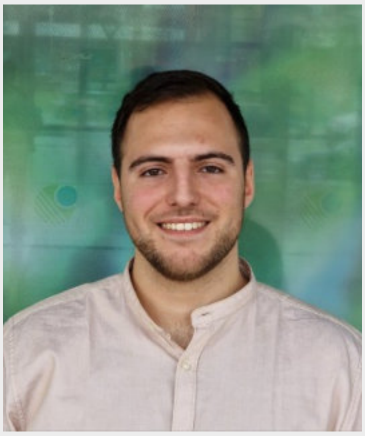


Hindol Mazumdar
DC2 - ATRYS HEALTH

I am Hindol Mazumdar, DC2 in the SIGNATURE Doctoral Network. I am originally from Kolkata, India, where I studied Pharmaceutical Technology and Pharmacology at Jadavpur University, and then worked as a research associate on biomarker discovery and early detection of atherosclerosis. Along the way, I've also been involved in projects around sustainability and ecology, and spent some time teaching as a guest faculty member in private institutes in India.

My PhD focuses on ***identifying biomarkers for Lupus Nephritis using machine learning, urinary miRNAs, and advanced imaging technologies***. I'm based at Atrys Health SA, with secondments at GENyO in Granada and Leiden University Medical Center. Outside the lab, I enjoy playing guitar and sitar, practicing mixed martial arts, traveling, exploring photography, trying new cuisines, reading widely, and speaking up for causes I care about, from social and climate justice to animal and human rights.

DC4 - Adrián Barreno



Adrián Barreno Sanchez
DC4 - DRFZ Berlin

My name is Adrián Barreno, and I am a DC4 researcher in the SIGNATURE Doctoral Network. I am from Madrid, Spain, where I studied Health Biology, and later completed my thesis at Umeå University in Sweden. After working in molecular biology and cancer research, I pursued an MSc in Computational Biology. Since then I wanted to combine wet-lab and bioinformatics to make a real impact on patients' lives, and SIGNATURE has given me that opportunity.

In my PhD, ***I study the complex interactions between the microbiota and the immune system in Systemic Lupus Erythematosus***. My goal is to identify new ways to stratify patients and uncover potential disease mechanisms. Outside the lab, I enjoy spending time outdoors hiking and cycling—whenever the German weather allows. I also have a strong interest in history and philosophy, as I enjoy learning from disciplines beyond my scientific background.

DC5 - M Serdar Koca

M. Sedar Koca
DC4 - GenYo (FPS)

I am M. Serdar Koca, and I am a DC5 researcher in the SIGNATURE Doctoral Network. I obtained my bachelor's degree in Molecular Biology and Genetics, during which I conducted RNA-seq analysis on Alzheimer's disease to better understand its pathogenesis. After completing my bachelor's degree, I realized that dry and wet lab research should not be separated. Therefore, I pursued a master's thesis focused on structure-based drug design targeting the circadian clock, where I also tested the designed molecules through in vitro assays.

Following my master's degree, I became interested in working with clinical data, as it offers the potential to impact patients' lives more directly and rapidly compared to purely laboratory-based studies. This led me to the opportunity to join the SIGNATURE Doctoral Network. During my PhD, I study systemic autoimmune diseases using a multi-omics approach. My goal is to identify new ways to ***stratify patients and to uncover potential disease mechanisms.*** Outside the lab, I enjoy playing computer games, watching Real Madrid matches, and spending time enjoying the beautiful weather in Granada.

The Journey Begins: SIGNATURE's First Training Event

Training is a central pillar of our doctoral network. Across the project, Doctoral Candidates participate in a rich programme of scientific workshops and transferable skills sessions that strengthen both their research capacity and their professional development. From experimental approaches to computational methods, these activities are designed to equip the next generation of researchers with the knowledge and tools needed to advance translational science.

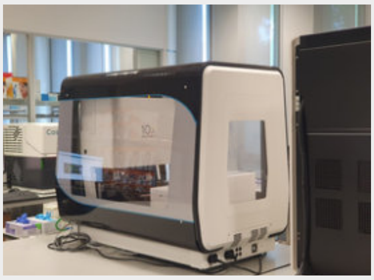
Follow our journey through single-cell genomics and spatial technologies.

SIGNATURE workshop on Single-cell Genomics and Spatial-Technologies
Single-Cell Genomics and Spatial Genomics Teams, CNAG, Barcelona
26-28th June 2024

Day 1: Visit at CNAG

We started our day with Holger Heyn and Ana Pascual who introduced us to the applications of single cell and spatial technologies technologies in research and business.
Later, Laura Jiménez-Gracia and Juan C. Nieto talked to us about the vital role of the experimental design when performing single cell experiments.

We continued with Ginevra Caratù who showed us the laboratory where samples are prepared for sequencing and Javier Gutiérrez Cuesta who gave us a tour in the sequencing lab were we state-of-the-art technology is used to produce high-qualitysequencing data.

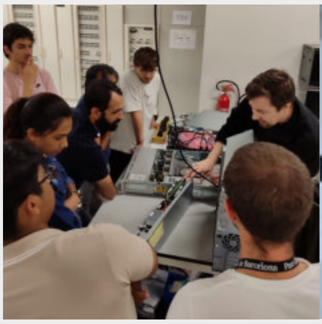


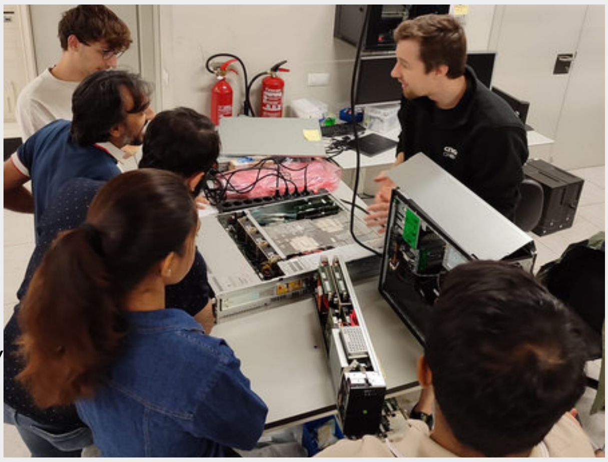
Day 2: Visit at ATRYS Health

We closed our day with a visit to Atrys where Nadina Erill Sagalés informed about the company and how they process and analyze biological material.

Day 3: CNAG

We started day 2 with a hands-on session with Laura Jiménez-Gracia and Paula Nieto García who guided through the analysis of single cell and spatial transcriptomics data.





Next we visited the Data Centre of CNAG, guided by William Blevins.

Finally Max Ruiz Gil & Patricia Lordén Rodríguez showed us around the laboratory where samples are prepared for Spatial Transcriptomics!

omniscope

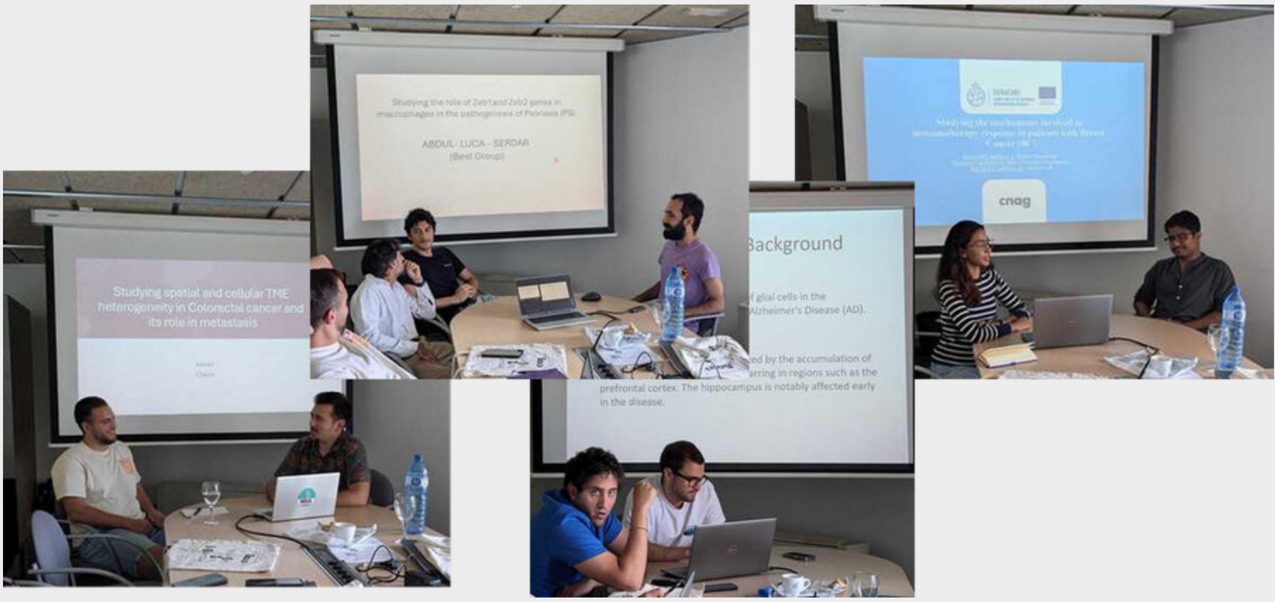
We had the oportunity to hear from omniscope's founding members Vijay Vaswani (CEO) and Lynnette Ang (Chief Growth Officer) who briefed us into what it takes to found a company in the field of diagnostics using state-of-the-art technology

Day 4: Spatial transcriptomics demonstration at CNAG

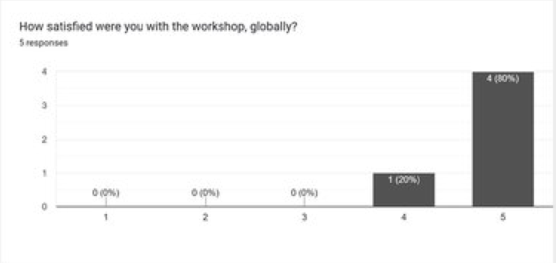
We started with Sam Morabito and Helena Crowell who demontrated the analysis of spatial data with actual datasets.

Hackthon at CNAG

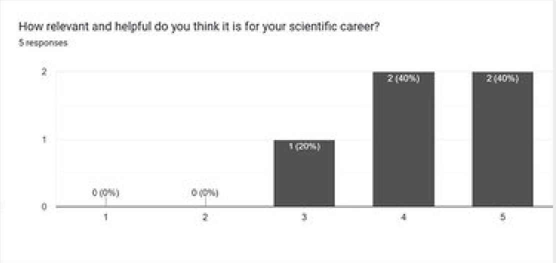
We finished with a fascinating HACKATHON where we had to propose an analysis pipeline for real scientific problems and every team gave a presentation in front of the rest DCs and Laura Jiménez-Gracia and Juan C. Nieto.



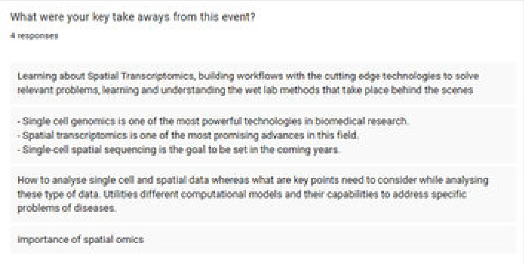
One Network, Many Stories : Reflections from Our DCs


How satisfied were you with the workshop, globally?

5 responses


How relevant and helpful do you think it is for your scientific career?

5 responses


What were your key take aways from this event?

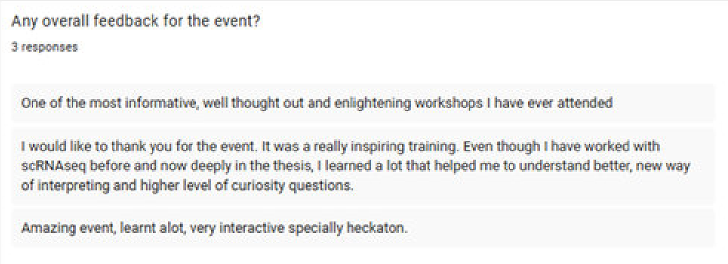
4 responses

Learning about Spatial Transcriptomics, building workflows with the cutting edge technologies to solve relevant problems, learning and understanding the wet lab methods that take place behind the scenes

- Single cell genomics is one of the most powerful technologies in biomedical research.
- Spatial transcriptomics is one of the most promising advances in this field.
- Single-cell spatial sequencing is the goal to be set in the coming years.

How to analyse single cell and spatial data whereas what are key points need to consider while analysing these type of data. Utilities different computational models and their capabilities to address specific problems of diseases.

importance of spatial omics


Any overall feedback for the event?

3 responses

One of the most informative, well thought out and enlightening workshops I have ever attended

I would like to thank you for the event. It was a really inspiring training. Even though I have worked with scRNAseq before and now deeply in the thesis, I learned a lot that helped me to understand better, new way of interpreting and higher level of curiosity questions.

Amazing event, learnt alot, very interactive specially heckaton.

Overall we found the workshop very informative and useful for our careers. We learned a lot about spatial transcriptomics and single cell analysis, as well as their applications in science, health and business. And ofcourse, we had a lot of fun!

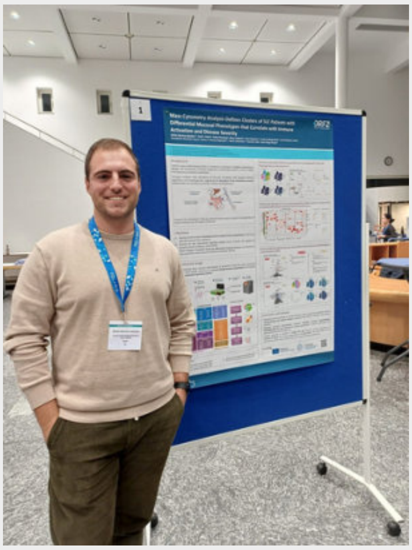
Coming from different countries, cultures and academic backgrounds, the DCs did not begin as a readymade group. Building connections took time, openness and effort. But through shared experiences, scientific exchange and everyday moments together, they have grown into a supportive and dynamic community, proof that diversity, while challenging at times, can become one of a network's greatest strengths.

SIGNATURE Shines in Heidelberg

This January 2026, SIGNATURE PhD students Akhiya ANILKUMAR REKHA, Mehmet Serdar Koca, and Adrián Barreno Sánchez took part in the **9th German Mass Cytometry User Forum**, hosted by the German Rheumatology Research Center, in Heidelberg.

Akhiya Anilkumar Rekha, delivered an oral presentation titled “AltraFlowSOM: A Semi-Supervised Framework for Imaging Mass Cytometry”

Mehmet Serdar Koca presented an oral talk titled “Center Harmonization for Multicenter CyTOF Immune Monitoring”



Adrián Barreno Sánchez presented a poster titled “Mass Cytometry Analysis Defines Clusters of SLE Patients with Differential Mucosal Phenotype that Correlate with Immune Activation and Disease Severity”

The GMCUF is more than just a conference, it’s a vibrant community where mass cytometry enthusiasts come together to inspire each other, spark new ideas, and push the boundaries of what mass cytometry can achieve. Whether you are an experienced user, a newcomer, or somewhere in between, this meeting offers a unique chance to explore the latest advances, troubleshoot challenges, and build lasting collaborations.
Book of abstracts and other information are available on the website: https://masscytometry.de/

It was an exceptional opportunity to connect with experts in the field, receive valuable feedback, and showcase the impactful research emerging from the SIGNATURE EU project.

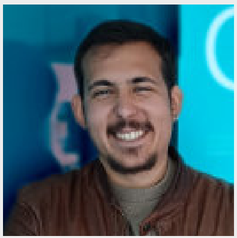
On the Scientific Stage : Candidate Participation and Recognition

Across conferences, workshops and specialist meetings, SIGNATURE doctoral candidates have been actively sharing their research, building visibility for their work, and earning recognition across a wide range of scientific fields.

DC1 | From posters to the podium

Presented work on scRNA-seq in kidney biopsies from SLE patients and on drug synergy across autoimmune conditions at international meetings in Barcelona, Toronto, Granada, Stockholm and Hinxton.

Highlight: Oral presentation at the 3TR Conference, Barcelona (2025)



Charisios Triantafyllou

Hindol Mazumdar

DC2 | Advancing liquid biopsy and extracellular vesicle Research

Shared research on extracellular vesicles, autoimmunity, liquid biopsy and digital PCR through conference contributions in Spain.

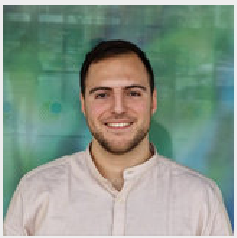
Highlights: Poster and flash talk at the 7th GEIVEX Symposium for EVs (Palma de Mallorca, 2024) and a poster presentation at GENyO.

DC3 | Bringing STAMP to an International audience

Contributed to scientific dissemination through an online Bruker webinar focused on STAMP and its translational potential.

Highlight: Oral presentation in the STAMP Webinar – Bruker

Emanuele Pitino



Adrián Barreno Sánchez

DC4 | Bridging the gap between gut health and immunity

Presented his research in gut microbiota-immune interaction in multiple national and international conferences.

Highlights: oral presentation and poster at the German Mass Cytometry User Forum (2024, 2025, 2026). Poster presentations and flash talks at the European Workshop for Rheumatology Research 2025 and The Human Microbiome EMBL Symposium 2025.

DC5 | Showcasing Mass Cytometry across centres

Presented research on CyTOF harmonisation and multicentre immune monitoring at leading specialist meetings in Germany and Spain.

Highlights: Oral presentation at the 8th German Mass Cytometry User Forum (2026) and poster presentation at the XII GENyO Scientific Meeting (2024).

Mehmet Serdar Koca

Luca Leomazzi

DC6 | Computational Science across disciplines

Built strong visibility across meetings focused on computational cytometry, benchmarking, FAIR principles, deep learning and reproducibility.

Highlights: Poster presentations at the 3TR Conference, CYTO2025, Modern Benchmarking (Ascona) and Flanders AI.

DC7 | Recognition on the International stage

Presented work on histopathology and molecular signatures at an international congress in London.

Highlight: Awarded the ESOT Full Bursary, including congress registration, travel support and membership benefits.

Giorgio Buzzanca

Íñigo Clemente Larramendi

DC8 | Exploring AI in Single-cell transcriptomics

Presented research on graph neural networks and self-supervised learning in single-cell transcriptomics at international meetings in France and the USA.

Highlights: Oral presentation at IBSAM (Brest, 2024) and poster presentation at FOCIS (2025).

DC9 | From Bioinformatics to autoimmunity

Contributed to meetings spanning autoimmunity, computational spatial transcriptomics and biomedical informatics.

Highlights: Poster at FASEB Autoimmunity (New York, 2025), quick talk in Lipari, and an oral lecture at the IEEE International Conference, Lisbon.

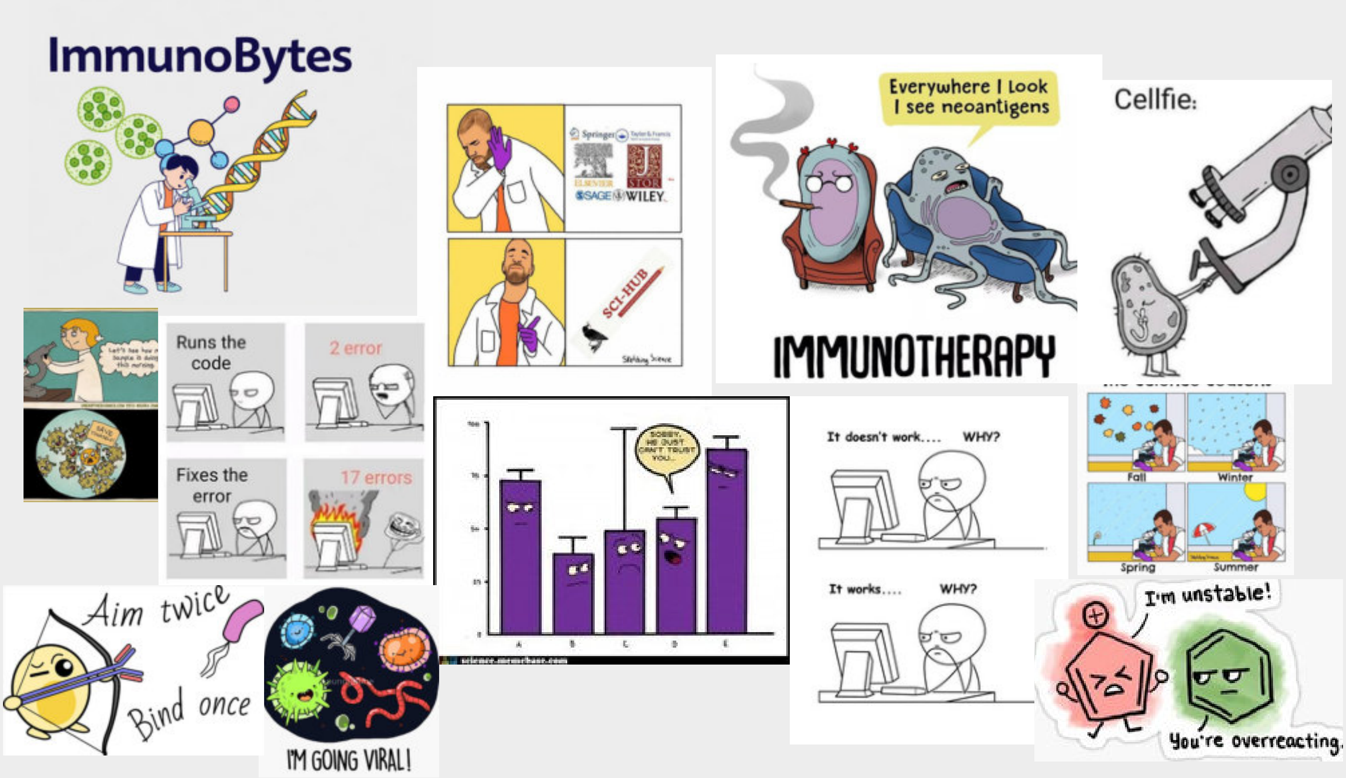
Abdul Wahab

Akhiya Anilkumar Rekha

DC10 | Where Biology Meets Bioinformatics

Presented work on A Semi-Supervised Framework for Scalable Phenotyping of imaging mass cytometry data and participated in specialised training in single-cell spatial transcriptomics.

Highlights: Oral presentations at the German Mass Cytometry User Forum 2026 and IBSAM (2026), plus participation in the AI/ML workshop in Lyon.



SIGNATURE Partner Institutions

At the heart of SIGNATURE is a strong and diverse partnership of institutions working together across disciplines, countries and sectors. Our main partners provide the scientific foundation and training framework of the programme, while our associated partners enrich the network through collaboration, expertise and broader engagement. Together, they form the international community that makes SIGNATURE possible.

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