the SUNDARI JOURNAL

SHINEDocs Unveiling New Discoveries and Research Innovation

#4 2026

Summary

EDITO: A Moment of Transition

When SUNDARI was first imagined, it was driven by a simple conviction: our scientific community needed a space of its own, a platform to make visible the excellence, collaboration, and intellectual diversity that define our R&D ecosystem. What began as an individual initiative gradually became a shared endeavor, shaped by those who chose to contribute to it.

This issue reflects that evolution well. While Saclay is often perceived as the hive of our ecosystem, innovation extends beyond it. Across three major research hubs, our "three Bs", Ballerup, Boston and Budapest, scientific expertise and strategic ambition develop in parallel, enriching the whole. In this volume, we spotlight the first of these hubs, the SRIMC from Budapest, illustrating how decentralized excellence reinforces Servier's One Research vision.
With this issue, my role as Editor-in-Chief comes to an end, coinciding with the conclusion of my postdoctoral chapter and the beginning of a new phase within the organization.
Developing SUNDARI reinforced a belief I hold strongly: nothing meaningful is given. It emerges through curiosity, perseverance, and collective trust. I step away confident that the foundation is solid and the ambition intact. The hive is larger than one site. The story is larger than one voice. And it continues from Saclay and beyond.

Sergio Gonzalez Duque
Founding Editor-in-Chief
SUNDARI Journal

DIRECTOR'S INSIGHTS

Wesley Blackaby (PhD.)
Chemistry Director Drug design small molecules,
Institut Servier d'Innovation Thérapeutique

It is with immense pride that I introduce the fourth issue of the SUNDARI Journal, continuing our journey of scientific exploration and collaboration. The SUNDARI journal, is a testament to the diverse perspectives, dynamic community, and inclusivity of Servier global scientific research, and is dedicated to celebrating the incredible work and groundbreaking research conducted by our talented postdocs and Ph.D. students. SUNDARI, signifies 'SHINEDocs Unveiling New Discoveries and Research Innovation,' and epitomizes our commitment to innovative scientific communication and collaboration.

Having spent the last two weeks visiting Servier Symphogen in Ballerup and the Servier Institute of Medicinal Chemistry (SRIMC) in Budapest, I was reminded of the power of our diverse culture, and the multiplicity of approaches to problem solving at our disposal to address the challenges our industry faces. The SUNDARI community embodies these principles, creating a platform where the brightest minds from various disciplines can come together, sharing insights to inspire innovation and advance scientific knowledge. Every page tells a story of collaboration and relentless pursuit of knowledge, reflecting the values of our R&D. Our work is more than a scientific endeavor; it's a journey towards understanding complex biological mechanisms and translating these insights into therapeutic solutions.

In the 'Guiding Lights' section of this issue, you will discover SRIMC, its history, evolution and its pivotal role within the Drug Design Small Molecule Unit and Servier Research as a whole. In the 'In focus: Research Updates' section you will hear testimonies from SRIMC collaborators, their personal career stories, and motivation, bringing to life the passion behind our scientific achievements, and celebrating the hard work and dedication of our research teams.
At a time when our industry faces unprecedented challenges, we are presented with unprecedented opportunities with the potential of Artificial intelligence and automation to aid us in our mission. Providing these tools with the right data, and combining them with human ability, experience, curiosity, and resilience will enable us to leverage them effectively to aid us in our mission to bring transformative medicines to patients.

As you browse this issue, draw inspiration and motivation from each other's work. Let's continue to cultivate a workplace of constant learning and mutual support, where no questions are off limits, and where we openly challenge each other with the motivation that collective insights and collaboration will drive us forward. Together, we can redefine the future of healthcare. Thanks to the SHINEDocs community and SUNDARI editors for your relentless pursuit of excellence, making SUNDARI a testament to the innovative spirit thriving at Servier.

Welcome to the fourth issue of SUNDARI!

GUIDING LIGHTS

SRIMC* and DDSM**: an innovation engine with seamless cross-border collaboration

Andreas Kotschy (PhD.)
Head of research science team,
SRIMC-Hungary

Small Molecule Drug Discovery

In the rapidly evolving landscape of drug discovery, the Drug Design Small Molecule Unit (DDSM) at Servier stands as a testament to innovation and excellence. We design, prepare, and characterize all of the small molecules, and sometimes also the bigger ones, that fuel Servier's drug discovery programs. Distributed across two continents and three research centers—with major presence at SACLAY and in the Servier Research Institute for Medicinal Chemistry in Budapest (SRIMC), and a small but equally important team in Boston—this unit comprises of around 150 collaborators, which also includes postdocs, PhDs, apprentices, and trainees. With a robust structure and diverse expertise, the unit is poised to address the complexities of modern medicinal chemistry and drug design and also acts as a bridge between research and chemical development. The unit's core activities include Medicinal, Synthetic, Analytical, and Computational Chemistry with a breadth of expertise encompassing more than 15 core competencies ranging from Process Chemistry and Biotechnology to Chemoinformatics and AI/Machine Learning.

SRIMC's evolution – from an outpost to an integrated research hub

The concept of a Hungarian research center dedicated solely to Medicinal Chemistry came from our founder Jacques Servier around 2005, and it was rapidly turned into reality with our official opening in January 2008. If you wonder why Hungary, then this might be linked to the fact that the first Research director of Servier and a close friend of the founder, Dr Laszlo Beregi was a Hungarian chemist who left the country after the 1956 revolution. It is difficult to understand in today's global environment how challenging it was to amalgamate a foreign research center with its specific culture, communication, and personalities into the traditionally French research system with little precedence in the company's life until that point. We are proud to say that for the last couple of years the notion of "one chemistry research engine" is a reality. Working in cross-site teams is now daily routine, which is strengthened by face-to-face meetings and personal contacts. The stability of the DDSM workforce and the supportive management have also been key to this development.

The evolution of our role

Since its opening SRIMC has been able to recruit highly qualified collaborators,

**SRIMC : Servier Research Institute for Medicinal Chemistry in Budapest*
***DDSM : Drug Design Small Molecule Unit*

which ensures their ability to bring innovative solutions to complex problems. Most participate in drug discovery programs and over the years, responding to projects' needs, several expertise platforms were also developed. Some of these platforms, serving a need for fast turnaround or close interaction, have their twins in Saclay, while centres of excellence are located on one site. At SRIMC we developed excellence in Process Chemistry, Biocatalysis, Enzyme Engineering, and Targeted Protein Degradation. In parallel, excellence in High Throughput Synthesis & Purification, Late Stage Functionalization, Antisense Oligonucleotides, and Computational Chemistry was built-up at Saclay. Our Antibody-Drug Conjugate platform is unique in combining linker-payload synthesis at SRIMC and bioconjugation at Saclay.In the analytical division innovative NMR approaches were developed, implemented and shared across sites both for small molecules and proteins.

Challenging times require innovative solutions

The recent decades led to the emergence of challenging, usually hard-to-drug targets, and the chemists who are in charge of delivering the drug candidates had to adapt to these circumstances. Anticipation of innovative approaches, their adaptation to the industrial environment, and building the critical expertise in-house were our answer, and the innovation was spearheaded by our postdocs and PhD students. Just to name a few approaches, the TPD (targeted protein degradation), ASO (antisense oligonucleotide), ADC (antibody drug conjugate), HTE (high throughput experimentation), and biotechnology platforms all emerged through systematic innovation and implementation. Today they all serve and fuel discovery programs and several of them are led by former ShineDocs, who became valued collaborators.

Innovation driven by a vibrant ShineDoc community

SRIMC as an industrial research center is in a unique position in the Hungarian scientific ecosystem. Our commitment to innovation and our achievements have been attracting both talented students and funding both from national and European grants, which enabled us to expand our innovative precompetitive research activities. All this, in combination with our internal NTech Dev programs results in a vibrant early-stage researcher community at SRIMC that we are very proud of. Servier's commitment to innovation and nurturing talent is also manifested in the Beregi scholarships. 8 PhD students from 2 of the leading universities receive financial support both for their personal and professional development in research areas linked to drug discovery, and enrich the ShineDoc community.

Visibility

The SRIMC collaborators, and ShineDocs in particular, are the major contributors to the DDSM unit's scientific visibility, with 11 publications, 9 posters, and 14 oral presentations in 2024 alone. These achievements not only enhance the reputation of Servier's chemistry but also underscore the unit's commitment to advancing the field of drug discovery through rigorous research and innovation.

Future Evolution

We at SRIMC, as an integrated part of the Drug Design Small Molecule Unit, will continue to evolve, identifying and addressing the unmet needs in drug discovery over the next decade. Beyond discovery chemistry the seamless integration of data, facilitated by automated tasks and Agentic AI, will become increasingly prevalent in our daily life. By driving innovation in our fundamental vocation, synthetic and analytical chemistry, as well as in new therapeutic approaches we want to ensure that Servier's innovative research portfolio receives the best possible support from us, fueled by our "amour du métier".

Conclusion

The Drug Design Small Molecule Unit at Servier is a beacon of innovation and excellence in the field of drug discovery and SRIMC is one of its bright lights with its vibrant ShineDoc community. While the boundaries between the twin research teams of Saclay and Budapest became blurred through mingling, their cultural diversity is a permanent inspiration of out-of-the-box ideas with differentiated ways of thinking, approach to problem solving and collective challenge. With SRIMC's innovative scientific contribution the DDSM unit sees the challenges ahead of us more as an inspiration than a threat to the delivery of transformative medicines to patients.

GUIDING LIGHTS

ShineDocs turned innovation drivers

“After earning my PhD at EGIS I joined SRIMC as a postdoc working on the field of Targeted Protein Degradation within the EUbOPEN consortium. During this period, I was also member of the ShineDocs community. This was a fantastic experience where I not only learned heaps but also got the chance to sharpen my soft skills and participate on Seedpods Days. Plus, I met a bunch of talented people whom I really admire. After 3 years I landed a permanent position as a Researcher. Nowadays, I split my time between working on Servier projects and coordinating pre-competitive research projects including E3 ligase binders and PROTAC development. On top of that, I have also mentored foreign interns and PhD students, helping them navigate their own research journeys. During my time at Servier, I received continuous support to develop my skills, which I hope will contribute to the development of innovative therapies and fit well into the multidisciplinary science of drug development. What truly drives me is the chance to improve patients' lives through cutting-edge drug research and development.”

Tímea Szabó, Targeted Protein Degradation

“I started my work in SRIMC as a summer intern during my BSc studies in 2014 and rapidly became fascinated by the synthetic topic and the quality of work I could pursue in SRIMC. I continued it as an MSc thesis work in a collaboration between the institute and an academic research group, and later developed the topic into a PhD research program, still within the confines of Servier and academics. On completion of my PhD, in 2020 I joined the medicinal chemistry team of SRIMC* and since then I’ve been working on various interesting projects. Both the strictly professional and the site-specific experience gained during my journey as a student in Servier are now helping me to give my best performance in my current role and contribute to the medicinal chemistry projects I am working on.”

Márton Zwillinger, Synthetic chemistry

"As a PhD student, I had the opportunity to establish the photochemistry platform at SRIMC. This innovative technology inspires us to explore novel synthetic approaches in medicinal chemistry projects. Throughout my PhD studies, I gained extensive experience in this field, which is essential for the successful implementation in our projects. Through hands-on experimentation, I developed a deep understanding of the principles of photochemistry and its applications in drug discovery and process chemistry. Additionally, I regularly share my findings within the Servier community. The successful examples, like the scale-up of the synthesis of a key intermediate, motivate me to push the boundaries of this emerging technology. Overall, my experience at SRIMC* has equipped me with the technical expertise and collaborative spirit necessary to contribute effectively to future research initiatives. I am excited to leverage this knowledge in my upcoming projects and continue exploring the potential of photochemistry to advance medicinal chemistry."

Nándor Györfi, Photochemistry

"I started my career at SRIMC as a postdoc in 2018, which offered a great opportunity to apply my learnings in a real industrial environment, moreover, in Hungary, my home country. The beginning was fairly challenging as no precedent for systematic use of enzymes for synthesis existed within the DDSM*. I started building a platform with the aid of trainees, and after two years Servier offered me a permanent position. Over the years, I could contribute to several projects and we built an expert community across sites with teams in Saclay, ORIL, Egis. We also continued developing the platform at SRIMC through various external and internal funding opportunities including a Horizon Europe project. Today our team includes a PhD student and 2 postdocs (all ShineDoc community members), one of whom is also a former PhD student. Over the years, we have been implementing new techniques and approaches from medium-throughput screening to cell-free enzyme engineering, and the journey continues in the era of artificial intelligence to make white biotechnology a strategic asset within Servier."

Gábor Tasnádi, Biocatalysis

FOCUS

DDSM Saclay and SRIMC

Discover the ShineDocs working in Chemistry

Raphael Steimbach

Postdoc: Revolutionizing Chemical Research: the era of high-throughput experimentation

Tony Biremond

Postdoc: Development of a continuous-flow electrochemical platform for the synthesis of drug metabolites

DDSM Saclay

Victor Lehot

Postdoc: Bioconjugation improvement of Thiomab-ADC

Christophe Cardone

Postdoc: Enabling phosphatase inhibitor discovery

Andras Telek

Research Associate II, Postdoc Biocatalysis

Gergo Dargo

Postdoc: Industrial application of enzymes of marine origin for biocatalysis

Mate Major

Postdoc: New degradation modalities to broaden toolbox of TPD for Key therapeutic targets

SRIMC

Simon Bodonyi

PhD: Exploring Targeted Protein Degradation

Viktor Gajak

PhD: Development of an enzyme panel for the synthesis of non-natural nucleosides

AI-Enhanced Cell-free Enzyme Engineering for Sustainable Chemistry

At Servier sustainability is central on many levels. When manufacturing the active pharmaceutical ingredients (APIs) for our drug products at scale, traditional chemical synthesis often struggles with efficiency, selectivity, and environmental impact. Biocatalysis, using enzymes for the synthesis, offers a promising alternative due to its inherent environmental friendliness, safety, and engineerability. Limitations such as enzyme instability under industrial conditions or low activity on non-natural molecules can be overcome by enzyme engineering. This highlight sheds light on the first successes of in-house biocatalyst development, that pave the way for more sustainable and efficient chemical processes.

Enzyme engineering can be simply described as modifying the amino acid sequence of enzymes to improve their catalytic properties. It is most often realized through the practice of the Nobel-prize winner directed evolution technology. This involves bacterial expression and iterative testing of huge enzyme variant libraries (10.000s of variants), that makes it efficient but very laborious and expensive. Therefore, it is only feasible at the later stages of chemical development. Simpler and more accessible alternatives could promote adoption of biocatalysis earlier, resulting in more green synthetic routes reaching manufacturing stage.

My PhD research contributed to making enzyme engineering more accessible by the development of the Rapid *In vitro* Semi-rational Engineering (RISE) workflow *(Figure 1)*.

The idea was to create a method that allows chemists to engineer enzymes quickly and efficiently and without using any living organism. An innovative modification of existing protocols resulted in a cell-free workflow that enables the production and screening of focused enzyme variant libraries (10s to 100s of variants) in less than 2 days even in a chemistry lab. It involves 5 key steps:

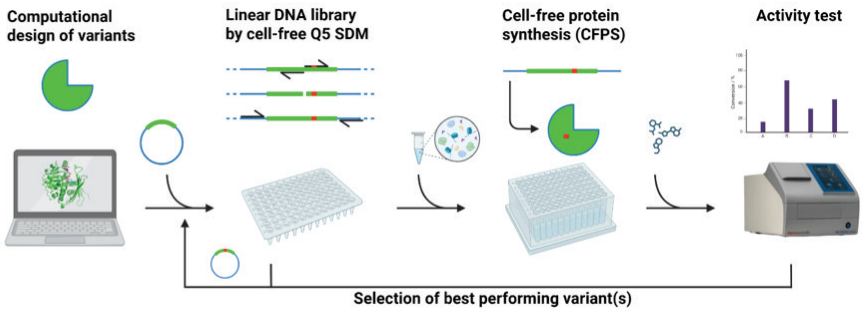


Figure 1: General workflow of RISE

- Computational design of enzyme variant library
- Mutagenesis and DNA amplification
- Cell-free protein synthesis
- Activity screening
- Selection of best performing variant(s) for iterative mutagenesis, expression and testing

The innovative step, the cell-free DNA amplification after mutagenesis, was a simple idea. So simple, it must have already been described or cannot work at all, I thought. Still, I insisted on trying it and it worked. Even the simplest idea can be a foundation of an exciting innovation!

I still needed a proof-of-concept, so I have applied RISE to engineer a ketimine reductase enzyme (RnKIRED) for the synthesis of a key pharmaceutical intermediate. In one application, RISE was able to switch the selectivity of the enzyme, and in another application, it improved its activity 400-fold. This development led to a gram-scale synthetic process for the pharmaceutical intermediate. A good start, but why stop here?

The initial version of RISE involved collection of beneficial mutations in the enzyme one-by-one. This significantly limits the exploration of the variant sequence space thereby compromising efficiency in finding the optimal biocatalyst. Therefore, my current postdoc project aims to apply artificial intelligence (AI) to enhance the capabilities of RISE. In collaboration with computational chemists and data scientists, we leverage a combination of protein language models (PLMs) with machine learning (ML) algorithms to navigate the complex "enzyme fitness landscape". Active learning strategies are also being implemented to efficiently guide the engineering process.

> "Even the simplest idea can be a foundation of an exciting innovation!"

Andras Telek,
Research Associate II,
Postdoc Biocatalysis

The development of RISE laid the foundations of enzyme engineering at Servier. The workflow is currently being used in other precompetitive and new technology development (NTechDev) projects as well. The integration of AI/ML promises to further enhance these in-house enzyme engineering capabilities, allowing for more sophisticated and efficient navigation of enzyme design space. In a wider view, I also think RISE changed the perspective of biocatalysis at Servier. As enzyme engineering becomes more accessible and cost-effective, biocatalytic processes have increased chance of prevailing in the competition against traditional chemical syntheses in the fast-paced early chemical development. RISE effectively forms a bridge between non-optimized wild-type enzymes and manufacturing-ready enzyme variants developed by costly directed evolution *(Figure 2)*.

These developments directly support Servier's commitment to innovation and sustainable practices in drug discovery and development. By enhancing the implementation of biocatalysis in chemical development, we can improve the efficiency and environmental footprint of our manufacturing processes, contributing to our CSR strategy. We are committed to deliver sustainable process alternatives where they are most sought for.

The proof-of-concept is there. The next step will be showing impact in running chemical development projects. Future work will also focus on refining the AI/ML models, integrating AI-enhanced RISE with automated experimental platforms, and exploring its application to a wider range of biocatalytic challenges. The goal is to continuously improve the workflow and expand the applicability of biocatalysis within Servier and the broader scientific community.

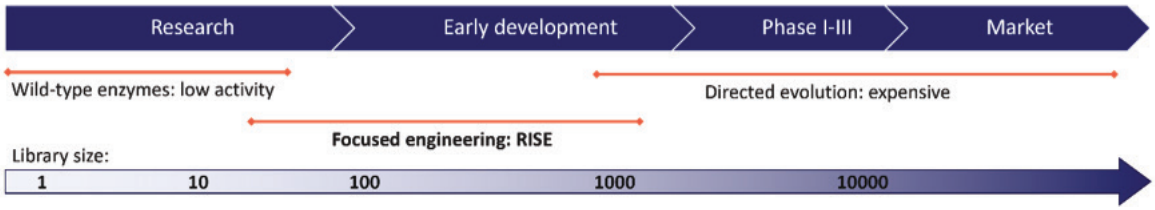


Figure 2: Proposed role of focused enzyme development by RISE in chemical development

NEW MEMBER'S SPOTLIGHT

Alexandra Rebak
Postdoc : Symphogen Presidency (CMC)

Enhancing Analytical Tools for the Development of Antibody Drug Conjugates

Antibody drug conjugates (ADCs) combine the power of potent small molecules with the selectivity of antibodies for cancer treatment. This allows for more efficient targeted treatment with fewer side effects for the individual.

The antibodies targeting the cells of interest are designed with sites that can be conjugated with the small molecule, known as the linker-payload, to combine the two. Prior to this conjugation, the antibody is primed so that the designated sites are ready to accept the linker-payload. The priming involves decapping the sites to remove any modifications that may block the conjugation.

It is crucial that the priming, also known as reduction, is successful to produce high-quality ADCs. This includes all designated sites must be fully reduced to conjugate to the linker-payload while not disrupting the natural organization of the antibody to ensure full functioning. The current focus of my project has been to develop analytical tools that can assess the reduction state of the antibody prior to conjugation. The first analytical method we developed relies on the same chemistry as linker-payload conjugation to the antibody, based on maleimides. By conjugating the reduced antibody with smaller maleimide molecules and analyzing by size-exclusion-mass-spectrometry, we can assess whether the antibody is fully reduced while evaluating whether the antibody structure has been disrupted.

This analytical method will assist antibody purification development and ultimately speed up the development of safe, efficacious, and stable ADCs to benefit patients worldwide.

Development and characterization of a human Gut–Liver organ-on-chip model for ADME applications

Understanding how orally administered drugs are absorbed and metabolized before reaching systemic circulation is critical for optimizing their efficacy and safety. The intestine and liver, through their coordinated function known as the gut–liver axis, are key organs involved in first-pass metabolism. Yet, traditional models often fail to reflect the physiological complexity of this interface. 2D static cultures oversimplify tissue architecture and lack dynamic interactions, while animal models suffer from limited predictivity due to species differences. To overcome these challenges, our project focuses on developing and characterizing a human-based gut–liver organ-on-chip model within a dynamic flow system (CNBio platform).

This model connects human intestinal cells and hepatocytes through microfluidic channels that mimic blood flow and directional transport, enabling the study of drug absorption, metabolism, and biotransformation under physiologically relevant conditions. Barrier integrity (TEER), paracellular permeability, enzyme induction, transporter activity (e.g., P-gp), and metabolic clearance will be evaluated using both functional and analytical assays.

One of the key advantages of this model is its ability to track drug concentration over time, in both compartments, and to identify active or potentially toxic metabolites produced by intestinal or hepatic enzymes. This allows for a more detailed understanding of compound fate and drug–drug interaction risks at an early stage of development. Ultimately, this approach aims to provide a predictive, human-relevant, and ethically aligned alternative to animal testing helping to make drug testing faster, safer, and more reliable.

Fahd Tibourtine
Postdoc : ADME In Vitro Technologies (Translational Medicine)

NEW MEMBER'S SPOTLIGHT

Martin Soucail
PhD student: Quantitative Pharmacology

Automated Tumor Growth Inhibition Modeling with Machine Learning

This PhD project brings together pharmacometrics, oncology, and artificial intelligence with the objective of improving the understanding and prediction of tumor dynamics under treatment, thereby contributing to the development of more precise therapeutic strategies.

In oncology, modeling is fundamental to the structuring and interpretation of complex data generated during preclinical and clinical development. Tumor Growth Inhibition (TGI) models are widely used to describe disease dynamics, quantify treatment effects, and compare different therapeutic strategies at both the individual and population levels. As such, they constitute a valuable decision-support tool throughout drug development, enabling the anticipation of tumor response and the optimization of treatment regimens.

However, the construction of these models often relies on complex and time-consuming approaches that are difficult to generalize, particularly when data are heterogeneous or limited. The aim of this PhD project is to explore how machine learning can enrich traditional modeling approaches, complementing rather than replacing existing methodologies. The overall objective is to improve the quality, robustness, and efficiency of oncology modeling while preserving biological interpretability.

By enhancing the efficiency and predictive performance of TGI modeling, this project has the potential to impact multiple stages of drug development. In early phases, it may enable a more effective use of available data to compare therapeutic candidates and support informed decision-making in compound selection. In clinical phases, these approaches could facilitate more individualized predictions of tumor response, supporting treatment optimization and reinforcing personalized medicine strategies.

Understanding what is driving the differential biodistribution of antisense oligonucleotides

Antisense oligonucleotide (ASO) therapeutics are emerging as a potentially transformative approach for the treatment of certain brain disorders that currently lack effective therapeutic options. However, the pharmacokinetics, biodistribution, and brain uptake of ASOs are not yet well characterized. Gaining a deeper understanding of their distribution and uptake in the central nervous system (CNS) could significantly advance the development of new ASOs targeting specific pathologies.

My project aims to investigate the factors that drive the differential biodistribution of ASOs observed in the CNS following an intrathecal (IT) injection. The hypothesis is that this variation in distribution and uptake is driven by protein binding. To address this question, I plan to undertake a cross-functional project, using various resources and collaborating with several departments.

The project will commence with the Proteomics team, where I will conduct a pull-down assay using non-human primate (NHP) cerebrospinal fluid (CSF). This assay will help identify which proteins bind to specific, well-characterized ASOs that have shown superior distribution. The goal is to uncover patterns or families of candidate proteins associated with enhanced ASO uptake.

Subsequently, I will employ additional tools, including in vitro and in vivo models, and collaborate with several departments collaborating with several departments (Research, TxM, NeuroTA), to further investigate the distribution mechanisms and validate the findings from the proteomic analysis. This comprehensive and transversal approach aims to enhance our understanding of ASO behavior in the CNS and pave the way for the development of targeted therapies for brain disorders.

Maria Querol Canut
PhD student: Neurology Research ASO

NEW MEMBER'S SPOTLIGHT

Louise Robinet de Plas
PhD student: Neurology
Research Small Molecules

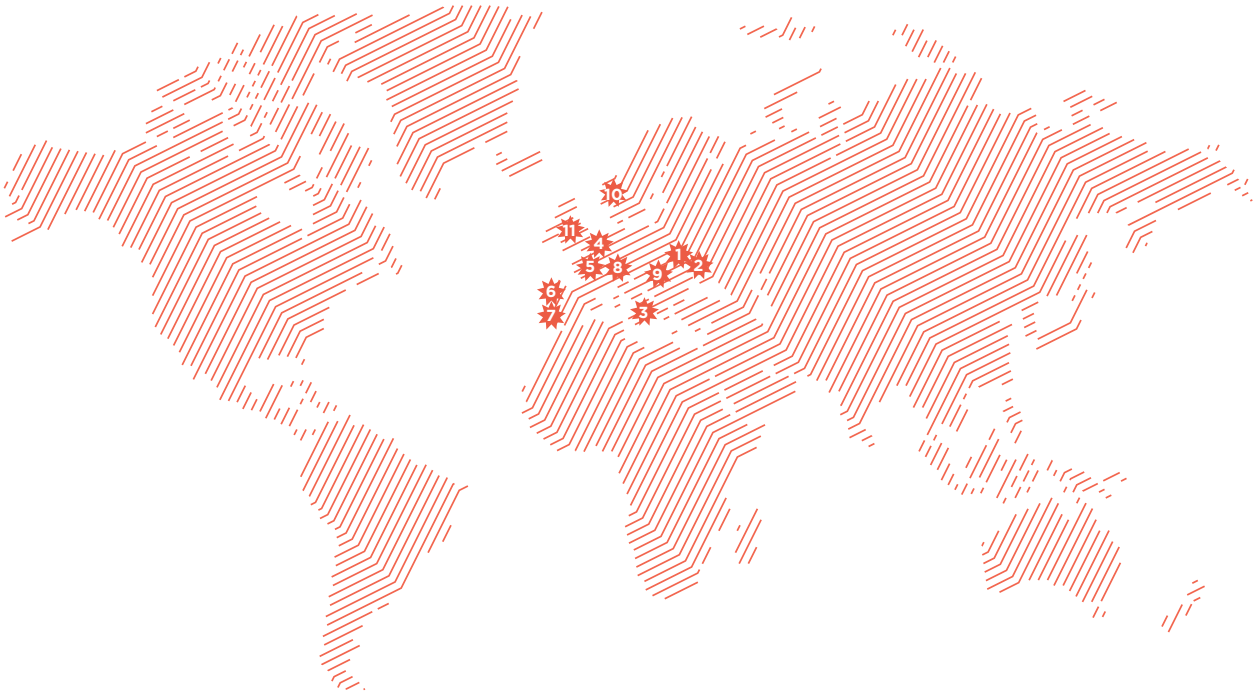
Functional characterization of genetic variations in an epilepsy associated gene

Epilepsy, particularly in its infantile form, is a significant neurological disorder associated with high morbidity. Despite extensive research, the genetic bases and mechanisms driving developmental epileptic encephalopathies (DEE), a rare and severe group of epilepsies, characterized by early seizures, frequent epileptiform activity, and developmental slowing or regression, remain poorly understood. Among these disorders, those caused by mutations in genes encoding ion channel subunits are of particular interest, as these channels play a fundamental role in neuronal communication.

Although genotype–phenotype correlations are emerging to better understand disease mechanisms, functional studies largely rely on heterologous systems, highlighting the need to investigate variants in human iPSC-derived neuronal networks. Genetics sequencing technologies and the use of patient-derived induced pluripotent stem cells derived offer relevant in vitro models to study variants and their impacts on epileptic activities. DEE patients are selected based on clinical observations at the Center for Rare Epilepsies at Robert-Debré IHU. Somatic cells from patients will be reprogrammed into iPSCs, which will then be differentiated into neurons. These patient-specific models will be characterized using electrophysiological readouts to correlate the impact of mutations on ion channel function and neuronal network activity in iPSC-derived neurons cultures. These analyses will be correlated with clinical phenotype severity to move closer to the development of functional and adapted treatment potential.

SHINEDocs' pulse: spotlights

Congress' participation in 2025



1 Novel Enzymes 2025, Budapest, Hungary | 25-28th March

András Telek: Cell-free enzyme engineering for biocatalysis

2 SETAC Europe 35th Annual Meeting, Vienna, Austria | 11-15th May

Chrisna Matthee: Assessing a Primary Hepatocyte Monolayer Culture System for Studying Pharmaceutical Clearance in Fish

3 Population Approach Group Europe, Thessaloniki, Greece | 4-6th June

Chloé Burlot: Assessment of S65487 PK differences from therapeutic doses to microdose: exploring linear ans nonlinear processes

4 MPS, Bruxelles | 9-13th June

Hélène Le: Ex vivo model from CRC patients to assess immuno-oncology drugs

Fahd Tibourtine: Evaluation of a gut-liver-on-chip system as an alternative to current static in vitro models

5 European Proteomic Association Meeting, St-Malo, France | 16-18th June

Charlotte Brun: SPACE: Surface Proteomics for AML-derived Cells Explores potential new targets and biomarkers through multi-omics strategy

6 EACR, Lisbon, Portugal | 24-27th June

Julie Le Naour: Patient-derived models for target identification and validation in PDAC

Daniel Herrero Saboya: Molecular and immune landscape of recurrent and/or distant metastatic squamous cell carcinoma of the head and neck: an IMMUCAN project

Malina Xiao: Development of relevant mouse models for the R&D of therapeutics for PDAC

7 Splicing 2025, Caprica, Portugal | 24-27th June

Marion Leblanc: Leveraging long read sequencing to guide ASO design

8 Festival of Biologics 2025, Basel, Switzerland | 30-2nd October

Estefania Tumbaco: Immunogenicity and Internalization of Therapeutic Antibodies

9 OTS, Budapest, Hungary | 19-22nd October

Nell Hirt: Leveraging Extracellular Vesicles to Advance Neurological Disease Research and ASO Therapeutics

Marion Leblanc: Leveraging long read sequencing to guide ASO design

Marius Halliez: In vivo pharmacology ASO screening workflow in Servier: learning through experience

10 Enzyme Engineering XXVIII, Helsingor, Denmark | 19-24th October

András Telek: Accessible biocatalyst development by Rapid In vitro Semi-rational Engineering (RISE) of enzymes

11 Tumor Models Summit London, England | 3-4th December

Malina Xiao: Development of relevant mouse models for the R&D of therapeutics for PDAC

Science Days in Servier

ASO Day

24 March 2025

During the ASO Day at Servier's R&D center in Saclay, collaborators showcased the impressive progress achieved since 2019 with antisense oligonucleotide (ASO) therapies, an innovative cure for rare neurological diseases. ASOs target non-functional mRNA to ultimately modify protein expressions by impeding the synthesis of defective proteins. ASOs design and manufacturing process were presented. Diverse subjects such as regulatory frameworks, ASO' safety, PK modeling, and clinical trial design were also discussed. Currently, Servier has 7 ASOs projects in its pipeline and one of them was featured as its entry in clinical phases is prepared. Below is an overview of our post doctorates' posters presentation:

MELO DE FARIAS ANA RAQUEL
| DSDM, Functional Genomics & Proteomics, Integrative Molecular Pharmacology
RHU iNNOV4-ePiK on Rare and Refractory Epilepsies: WP4 - Focus on iPSC-derived Models for KCNA2 Mutations and Therapeutic ASO Development

HALLIEZ MARIUS
| In vivo Pharmacology, Translational Medicine, NITA
Blood biomarkers exploration in A SCA3 transgenic mouse model Home-Cage Monitoring for Transgenic Mouse Characterization and Phenotypic Rescue by ASO treatment

HIRT NELL
| Integrative Molecular Pharmacology and Translational Medicine
Promise of brain derived extracellular vesicles for biomarkers identification

COSSA ANTOINE
| Translational Medicine DDIS Global Biometrics NITA
How can MR imaging biomarkers and disease modeling support ATXN3 project development

LEBLANC MARION
| NITA, Translational Medicine, IVP, Integrative Molecular Pharmacology
RNA modulation with Steric-Hindrance ASOs

Research Pharmacology & Global Central Lab Science Days

26-27th November 2025

Drugs platforms were presented such as the ADC franchise and the ASO one. ADC are based on antibodies targeting CD7 (cell surface protein overexpressed in leukemic T-ALL blasts) or EPCAM (cell adhesion molecule overexpressed in solid tumor cells). The antibody is linked to Bcl-xL inhibitor (Bcl-xL is an antiapoptotic protein from Bcl-2 family). ASOs were also presented by the neurology team of in vitro and in vivo pharmacology team.

With these promising therapies, success in clinical phases is expected. However, there is a harsh reality: when arriving in clinical phases, a 90% attrition rate is observed. This demonstrates the need for relevant preclinical models that have a predictive "power" before advancing in clinical phases. To innovate in preclinical models, the implementation of the 3Rs (Reduction, Refinement, Replacement) is crucial for ensuring ethical compliance and adherence to regulations in research.

From these Science Days, a great bridge was observed between the In vitro and In vivo pharmacology teams. In the In vitro departments, postdoctorates Helene Le and Julie Le Naour developed ex vivo models in CRC and PDAC indications respectively. Ex vivo models are more complex and relevant than spheroids or organoids, as they recapitulate the tumoral tissue structure with all the tumor microenvironment.

In the 3Rs, the word "Replacement" is misleading. Indeed, the In vivo pharmacology department, postdoctorates Marius Halliez and Malina Xiao aim to develop innovative murine models to replace conventional murine models that lack human clinical features, in PDAC and neurological diseases respectively.
Like the ASO day, communication and application of 3Rs understanding will help to advance in the development of innovative models for better understanding of our lead candidate drugs.

A WINDOW TO THE PAST

From Postdoctoral Innovation to Research Leadership at Servier

Could you tell us about your background and what initially inspired you to pursue this career path?

My journey began with a childhood dream: playing a part in the discovery of new medicines. I qualified as a Pharmacist Researcher, completing my PharmD at the University of Lille. Fascinated by immunology during my second year, I pursued a Master's in Immunotechnologies and Biotherapies at Sorbonne University alongside my final year of pharmacy. After completing my PhD in Immuno-oncology at the Cordeliers Research Centre, I joined Servier for a postdoc in histopathology. I then spent five years as a Clinical Biomarker Project Leader, managing early-phase (Phase I/II) projects to identify responder subpopulations and refine dosing. In December 2025, I transitioned to Preclinical Lead in Oncology, where I now provide the preclinical rationale needed to build confidence in our drugs and drive them into clinical development.

What were the most significant lessons from your postdoc at Servier?

It was a total immersion. Scientifically, it was mind-opening; rather than just managing, I spent this time observing the R&D pipeline and discovering the sheer variety of professions involved. I also participated in implementing cutting-edge technologies, such as Multiplex IHC (Immunohistochemistry). Beyond the science, I discovered the corporate world. I learned how to manage time extremely efficiently across multiple projects while balancing the specific priorities of various stakeholders and navigating the company's organizational structure.

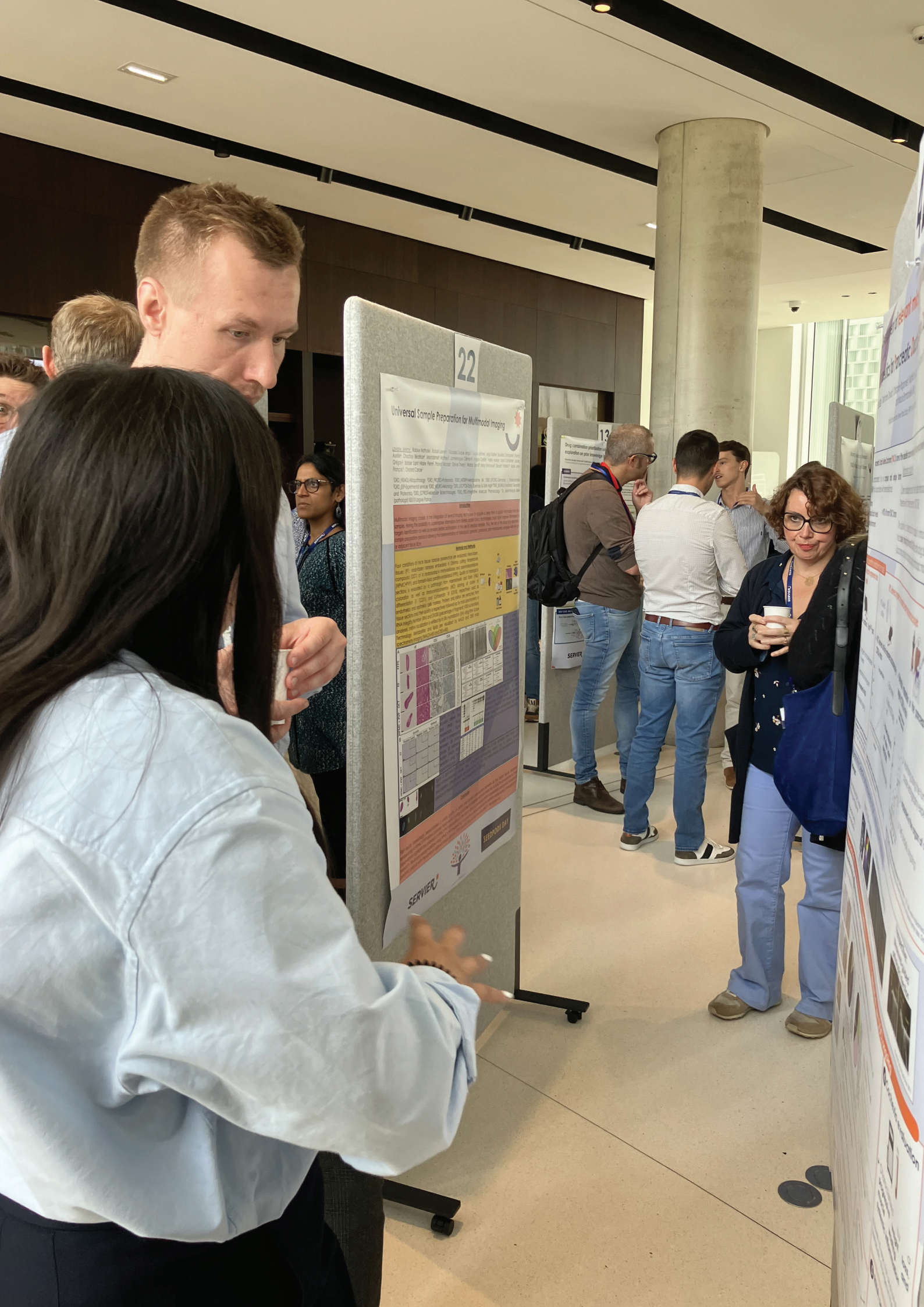
How does that postdoc fit into your long-term career plan?

Histopathology is at the heart of the drug discovery process, impacting every stage from target validation to clinical outcomes. Specializing in this field gave me a strategic "big picture" view of the R&D organization and allowed me to build a strong network and understand what different teams do. Moreover, I felt a strong alignment with Servier's core values. This foundation was essential in building my career plan: I knew I wanted to stay in research while supporting the clinical transition to ensure we make highly informed, data-driven decisions.

What advice would you give to current postdocs to prepare for their next move?

A postdoc in a corporate setting is not just about conducting a research project; it is a unique opportunity for immersion. The main advice is to anticipate the next step very early. Take the time to reflect on your own interests and "appetites," observe what other teams are doing, and engage in broad networking beyond your own department. Furthermore, it is vital to be aware that in industry, projects can change rapidly. Success requires the ability to remain flexible and adapt to a highly dynamic environment. It is the perfect time to understand the global ecosystem before making a career choice.

Hélène Kaplon (PhD.)
R&D Project leader, Oncology TA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Universal Sample Preparation for Multimodal Imaging
SERVIER

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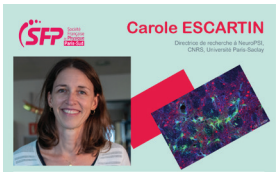
UPCOMING EVENTS

April / July 2026



02.04.26

SFP Paris-Sud Conference by Carole Escartin

Pierre Lehmann Auditorium, Building 200, IJCLab Laboratory, Paris-Saclay University Campus.
"Glial cells in neurodegenerative diseases: emerging roles and therapeutic potential".

université PARIS-SACLAY

13.04.26

"R&D" Track – Doctoral Career Days (Health, Biotech, Medtech theme)

Paris-Saclay University.
Deepening knowledge of corporate R&D processes through interventions by industry leaders and experts. Servier will be present.

07.05.26

AI and Digital Health

Paris-Saclay Faculty of Medicine.
Part 1 on using connected objects and AI for research data collection, and Part 2 on ethical and regulatory challenges in digital health.

11.06.26

Seedpods Day

Servier Saclay.

18.06.26

Doctoral School Day

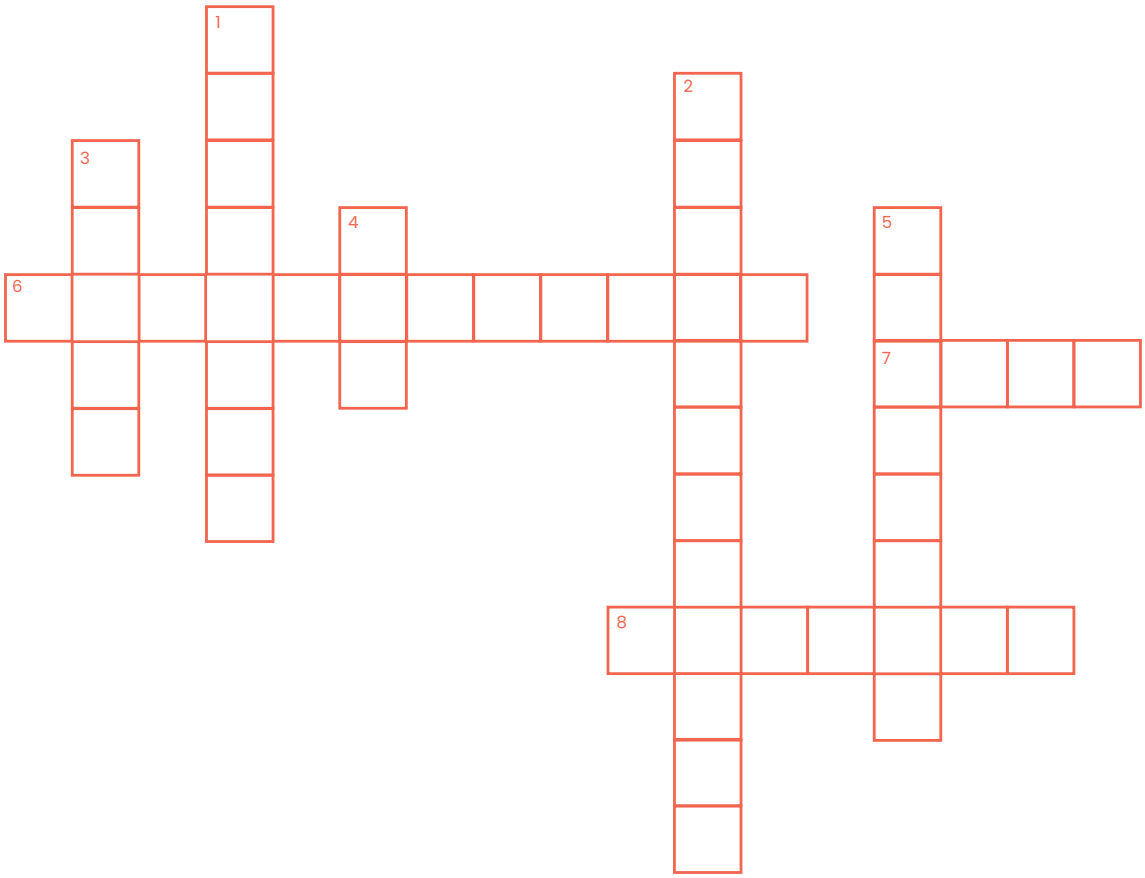
Pharmacy Faculty (Henri Moissan Building), Paris-Saclay University Campus.
Organized by the ADIT (Association of Doctoral Students in Therapeutic Innovation) with Servier's participation.

29.06 to 01.07.26

R&D on Air

Servier

BEHIND THE SCENE

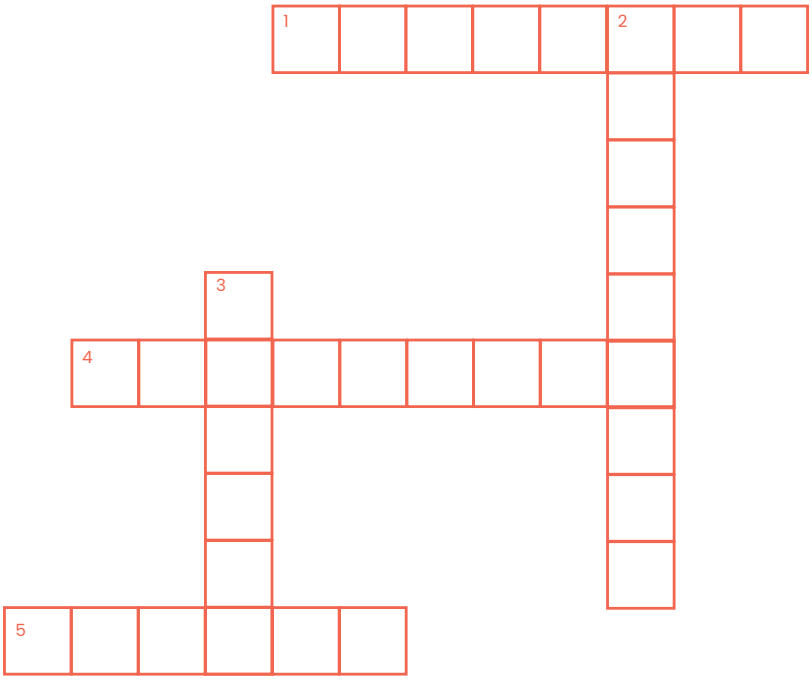


Vertical

1. Chemical entity made of a group of atoms bonded together
2. The act of removing impurities to make something clean or pure, especially in chemistry
3. Servier Research Institute for Medicinal Chemistry in Budapest
4. High throughput experimentation
5. In silico technique used to better understand the behaviour of complex molecules and proteins

Horizontal

6. Catalytic process accomplished by a biological entity, typically involving natural enzymes
7. Drug Design Small Molecule Unit
8. A type of alcohol used as fuel and its chemical formula is C2H6O



Will you guess the topic of the next edition ?

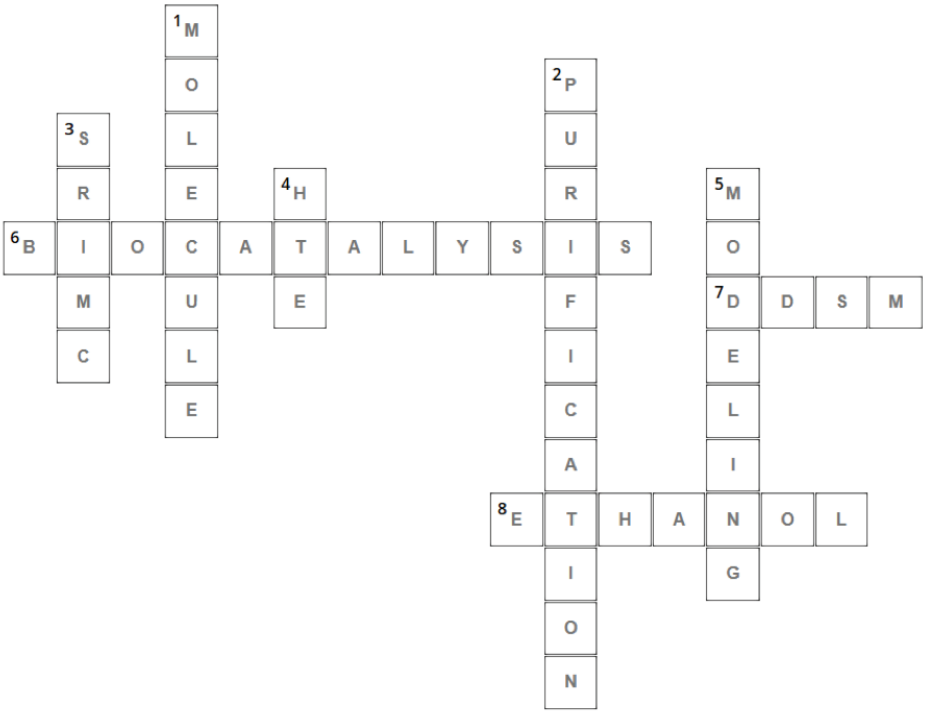
1. Protein produced by B-cells to fight pathogens
2. Mini organ grown in lab
3. Resistant to infection
4. Servier's Biotech company name and I am the next issue topic
5. White blood cell that makes antibodies

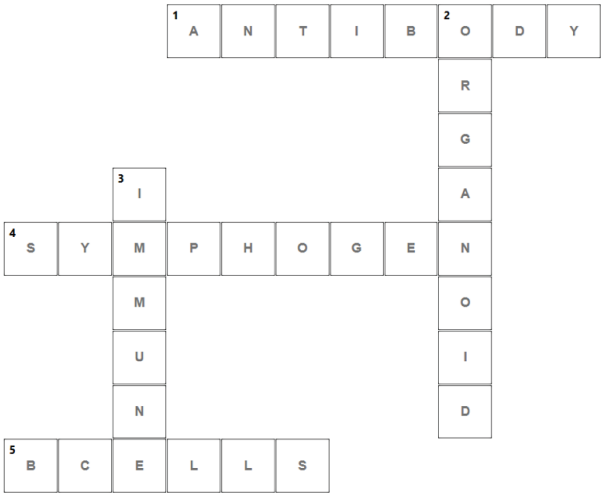
BEHIND THE SCENE

Next issue

Big news! The upcoming issue of the **SUNDARI Journal** is going on a special mission to Ballerup, Denmark, to spotlight **Symphogen**, Servier's powerhouse antibody platform. In this edition, we are diving deep into how we leverage our antibody platform and expertise to discover and develop next-generation, differentiated therapeutics. Get ready for an inside look at cutting-edge research, moments in innovation, and the collaborative spirit defining our future. We are taking SUNDARI on an exciting road trip **from Hungary all the way to Denmark! Stay tuned.**

Arrowword Answers





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We encourage contributions from our community. If you have research findings, insights, or stories to share, please reach out to us. The Editorial Board welcomes submissions that align with our commitment to advancing science and knowledge. For guidelines and submission details, or to discuss potential contributions, please contact us at sundarijournal@servier.com
We look forward to your valuable input and collaboration in shaping the future issues of the SUNDARI Journal.

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