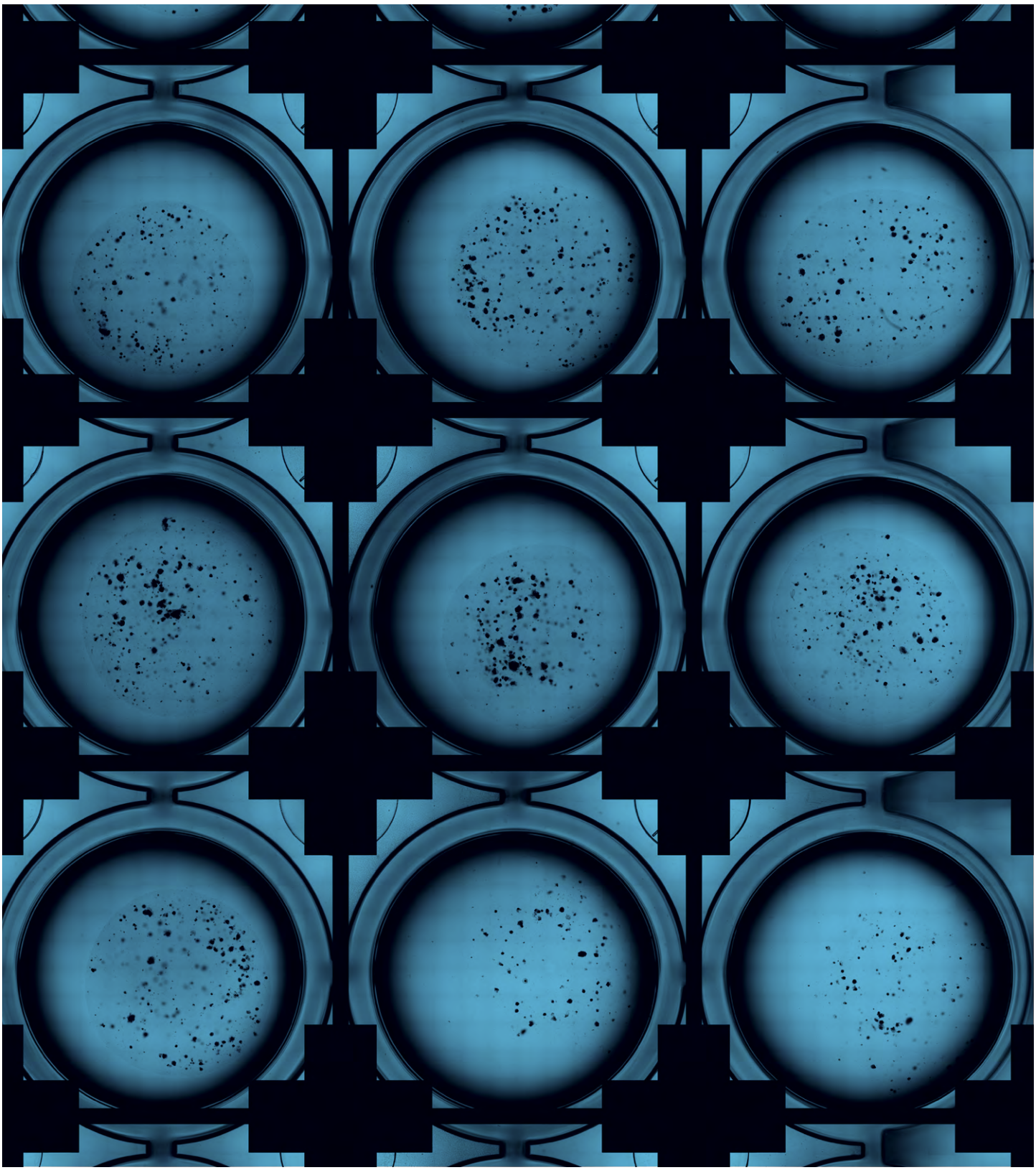
ANNUAL REPORT 2023



60TH

THE ISREC FOUNDATION
INVOLVED IN THE FIGHT
AGAINST CANCER
SINCE 1964

ISREC
Fondation Recherche Cancer

ANNUAL REPORT 2023
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2023 — COMMITMENT AND COOPERATION : UNITED IN OUR FIGHT AGAINST CANCER

Supporting translational cancer research and encouraging young academics have been the two main missions of the ISREC Foundation since it was established in 1964. Drawing on sixty years of experience, it provides independent support for members of academic institutions, based on a rigorous scientific selection process and careful monitoring of the projects it finances.

On the eve of our 60th anniversary, the Foundation continues its unflagging commitment to the fight against cancer. It acts as a link between scientists and donors, and we are convinced that it is necessary to pool our efforts and to move forward as one to support cutting-edge research.

In 2023, the members of our Foundation Council, Scientific Board and management joined forces to promote exceptional individuals and support invaluable projects (page 30). Their commitment deserves great recognition, as does the Foundation's teams' tireless day-to-day work. Our heartfelt thanks also go to our partner institutions in the Lake of Geneva area. Close collaboration with all of these is essential for the implementation of our projects, and also brings to life our magnificent AGORA building, which hosts interdisciplinary teams from CHUV, UNIL, EPFL, HUG and UNIGE.

Prof. Pierre-Marie Glauser

President

The second call for TANDEM projects, aimed at supporting projects co-directed by a basic researcher and a clinician, was very well received and led to over 30 letters of interest. Our Scientific Board carefully evaluated 22 projects addressing essential oncological issues, both from a clinical perspective and with a view to improving patient care. Thus, in 2023 and for the second year running, the Foundation Council allocated 3 million CHF to collaborative projects involving clinicians and basic scientists (page 16).

Last September, Prof. Nicolas Thomä, a world-class structure biologist committed to innovative drug development, was appointed to the Paternot Professorship at the EPFL. His position is financed by the ISREC Foundation for the coming six years. This nomination bears witness to our ongoing commitment to accelerating progress in oncological research (page 8), and represents a further step towards achieving our ambitious research and innovation goals in this field.

Finally, the ISREC Foundation strives to develop cooperation with other philanthropic institutions, in order to join forces to support innovative cancer research. In 2023, this commitment took concrete shape in a new collaboration with two donor foundations active in the oncological sector : the FIAMMA program, which supports a major project focused on treating childhood leukemia (page 10).

It is thanks to the unwavering support of our donors that we are able to deliver on our commitments. Through fruitful collaborations with other foundations, a rigorous selection of the best projects, and a thorough follow-up both scientifically and administratively, we have strengthened our impact on translational cancer research. We are deeply grateful to all who support us and who enable us to carry out our missions, achieving significant progress each and every year. Thank you from the bottom of our hearts for your trust and commitment ! They are the driving forces that inspire us to move forward.

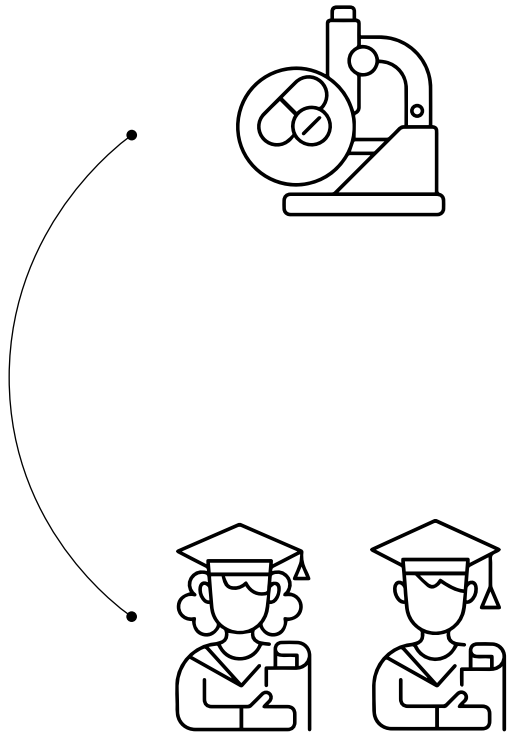
THE FOUNDATION'S MISSIONS

Funding Translational Oncology Projects

The ISREC Foundation identifies, selects, and supports projects that promote knowledge transfer and collaborations between basic research and clinical applications. In order to establish novel diagnostic and therapeutic approaches, it is necessary to take a systems' approach to understand cells, their interactions with their environment and the immune system, and to be able to counteract the dysfunctions driving cancer.

Supporting Young Scientists and Clinicians in Switzerland

The ISREC Foundation grants scholarships to students, PhD candidates and clinicians working in the fields of biology, bioengineering or medicine, and whose research is focused on forefront innovations in oncology.



Established on June 18, 1964, the ISREC Foundation is a private non-profit foundation devoted to supporting experimental cancer research. Over the past 60 years, approximately 150 personalities from Switzerland and abroad, including five Nobel Prize winners, have served on the various boards of the ISREC Foundation. The Foundation has financed significant research projects and discoveries, notably in the areas of mutagenesis, genome instability and repair, immunology, immunotherapy, the cell cycle, cell biology, tumor virology, oncogenes, cell differentiation and bioinformatics. For decades, research accomplished by many scientists and supported by the Foundation has contributed to a better understanding of the mechanisms underlying cancer, and to the identification of novel therapeutic targets and techniques.

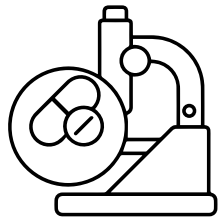
Since translational medicine has a strong forward-looking component that needs to be implemented, the ISREC Foundation's efforts today are focused on funding projects that bridge the gap between basic medical research and clinical practice.

The aim of translational research is to convert scientific theories and laboratory discoveries into concrete medical applications, in order to improve the quality of medical and pharmaceutical care for patients. However, if translational research is to flourish, considerable resources are required to secure equipment and talent that cannot be systematically financed in the framework of standard budgets. Moreover, clinical studies require lengthy interactions with authorities and with patients and present a major hurdle for clinicians.

In order to have access to such innovations and to be able to improve patient care, we must eliminate obstacles and promote endeavors at the intersection of many different disciplines.

The ISREC Foundation is proud to be in a position to support efforts that are in line with its two core missions.

39
projects were evaluated



8
new projects were approved by the Foundation Council

including 6
collaborative **TANDEM** projects

In 2023, 7 million CHF were allocated to oncology research projects:

- Young scientists

  4 scholarships
  CHF 260 000.–

  3 professorships
  CHF 2 650 000.–

- Research projects

  15 oncology research projects
  CHF 2 120 000.–

- Collaborative TANDEM projects

  12 oncology research projects
  CHF 2 000 000.–

- Scientific conferences and symposiums

  30 scientific events
  CHF 100 000.–

Summary of funds allocated to projects over the past 15 years

- Young scientists

  Scholarships
  CHF 4 000 000.–

  Professorships
  CHF 28 900 000.–

- Research projects

  Oncology research projects
  CHF 57 200 000.–

- Collaborative TANDEM projects

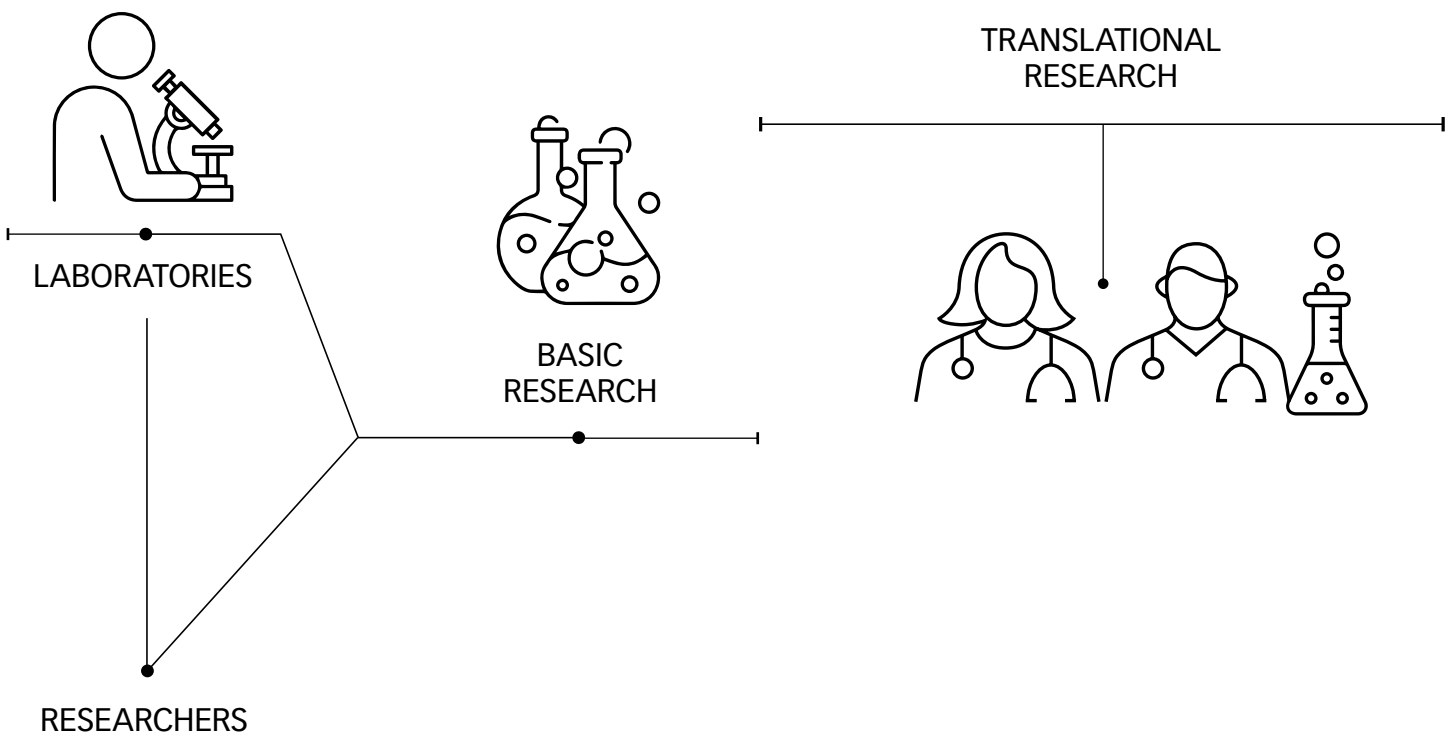
  Oncology research projects
  CHF 6 000 000.–

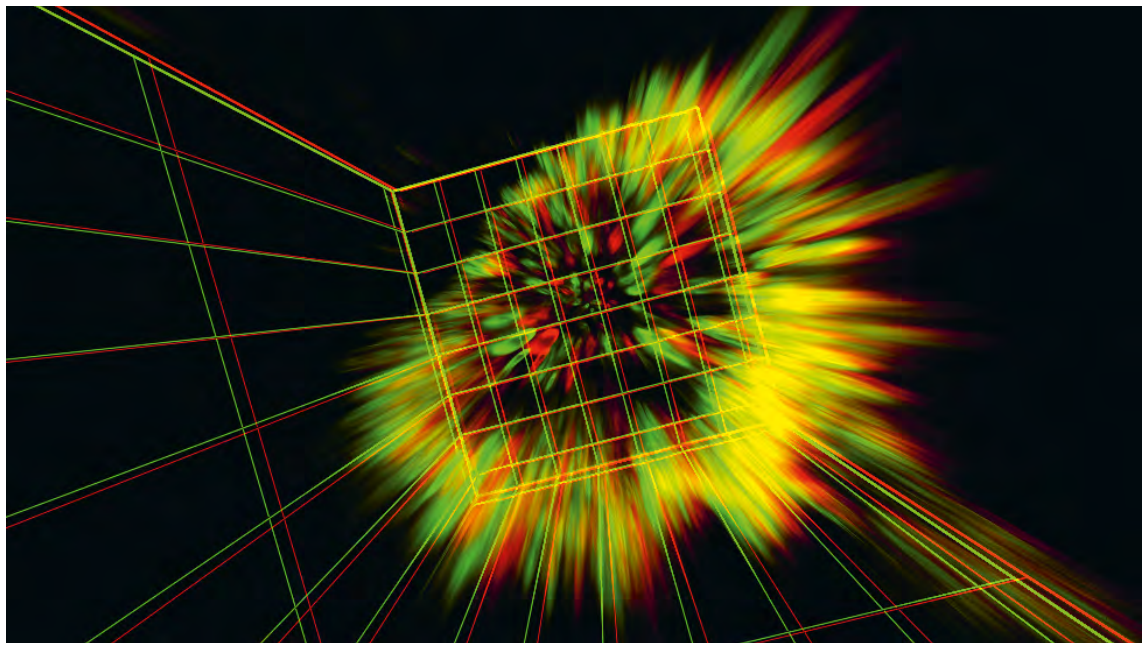
- Scientific conferences and symposiums

  Scientific events
  CHF 500 000.–

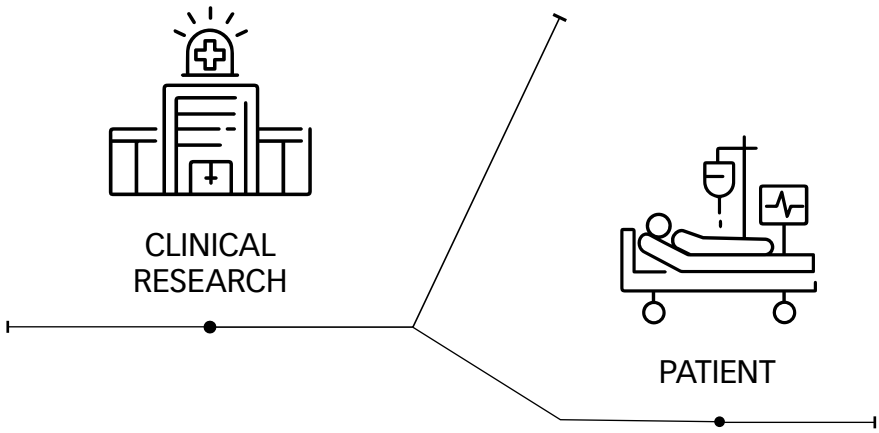
TRANSLATIONAL RESEARCH

By promoting collaborative research between clinicians and basic scientists, this discipline aims to enable patients to benefit as much as possible from new therapeutic discoveries.





Quantification of the infiltration of immune cells in an organoid: this confocal microscope image shows the projection analysis of an organoid used to quantify the infiltration of immune cells within its three-dimensional structure. This technique provides insights into the cellular interactions within the organoid, opening up new perspectives for the study of immune responses within tissues.



Prof. Nicolas Thomä

Paternot Chair for Interdisciplinary Cancer Research

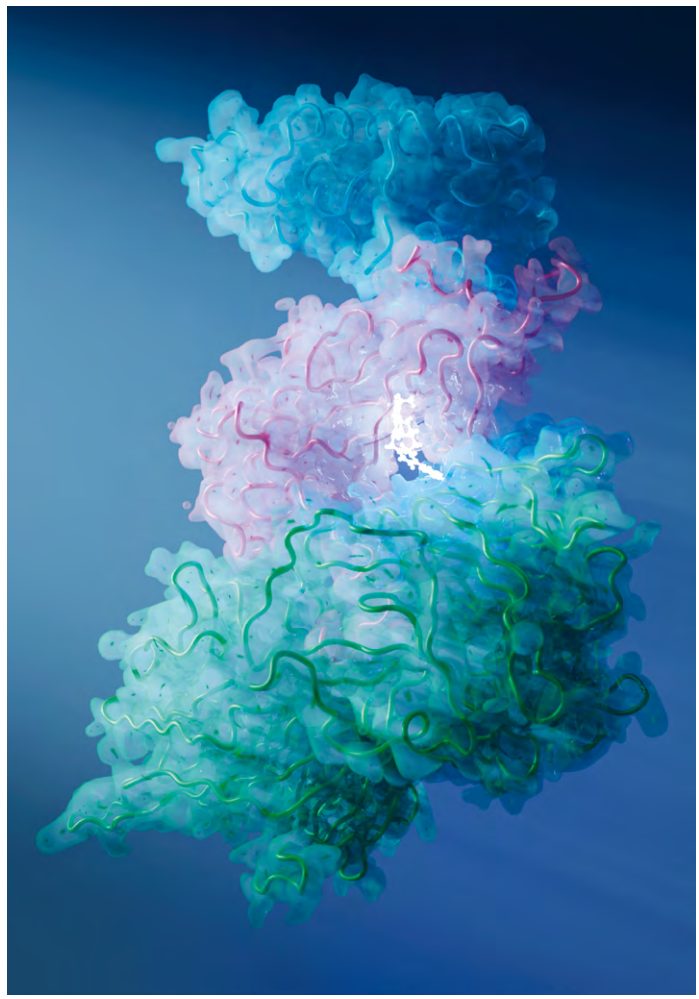
Professor Nicolas Thomä, holder of the Paternot Chair for interdisciplinary cancer research at EPFL, explains why the ISREC Foundation's donation is a game-changer.

Professor Nicolas Thomä was appointed full professor at the EPFL School of Life Sciences in Lausanne in 2023. He came from the Friedrich Miescher Institute for Biomedical Research in Basel, where he had been leading a world-class team of scientists in the fields of structural and chemical biology since 2006. In September 2023, Prof. Thomä took up his research position at the EPFL, as the head of the new Paternot Chair for interdisciplinary cancer research, financed by a donation of the ISREC Foundation amounting to 7.5 million CHF, spread over six academic years.

Prof. Thomä, a German citizen, is a chemical biologist and an expert in X-ray crystallography and cryogenic electron microscopy, two cutting-edge technologies which he uses to study the key protein assemblies involved in human diseases. He is responsible for groundbreaking discoveries regarding the key structures and molecular interactions involved in the targeted degradation of pathological proteins, thus paving the way for new approaches to drug discovery in cancer.

«The contribution of a private donation is vital», explains Nicolas Thomä. «It provides the support needed for an approach that breaks the mold and combines elements that do not necessarily go together.» In Prof. Thomä's research, the combination of structural biology and cancer drug development calls for «a certain hunger for innovation, which private donors can more easily support».

Nicolas Thomä goes a step further: «We need to think about how Lausanne, a relatively small town, can position itself on the world map in the fight against cancer. We are building tomorrow's impact on these diseases today, thanks to its niche position, to a combination of opportunities and talents that brings together computational sciences (with artificial intelligence), basic research and research in the field of molecular therapies, and thanks to the multidisciplinary and patient-oriented environment that is to be found at AGORA. In the same way that the pioneers, a century ago, had the insight to join forces to better understand cancer. It's obvious, but also revolutionary!»



Structure of DDB1 linked to CDK12-cyclin K engaged in CR8 (ID PDB: 6TD3).

FIAMMA PROJECT — A COLLABORATION BETWEEN TWO DONOR FOUNDATIONS

Jean-Philippe Rochat, President of the Jan Baron Mladota Foundation
Pierre Henchoz, President of the Jacqueline de Cérenville Foundation

The ISREC Foundation announced the payment, on July 1, 2023, of the first of five instalments of a donation amounting to 2.8 million CHF for the funding of the FIAMMA research project. PD Dr. Francesco Ceppi, senior physician in the pediatric hemato-oncology unit at the CHUV, and Prof. Caroline Arber, senior physician in the oncology department UNIL/CHUV (immuno-oncology and hematology wards) are collaborating closely to conduct this project. The aim of this pioneering endeavor is to develop a novel cellular immunotherapy for children and adults with acute myeloid leukemia (AML) in relapse after standard treatment.

«This model is an example for the future»

The lawyer Jean-Philippe Rochat and the banker Pierre Henchoz, presidents of two Lausanne-based foundations, explain how the support for the FIAMMA project, coordinated by the ISREC Foundation, came into being. They are convinced that their approach will inspire other foundations to support similar enterprises. This project, led by two CHUV professors, aims to fight childhood leukemia through immunotherapy.

Pierre Henchoz is a well-known personality in the canton of Vaud : after his return from New York in the 1990s, he was a very active private banker in the Lausanne area, but also a philanthropist and a coordinator of major projects in the medical field (notably for the Fondation Asile des Aveugles). He is president of the Jacqueline de Cérenville Foundation, and he and the lawyer Jean-Philippe Rochat, another respected personality in Lausanne, are members of this family foundation's board. The purpose of this foundation is to « disinterestedly devote itself to charity, education, training, health, teaching and any other undertaking of public utility ». Jean-Philippe Rochat is also the president of another Lausanne-based institution, the Jan Baron Mladota Foundation, the purpose of which is « to promote and support any humanitarian, cultural or scientific activities it deems useful, inter alia in the field of health, in particular the fight against cancer (…) ».

The two friends are at the heart of an innovative initiative centered around the ISREC Foundation : the goal is to pool the resources of small and medium-sized foundations, backed by an independent scientific structure and the experience of a specialized foundation, in order to maximize the effectiveness of the committed funds. Jean-Philippe Rochat and Pierre Henchoz explain how the project came into being and why it should be followed by others.

How and when did the plan arise to participate in joint funding, coordinated by the ISREC Foundation ?

The FIAMMA project began as an independent initiative of the ISREC Foundation. It stemmed from the observation made by each of us that collaborations between small and medium-sized foundations in the Lake of Geneva area are insufficient. Our philanthropic experience thus led us to a first conclusion: the pooling of financial resources from foundations that have neither the size nor the means to support large scientific projects creates genuine leverage and support for major projects that none of the small or medium-sized foundations could carry on their own.

The first challenge was to find a common denominator between the goals of the Jan Baron Mladota and the Jacqueline de Cérenville Foundations. We discovered it in the areas of health and children, and thus decided to focus on supporting research in the field of childhood diseases.

We then moved on to the next phase, in which we needed to find a project that was suitable in terms of topic, characteristics and size. That is how, through professors and connections we had, we spontaneously came into contact with Prof. Caroline Arber, who introduced us to the FIAMMA project.

The project was subsequently presented to our respective Foundation Boards, and it was then refined and a figure was put on costs. This enabled us to obtain the agreement of our Foundations.

The ISREC Foundation was called upon in the final phase : having identified the project we wanted to back, we contacted the Foundation to obtain confirmation that the project was scientifically valid. We also inquired about the possibility of an annual monitoring, allowing our Board members, who have no scientific experience in this particular field, to ensure that the development of the project meets the predefined milestones.

It was only at this point that the ISREC Foundation stepped in, and at our request also agreed to contribute a minor part of the funds, enabling us to settle the financial aspect of the project.

Why cooperate with the ISREC Foundation ?

Thanks to the ISREC Foundation's scientific expertise and its reputation, we were able to validate the quality of the project. The Foundation also guarantees annual monitoring, which enables our Boards to assume responsibility, both in terms of proper funds allocation and proper management of the project itself. This initial experience shows us that in future the ISREC Foundation could also help other foundations launch quality projects. We both realize that at the present time there is not so much a lack of funds in the Lake of Geneva area, as a lack of good projects that are accessible to institutions such as ours, i.e. foundations that do not have a scientific board or the contacts required to implement such projects. The ISREC Foundation must therefore be in a position to offer these foundations the opportunity to implement high quality scientific projects.

What aspect of the FIAMMA project particularly appealed to you?

We were especially impressed by two key elements of the endeavor:

a) Firstly, this project addresses the urgent need for better solutions to combat acute myeloid leukemia, a disease that affects children. The intensity of this disease and the number of cases are not sufficient factors to preferentially mobilize research funds.

b) Secondly, the innovative nature of this project, based on cell immunotherapy, attracted us. This approach has its risks, but taking risks opens up possibilities and opportunities for the future.

How will you keep abreast of the developments in the project?

Our Boards are regularly involved in the monitoring of this project, and beyond the launch meetings with the initiators, our two Boards plan to hold yearly meetings with the scientists, in order to assess the progress and the proper conduct of the research. The annual report on the scientific monitoring, provided by the ISREC Foundation, is also an essential element we can rely on.

What are the benefits of this cooperation for your foundations?

The collaboration between our two foundations makes it possible to support a project that neither of our institutions could have supported alone, without overly exposing ourselves to the inevitable risks associated with scientific research. What's more, the credibility and the scientific backing provided by the ISREC Foundation enable us to fill in any gaps in scientific expertise that our Foundation Boards may have.

Can this model be used for other projects? Have you received any requests?

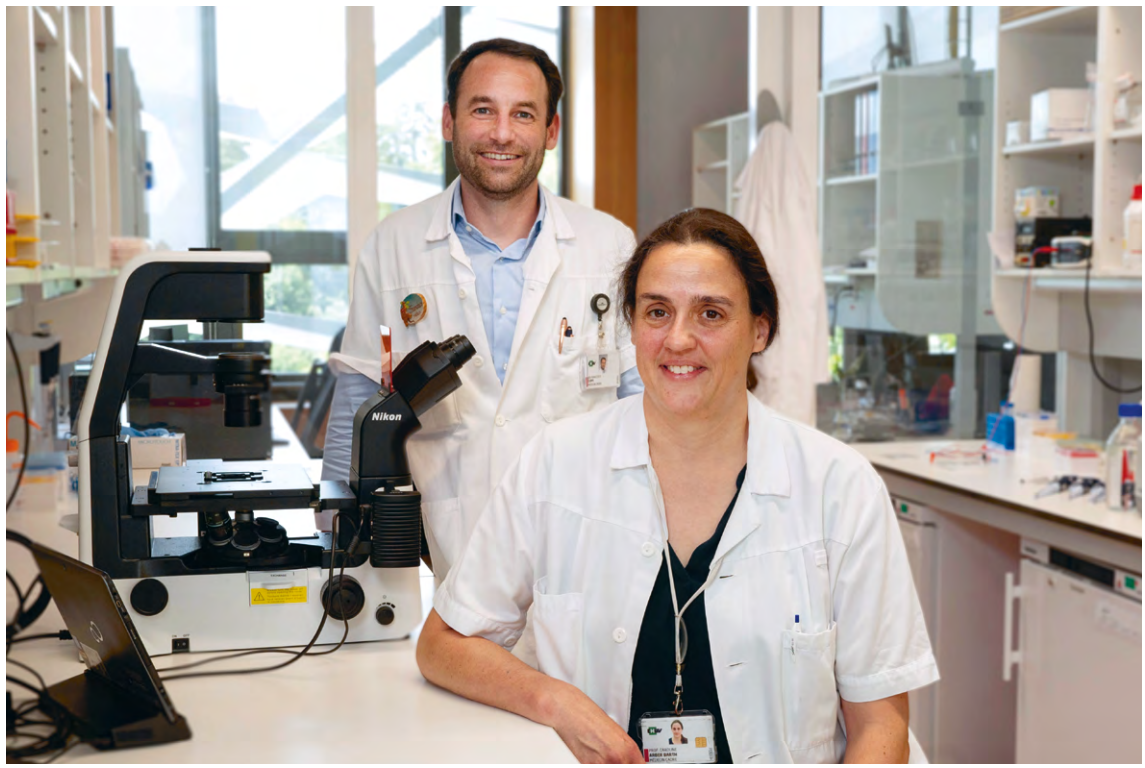
The FIAMMA project is the result of a spontaneous initiative taken by our two foundations, and to date neither has been approached for similar collaborations. It is therefore a highly innovative strategy, all the more so because it comes from the «roots». And we are convinced that whatever the outcome of the project, this model will serve as an example for future endeavors.

Based on this experience, the ISREC Foundation has already called upon several foundations to inquire about their position and their expectations. First meetings have shown that the ISREC Foundation could coordinate major projects and also encourage foundations in the Lake of Geneva area to jointly participate in large-scale projects. To this end, an important step forward would be to systematically send project topics to foundations, offering them the possibility to find out about the type of projects, project costs and possible partners.

The scientists' perspective

The two clinician scientists greatly appreciate the private support their project is receiving. «The most difficult part of a clinical trial is finding the financial support required for the so-called phase 1, the very first stage of the project,» explains Dr. Francesco Ceppi. «Unlike the United States, where the National Cancer Institute (NCI) provides centralized support for clinical studies, Switzerland has no such instrument. In the USA, a phase 1 clinical study with 12 to 14 patients can expect 5 to 6 million dollars from the NCI. The situation is different in Switzerland, and this makes the FIAMMA project so interesting.»

The practicing physician explains that the desire of two Lausanne-based foundations to commit to a pediatric oncology project that can be supervised from A to Z was the incentive for this enterprise. «Prof. Arber, whose lab set up the therapy, and I had discussions with the members of both Foundation Boards, and then developed a strategy with the ISREC Foundation. It is amazing to be able to count on the expert eye provided by the ISREC Foundation's Scientific Board. We plan to meet with the foundations at least once a year.»



Dr. Francesco Ceppi and Prof. Caroline Arber, principal investigators of the FIAMMA project.

Following Swissmedic's regulatory recommendations on «Good Manufacturing Practices», the FIAMMA project has gone into the preparatory phase, ordering the viruses and establishing all the parameters for cell production. «This is a very lengthy process, involving lawyers, monitoring at every stage, and many people working at a very small percentage on very specific tasks,» explains Dr. Francesco Ceppi. «But the CHUV's Oncology Department was designed to meet these requirements, and our work is well worth the effort: projects such as this one allow us to treat patients here, rather than having to send them abroad.»

LAUREATE OF THE PRIX DU RAYONNEMENT
OF THE SOCIÉTÉ ACADÉMIQUE VAUDOISE,

Prof. Mikaël Pittet

«Our understanding of tumors has greatly progressed»

Holder of the ISREC Foundation Chair at the University of Geneva and laureate of the Prix du Rayonnement of the Société Académique Vaudoise, Prof. Pittet, a Lausanne native, explains the latest advances achieved in his lab and the Foundation's decisive contribution to his work.

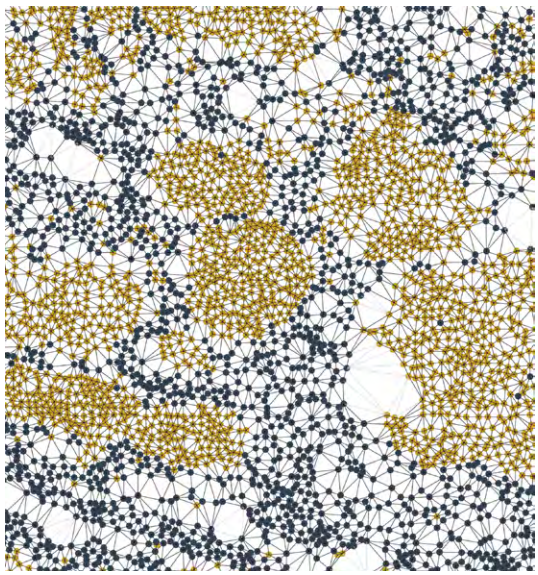
«It may be that we only need a few parameters to identify tumors, and that these parameters are not located within the cancer cells!» The lively flow of Mikaël Pittet's speech accelerates, his eyes are lit up, and his body language conveys added intensity. He is very obviously passionate about cancer research. Under the auspices of the ISREC Foundation's immuno-oncology chair in the UNIGE Faculty of Medicine (Translational Research Centre in Oncohaematology (CRTOH) and Pathology Department), Prof. Pittet heads a laboratory at AGORA. His latest research has delivered great insights in 2023, progress which in turn will open promising prospects for cancer patients.

«Until now, we have thought of a tumor as a chaotic mass that dictates the course of the disease, including the body's dysfunction. However, we now realize that a tumor is a coherent and organized entity», explains Mikaël Pittet. «The key elements that allow us to identify the unique characteristics of a tumor are not necessarily very numerous, and not perforce to be found in the cancer cells themselves. Rather, they are located in apparently healthy cells that are usurped to form part of the tumor's ecosystem.»

This work is crucial and heralds a novel approach: by understanding just a few extra-tumoral elements, as opposed to all the components of the tumor, it will be possible to determine the evolution of the disease and the best therapies to fight it. Better yet, the determinant elements in the tumor microenvironment recur in different types of cancer. Suddenly, the hitherto seemingly infinite range of variables is reduced. «The analysis of tumor cells from large numbers of patients

has not led to the expected identification of common and repetitive patterns. Rather, the study of non-tumor components, the tumor microenvironment, allows us to do so. These help us understand the interactions between the disease and the immune system.»

From now on, and for years to come, artificial intelligence will make it possible to analyze the huge volume of collected data, and to understand the spatial organization of the cells in the tumor ecosystem and their communication system. «We will investigate how best to exploit this data for the benefit of patients.»



Cellular networks within a pulmonary adenocarcinoma.

«Trust breeds efficiency»

And this is where AGORA really comes into its own. «This is a unique facility, and I weigh my words carefully. The day-to-day cooperation between multi-disciplinary scientists, clinicians and bioinformaticians from different institutions, but all working in the same place, generates momentum at all levels. This is what captivated me when I was approached while in Boston.» Prof. Pittet, a Lausanne native, had planned to spend just three years at Harvard at the beginning of his career, but ended up working 17 years in Benjamin Franklin's hometown. «I still had ties to Lausanne and I talked to many people who were able to convince me to accept the position. Catherine Labouchère, then president of the ISREC Foundation, also helped me make my decision. The AGORA project is remarkable: I received funding through a chair at the University of Geneva to work in the AGORA, a building that facilitates continuous exchange among scientists and clinicians from the entire Lake of Geneva area.»

Mikaël Pittet insists that this trust, the shared commitment and the translational character of the research performed at the AGORA are what makes this project of the ISREC Foundation so unique. «Unlike conventional funding, dictated by a predetermined plan, the focus here is on flexibility. We are at liberty to rapidly adapt our research to the discoveries we make in the lab. The trust placed in us by the ISREC Foundation enables a working efficiency that I have never before experienced. Also, the AGORA building puts a smile on our face every morning. A truly extraordinary ecosystem.» A research ecosystem designed to thwart the tumor ecosystem!

Created in 2014, the Prix du Rayonnement Académique of the Société Académique Vaudoise honors individuals who significantly contribute to the national and international reputation of the University of Lausanne and the academic setting in the Lake of Geneva area.

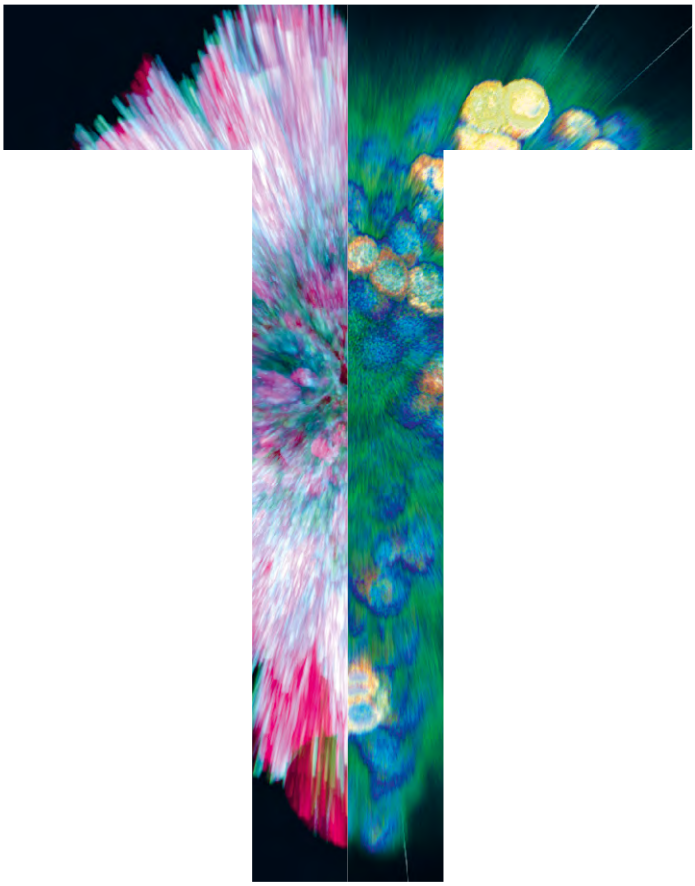
«Two minds are better than one!» is an aphorism that seems to be reinforced by the resounding success of the TANDEM grant program initiated in 2021 by the ISREC Foundation.

Prof. Susan M. Gasser

Director

TANDEM — Transformational Cooperations in Translational Cancer Research

Focused on uniting clinicians and basic scientists in the common goal of establishing new and more effective cancer treatments, the ISREC Foundation makes an annual call for grant applications outlining cooperative projects involving a basic scientist and an active oncologist or pathologist. With over 100 applications received, the interest in this program has been remarkable. After rigorous international review, six projects were chosen in 2022 and in 2023, and six or seven more will be selected in 2024.



The impact of scientific research on cancer therapy has been enormous over the past 20 years. Advances range from the establishment of elaborate molecular diagnostics for a better use of targeted inhibitors to improvements in radiotherapies. There are also highly specific inhibitors available now, that block oncogenes amplified in select tumor types. Still, cancer cases increase, and innumerable challenges remain.

One of the more recent advances with broad clinical impact was the discovery of the immune-checkpoint pathway that blocks a person's own immune response to cancer. While immune-checkpoint inhibitors (ICI) are now readily available, both clinicians and researchers face the challenge of understanding which tumors allow an immune response against cancer and which do not, and why. It requires a highly detailed characterization of immune cells and their position within the tumor, something that only the most advanced imaging technologies coupled with machine learning can resolve. While the ability to program immune cells to recognize our tumors was a game-changer, again we do not understand why many tumors do not respond. These are just a few of the topics that require the creativity and innovation that stems from the interface of two mind-sets – that of the clinician who is close to the patients, and that of the researcher who understands the language of tissues and cells.

The interdisciplinary TANDEM teams funded by the ISREC Foundation have triggered collaborations across all of Switzerland, including a handful of the scientists based in the AGORA cancer research center. The AGORA was created to unite researchers from different institutions together in multidisciplinary cancer research, and TANDEM funding helps support those projects co-supervised by a clinician and a scientist/engineer. We hope for even faster «bench to bedside» innovation and even more «bedside to bench» communication in the years ahead, as young scientists and clinicians learn to work shoulder to shoulder.

Communication is key to long-term success in our struggle to improve the outcome for cancer patients, and with this in mind, we communicate here the efforts of our lucky grantees.

CONGRATULATIONS TO OUR TANDEM 2023 LAUREATES

ANALYZING THE ROLE OF THE TUMOR MICROENVIRONMENT IN PLATINUM DRUG-RESISTANT OVARIAN CANCER.

Dr. **INTIDHAR LABIDI-GALY**, HUG — Dr. **SVEN ROTTENBERG**, UNIBE

Ovarian Cancer

High grade serous ovarian carcinoma (HGSOC) is the deadliest gynecological cancer, with a median survival rate of 3 years. Standard treatment involves surgery followed by chemotherapy, typically using platinum and taxane agents. While chemotherapy frequently works well initially to shrink tumors, most women later develop platinum-resistant tumors, that are often fatal. This TANDEM project aims to understand the underlying factor of this resistance, in order to improve immunotherapeutic approaches and develop more effective treatments.

Treatment of HGSOC is a major clinical hurdle, not only because of the commonly developed resistance to chemotherapy, but also due to the fact that it does not respond to recently discovered therapies such as immune checkpoint and targeted T-cell therapies. The reasons for its chemotherapy resistance and insensitivity to immune checkpoint therapy remain unclear.

In this project, the team uses a unique set of patient-derived samples that were collected after resistance had developed and applies cutting-edge molecular technologies to analyze the spatial distribution of cellular and subcellular compartments. Through this, they aim to understand the disease heterogeneity and pinpoint changes that result in resistance.

Preliminary data suggest that platinum-resistant HGSOC is characterized by the accumulation of immune cells called tumor-associated macrophages. These cells are the most common cells in the tumor microenvironment and play a vital role in cancer survival and progression. Leveraging imaging and sequencing tools, the team will identify cell types responsible for resistance, and will gain insight into the spatial distribution and status of the tumor associated macrophages. In this way, they hope to decipher the role these macrophages play in the platinum resistance of HGSOC. Ultimately, these results may lead to an improvement of immunotherapeutic approaches, specifically in the case of platinum-resistant HGSOC.

IDENTIFICATION OF NEW TARGETS TO TREAT PROSTATE CANCERS THAT ARE NON-RESPONSIVE TO AVAILABLE TREATMENTS.

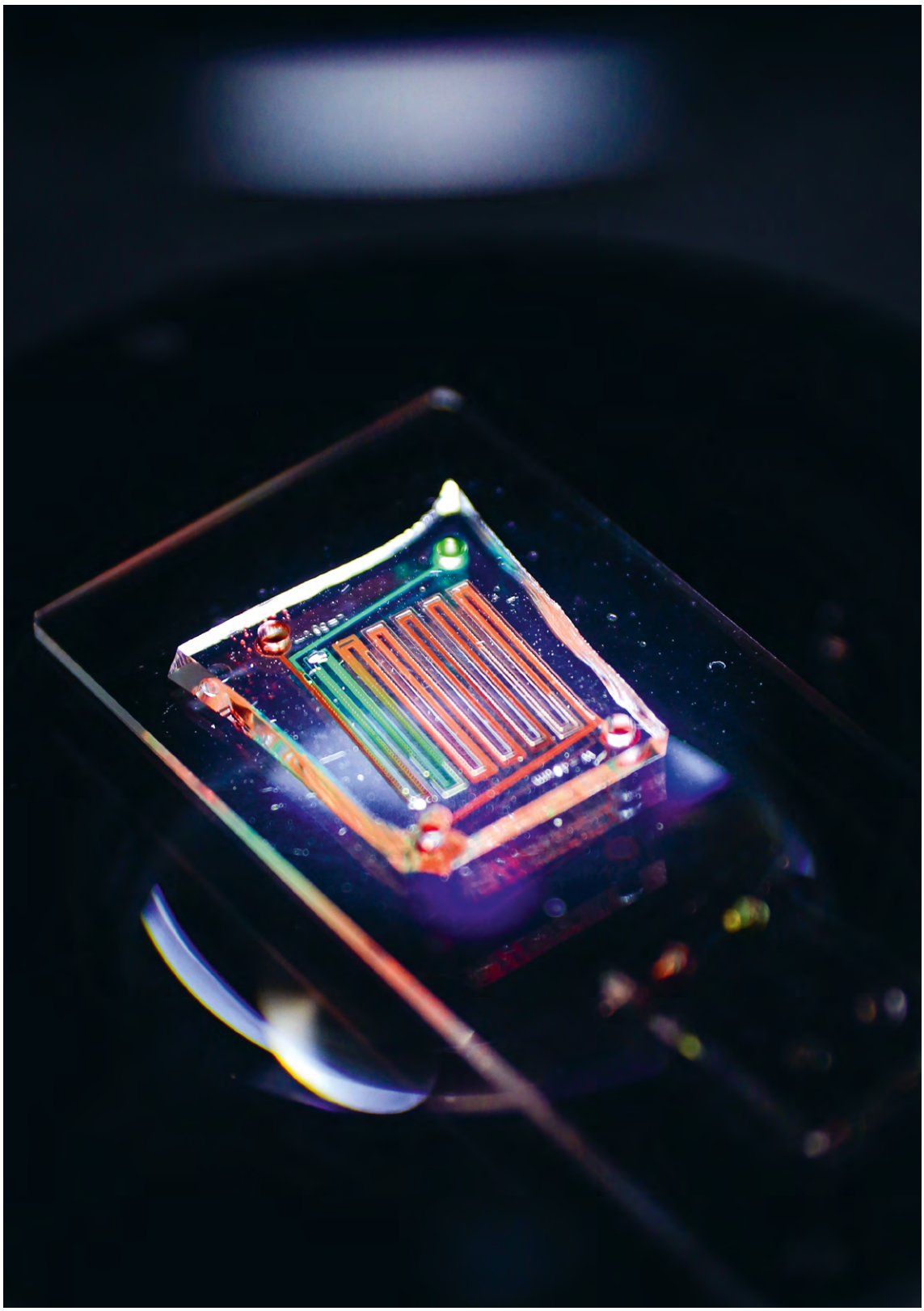
Prof. **MARK RUBIN**, UNIBE — Dr. **SILKE GILLESSEN SOMMER**, IOSI

Prostate Cancer

Prostate cancer is the most common cancer among men, affecting 1 in 8, and is a leading cause of cancer-linked mortality and morbidity. Even though localized prostate cancer is highly treatable with surgery, radiation therapy, or active surveillance, survival rates are poor for men with metastatic disease. Existing hormonal therapies in general induce responses initially, but in the majority of cases, their initial effectiveness fades and eventually fails, leading to metastatic castration-resistant prostate cancer (mCRPC).

In addition to hormonal therapy, one of the most promising current treatment regimes for mCRPC uses radioactive compounds linked to antibodies targeting a cell surface protein on mCRPC cancer cells. Such targeted markers are unique to tumor cells, and the binding of high-energy radioactivity, which acts over a small distance, kills these cells efficiently. Unfortunately, up to 30% of patients fail to express the proteins necessary for the radioactive antibody conjugate to recognize the tumor cells and are thus not eligible for this therapy. In addition, only 50% of the patients that express the appropriate marker protein respond well to the treatment.

The main goal of this project is to nominate new therapeutic targets for patients with mCRPC who are not eligible or resistant to this treatment by identifying new surface proteins unique to prostate cancer. This is a laborious process as many tumors need to be sampled and tested to find proteins uniquely expressed on the surface of the cancer cells and not on normal cells. Such probes will ensure that only the tumor cells are being targeted by the radioactive substance during the treatment. This is particularly important as the probe gets introduced into the bloodstream and not injected locally. Not only would this provide treatment for men who at the moment are not eligible for a theranostic treatment, but it could also lead to the further development of other therapy modalities for these patients, using targeted therapies such as CAR-T.



Fascinating view of the microchannels on a microfluidic chip. This chip, no larger than a coin, features microscopic channels through which fluids can circulate in a highly precise manner. In the search for cancer therapies, this technology makes it possible to perform high throughput screening of cancerous cells encased in micro-droplets, opening up countless new opportunities for biomedical research.

INVESTIGATING THE CONNECTION BETWEEN CIRCADIAN SYSTEM AND LUNG TUMOR GENERATION TO PERSONALIZE TIME SCHEDULES FOR CHEMO-IMMUNOTHERAPY.

Prof. **CHARNA DIBNER**, UNIGE — Prof. **ALFREDO ADDEO**, HUG — Dr. **WOLFRAM KARENOVICS**, HUG

Lung Cancer

Lung cancer is one of the most prevalent causes of cancer-related deaths world-wide, largely because most patients have already developed metastases at the time of diagnosis. Besides a need for earlier diagnosis, there is a fundamental lack of effective therapies for lung cancer. As a result, lung cancer has a poor prognosis and low survival rate. In this collaborative TANDEM project, a basic scientist, a surgeon, and an oncologists aim to innovate lung cancer therapy by making use of the body's internal «circadian» clock to maximize therapeutic impact.

The circadian system evolved in light-sensitive organisms to serve as an intrinsic biological clock with oscillation periods close to 24 hours, in line with geophysical time. It is the molecular time-keeping system operative in most of the cells in the body which drives our physiological activities. Additionally, linked to this is a cell division clock, which drives both normal growth and tumor development. Upon malignant transformation, that is the generation of cancer cells from normal cells, both of the above-mentioned cell-control systems undergo massive changes, resulting in tumor formation.

This project proposes to optimize chronotherapy for lung cancer. Chronotherapy means that the «treatment schedule» is timed in order to align the introduction of medicine with the patient's natural circadian rhythms. Preliminary data show that for certain types of cancer, the coordination of the administration of anti-tumor drugs at certain times of day improves the effectiveness of chemotherapy and reduces toxicity. Inspired by this emerging potential, the TANDEM team will study the chronobiology of lung cancer, to see if the coordination of therapy with the circadian cycle can improve the outcome for lung cancer patients.

The project has two goals. First, they will refine the diagnostics of lung cancer, and second, they will develop personalized time schedules for the administration of chemo-immunotherapy. This will be achieved by analyzing the interaction of the circadian clock with lung cancer progression, and secondly, by analyzing the reaction of the patients to therapy administered at different daytimes. This should enable an optimization of lung cancer therapy and improve personalized care.

CONGRATULATIONS TO OUR TANDEM 2023 LAUREATES

USING TISSUE DERIVED FROM THE PATIENT TO PREDICT EFFECTIVENESS OF DIFFERENT TREATMENTS TO FIND THE BEST ONE FOR EACH PATIENT.

Prof. **ELISA ORICCHIO**, EPFL — Dr. **ANNE CAIROLI**, CHUV

Lymphatic Cancer Organoids

The use of molecular and genetic approaches to personalize medical treatments is well on its way to transform cancer therapy. This is because personalized medicine can generate customized therapies and avoid the use of ineffective, and often debilitating, molecules. Currently, cancer treatment is based on tumor stage, mutation profile, and clinical history, while crucial factors such as the tumor heterogeneity and its microenvironment are rarely taken into account. These latter factors, however, are often the most variable and can influence therapy response. Thus, there is an urgent need to incorporate patient-specific data into decisions on the choice of treatment. This project aims to develop an automated culture system of patient-derived tumor explants. These tumor avatars are unique to individual patients and provide a platform to test sensitivity of each tumor to various treatments. This information could be used to anticipate clinical response, and therefore could guide the hemato-oncologist in selecting the most effective molecule for each patient. In this project the team works with patients affected by non-Hodgkin lymphoma, a group of cancers originating from mature lymphocytes (type of white blood cell).

The team has a number of promising preliminary results. First, the basic research team has developed a method to culture small fragments of the tumor tissue taken from the patient in such a way that key features of the tissue including the cellular composition and architecture are preserved. These fragments, called lymphomoids, can subsequently be used to test the sensitivity to various therapies. Ultimately, the goal is to optimize the lymphomoid technology as a clinical tool to find the most suitable treatment for each lymphoma patient. The team will use cutting-edge image analysis of spatial features to understand the effect of the treatment on both the lymphoma and the neighboring cells forming the tumor microenvironment. In addition to better tailoring existing treatment to specific patients, this technology can also be used to discover novel therapies.

Ineffective therapies are associated with potential toxicities and ultimately lead to the emergence of resistant diseases that are more difficult to treat. Therefore, implementing a technology that could directly identify these inefficient treatments in routine clinical practice would be ground breaking and could significantly improve patients' prognosis and their quality of life.

ANALYZING TERTIARY LYMPHOID STRUCTURES AS PART OF THE BRAIN TUMOR ENVIRONMENT TO DEVELOP IMMUNE THERAPIES AGAINST GLIOBLASTOMA.

Prof. **DENIS MIGLIORINI**, UNIGE — Dr. **GIOELE LA MANNO**, EPFL

Brain Tumors (Glioblastoma)

Glioblastoma (GBM) is the most common and malignant primary brain tumor in adults. The aggressive and invasive nature of the tumor and its heterogeneity often render it resistant to standard therapies, including chemotherapy, radiation and surgery, leading to a survival rate of less than two years. In this TANDEM collaboration, the team hopes to improve the outcome of GBM treatments by advancing their understanding of the interaction between this tumor and the cellular environment that surrounds it.

Tertiary lymphoid structures (TLS) are ectopic (misplaced) parts of the lymphatic system that develop in non-lymphoid tissues, and which form, importantly, at sites of chronic inflammation such as tumors. Past work has shown that TLS are highly relevant to the prognosis of cancer patients as they form part of the cellular environment that surrounds the tumor, the TME. A major focus of anti-cancer research has been on the macrophages found in TLS, as these white blood cells can either promote or hinder tumor growth, by helping remodel the tissues that surround and support the cancer.

The researchers aim to understand how tertiary lymphoid structures interact with the TME in glioblastoma patients, in order to eventually trigger an anti-tumor immune response in the TLS. Specifically, the project will characterize the repressive TME that blocks normal immune system function, with the ultimate goal of reprogramming the TLS and combining it with CAR-T cell treatment, an advanced T-cell-specific immunotherapy in which T lymphocytes are programmed to recognize tumor cells.

Over the next three years, the team will apply cutting-edge technologies based on the *in vivo* imaging of gene expression in cells within normal and tumor-containing tissue sections, in order to identify and analyze the contents of the TLS. They aim to understand the intricate interactions of the lymphoid structures with the TME, which helps sustain both the tumor and the TLS. This new knowledge may serve to generate new avenues for therapy, namely the reprogramming of macrophage states in order to support the attack of programmed T cells (CAR-T) on the tumor. The extremely aggressive behavior of glioblastoma and its high mortality rate add urgency to their search for new therapies.

CONGRATULATIONS TO OUR TANDEM 2023 LAUREATES

DEVELOPMENT OF AN ENDOSCOPE TO BETTER DEFINE TUMOR MARGINS DURING SURGERY.

Prof. **CHRISTIAN SIMON**, CHUV — Prof. **CHRISTOPHE MOSER**, EPFL

Head and Neck Cancer Surgery

Neck and head cancers (HNC) are lethal and mutilating. With over 150 000 new cases diagnosed each year in Europe alone and 370 000 deaths world-wide, these cancers have a significant impact on the human population. The main issue with HNC is that they have characteristic infiltrative growth, which means that the disease can escape eradication by local surgery and spread. This TANDEM project aims to improve the technology used to make HNC surgery more efficient.

For more than 50% of the HNC patients the first-line treatment is surgery. During those interventions it is essential that the surgical margin (the «border» between the tumor tissue and healthy tissue) is negative for cancer cells. This requires the excision of the cancer such that even on the microscopic level no tumor cells are left behind. Residual disease can lead to local reoccurrence and death of the patient.

The routinely used surgical techniques have limited resolution and surgeons often have poor visibility of the extension of the tumor, which leads to diseased cells around the edge not being detected. So, even though the surgery is deemed successful, in about 20% of the patients, it is not. Consequently, such patients must undergo further treatments such as chemical and radiation therapy which are aggressive and seriously impact the patient's quality of life.

This collaboration between clinicians and engineers aims to use recently developed ultra-thin endoscopes – which are minimally invasive due to their small size (thin as a hair !) while still providing high resolution images – that will enable a more precise visualization of tumor cells *in situ*. Importantly, this technology will be implemented in real time during surgery to enable the surgeon to predict with much higher accuracy where the tumor tissue ends and the healthy tissue begins. Ultimately this will improve the reliability of diagnostics and the rate of success of HNC surgery for these cancer patients.

OTHER ONGOING TANDEM PROJECTS

Prof. **Giovanni Ciriello** (UNIL), and Dr. **Igor Letovanec** (CHUV) – **Lung Cancer (adenocarcinoma)**
Project aimed at understanding disease progression in lung cancer.

Prof. **Michele de Palma** (EPFL), and Dr. **Nahal Mansouri** (CHUV) – **Small Cell Lung Cancer**
Project aimed at expanding the knowledge on the potential of cancer vaccines.

Dr. **Virginie Hamel** (UNIGE), and Dr. **Benita Wolf** (CHUV) – **Microscopy in Translational Immuno-Oncology**
Project aimed at using new visualization technologies to further the understanding of CAR-T cell therapy.

Prof. **Camilla Jandus** (UNIGE), as well as Dr. **Francesco Ceppi** and Prof. **George Coukos** (CHUV) – **Pediatric Leukemia**
Highly translational project aimed at harnessing the tumoricidal activities of CD4+ T cells to optimize cancer immunotherapies. The project includes preclinical validation of TCR-engineered CD4 T cells and the setup of a phase 1 clinical trial for relapsed and refractory solid tumors in both adult and childhood cohorts.

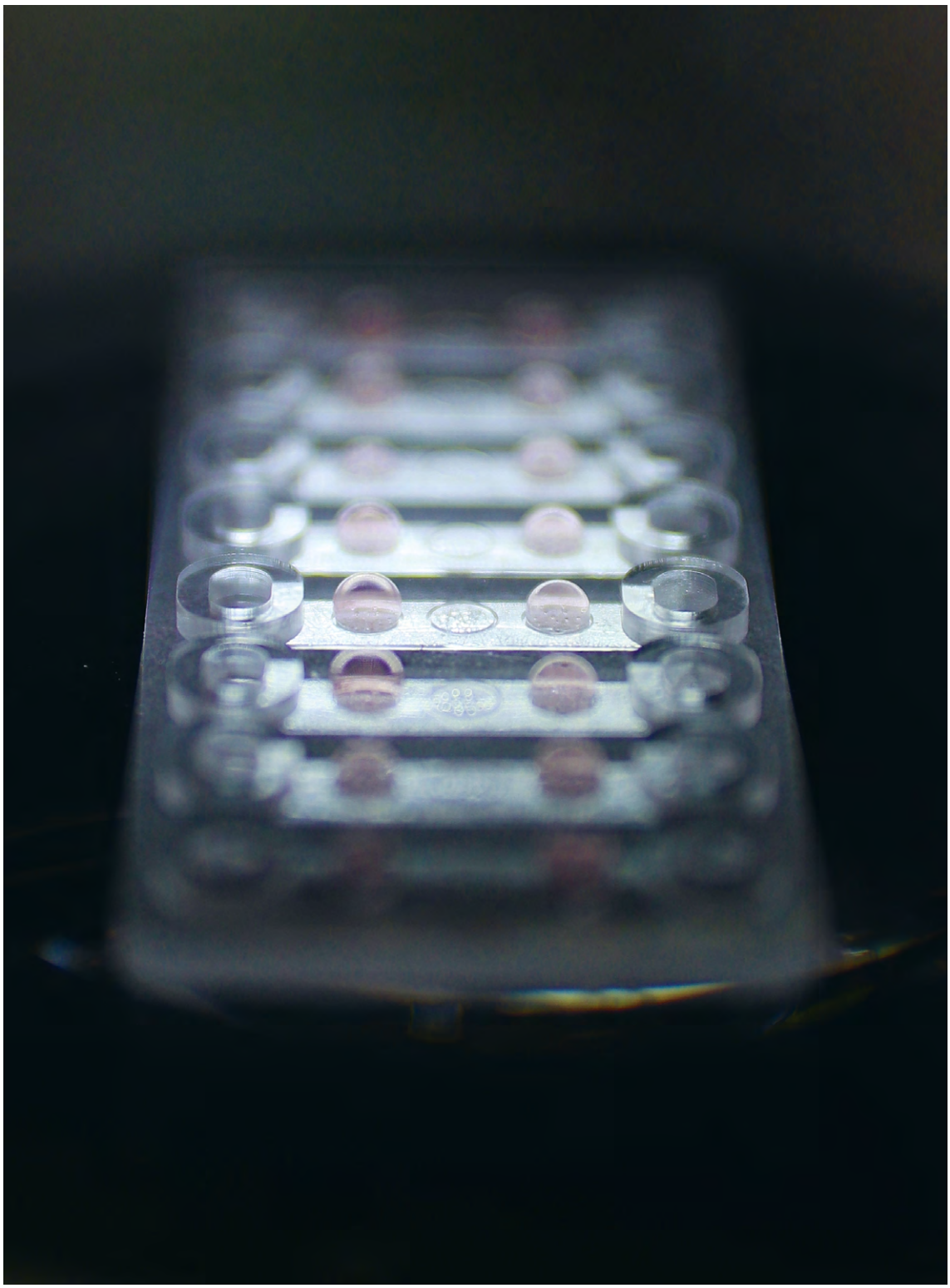
Prof. **Marianna Kruithof-de Julio** (UNIBE), and Dr. **Bernhard Kiss** (Inselspital) – **Bladder Cancer**
Project aimed at developing AI systems to assist in staging and treatment of bladder cancer patients.

Prof. Dr. **Michael Scharl** (USZ), and Prof. Dr. **Isabelle Arnold Wallén** (UZH) – **Colorectal Cancer**
Project aimed at developing a new therapy for patients with resistant colorectal cancer.

The Scientific Board of the ISREC Foundation vouches for the development and scientific monitoring of these projects. Supervision and financial management are ensured by our administrative and financial management office.

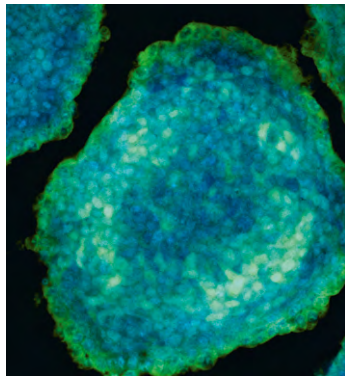
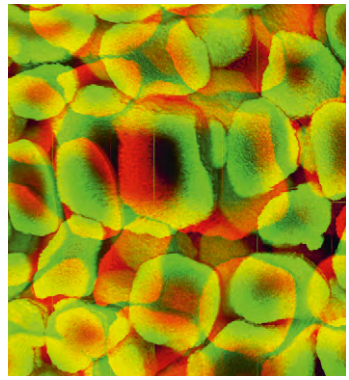
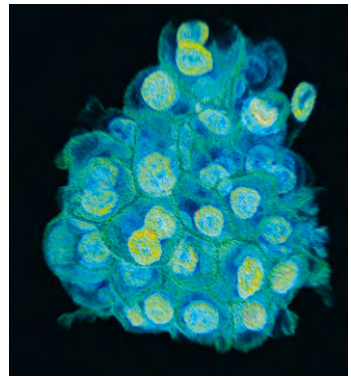
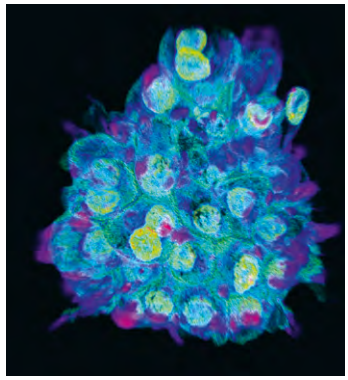
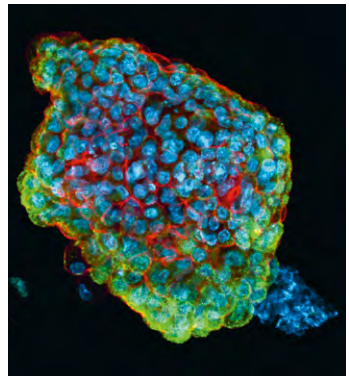
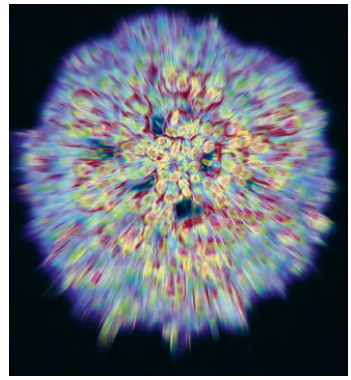
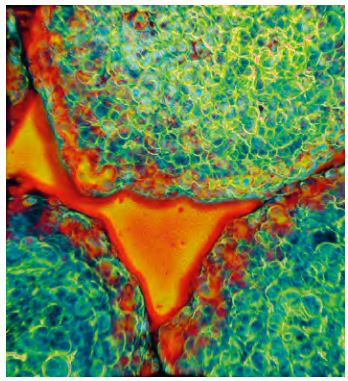
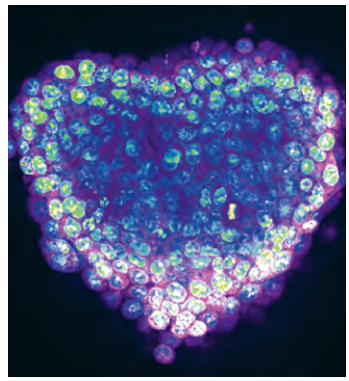
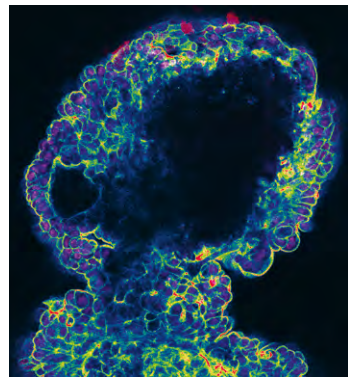
Information on TANDEM projects

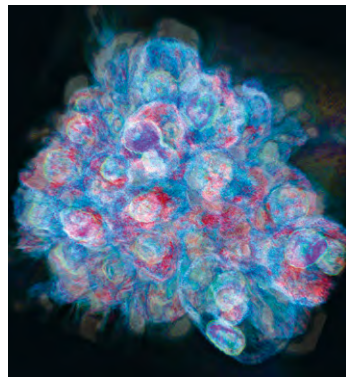
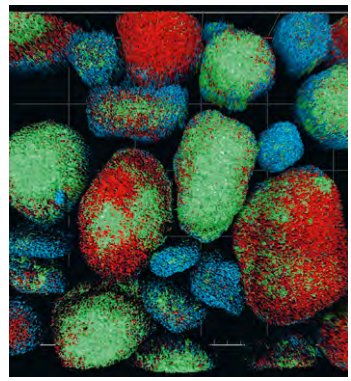
AGORA
PÔLE DE RECHERCHE
SUR LE CANCER

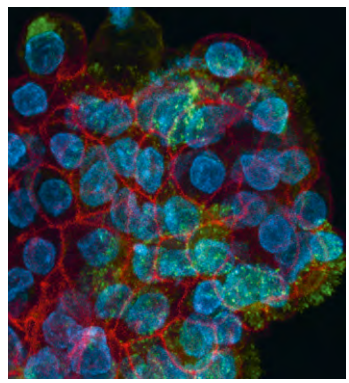
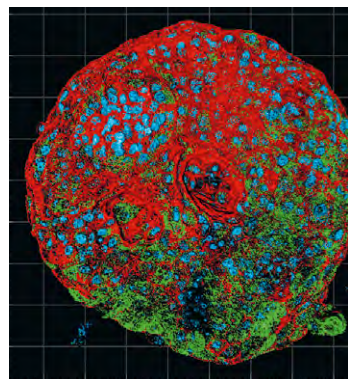


Development of a microfluidic chip for the culture of biopsy explants. This microfluidic chip, created using a precision 3D printer, is designed to improve the viability of cultured biopsy explants. To ensure a physiologically adequate environment, the explants are carefully wrapped in a suitable biomaterial. Thanks to a capillary system, the cells receive a continuous supply of culture medium, ensuring their hydration and survival. This innovation is an invaluable tool in the study of tissues and the development of novel therapies, and thus opens up new perspectives in biomedical research.

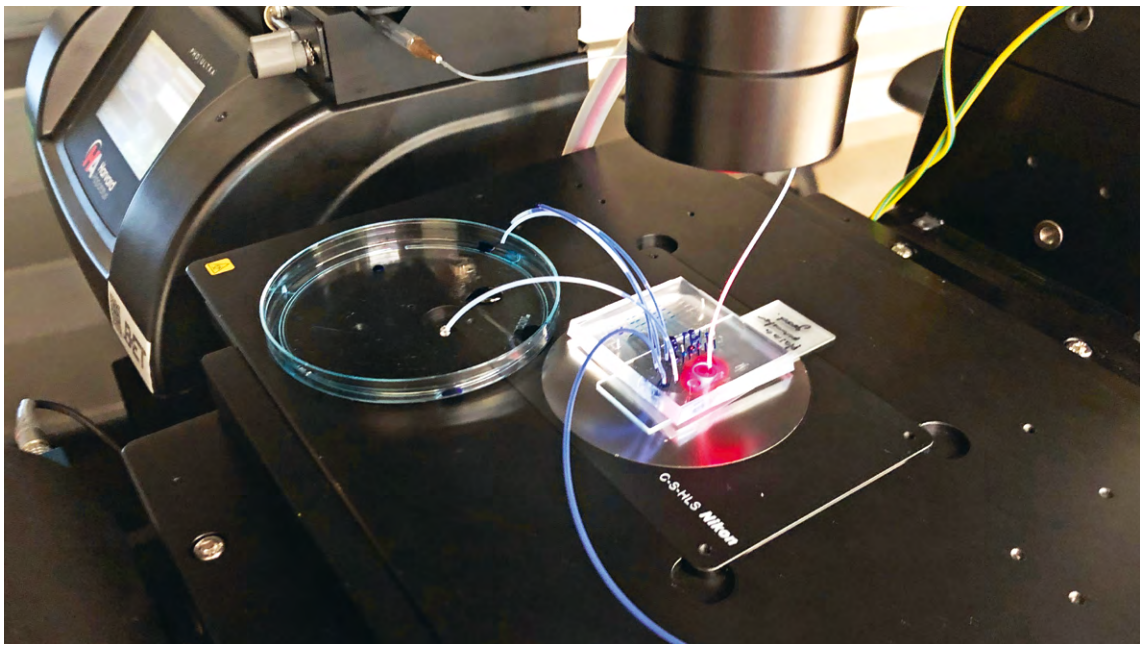
Page 27 : Images from the BET technology platform located within AGORA.

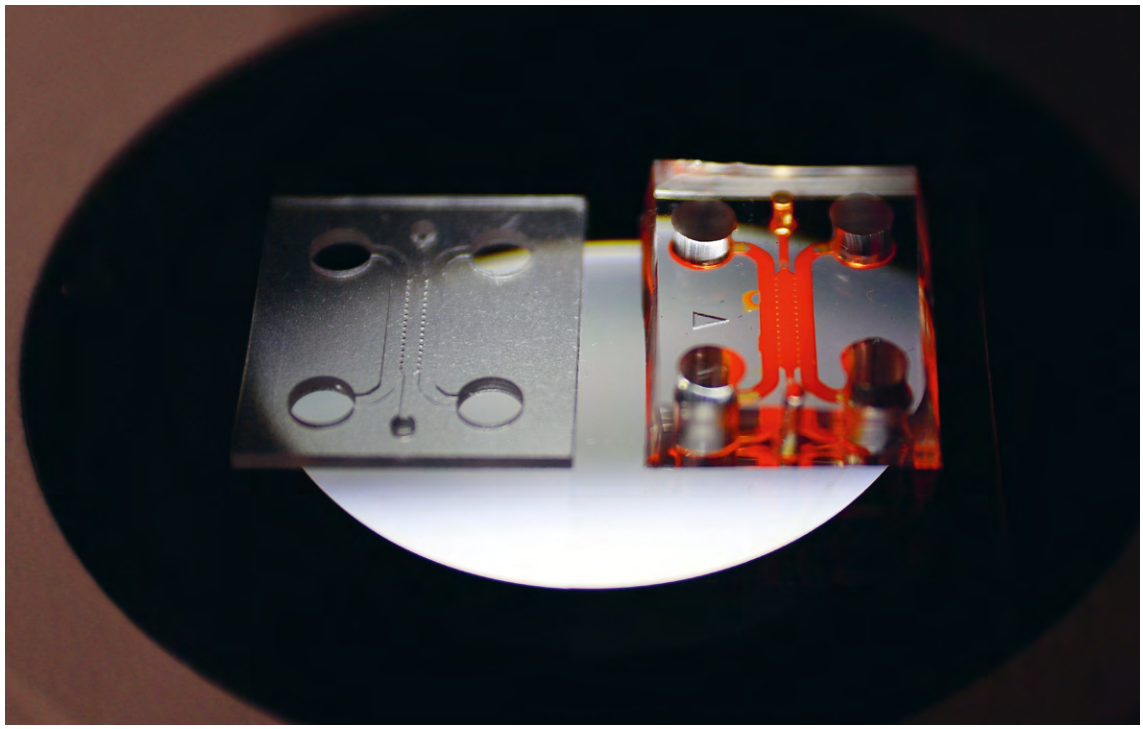



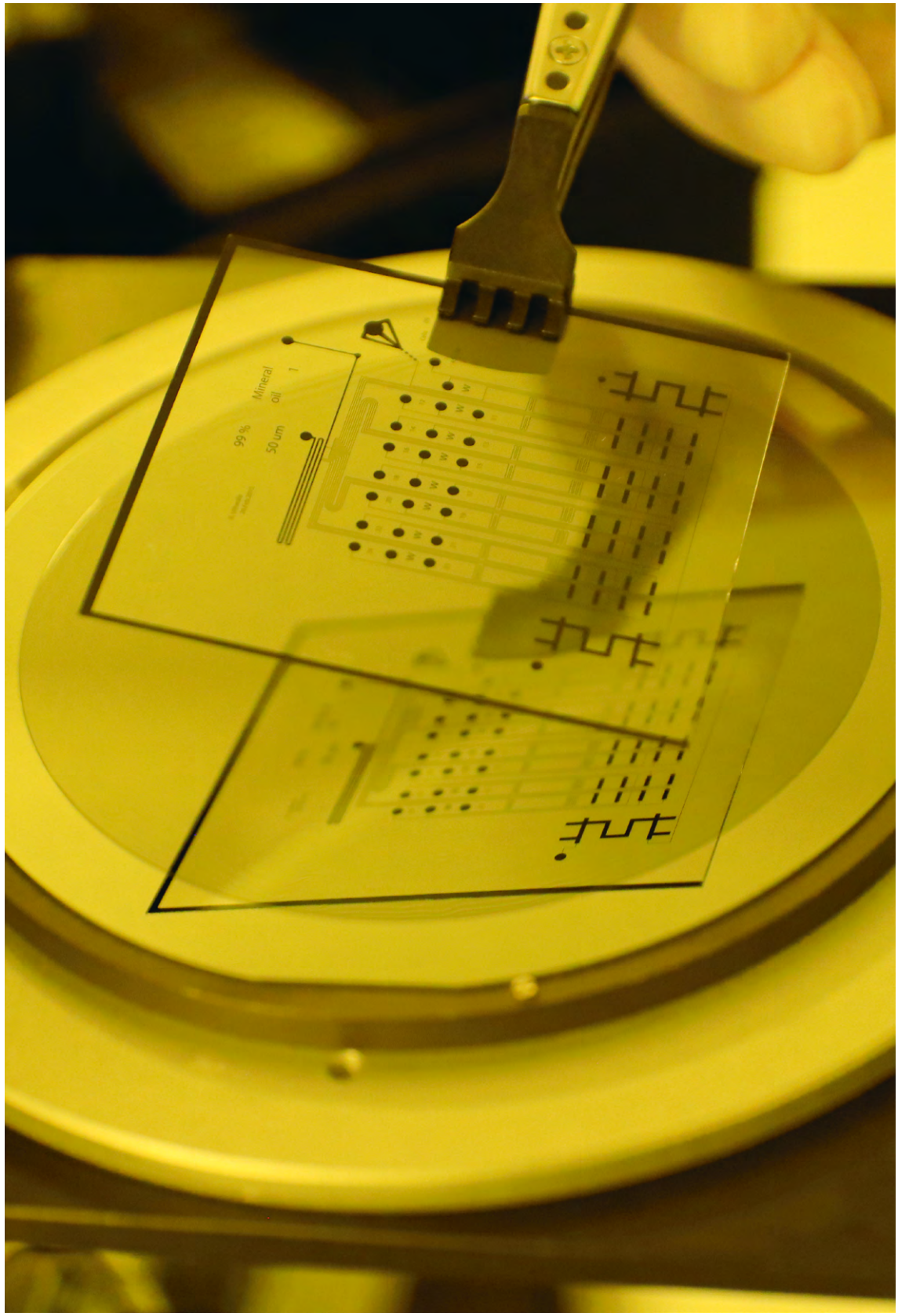
AGORA
PÔLE DE RECHERCHE
SUR LE CANCER



Microfluidic chips for high throughput drug screening. This image is a snapshot of a scientific experiment, in which tumor cells are carefully analyzed using state-of-the-art laboratory equipment. In the foreground is a microfluidic chip under the microscope. Micro-droplets containing cancerous cells are subjected to various treatments.
The red light emanating from the microscope highlights features imperceptible to the naked eye, illustrating the perfect fusion of cutting-edge technology and scientific exploration in cancer research.



Captivating view of a microfluidic chip used in the immunotherapy of solid tumors. This chip, initially developed to reproduce the blood-brain barrier and study permeability, was adapted to enable the analysis of the infiltration of immune cells in solid tumors. Immunotherapy is a powerful and targeted weapon in the fight against cancer. It harnesses the immune system's potential to eliminate malignant cells and therefore, thanks to immunological memory, offers a glimmer of hope for long-term control and prevention of relapses.



Detailed view of the process used to micro-manufacture a silicium mold for the production of microfluidic chips.
This image documents the process used to micro-manufacture a silicium mold in a cleanroom, i.e. in an environment with a very low concentration of airborne particles. This is a crucial step in the production of microfluidic chips. The scientist, wearing sterile gloves, positions foils on which are printed detailed patterns. These foils play a key role in the making of the microscopic channels that will guide the fluids within the chip.

SUPPORTED PROJECTS

YOUNG SCIENTISTS

The ISREC Foundation supports PhD students in the fields of biology and medicine.

***Students** supported in 2023 :*

Andrea Agnoletto
Lab of Prof. Cathrin Brisken, EPFL/SV/ISREC
ISREC PhD grant to study androgen receptor signaling in the normal breast epithelium and in estrogen receptor alpha-positive breast cancer.

Daniela Cropp
Lab of Dr. Grégory Verdeil, Department of Fundamental Oncology, UNIL
ISREC PhD grant to study the role of nfat5 in tumor-specific T cells.

Benoît Duc
Lab of Prof. Johanna Joyce, Oncology Department, UNIL/LUDWIG/CHUV
ISREC PhD grant aiming to model and investigate the tumor microenvironment of non-small cell lung cancer brain metastasis.

Benedetta Fiordi
Lab of Prof. Camilla Jandus, UNIGE
ISREC MD-PhD scholarship to study the role of the brain-derived neurotrophic factor in the neuro-immune control of acute myeloid leukemia.

Christoph Iselin
Lab of Prof. Emmanuella Guenova, UNIL
ISREC MD-PhD scholarship to study the role of natural killer cells in cutaneous T cell lymphoma : pathophysiological mechanisms and clinical implications.

Silvia Podavini
Lab of Prof. Margot Thome Miazza, Biochemistry Department, UNIL
ISREC PhD grant for the biochemical identification and characterization of PD1 signaling components.

Simge Yücel
Labs of Prof. Douglas Hanahan and Michele De Palma, School of Life Sciences, EPFL/SV/ISREC
ISREC PhD grant to study the mechanisms and therapeutic targeting of the neuronal NMDAR signaling pathway promoting breast cancer pathogenesis.

Supported scholarships

Information on professorial chairs

PROFESSORIAL CHAIRS

Professorships enable young professors affiliated with a Swiss academic institution to launch their research careers.

*The **chairs** financed by the ISREC Foundation in 2023 :*

Prof. Denis Migliorini UNIGE/AGORA –
ISREC Brain Tumor Immuno-Oncology Chair
This ISREC immuno-oncology chair is dedicated to the immunology of brain tumors. The associated research in this program explores new therapeutic approaches for brain tumors and in particular for glioblastoma, a highly aggressive form of the disease.

Prof. Mikaël Pittet UNIGE/AGORA –
ISREC Immuno-Oncology Chair
This ISREC immuno-oncology chair is dedicated to the study of cancer immunity in context. The associated research in this program aims to discover how the immune system controls cancer and other diseases, and how it can be exploited for therapeutical purposes.

Prof. Nicolas Thomä EPFL – **Paternot Chair for Interdisciplinary Cancer Research**
The goal of the Paternot Chair for Interdisciplinary Cancer Research is to study the protein-protein interactions that play a role in cell fate decisions, with the goal of chemical intervention in those that are disease-causing (page 8).

TRANSLATIONAL RESEARCH

Translational research projects encourage collaborations between basic and clinical research. Their goal is to study cells and their interactions with the environment, and to provide impulses for novel therapies and clinical approaches designed to act on the causes of cellular malfunction.

***Projects** supported in 2023 :*

Chantal Arditi Unisanté –
Analysis of Oncology Patient Data
Research project in the field of oncological care, aiming to develop a survey on cancer patient-reported healthcare experiences in Switzerland.

Prof. Holger Auner CHUV –
Multisystem Cancer Biology
Translational research project in the field of multisystem cancer biology aimed at targeting the interplay between intra- and extracellular proteostasis.

Prof. Jean Bourhis CHUV – **FLASH Therapy**
The FLASH project is exclusively funded through a donation made by the Biltema Foundation. In collaboration with the CERN and Theryq SA, a medical technology company, this program aims to study the clinical translation, development and clinical modelling of FLASH radiotherapy treatments. This unique model will eventually enable the treatment of all types of deep-seated tumors.

Dr. Francesco Ceppi CHUV and
Prof. Caroline Arber UNIL – **Immunotherapy for the Treatment of Myeloid Leukemia**
The FIAMMA project (Chimeric Antigen Receptor T Cell Therapy for Children and Adults with Relapsed Acute Myeloid Leukemia) is supported by a donation from the Jacqueline de Cérenville and the Jan Baron Mladota Foundations (page 10).

Dr. Antonia Digklia CHUV and
Dr. Melita Irving CHUV – **Immunotherapy for Sarcoma Treatment**
Translational research project aimed at improving the treatment of sarcomas thanks to a tyrosine kinase inhibitor administered in combination with an innovative CAR-T cell therapy.

SUPPORTED PROJECTS

Prof. Camilla Jandus UNIGE and
Prof. Grégory Verdeil UNIL – **Bladder Cancer**
Translational research project targeting novel molecular networks underlying bladder cancer recurrence and progression.

Prof. Johanna Joyce UNIL/LUDWIG –
Brain Tumors
Translational research project to explore the role of neutrophils in brain metastasis.

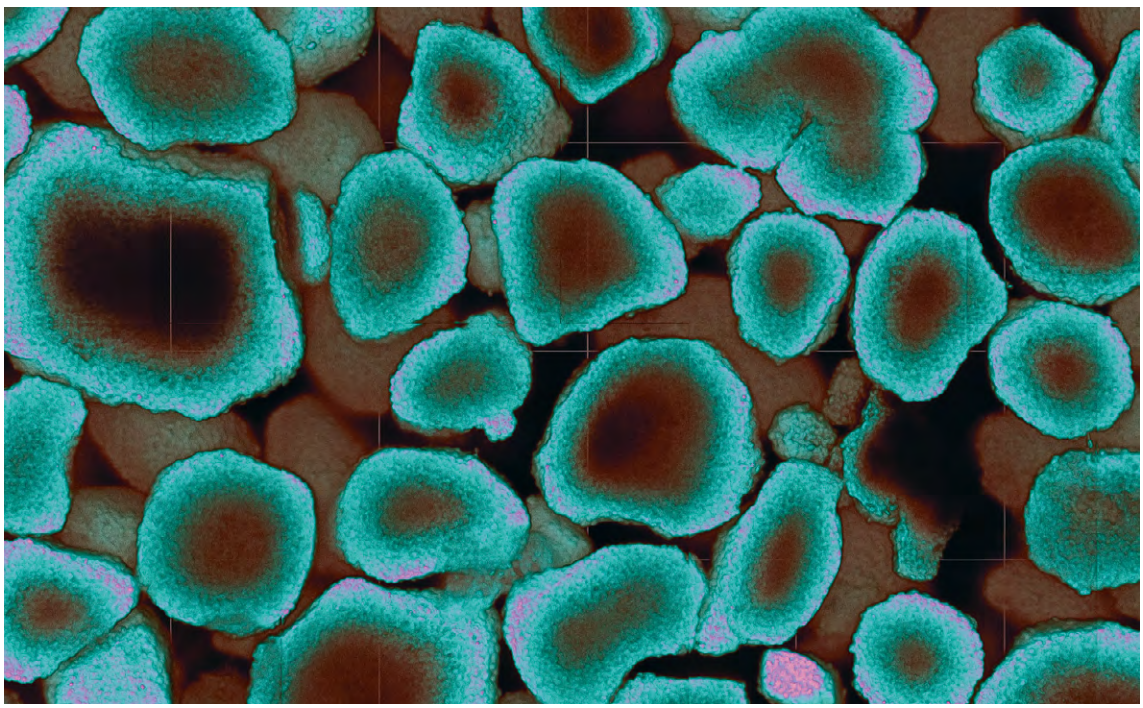
Prof. Chantal Pauli USZ – **Identification of Personalized Therapeutic Strategies**
Translational research project aiming to customize treatment in cancer patients and to uncover cancer vulnerabilities.

Prof. Davide Rossi USI/IOR –
The Lymphoma Microenvironment
Translational research project aiming to understand how clonal hematopoiesis feeds lymphoma.

Prof. Mark Rubin UNIBE – **Prostate Cancer**
Translational research project on the use of advanced in vitro models of prostate cancer metastases to unravel and overcome ARSI resistance.

Prof. Curzio Rüegg UNIFR –
Breast Cancer Screening
Study aimed at developing a test for the early detection of primary breast cancer and breast cancer relapse.

Information on supported projects



Visualization of tumoroids from colorectal cancers after tissue clearing. Biological tissue constituents have varying optical properties, which often limit in-depth observation due to light scattering and absorption. Clearing methods attenuate these limitations by homogenizing the refractive index. This allows a more in-depth and preciser exploration of tissue structures. The panoramic image shown here showcases a remarkable preservation of the cytoplasmic (green) and cytoskeletal (pink) fluorescence, and an in-depth view of these mini-tumors.

Congratulations
to these promising students!

Dana Almbark Ortiz
c/o Prof. Ileana Jelescu – UNIL
Bahçesehir University in Istanbul, Turkey

Nithyasshree Maheswaran
c/o Dr. Fabio Martinon – UNIL
Anna BIT-Campus University in Tamil Nadu, India

Karina Araslanova
c/o Dr. Can Aztekin – EPFL
Lomonosov University in Moscow, Russia

Alireza Gargoori
c/o Prof. Gioele La Manno – EPFL
Sharif University of Technology in Teheran, Iran

Cailyn Mae C. Ong
c/o Prof. Jacques Fellay – EPFL
Diliman University in Manila, the Philippines

Dessislava Ilieva
c/o Prof. Pierre Gönczy – EPFL
Manchester University, Great Britain

SUR/SRP Summer Program

In 2023, the ISREC Foundation supported six undergraduate students participating in the SUR/SRP «Summer Research» program, a collaboration between the UNIL and the EPFL.

Since 2006, this scientific program has offered more than 300 international students a unique opportunity to engage in research in Lausanne. Positive feedback and the many enthusiastic comments of past participants underscore the impact that this program has had on their choice of studies and career. It is an unforgettable and gratifying experience for all involved. This eight-week internship offers the selected young biologists a first insight into the world of research and an opportunity to network on an international level. The host laboratories, on the other hand, are given the chance to discover brilliant students who might, someday, return for a Master's or PhD degree.

Scientific conferences, symposia, and workshops

In 2023, more than 150 events, **symposia** or **scientific lectures** were held in the Paternot auditorium and the lecture rooms of the AGORA Cancer Research Center, most of them directly related to research and oncology.

The ISREC Foundation also co-organized two **workshops**. In January, approximately 200 researchers, physicians and scientists attended a workshop on **the use of spatial multi-omics in biology and medicine**. And in February, close to 130 participants gathered to discuss **multimodal imaging in life sciences and cancer research**.

The ISREC Foundation will continue to prioritize oncology events in the AGORA Center's program of activities, reflecting its two main missions, namely promoting experimental, translational, and clinical research, and supporting the next generation of scientists and physicians in this field.

HIGHLIGHTS IN 2023

JANUARY

As of January 1, 2023, **Prof. Andrea Alimonti** is a member of our Scientific Board. He is a specialist in solid tumors, a renowned immuno-oncology expert and the Director of the Institute of Oncology Research (IOR). Prof. Alimonti has received numerous Swiss and international awards honoring his remarkable contributions to cancer research. He is in particular renowned for his groundbreaking research in the field of prostate cancer biology. His work has led to promising new therapeutic approaches for this common malignant tumor in men.

On January 30, our Director, **Prof. Susan M. Gasser**, was granted the Lelio Orci Award 2022, which is awarded for outstanding performance in fundamental cellular biology by the Life Sciences Association of Switzerland. She is recognized for her contributions to understanding telomeres, heterochromatin-mediated spatial genome organization, and the role of nuclear pores for gene expression and DNA repair.

FEBRUARY

Prof. Nicolas Demartines, General Director of the CHUV, is appointed member of our Foundation Council, taking over from Prof. Philippe Eckert. **Fritz Schiesser**, lawyer and notary public, former member of the Swiss Council of States, former president of the Foundation Council of the Swiss National Science Foundation, former president of the Board of the Swiss Federal Institutes of Technology, is also elected member of our Foundation Council.

APRIL

Prof. Susan M. Gasser, our Director, and **Prof. Federica Sallusto** (ETH Zurich), member of our Scientific Board, are elected international members of the National Academy of Sciences (NAS). Election to the National Academy of Sciences (NAS) is considered a mark of excellence and one of the highest honors in the scientific field. Scientists are nominated by current members, in recognition of their exceptional contributions to research.

Prof. Susan M. Gasser and Prof. Federica Sallusto during their election into the National Academy of Sciences (NAS).

MAY

From April 21 to May 1, **Helder Amaral** participated in the **Marathon des Sables**, a 7-day, 250-kilometer foot race in the Moroccan Sahara, during which the participants must be self-sufficient. Mr. Amaral embarked on this adventure in memory of his father, who died of pancreatic cancer. The funds he raised were generously donated to institutions involved in cancer research, including the ISREC Foundation. A huge thank-you to Helder Amaral for this incredible initiative!

Helder Amaral in the Moroccan Sahara during the Marathon des Sables 2023.

Prof. Mikaël Pittet, winner of the Prix du Rayonnement Académique 2023 of the Société Académique Vaudoise.

JUNE

Within the context of the ISREC Foundation's second call for **TANDEM** projects, our Foundation Council validates the allocation of **3 million CHF for collaborations between clinicians and basic biologists** (page 16).

JULY

Press release announcing the allocation of **2.8 million CHF** to the **FIAMMA project** (page 10), in collaboration with the Jacqueline de Cérenville and the Jan Barton Mladota Foundations, both based in Lausanne.

AUGUST

24th edition of the Old-Timer Hill Climb in Corcelles-le-Jorat. The Club Team Girard, consisting of owners, pilots and connoisseurs of old motorcycles, has been organizing annual «Old-Timer» events since 1998. On August 25 and 26, 2023, more than 140 pilots, including teams with sidecars (most of which were built before 1985), gathered for the 24th edition of this race. The ISREC Foundation is greatly honored to be among the beneficiaries of this event, which, to date, has donated 47 500 CHF to cancer research.

OCTOBER

Prof. Mikaël Pittet, holder of the ISREC Foundation's Immuno-Oncology Chair, is this year's recipient of the **Prix du Rayonnement académique 2023** (page 14).

Granting of the **Paternot Chair for Interdisciplinary Cancer Research** to Prof. Nicolas Thomä at EPFL (page 8).

NOVEMBER

This year's annual ISREC Foundation conference, entitled «At the Heart of Oncological Research», was held on November 22. We were greatly honored to welcome the **president of the Executive Council of the Canton of Vaud, Christelle Luisier Brodard**. This event was a great opportunity to draw attention to the power of scientific collaborations as well as to the fundamental role played by private foundations. On this occasion, Mrs. Luisier Brodard was able to visit the AGORA research center and to exchange views with young scientists.

Executive Council President Christelle Luisier Brodard, during her speech at the ISREC Foundation's annual conference.

THE FOUNDATION COUNCIL

The Foundation consists of the following bodies:

THE FOUNDATION COUNCIL

The Foundation Council is the highest authority of the Foundation. It approves the allocations of resources, appoints its own members, those of the Scientific Board and the Management, as well as the Financial Auditors. It approves the annual budget and the Foundation's accounts.

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Lawyer and professor of tax law at UNIL (University of Lausanne), associate at Oberson Abels SA

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Independent administrator

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General director, CHUV (Centre Hospitalier Universitaire Vaudois)

Prof. Dr. Michael N. Hall
Representative of the Scientific Board, Professor at the Biozentrum, University of Basel

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Prof. Philippe Moreillon
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Prof. Didier Trono
Full professor, GHI (Global Health Institute), EPFL (École Polytechnique Fédérale de Lausanne)

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The Scientific Board is composed of experts of international renown in various fields of cancer research and is overseen by the Director. They cannot be members of the Foundation Council, with the exception of the president of the Scientific Board, by virtue of his position. The Scientific Board and the ISREC Foundation Director select the research projects to be funded, and present recommendations to the Foundation Council.

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Prof. Dr. Michael N. Hall
Professor at the Biozentrum, University of Basel

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Director of the Molecular Oncology Department, Institute of Oncology Research, Bellinzona

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Prof. Peter Johnson
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Foundation Council
From left to right: Nicolas Demartines, Claudine Amstein, Thomas Paulsen, Didier Trono, Béatrice Schaad and Fitz Schiesser
Front row: Pierre-Marie Glauser – president
Absent: Yves Henri Bonzon, Michael N. Hall, Bertrand Levrat and Philippe Moreillon

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Assisted by the Scientific Board, the Management selects and oversees the funded research projects. It develops and recommends a fundraising strategy and carries out the tasks defined by the Foundation Council.

Prof. Susan M. Gasser
Director

Aylin Niederberger
Administrative and Financial Director

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The financial auditors, whose duties are determined by law, are nominated by the Foundation Council. They are elected for one year. The 2023 mandate was entrusted to **PricewaterhouseCoopers** in Geneva, a fiduciary company recognized by the Swiss Institute of Certified Accountants and Tax Consultants.

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Since 1964, numerous donors have supported our cause through their gifts, subsidies or legacies and contributed to the progress of cancer research.

We are very grateful and thank each one of them most warmly.
Among these donors, more than six hundred and fifty appear in our Book of Donors:

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You all have contributed to the advancement and the success of our Foundation.

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Image of the cover page
Comparative study using intestinal organoids: radiotherapy plays an essential role in the fight against cancer. However, it also poses risks for the surrounding healthy tissues. FLASH radiotherapy, a recent innovation which rapidly delivers high radiation doses, is attracting growing interest due to its potential to reduce these undesirable side effects. The present study aims to compare the effects of FLASH radiotherapy and conventional radiotherapy on intestinal organoids, which are reduced models of biological tissues. By observing the regenerative responses of these organoids to varying radiation doses, the researchers can gain a better understanding of the mechanisms underlying cancer therapies.

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