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07.10.2024

Tags: [Switzerland](#), [ISREC](#), [AGORA](#), [Oncology](#), [PPPs](#), [R&D](#)

World-renowned oncologist Professor Susan Gasser outlines the innovative public-private partnership model in place at the ISREC Foundation at the AGORA Cancer Research Center in Lausanne. The unique model of ISREC/AGORA involves a reversal of the typical PPP structure, where the private foundation builds infrastructure and invites public institutions to collaborate, fostering a translational cancer research environment that bridges research and clinical application. Gasser, who also serves on the board at Belgian pharma company UCB, explains how AGORA emphasises the practical application of scientific discoveries, promoting direct collaboration between basic scientists and clinicians to bring new therapies to patients, highlighting the role of immunotherapies, AI, and cutting-edge techniques like Flash therapy.

Could you explain the unique model behind ISREC/AGORA and how it integrates multiple research institutions?

ISREC is a purely philanthropic organization, founded 60 years ago, with a long history of supporting experimental cancer research. In its earlier years, particularly through the 1980s, 1990s, and 2000s, the focus was very molecular, dealing with areas like oncogene identification and target discovery, without much direct interface with hospitals. Over time, much of the early research was absorbed by the Swiss Federal Institute of Technology Lausanne (EPFL).

The new ISREC/AGORA model represents a significant shift. We have built a cutting-edge research facility directly across from the university hospital, creating a public-private partnership (PPP) with an unusual twist. Typically, in a PPP, the public sector builds infrastructure and private entities invest in it. Here, it is the reverse: the private foundation, funded by donations, constructed this state-of-the-art building, and we have invited public institutions to join and occupy it.

We've brought together key partners—EPFL, the University of Lausanne, the Lausanne University Cantonal Hospital, and the University and University Hospital of Geneva. Each institution contributes financially and through their staff and professors, they form a collaborative albeit diverse group of team leaders within AGORA. This partnership fosters a highly translational cancer research environment, bridging the gap between research and clinical application.

AGORA integrates clinicians from the hospitals with technical experts from EPFL, which specializes in bioengineering, computation, and other cutting-edge fields. The University of Lausanne brings its strength in cellular immunology. The collaboration between these diverse fields has resulted in a dynamic and innovative research center, where young professors are enthusiastic about working together. The synergy among these disciplines has led to advanced capabilities in areas like imaging, bioengineering, computation, and informatics.

Over the past three and a half years, What would you highlight as AGORA's most significant achievements?

A key achievement was to open the door for collaboration between clinicians and basic scientists, and here we have been able to attract a critical mass of talent. AGORA now hosts around 300 people across 30 research groups, and there is significant interest from others wanting to join. One-third of the groups are led by clinician-scientists. It has been four and a half years since the building opened, and two of those were impacted by COVID-19. We launched in 2019, took a year to move in and set up facilities, and then much of 2020 and 2021 were hampered by lockdown restrictions. So, in terms of fully functioning time, AGORA has been running at full speed for about two and a half years. Despite the short time, the concept has really taken off and the centre is extremely productive.

The synergies created here have been fantastic. The open-bay, open-lab design promotes interdisciplinary collaboration. While some areas are grouped by interest, they are not divided by institutions, so you might find an EPFL lab next to a University of Geneva lab, alongside hospital researchers. This setup encourages cross-disciplinary interaction, which has been key to our

success. The core requirement is that all projects must be truly translational, aiming to impact patients as soon as possible. While we still use mouse models, we are increasingly working with organoid samples and actual patient biopsies, moving closer to real-world application.

ISREC, as a private foundation, funds core facilities and specific projects, but we insist on true collaboration between medical clinicians and basic scientists. It is not enough that a clinician provides some material: they must be equal partners in designing the research. This focus on collaboration and translation is what makes AGORA unique. We have had great successes so far, particularly in bringing together diverse expertise. There is more to come as we continue to build on this foundation.

As of today, what are the primary priorities and strategic focus areas for AGORA as it continues to advance translational cancer research?

The next major step for AGORA is to fully integrate pathology into our research efforts. Being right next to the University Hospital's Pathology Department, we see pathology as an untapped resource for advancing medicine. There is so much more information we can extract from biopsies, blood samples, and imaging data than we currently do. With advanced techniques like sequencing, tumour visualization, and machine learning through neural circuits applied to pathology sections, we are able to revolutionize how we understand and treat cancer. This is an area where we need to focus our efforts.

To move forward, we plan to fund collaborative projects that connect pathologists with basic scientists. While we already have successful collaborations involving oncologists, haematologists, and immunologists, pathology and radiology remain underdeveloped areas. We support a cutting-edge project in radiation therapy, but day-to-day pathology is not yet optimally integrated into our research efforts.

By optimized research, I mean maximizing the value of every sample, even if we do not immediately know how important it may be. This implies ensuring that biopsies and biobanks are accessible and that pathologists, who often have a strong background in basic science, are fully involved in diagnostics and decision-making, particularly within the molecular tumour boards. To achieve this, we also need to work closely with regulatory bodies like Swissmedic to ensure that advanced diagnostic tests, which are often more precise and not necessarily more expensive, are covered by insurance. This requires national coordination, as every procedure must be approved in Switzerland's healthcare system.

A big part of my focus is ensuring that we align the efforts of pathologists across Switzerland at both university and cantonal hospitals alike. We need to standardize data collection, share it in a national, encrypted patient database, and use this wealth of information in real-time clinical decisions and research.

Beyond that, AGORA is focused on optimizing several promising areas in cancer research. These include immunotherapies like CAR T cells, bi-specific antibodies, theranostics with novel radionuclide delivery, and Flash therapy, which delivers high-intensity gamma radiation in short bursts. Flash therapy has shown promise in sparing normal tissues while being as effective as traditional radiation on tumours, but we still have much to learn about how it works and on which tumours it is most effective.

Among the current leading-edge approaches to cancer treatment, which do you believe holds the most potential for breakthrough success?

One of the most promising approaches in cancer treatment today is immune checkpoint therapy, which is already widely used. However, the use of specifically designed CAR T-cell therapy, particularly the GMP-grade production and amplification of T cells for patient transplants, has yet to reach full swing. While Europe is still catching up with global leaders like the University of Pennsylvania, there are exciting advances here nonetheless, especially in challenging areas like glioblastoma. On this topic, experts from Geneva and Lausanne have been brought together at AGORA, enabling deep insight into the tumour microenvironment, tumour-infiltrating lymphocytes (TILs), and the interaction between tumour cells and the immune system. I would like to highlight outstanding AGORA researchers like Johanna Joyce, Doug Hanahan, Denis Migliorini, Mikaël Pittet, Michael de Palma, and George Coukos who are all doing impactful work on immunotherapy of tumours in the brain and in the lung, where CAR-T therapies have had limited success in the past.

Another exciting theme is Flash therapy. Through a USD \$25 million private investment, we are developing a Flash therapy centre for deep tumours. This is a collaboration with CERN, a French medtech company, and the University Hospital of Lausanne, involving its radio-oncology and radiophysics departments. While we are still at an early stage of development, Flash therapy shows great promise, particularly for treating deep-seated tumours beyond skin cancer. It is a project in progress, but it holds significant promise.

We are also focusing heavily on digital pathology and AI-driven analysis in molecular tumour boards. This collaboration between Olivier Michelin, David Feller, and EPFL, a leading AI centre, is

already showing strong results. EPFL's computational sciences expertise has been instrumental in advancing precision medicine in cancer research.

A fourth exciting area, still in its early stages, is the use of AI and cryo-EM for molecular design, particularly targeting small molecules that act like molecular glues. These molecules facilitate targeted degradation by bringing proteins together so that one can ubiquitinate and degrade the other. Success was recently reported for targeting KRAS for degradation *in vivo*. Such advances arise from the intensely collaborative work of computational modellers, synthetic chemists, molecular biologists, and structural experts who use tools like cryo-EM to understand how to model and optimize protein-protein interactions. Interdisciplinary teamwork is essential to advance on topics like this, and even if pharma companies take the lead on such developments, academic collaborations like ours are essential for developing the forefront methods in molecular design. This means that the collaboration of academics with startups, established biotechs, as well as larger companies like Merck or Roche, are ever more important. These companies and others follow closely developments that come from collaborations with AGORA and EPFL.

How do your research efforts at AGORA differ from your previous work at the Friedrich Miescher Institute for Biomedical Research (FMI) in Basel?

The research focus at AGORA actually differs quite significantly from what I was doing at FMI. While you might assume that FMI, given its connection to pharma and biomedical research, was more applied, it was actually largely focused on basic discovery science. At FMI, we set up cutting-edge technologies like cryo-electron microscopy, innovative imaging systems, bioinformatics, epigenetics, and organoid development long before these became widely applied in drug development. We were even exploring AAV delivery to the retina in 2008, although at that point it was only applied to mouse models of human disease. Basically, we were pushing scientific boundaries for the sake of innovation.

For this reason, I believe, the FMI is a small, yet highly prestigious research institute of exceptional quality. During my time there, we had about 20 ERC grants among just 24 group leaders. This level of funding and international recognition underscores FMI's role in driving fundamental research, whether or not it directly addresses a medical problem. We aimed to explore and understand cellular and organismal mechanisms, gene regulation, epigenetic processes, and cell-cell signaling, all relevant to disease, yet we were pushing the boundaries of technology and knowledge.

AGORA, on the other hand, is all about translation, particularly in cancer. Here, the goal is to take the insights arising from research directly to the patient, as soon as possible. It's a very different environment—highly applied, clinically focused, and aimed at finding real-world solutions for cancer. At AGORA, we are developing immuno-oncology therapies, mass spectrometry analysis of tumour antigens, and CAR-T optimizations in real-time. This is not research for a distant future; we are addressing immediate needs in patient care and treatment.

The biggest shift for me has been transitioning from asking fundamental questions about biology—like gene regulation or DNA damage response—to dealing with highly practical questions that have direct medical relevance. For example, with respect to work on Flash therapy, we are trying to determine whether high-energy radiation delivered in a short burst generates the same DNA damage and cytokine response as traditional gamma radiation. Research is needed because we don't fully understand the different outcomes, and yet we are preparing to use the therapy on patients. In medicine, one often has to apply a treatment that works, even if the scientific basis of its action remains only partly understood.

This type of research requires a different mindset. In basic research, you can control all variables and can be quite certain about your conclusions. In medical research, especially with human trials, you have to deal with far more complexity and accept uncertainty, that is, variability. Patient responses vary widely, patients themselves are a variable, and the results are as often as not, confusing. But even a mitigated success—such as a treatment that only helps 20% of patients—can be life-saving. So while the conclusions are usually less compelling, the impact is profound. At AGORA, we work to bring improved treatments to patients, knowing that even partial success can make a significant difference to people's lives.

How would you assess the current level of collaboration between academic researchers like yourself and private industry?

The relationship between academic researchers and private industry has evolved significantly in recent years, driven by the increasing complexity of biomedical research, the amount of detailed information we have about cells and molecules, and the demands of translational medicine. Historically, academic research was focused on pushing the boundaries of knowledge, with the understanding that one day it might be applied to improve human health. Now, however, the current landscape of translational cancer research requires a more integrated approach between academia and industry. The problems come from medicine, the technologies and know-how from

basic research, and the optimization of drug development and large clinical trials come from industry. All three intersect in one lab sometimes.

At AGORA, this is our reality. The research focus is highly applied, and there is a constant push to bring new treatments to patients as quickly as possible. Collaboration with industry is often essential, as pharma companies have bigger resources and the necessary infrastructure to bring treatments to market and navigate regulatory hurdles while managing production and distribution as well. However, they increasingly rely on academic partnerships to drive early-stage discoveries and innovation, which is the source of new therapies.

What has changed is that both academic and industry players are more aligned in their overall goals. Academic researchers, especially in translational fields like cancer research, are now deeply involved in applying their findings to real-world problems, and this has led to a more fluid exchange of ideas, data, and resources between academia and pharma. Both sides recognize the need for collaboration to bring meaningful medical solutions to patients.

In contrast to the recent past when pharma might have raced to be first to market with a new drug, the emphasis today is on being best in class and developing treatments that truly improve patient outcomes. This has led to more public-private partnerships like those we see at AGORA, where private industry and public institutions, such as hospitals and universities, collaborate closely. These collaborations are not just about securing funding but about ensuring that the research is aligned with patient needs and that treatments are developed and tested efficiently.

Pharma companies today must navigate a highly strategic environment, balancing innovation with regulatory approvals, market timing, and patient demand. This creates additional layers of complexity in commercialization, and often biotech startups will partner closely with academic researchers for early-stage research but hope to be acquired by larger pharma companies for production, regulatory and market challenges. It is in this middle ground that AGORA operates, even though the goal is not commercial: our focus is squarely on patient-centred solutions in hospitals. The research we do is closely connected to clinical realities—working directly with patient samples, understanding human systems biology, and optimizing therapies based on the body's response to both the tumour and the treatment. This approach is what defines modern biomedical research and sets it apart from the more isolated, fundamental research of the past.

Since joining the board of UCB in 2021, what value have you gained from the experience of working closely with the industry?

One of the key takeaways has been gaining a deeper understanding of how broad the range of expertise is, that is needed to successfully develop and market a pharmaceutical product. The coordination between patient awareness groups, real-world evidence collection, regulatory audits, and investor relations plays a crucial role in the overall success of a drug. I've come to appreciate the complexities behind these collaborations and the talents required to drive them forward.

As a mid-sized pharmaceutical company, UCB strikes a balance that avoids the communication issues often seen in larger organizations. I've learned how an optimal size allows UCB to remain nimble, while still achieving impressive results—this mindset of efficiency is one I try to encourage at AGORA as well. UCB's focus on biologics, particularly antibodies for inflammatory diseases, dermatology, and neurological conditions, has been central to its success. Their approach to biologics has been highly productive, but they have also maintained strength in the optimization of small molecules, and are pursuing gene therapies, convinced that a diversified portfolio will benefit their overall pipeline. In the end, it is the tight communication between strategy, patient need and operational measures that makes UCB so impressive.

Last time we spoke, you were critical of Europe's inability to translate its research and scientific excellence into application, suggesting that it needs to simplify its processes and expand both scope and working models. Has this situation improved or worsened?

I would argue there has been steady progress in Europe's ability to translate research into applications compared to only a few years ago. Primarily there has been a shift in mentality regarding translation. European researchers, venture capitalists, and policymakers now better understand the importance of turning scientific excellence into marketable products. This shift has been particularly evident in countries like Germany, Switzerland, Belgium, the Netherlands, and even parts of Scandinavia, where the ecosystem for startups and innovation is maturing. In particular, the success stories of companies like BioNTech during the pandemic showed that Europe can be competitive and globally relevant in biotechnology and pharmaceutical development.

This progress is marked by the increase of spin-offs from top-tier universities like EPFL and ETH in Zurich, which have seen record numbers of startups in recent years. The entrepreneurial culture in places like Switzerland, which combines strong medtech, AI, and computational resources, has also grown significantly. Government initiatives have helped ramp up these developments, particularly during the pandemic when public funding was mobilized to accelerate research in vaccines and

infectious diseases. This injection of funding has helped Europe's research sector realize its potential for innovation and commercial success.

However, there are still challenges when it comes to finances. The recent energy crisis, economic downturn, and geopolitical instability have created financial restraints, making it difficult for many startups to secure second-round funding or attract long-term investment. While the US market appears to be loosening up again, European startups are facing a tougher financial environment. This is a critical issue, as, without sustained investment, the gains in mindset and infrastructure might not be fully capitalized on.

That said, the long-term outlook is more positive than it was a few years ago. The realization that Europe can drive pharmaceutical development through strong academic and research institutions is becoming more widespread. Big pharma's willingness to acquire promising startups or buy into innovative products has also provided a clearer pathway for smaller companies to scale their ideas into practical applications.

Therefore, the main hurdles today seem to be financial rather than cultural. The mindset around innovation is shifting, and Europe's talent pool and university systems are excellent. Sustained funding and constant investment remain critical factors to ensure that this progress continues. The ecosystem is being built, but to fully realize its potential, the availability of capital must catch up with the innovation emerging from research institutions.

How would you assess the current talent landscape, both in Europe and specifically in oncology? In which areas do you see strong growth and expertise, and where do we still need to foster further development?

I see a significant gap in talent among scientifically trained MDs. While it does not necessarily have to be an MD-PhD, I believe it is crucial that medical professionals have engaged deeply in research. They should have a solid understanding of topics such as transcriptomics and single-cell transcriptomics, as well as the complexities of the extracellular tissue microenvironment. It is essential that they grasp the intricacies of biology, genetics and the interrelation of different biological processes both on a molecular and a systemic level. Medical professionals are usually trained in either clinical practice or research, but we need individuals trained in both; they must be able to communicate in both languages. The MD-PhDs was a model that developed largely in the United States, with considerable success. In the future, I hope to see an increase in similar programs here in Europe, and more "protected time" programs that allow clinicians to spend time

in a lab, in order to bridge this competency gap in our medical professionals.

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