José-Alain Sahel – Founder and Director, Institut de la Vision, France



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Professor José-Alain Sahel, founder and director of the Institute de la Vision in Paris, offers his insider take on the ophthalmology landscape in France, international perceptions of the country, and the future of the Institute.

Could you please describe to our audience your career path and introduce the Institut de la Vision?

I am an Ophthalmologist by training, and throughout my career I have developed a specialty in intractable retina disorders, especially orphan retinal degenerations. I have been involved in building a collaborative environment between the Quinze-Vingts National Ophthalmology Hospital, the Rothschild Ophthalmology Foundation and Ophthalmology Departments at Assistance Publique-Hôpitaux de Paris. Moreover, a large part of my career has been focused on creating the Institut de la Vision, a translational research center. Around ten years ago, my collaborators and I were able to turn a small lab in Strasbourg into a multidisciplinary institute that now has 20 teams and over 300 scientists, specializing in fields such as retinal development, stem cells, genetics, genomics, neuroscience, vision restoration and computation, photonics, innovative diagnostic imaging and therapies, and supervises over 100 clinical trials to name a few.

The Institute has had significant hurdles and successes; our work has led to 60 families of patents (many of which are licensed) and 80 industrial partnerships with Big Pharma, such as Sanofi, Novartis and Roche. The key to this success is having developed our own internal industrial strategy. France’s medical industry lost a lot of headway in our field in the 1980s and 1990s, so we have tried to close this gap; we currently have an incubator that has helped more than 30 companies in hearing and vision therapies and we have created 10 startups, two of which are on the stock market.

As we have focused on technologies for vision impairment, we have inevitably been led to explore artificial intelligence. We have additionally worked on phenotyping (high resolution imaging, analyzing data, etc.) as a crucial hybrid of an academic department and an as an industrial body.

All in all, the Institut de la Vision has a network of around 1000 professionals in our research centers and our hospital partners.

What was the inspiration behind the Institut de la Vision?

Our motivation is based on project developments and fostering innovation between the research lab and the patient. When I entered the field, bringing innovative practices to the patients was a complex process, as there were unnecessary barriers between the field workers, researchers and various professionals.

Accordingly, we decided to create an institute that could synergize the different professions involved in medical innovation around patients needs.

At the Institute, if you need to consult an expert in molecular biology, physiology or photonics, for instance, everything is there. You are assured of expert support, and when a project is mature enough to move on to clinical development, the center helps the project advance by finding resources for patenting and industrialization. If the industry doesn’t exist, we find investors, conduct clinical trials, and assess the real impact of the innovation.

The key question behind our research is: how does it impact the daily lives of the patients? Our approach is a matter of asking questions to the right people at the right time and not wasting energy. This is a way to ensure efficiency and that products serve the public.

Today the Institut de la Vision is one of Europe's leaders. How would you describe its positioning?

International experts from the National Evaluation Agency (HCERES) and other organizations say that we are the world leaders in our field. When experts and companies do assessments and benchmarks, we consistently rank in the top three worldwide. We also just were selected in the new competitive call for Univsersity-Hospital Institutes. This is great, because we did not exist ten years ago. I think this success can be attributed to our focused, energetic approach.

Why is France so strong in ophthalmology?

The Quinze-Vingts National Ophthalmology Hospital is actually the oldest institution in the world for the blind. It was created by King Saint Louis (Louis IX) in the 13th century. The hospital has always been a good place for vision care, but there was no structured research conducted when we arrived. Upon my arrival we decided to focus on innovation and research, and since that decision was taken and implemented, we have seen success. It is also important to note that we do not work in isolation. We don't believe that we know everything, so we collaborate with other institutes in France, and even more importantly, with other institutes worldwide. For instance, I just stepped down from chairing a ten-year collaboration in clinical research trials with a network of over 100 research centers in Europe with identical protocols. Moreover, the Institut de la Vision is now part of a network of other research centers, notably, Moorfields Eye Hospital in the UK. We have collaborated very closely with Moorfields (in fact, several clinician-scientists here trained also at Moorfields and still hold honorary teaching positions there; until last year, I had a position as a professor at UCL working with Moorfields but I decided to step down because of my new position in the US) and we still do. Next month we will for example have a meeting with Moorfields wherein scientists and physicians will meet and exchange updates on their research. We also collaborate with established institutes in Germany, such as the Tuebingen Center.

Recently, new institutes have been created – for example, in Basel, there is now the Institute of Molecular and Clinical Ophthalmology (IOB), started by two leading clinician and scientist and funded by Novartis, the University and Hospitals of Basel, and the Canton of Basel. They decided to create the institute modelling closely the Institut de la Vision; they came to visit us and decided to create a similar type of research center. We have fostered a strong collaboration with the IOB – in fact, I am actually the organization's chair of the scientific advisory board.

Would you say that the Institut de la Vision acts as a model for others worldwide?

In some ways, yes, it is a model because it is based on undisputable goals and a collaborative approach that should be obvious to all. For example, the RIKEN Institute in Kobe, Japan, decided to mimic our design and open a similar institute. In May, we reached a joint agreement to exchange programs in research on stem cells. We also offer a joint master's degree with a Mexican university and we are about to enter a partnership with a technological university in Singapore, as the new president is keen to make an agreement with us and Sorbonne Universite, our main parent organization with Inserm and CNRS.

However, perhaps the most significant program that we have is the one with Pittsburgh. Two years ago, the University of Pittsburgh and the clinical giant University of Pittsburgh Medical Center (UPMC) asked me to create something similar to what we have done here in Paris : a strong vision institute with a clinical and research element. UPMC, in particular, is a massive, international organization with an annual budget of over USD 20 billion and a presence in Ireland, Italy, Dubai, the U.S., and China, to name a few sites. It is one of the largest academic institutions in the United States, and functions in full integration with a very efficient health plan.

Last year, the presidents of the Sorbonne University, of Inserm and a international representative from CNRS came to the French embassy in Washington to sign an agreement with the Dean of the University of Pittsburgh Medical School to build a bi-national institute between France and the US. This is a huge opportunity – not because we want to become a large institution per se, but because we want to make sure that our work is developed beyond our bounds. There are very strong teams in Pittsburgh that will complement our teams very well – for instance, Pittsburgh researchers have made great strides in corneal regeneration with stem cells, optic nerve regeneration and even a crazy project to conduct an eye transplant. So, this is a unique opportunity for Paris, to evolve into the foundation of an international leader in vision care.

How would you describe the pros and the cons of the research environment in France? What changes would you implement, given your experience and international exposure?

I think that one pro of the French environment is the free access to high-quality healthcare. I consider it a major strength of the country, although there are of course some limitations that are being addressed by the government. I would say that another strength to the French system is free education, which gives anyone access to any degree, unlike its counterpart in the United States. Moreover, I would say that the tenure system for university researchers is important, as the job

security allows them to take some professional risks. For example, when I was 32 and coming back to France after studying at Harvard, I was given a full professorship. I can remember feeling confident in proposing ambitious projects because I knew that I would have the time to see it through. While it is true that a few people might become less committed due to the job security, those that have ambition have the opportunity to truly be disruptive in their fields in France.

However, there are also several limitations to the French research environment. Firstly, the landscape is extremely fragmented. We have too many institutions, too many systems, and it seems that whenever someone tries to simplify it, they end up adding one more layer of complexity. This is because nobody is daring enough to simplify the landscape. For example, we are in the middle of deciding if the system should be driven by the universities or the research institutions. These two groups tend to fight with one another and instead of trying to simplify the landscape, they are creating new structures. In general, I think that France has too much creativity when it comes to creating new models of bureaucracy! I think that it would be better if we focused on making things more efficient and limit wastes of time. For example, about ten years ago, they created the National Agency for Research (ANR), thinking that this would be an ambitious way to fund new programs. However, it ended up funding few programs and distributing very little money. In this sense, it cannot compare to the NIH or the National Science Foundation. In the end, it was really just one more “layer” in the landscape that diverted funds to an inefficient body. Hopefully this can be fixed, as funding projects has proven effective worldwide.

Unfortunately for the scientists, they are caught in the middle of this maze with so many agencies. Take, for example, when we produce publications and are required to list three, maybe four, entities that are all competing against one another; regarding applications to the the European Research Council (ERC), the CNRS, and the universities all want to compete on their own. And that causes problems for institutions like ours, as 25% of our scientists are funded by the ERC and belong to either by the University , CNRS, the French National Institute of Health and Medical Research (INSERM), but work in a joint Institute. It just doesn’t make any sense.

What is the major difference between INSERM and the CNRS?

Before the Second World War, medical research was supposed to be done at universities. However, they had a very fossilized system that did not conduct much research. There were not many French organizations conducting medical research at the time, a part from the Pasteur Institute. Then, the Rothschild family supported the Physical and Chemical Biology Institute (IBPC) led by Jean Perrin,

which ended up becoming the core of the CNRS. The CNRS hence traces its roots back to before the Second World War, and it soon became the multidisciplinary home for free research and a leading Institution, independent from Universities.

In the 1970s and 1980s, while the Hospital system had greatly benefited from the Hospital-University reform conceived by Robert Debré, professionals in the field realized that there was still not enough medical research being conducted in France. The government therefore decided to create INSERM, dedicated solely to medical research and run jointly by the Ministry of Health and the Ministry of Research. Tet, instead of being created as a complimentary entity to the CNRS and universities, it was independent. To this day, it makes it difficult for researchers, as we belong to multiple organizations. It is burdensome, as we have to report to many entities.

Some in government have seen the problem, though. For example, Valérie Pécresse, when she was Minister of Higher Education and Research, did a great job with the autonomy of universities and pushing forward the unique mandate for technology transfer. This has made our lives at the Institute far easier, as we now only have to report to the Sorbonne University, who will then share relevant information with the CNRS and INSERM (before, one had to report any patent to every single affiliated program). All in all, it is getting a little bit better, especially for us. Ten years ago, we attained the status of a Foundation for Scientific Collaboration, which allows us to bring together the hospitals, universities, the CNRS and INSERM. I think we now have an efficient model which is why we are able to do so much. We manage grants from Europe and from the US while simultaneously collaborating with industry; we have truly become a one-stop-shop.

Nonetheless, the entire system remains too complex and there is limited funding. I am jealous of the United Kingdom when I review their grants, as they have the Welcome Trust, the Medical Research Council and other sources of funding at levels that are not available here in France.

Do you think that the patient groups in France can one day become a source of funding for R&D?

As of now, the only civil society groups in France that raise significant amounts of money for research are the Fondation pour la Recherche Médicale and the French Muscular Dystrophy Association (AFM) and their Telethon. The only reason that France is currently so good at gene therapy is because of the AFM’s fundraising. While the French Foundation for Medical Research (FRM) does give away a fair bit of money, it does not compare to other global leaders. It is true that the French environment has a lot of advantages, but it is also far behind in some aspects. But, for

all that we know, this could change in a short amount of time.

Do you think that Brexit gives countries like France an opportunity to increase its presence in the global research landscape?

Frankly, I see Brexit as only bad news. I do not consider it a success when others are defeated. I am not happy at all with what is happening in the United Kingdom. I have a lot of respect and history with British universities and they have been great partners at the European level. We have worked together a great deal, and I don't think that anyone stands to benefit from Brexit. While it may lead companies to choose France over Britain in the future, I am generally not happy about what is happening. I do not want people to come to us because of Brexit, but rather because we do a good job. Success in a competitive system is not found in the weakness of others, but rather in collective strength.

While Brexit is a potential disaster, I think that the UK will recover. The people are smart and pragmatic, and I am sure that after a certain point, they will say, "enough is enough. Let's stop this stupid thing." And on the other hand, I think that Brexit should serve as a lesson to the bureaucracy of Europe. People need to ask themselves why these movements are happening in Austria, Hungary, Poland and Italy. Europe needs to understand why it is happening and fix it. Nonetheless, we are going to continue working with the British researchers and ensure that they do not lose too much from Brexit. Obviously, we are proud to be French and we want to advance our country and industry with the new government's help, but it is one world and we want to work with everyone.

Have you noticed a change in the landscape with the arrival of the Macron government?

I think that it has changed the image of the country. I think that the fact that it has not bowed to pressure from strikes and the unions has been good. I really hope that everyone can benefit from the government's policies and will not perceive it as a regime for the rich and powerful. After all, this country is based on a model in which everyone wins together. Overall, given the world around us, we are lucky to have such a forward-looking government and president. A five-year term is very short, but I hope that they are able to impulse positive changes in this country that will help a lot of people, within that time.

What are your ambitions for the Institute in the next five years?

We recently co-authored an article in *Nature* (the May 2017 issue) about the potential of the study of vision restoration. We are very fortunate, as we are entering a new era in ophthalmology where vision restoration through prosthetics, gene therapy, and stem cells is becoming possible in some patients. This opens the opportunity to work on brain plasticity, rehabilitation, and artificial intelligence, all of which will make a real change in patients' lives. Thanks to the IHU (*Instituts hospitalo–universitaires or University Hospital Institute)* support, we plan to work with Pittsburgh, and others, including Stanford in bringing remote access to diagnosis, artificial intelligence and analytics to adapt and facilitate delivery of care. We are truly entering a disruptive era.

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