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The CNRS has activity in nearly every field of science

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Dr. Catherine Jessus, Director of the INSB (Institute of Biological Sciences), the largest branch of the CNRS (National Center for Scientific Research) in France, discusses the strengths and weaknesses of the French biological research ecosystem, public-private partnerships, and post-Brexit France.

The CNRS (French National Center for Scientific Research) features some of the world's elite researchers. Could you introduce the CNRS and the INSB (Institute of Biological Sciences) and its key mission to our international audience?

The CNRS is the main research organization in France – it has approximately 33,000 employees, 25,000 of whom are permanent workers, with the remaining 8,000 working on a contract basis. Among the 25,000 permanent workers, approximately 12,000 are researchers working in labs. The rest are engineers and technicians, either in the lab or in the administrative offices. Most of our labs are run under a partnership with other organizations, such as some French universities, INSERM (*Institut national de la santé et de la recherche médicale*), INRA (*Institut national de la recherche agronomique*), and CEA (*Commissariat à l'énergie atomique et aux énergies alternatives*), to name a few concerning biological sciences. Our labs are located all across the country, but we are primarily based in large cities. 30% of our labs are hosted in CNRS-owned buildings while the rest are typically located in university facilities. In our labs, you have a mix of university and CNRS employees; we work with a mixed population and source of financing.

The CNRS has activity in nearly every field of science. The CNRS is divided into ten institutes that each focus on a particular domain of scientific research. Each institute has its own set of labs,

researchers, and so forth. The life sciences institute, or INSB, is the largest institute of the ten, and it controls nearly 20-25% of the CNRS's manpower, budget and laboratories. We have between 200 and 250 labs and 5,000 researchers and engineers. In our labs, about half are made up of CNRS researchers, while the other half is comprised of researchers from universities or other French organizations (INSERM, INRA, etc.).

The mission of the INSB is to cover all of the domains of life sciences and to support research that does not have a preexisting program. Our goal is to find out how life functions and exists on Earth (now and in the past, and, in the future, on other planets!). We are not focused on one aspect of biology (i.e. we are not simply a medical research organization that is focused on human biology), but on all aspects of biology. From molecules to cells, cells to tissue, tissue to bodies, individuals to populations, we are concerned with each and every ecosystem of living things. We want to have a comprehensive picture of the history of life, to date, so that we can eventually predict how life will evolve and change in the future. It is a massive objective.

We dedicate a lot of our research to unexplored, pioneering fields. One example among others: the study of microbes. This has implications in the study of pathogens, but the field is largely unexplored and we know very little about microbes. Only very little is known about the large presence of microbes in the oceans and elsewhere, and there are potentially huge discoveries to be made that have implications not only on healthcare and medicine but also on ecology and energy. We are also in the midst of understanding new forms of life, like megaviruses and unknown bacteria, new metabolic systems, and new genomes. From studying single-celled life forms living in highly acidic environments to decoding the mysterious junk DNA, the INSB takes on new scientific frontiers.

A second mission of the CNRS and the INSB is to help shape the applications of discoveries when they appear. The "motor" behind the CNRS is to decrypt, understand, and explain not only the *source* of discoveries, but also the practical application of scientific discoveries – we do not merely reside in an Ivory Tower. We need to stay aware and think of applications for untargeted scientific research that, with a clever application, can become disruptive innovations. Take Crispr-Cas9, for example. This discovery stemmed from fifteen years of rather arbitrary research. It was at first an intriguing, yet unapplied, way of studying bacterial genomes and bacterial defense against viruses that eventually turned out to be dependent on gene splicing and editing; then, one day, somebody said, "hey – this would be great in a biotechnological application." Then, of course, they applied the science and it has been disruptive. There are countless stories like this. Innovation is often the product of aimless research. We at the CNRS want to stay aware of current scientific research in

the event that it could be utilized in an innovative way.

Lastly, we also try to communicate with the public – however, we could probably do a better job on this front. We naturally have a great deal of communication at the academic level with our partners, but it is incumbent upon us to also keep the French people aware of our work, discoveries and innovations.

Why do you think it is a pivotal role of the CNRS and INSB to communicate effectively with the French public?

Firstly, we have to explain what we do because we are publicly funded. The people finance our activity with their taxes. Secondly, it is really important to communicate with the public, now, because we are facing an explosion of new knowledge, whether in the fields of microbiology or genomics or neurosciences and many others. We are only at the tip of the iceberg in these fields, as well, as we have only recently acquired the capacity to study life at the atomic level. We are seeing a paradigm shift in science, more generally, and the public needs to be updated. Lastly, since we don't communicate enough as is, some members of the public are no longer very confident about the positive impact of scientific research for society. People are a bit frightened by frontier research fields, like stem cells, genetic editing, etc. Some are horrified by the use of animals in research. These practices provoke justifiable questions from the public, and it is important that we defend our rationale and explain our procedures so that they do not think we are spending their money on immoral activities and that they are confident that our work is dedicated to the benefit and progress of the society, based on a rational scientific method.

What are the differences between the INSB and INSERM?

There is a fair amount of overlap between the two, but the broad difference is that INSERM is focused on basic medical research and *human* health. The INSB sometimes studies these fields and has roughly the same size, but we, again, cover all biological science, from microbiology to genomics, from molecular biology to cell biology and physiology. All of INSERM's work is connected with health implications, while our work is not constrained to such parameters. That said, we do collaborate a great deal – 20% of our labs are partners with INSERM. INSERM is actually our largest non-University partner organization, and we work together in three major domains: physiology and cancer, immunology and infectiology, and neuroscience. Once per month, we get together with the

President of INSERM and coordinate these initiatives.

INSERM and the CNRS also have a framework agreement that has standardized our regulatory processes. Each organization follows the same rules insofar as research, authorization and talent acquisition is concerned, and this accord has helped us work efficiently together.

Moreover, we have a very important joint program called Atip-Avenir that invites young scientists to partner with and work in INSERM/CNRS labs in France. We give them the money to start their own team and work for three years, with a potential two-year extension. We have an international committee that selects the best 20 of 150 candidates, ten going to INSERM and ten going to the CNRS. These young PI must not set their team in a lab where they have done their PhD or have been studying more than 18 months. This helps circulate France's brightest minds and keeps the program fresh. Furthermore, we encourage our laureates to apply for grants from the European Research Council (ERC), and we are typically very strong at this – more than 50% are successful in getting ERC grants.

The CNRS and INSERM have other common action. We write position papers together, we work together in finding alternatives to animal testing. Both of our organizations are also key members of the Alliance Aviesan, a group that seeks to unite international medical and biological research institutions. The president of INSERM is currently the president of the Alliance, and I am vice president.

We work together in consulting and reporting to the ministry of Higher Education, Research and Innovation. Importantly, we contribute to shape the strategy of the ANR (National Research Agency), and the INSERM and CNRS work very much in concert in this regard.

That said, I would say that the best asset of biological science is to be part of the CNRS and not of INSERM – we have access to interdisciplinary teams and a higher exposure to technological innovations.

What do you believe are France's strengths when it comes to its research environment?

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One great part of our research environment is that the French public research institutions have tenured, full-time positions. What this permits is the development of the lengthy research projects

necessary for scientific progress. Without such safety nets, politicians and budgeters likely wouldn't give researchers an adequate timeline to conduct long-term studies. This permanence allows some risk taking on the side of the researchers, and it is the best way to get a return on scientific investment. It takes time to see the payoff, but only allowing scientists to do work in the short-term would be a mess.

Our researchers have the opportunity to leave their position at any time they like (a permanent position does not imply that you are obliged to keep it for ever), but this does not happen often. We even offer our researchers the opportunity to go abroad and work elsewhere for a time, and they are always welcomed back if they wish to return. This is actually a win-win for both parties – researchers can give their brains a rest while we save on salary expenses, and when they are rejuvenated, they come back ready and great work gets done.

The second factor behind France's favorable scientific ecosystem is our 'critical mass.' We have a wealth of laboratories and scientists, rich in human capital. We are very well ranked, globally. The French system is powerful due to its strong public research institutions. Moreover, the national organizations, as CNRS or INSERM, implement a national vision for how the research ecosystem should be shaped in the country. It is more difficult for universities to have this vision at a national scale and it is why the French research organizations are so important.

Finally, we are very strong in interdisciplinary research projects because of the CNRS. The CNRS is great at mixing and matching scientists from all sorts of backgrounds, and this is a huge asset – we have dynamic labs that help us attack the issues from new angles. This is particularly true when it comes to life sciences. We partner with researchers in engineering, informatics, mathematics, environment, and physics, to name a few cases. The physics applications have been particularly useful. More and more, mathematics are becoming integrated in life sciences, as AI and informatics are helping us perform our research. The CNRS has an incredible network of diverse scientists.

What are the threats and weaknesses of the French life sciences industry?

I think that we are vulnerable to politics. It would be terrible for us if political prudency prevented us from being able to invest in the "aimless" research that I mentioned earlier. If every project is only funded because it has a targeted goal, you will see innovation rates decline. Furthermore, a unique characteristic of French laboratories is that they are less compartmentalized than are their Anglo-Saxon counterparts. In other words, our labs mix scientists from several different disciplines that have an excellent communal and collegial culture. We call these UMRs (*unité mixte de*

recherche). Scientists from different teams share ideas, support services (including administrative ones) and technological platforms and it creates a great research environment. What people may not realize, though, is that under a constrained budget, this eclectic staff makes fiscal sense, as these different professionals share ideas and resources and create a higher return on investment.

Nonetheless, there is not sufficient funding available for France's labs as is. Keep in mind that labs are regularly audited and examined. Every five years, when these analyses are done, there are some cuts. Labs open and close according scientific performance criteria. Research is, after all, an international competition. Labs are given funding by two sources: grants from public institutions like the CNRS, INSERM or universities and individual fundraising from the teams themselves. Nonetheless, these sources are not enough, and the ANR (National Research Agency) doesn't have the funds necessary to offset the shortage of financing. This is a real problem – unless we can, politically, find a way to fix this issue, labs are at risk and we will asphyxiate important branches of French scientific research.

As I said early, we need to protect all of these different fields and labs. After all, the innovation and discovery of tomorrow will come from them, even if they aren't searching for it.

Do you see Brexit as an opportunity for France to take a leadership role in international research?

Not at all. Research is an international endeavor. France cannot be excellent without the collaboration with other strong countries, as the British. Note that more than half of our publications are done with an international team. The UK has excellent research facilities. It is a shame to not be able to include them in the European research network, and we are already working with them to find a way to keep them involved in our research. It is tragic that our closest partners are becoming removed from the rest of the continent. It is a lose-lose situation. We will simply have to create new partnerships.

How is the CNRS and INSB incorporating the private sector?

At the CNRS (same for INSB which is part of it), we do not pass up opportunities to create economic value. In the INSB portfolio, we have around 1600 families of active patents and at least 500 contracts underway. Moreover, the INSB has helped create or collaborates with 225 startups that use our facilities. We support doctorate theses that collaborate with industry, and we work with

them in our labs. The CNRS is the first public research organization that I know of in France to host a program of “pre-maturation” in which we supply an early injection of investment into research projects that we think are promising and can transfer over into other fields. It is a risky investment that we make, but we will provide funding for one year, or even eighteen months, in some cases, for promising, original research to obtain a proof of concept. This program is only four years old, and we have already had some success stories. I think that this is a crucial program, helping scientists to stay focused on their science, while funding another side of their research dedicated to application.

In addition, we have partnerships with industrial companies sich as Bayer, PSA Group, Servier or Sanofi, to name a few, in a variety of research fields, from biology to automated vehicles.

Do you have any concluding remarks for our international audience?

I think that “Better Together” is an important doctrine to keep in mind when talking about the French life sciences sector. From the outside, the French ecosystem might seem very complex, but from an insider’s perspective, I can tell you that it is not that complex or hard to navigate. I think that we have a unique strength in that our research prowess lies in our national organizations, in partnership with our universities that are rising in strength. We work together very well. Thanks to our national vision of research throughout France, we can effectively organize networks of laboratories and technological platforms based on the respective and specific strengths of each local node. The notion that the French life sciences sector is a web of complexity is a myth. Moreover, we have large, interdisciplinary bodies like the CNRS that creates a mixture of ideas and collaboration.

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