Interview: Gianvito Martino – Scientific Director & Director of the Division of Neuroscience, San Raffaele Scientific Institute (SRSI), Italy

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22.03.2017

Tags: Italy, San Raffaele Scientific Institute, SRSI, Neuroscience, R&D, Research

The division of neuroscience at the San Raffaele Scientific Institute is one of the best worldwide performers in academic research. Division director Professor Gianvito Martino discusses the institute's unique operative model, national limitations, and the future of the neuroscience field as an investment opportunity.

Prof. Martino, to start off, the Division of Neuroscience at the San Raffaele Scientific Institute (SRSI) oversees more than 300 researchers split into 38 research units. What position does the division occupy within the Italian and the European scientific community for neuroscience?

Quantitatively, in Italy, the SRSI has the largest division of neuroscience both in terms of number of people working in, and volume of publications. In fact, our division of neuroscience publishes more than 250 scientific publications per year.
Qualitatively, translational medicine it is a field where the SRIS is particularly strong. This hospital performs well in basic science and clinical science, but it is the translational science field what really differentiates us. Indeed, we can consider ourselves as one of the top hospitals in this field, and this is the main goal of the SRSI: to translate the research into new therapies.

As you said, the SRSI holds a leading worldwide position in the translational science. Why is your model leading and unique?

The beauty of this approach, our division is pursuing as a main pillar of its activity, is the balance between the clinical research and the basic research; we have 38 research units in total, with roughly half dedicated to basic research and half to clinical research. This means that inside the Division it is possible to find purely basic research oriented teams – e.g. Cell Adhesion Unit or Axo-Glia Interactions Unit – together with more clinical teams, such as Psychiatry and Clinical Psychobiology Unit or Experimental Neurointensive Care Unit. When you take a look at the publications records, the again roughly half are in each segment. This balance is what makes this division unique and successful, as it not only fosters but necessitates collaboration and cooperation between scientists and physicians, and it is something rarely seen in other institutions in Europe or the USA.

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Could you share with us some of your biggest projects that the SRSI neuroscience division has recently completed?

If I had to highlight some of our achievements I would like to mention three. Firstly, we have been among the first working on stem cells and cell reprogramming – a smart way to differentiate easily obtainable cells into highly specialized neural type of cells – an approach that represents a smart and novel way to generate in vitro several types of neural cells that might be useful in the future for regenerative medicine approaches. In the same research area, we have been the first institute to demonstrate the potential therapeutic efficacy of neural stem cells in inflammatory neurological diseases such as multiple sclerosis and we are very close to prove the preclinical results we obtained in human patients. Secondly, we have been developing several state-of-art technologies to use neuroimaging to decipher pathological aspects and improve prognosis and diagnosis of several inflammatory and degenerative neurological diseases as well as psychiatric disorders. Thirdly, I have to mention that we are also state-of-art in myelin disorders where we have been working hard to understand the genetic basis of such disorders in order to identify novel therapeutic targets to tackle. .

How long does it take to bring these therapies from bench-to-bedside? And, could you briefly explain how you develop them?

It is a long-term process. Indeed, in order to develop novel therapies it can take even more than 15 years, this is the necessary time to translate the results of research done in the laboratory into new ways to treat patients. It is a long process where we first prove the therapies using informative pre-clinical animal models, afterwards we need human validation tests and finally, if there is any

reasonable possibility, we might go into humans.

Besides being the therapies development our division main goal, we do not confine our science to new therapies' development. As I said before, we know that if we want to do something we need to start from something. It means that we start from basic science to find out the knowledge that will help us to develop new therapies for neurological and psychiatric disorders.

Therefore, basic science is an important underpinning in our operative model. It means that, in the division, we have neurobiologists as well as cellular and molecular neuroscientists. It is important to understand that all these figures and the areas where they work are crucial for developing real translational medicine.

A large number of basic and clinical research groups, which make up the division, have been assembled under the Institute of Experimental Neurology (INSPE). The aim of this institute is to combine competences in clinical and pre-clinical research together with a high level of basic research. How have you sought to build excellence in this area?

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If you want to build the excellence you have to start with excellent people. We applied this argument in our SRSI recruitment policy. Indeed, we look for professionals that have international experience, which helps keep us connected and aware of the important research developments on-going outside of Italy. These experts come back to Italy with some competencies that are fundamental and crucial for us, and it is through these excellent people that we build our excellence in experimental neurology. Of course, transparency and meritocracy are the main pillars of our recruitment policy.

So, knowing that the research is a priority for the government, how do you manage to attract and retain your experts?

Unfortunately, research in Italy is not a key issue for the Government. There are very few investments coming from public funds because the politicians do not understand how important is the research and the way this field performs (payback returns, quantity of investment needed, etc.). Luckily, things are starting to change in the last years.

Indeed, in SRSI we push people to compete worldwide and share their ideas with their peers. We foster peer reviewing in order to discard those ideas that are not great and to choose the best ones. It is the only way to make them growing both intellectually and professionally. We have also this mindset in our management, the bottom line is that we have to compete worldwide in order to find monetary support and this is the way making us international competitive.

You have said that the best way of doing research in Italy has been changing in recent years; how has the SRSI played a role in this change?

My generation was the new one going massively out of Italy to learn how to best perform in research. In fact, when I graduated at medicine there were very few research jobs in Italy, so to a certain extent we were obliged to leave the country to develop our professional careers. After some years, we had to come back with all those aforementioned competencies, and those of us who were able to get good positions started to drive a change in the mindset within Italian research institutions.

At that time, this hospital grew very rapidly and started to recruit people with that international background. It was a great opportunity to find a position here in Italy, and a lot of talented individuals joined this organization. Finally, after many years, the critical mass was enough for this internationally experienced generation's mindset to become dominant, and dictate the way research is actually being done in Italy.

A common topic is the willingness division heads are showing to promote collaboration with the industry, and to move towards a more efficient model for the development of new therapies. Where do you see the advantages of working more closely with the industry?

Just to give you a rough number, we are running studies of more than 50 drugs in this research division. It means that we are collaborating a lot, and this institute has many partnerships drug companies. We are very keen to work with different organizations within the industry, and there are many reasons to collaborate: cost effectiveness, innovative thinking from academies and expertise from drug companies. For example, the SRSI is really good at developing alternative ways of thinking regarding drug development, and finding alternative treatment methods; drug companies are less flexible, as they think in terms of the molecules that they have invested in. However, we also need the expertise of the drug companies. We don't know how to develop a drug from the beginning to the end, and they can figure out very quickly if an idea has the potential to be developed into an effective and commercially sustainable treatment.

Besides Merk Serono, which other companies are youcollaborating with?

We are working hand to hand with leader companies and we are collaborating with all the major companies that have presence in the neuroscience field. Sometimes it is hard to find collaborations for a project because pharma companies do not take too much risk when they invest in neuroscience. We are trying to break this fear wall transmitting that neuroscience projects can deliver, have an economically sustainable outcome, and of course improve patient care.

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You mentioned that drug companies do not take too much risk when they invest in neuroscience. What are the reasons that make neuroscience a complicated field?

There are two main reasons that make treating neurological disorders particularly complicated. On one hand, the brain is protected and covered by the blood brain barrier, so it is difficult to deliver the drug into the brain. This also makes it difficult to study the brain in order to understand the internal mechanisms of the diseases.

However, besides these difficulties, it is a field where I see a lot of potential. Investing in this field is an opportunity because there is a lot of room to find new therapies (e.g. cell and gene therapies, etc) and there will certainly be more targeted therapies for neurological and psychiatric disorders in the future.

What is more and really interesting, from a scientific point of view, we understood among the last twenty years that the brain has an internal mechanism that repairs itself. In the past we thought that the brain was a sort of issue that cannot change. However, now we know that the brain changes a lot, it is a dynamic organ. And now we are trying to understand this mechanism. The idea is to start fostering this type of intrinsic mechanisms in the future through developing more 'natural' therapeutic applications.

Finally, what are your expectations for the potential of the field over the next few years, and what are your personal ambitions for the Neuroscience division at the SRSI?

The future challenge of the industry is to find a solution for the neurodegenerative diseases such as Alzheimer, Parkinson and ALS. Indeed, at the moment, there is not any relevant 'therapeutic' advance in this field. I expect that there will be some major discoveries in terms of targeting therapeutic approaches to these diseases over the next years. The aim is to understand better the molecular mechanisms of the neurological degeneration in order to find target therapies to hit these diseases through drugs or other approaches.

Referring to the neuroscience division of SRSI, my expectation is that it will be able to understand better the reason why the brain degenerates itself overtime. It can be due to physiological reasons or due to certain pathology, but if we can better understand these mechanisms, we will be able to develop a therapy based on the aforementioned concept of natural medicine through fostering the intrinsic repair mechanism.

I also expect that there will be major advances made in the area of brain-machine interfaces and neural prosthesis that could potentially improve the treatment of neurological problems and the quality of life of disabled neurological and psychiatric patients.

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