Interview: Luca G. Guidotti – Deputy Scientific Director, San Raffaele Scientific Institute (SRSI), Italy

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Prof. Luca G. Guidotti discusses the esteemed positioning of San Raffaele within the global scientific community, their core mission of translational medicine and the challenges Italy faces today with the development of young scientific talent and the bridging of the public-private gap.

Prof. Guidotti, could you begin by describing the position of the San Raffaele Scientific Institute (SRSI) within the Italian and European academic communities?

SRSI constitutes the research institution within the San Raffaele Hospital (OSR), which is one of the largest university hospitals in the country and also a private institution. From the very beginning, since OSR was founded in the 1970s, its fundamental mission has been – and still is – to promote what is referred to as 'translational medicine', meaning essentially the promotion of research that moves from the laboratory to patients as quickly as possible.

As a research hospital, it is one of the largest campuses in Europe on a variety of metrics: clinical trials, from early to late phases; number of employees (6,000) and land area (150,000 square meters of laboratory and 150,000 square meters of hospital space).

Following our new ownership in mid-2012, we are now part of the San Donato group, which is among the largest healthcare-related groups in Europe.

One of the most significant aspects – and advantages of OSR – is its size, which gives it the critical mass necessary to successfully accomplish its goals.

When the institute was granted IRCCS status in 1972, its main focus was on Diabetes and Metabolic Disease. Today, the institute operates in a wide range of areas, but what would you say are its main pillars?

Both in terms of research and clinical care, we do not think in terms of single specialty areas. Instead we cover all biomedical areas and, research wise, our activities are organized within five different Research Divisions (*Genetics and Cell Biology; Neuroscience; Immunology, Transplantation and Infectious Diseases; Regenerative Medicine, Stem Cells and Gene Therapy; Experimental Oncology*), 4 internal Research Institutes focusing on specific themes (*the San Raffaele Telethon Institute for Gene Therapy [SR-TIGET], the Diabetes Research Institute [DRI], the Institute of Experimental Neurology [INSPE] and the Urological Research Institute ([URI]*), 3 Research Topic Areas (*Area of Cardiovascular Research, Area of Feto-maternal, Newborn, Child and Adolescent Health and Area of Oral Pathology and Implantology*) and 3 Research Centers (*Experimental Imaging Center, Center for Translational Genomics and Bioinformatics Center for Advanced Technology in Health & Wellbeing*).

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Nevertheless, there are what we call ‘hotspots’ of activity at OSR and these are mostly linked to the reputation and talent of single individuals. For instance, Prof.. Luigi Naldini is a world-renown expert in gene therapy at SR-TIGET, which has been at the forefront of biomedical scientific activity in gene therapy worldwide.

The phrase ‘translational medicine’ has become a buzzword in the healthcare industry. How is this being concretely realized at OSR?

As mentioned, OSR has translational medicine at the core of its efforts. It is true that the phrase ‘translational medicine’ is an incredibly overused word in the healthcare industry today and often the reality does not match up to the phrase because it is a very difficult concept to implement.

At OSR, we have it as our foremost mission and we do our utmost to practice it in our daily operations. For example, all physicians at OSR must be fully involved in research, understand laboratory processes and in general also be good scientists. Similarly, scientific researchers must understand the processes of good medical practice. This fosters better communication between the two and helps contribute to an environment where translational medicine is possible and realized

everyday.

In terms of practical matters, this also ensures our financial survival in the long-run. As translational medicine involves the development of science from early, basic research to clinical trials and patents, we are able to produce products that are of direct interest to the private sector, be it the pharmaceutical industry or private investors. It is important to be able to have a tangible product with clear potential market value in order to remain competitive in today's healthcare environment.

This is also related to the complexity of the industry nowadays, partially due to the regulations imposed by external regulatory authorities. For instance, discussion with the FDA cannot be based on the basic science of a therapy alone. They also want concrete details on the therapy's impact on the hospital infrastructure and the overall healthcare system, for example, the time it would take for the therapy to reach the patient or the number of contact time with doctors it would replace. This is even more applicable if we are offering a novel technology like the first human use of biologics worldwide. From the very beginning of the process, even at the initial scientific stage of basic research and development, we need to consider the overall strategy and investment choices of the final marketing of this product. There needs to be a long-term perspective to guide the entire development process.

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This is a very different undertaking compared to the provision of standard healthcare, and our success is our emphasis on – and actual ability to do – translational medicine.

As the largest scientific institute in Italy, what are some of the unique strengths you are able to draw on, which have led to the institute's success?

Two fundamental aspects stand out. The first is the intimate connection between research, clinical activity and education that we foster here through the coexistence and proximity of the hospital, the university and the research institute.

The second is our size, which gives us the critical mass necessary to successfully perform translational medicine. My pitch to both students and investors is this: the entire process at OSR is derived from ideas. Ideas – strong, scientific ideas – are at the core of any innovation, research and development. This means that our primary and basic objective is to foster and encourage good science as much as possible, regardless of specialty areas or field. It does not matter whether the scientist works in basic science, specific medical subfields or pure chemistry or physics.

The magic comes when they interact and exchange ideas. Synergies develop through collaboration between scientists from different fields and areas of expertise, be it at professional networking events or the simple act of sitting down for lunch at the same table. The price we need to pay for this invaluable synergy is the maintenance of a critical mass and a large institution. OSR does pay for some of this research activity out of our own pockets. 80 to 90 percent of our funding comes from public sources but in Europe, public funding does not take into account indirect costs of research, which includes the daily operational costs of the institution (which are taken into account by the National Institute of Health in the US), so our public funding only covers direct research costs. We fund the remaining through private donations because we understand very clearly how much our reputation depends on the quality of our research.

As big as we are now, with over 1000 scientists, we want to – and should – be even bigger, in order to really compete with the major institutions in the US. There are plans for further expansion and in 2017, construction has begun on new buildings on the various campuses of OSR.

An issue we have heard some concern around is the difficulty for young scientists face when looking to join and build their career at scientific institutes. With Italy's scientific renown being a major draw for international companies, how would you rate the current pipeline of talent in Italy?

Going beyond the obvious, usual complaints about the instability Italian political system, there are two main challenges in terms of the development of young talent in Italy.

The most basic is simply the language barrier. The language of science remains English, and competence in the language is absolutely essential. From the very beginning, there is a price for Italian scientists to pay because they do not live in an English-speaking country.

Secondly, whether we like it or not, the US still dominates the scientific research ecosystem. Top institutions like Harvard, MIT or Stanford possess a prestige and a reputation that even the best universities in Europe, with the exception of Oxford or Cambridge, simply do not, despite the top quality of European institutions. This is very important for young scientists and given the option, Italian post-doctorates should absolutely go to these institutions. We do lose a lot of promising talent this way.

At OSR, we have our own PhD programs and we have done very well in developing and maintaining young talent, but we also give them the opportunity to perform very good postdoctoral programs abroad. There is this gap of a few years where many of the best young researchers go abroad, but often we do find that they like to return to Italy after their postdoctoral programs, with the

significant caveat that they manage to find grants from Italian universities. In this regard, there have been a number of programs in Europe to encourage this, like the European Research Council program, through which we receive many applicants.

In France, we have heard about a cultural attitude that discourages academic researchers from going into private or industrial research because there is an aversion to the idea of 'profit'. How would you rate the willingness of Italian research institutes, both the SRSI and more broadly, to collaborate with the pharmaceutical industry?

This cultural attitude is definitely present in Italy. It is changing, but very, very slowly, and it varies between institutions, particularly between private and public institutions. It is crucial that we continue opening and that we open more rapidly, because the private industry sector is very reactive and quick.

Industry has been seen rather as a devil for a long time. As research and healthcare institutions, it is clear that the environment today is such that we cannot hope to support ourselves in the old ways one or two decades from now. Money for healthcare and science is decreasing and it will only continue to do so. Partnerships with industry and private entities are crucial, now more than ever, to our survival.

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Going back to my earlier point about young talent development, this is another reason we need industry in Italy. Academic science has a particularly merciless hierarchical system, with many people at the bottom and only a few at the top. The competitiveness means that there must be backup plans and exit strategies for all the people who do not make it all the way to the top. These are still highly skilled, valuable professionals, in their mid-thirties or mid-forties, who now require other career options commensurate with their experience and expertise. We need a thriving industry to soak up this talent. In the US, this is easy because there are so many pharma and biotech companies, but it is much harder in Italy and this discourages some from pursuing a career in science in Italy.

We need to create a more conducive environment for business in Italy. We are very well-placed for clinical development and research activities, because of the pool of talent and expertise here, which is not always or even predominantly the case in Asia, and its public, universal healthcare system, which is not true of the US. These two factors should position us as the ideal hub of R&D, and there is a lot of clinical research activity in Italy. But international companies continue to keep

their research and manufacturing HQs in the US. It would be wonderful if we could work on changing this.

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