# Interview: Prof. Manuela Battaglia & Prof. Lorenzo Piemonti – Vice-Directors, Diabetes Research Institute (DRI), San Raffaele Scientific Institute, Italy

22.01.2016

Tags: Pharma, Pharmaceuticals, Italy, Government Relations, PPP, Public Private Partnerships, Doctor, Academia, Education, University, DRI, Drugs, Diabetes Research Institute, Manuela Battaglia, Lorenzo Piemonti, San Raffaele Scientific Institute, Interview, Insight

*Prof. Manuela Battaglia (MB) and Prof. Lorenzo Piemonti (LP) discuss the positioning of the Diabetes Research Institute (DRI) within the San Raffaele Scientific Institute and the global diabetes care community, their respective specialty areas and DRI's commitment to translational medicine.*

**The Diabetes Research Institute (DRI) is part of the International DRI federation, which includes 12 other institutes around the world. What are the key characteristics and activities of the DRI at SRSI that differentiates it from other institutions?**

**MB**: As you know, SRSI itself is centered on the mission of translational medicine. Our strength derives precisely from this integrated effort, both in terms of specialty areas, where we combine the fields of immunology and beta-cell replacement, and in terms of industry, where we have major collaboration with Big Pharma.

The key feature of the SRSI – and therefore the DRI – is the coexistence of laboratory, hospital and university, which is a rare occurrence even globally. Very tangibly, it is uncommon for a researcher to be able to cross a street and obtain patient samples for use in the laboratory, and our interactions with researchers in the US have impressed on us the rarity of our work situation. We

have both clinicians and university students active on our research projects and this generates a lot of synergies.

Diabetes itself has been one of the original focuses of SRSI. In 2007, the then-scientific director decided to collect all the different sections related to diabetes in one institution; before, the organization was very fragmented, which diluted the effectiveness and influence of all the expertise available. A year ago, we were lucky enough to move to a brand new campus with new laboratories, and we are continuing to expand.

Specifically, in DRI, we have two areas of focus within diabetes: firstly, islet transplantation and beta-cell replacement as a new approach, which is Dr. Piemonti's specialty, and the immunology of diabetes, mainly type I for now, which focuses on preventive care and is my area of speciality. We also have a broader emphasis on screening and preventing type I diabetes, for instance, we collaborate with TrialNet, an US-based organization that screen subjects at risk of diabetes.

**Can you briefly discuss your respective areas of specialty and the projects you are most excited about?**

**MB**: The most exciting development in immunology is the idea of resetting patients' immune systems, to have the tools to understand the disease development in patients in terms of immunological response, and the tools to intervene as early as possible, even before the condition appears. We can now recognize patients at risk for diabetes and this paves the way for us to develop preventative care. This represents a huge change in mentality and in approach. We can intervene earlier, faster and better.

**LP**: It is also a really exciting period in terms of my specialty area. Our research into islet transplantation has taught us two things: we can cure diabetes, but we require a personalized approach. A cure means restoring normal glucose control to diabetic patients, and this is unequivocally possible with cell or tissue therapy, depending on your definition. But there are limitations and this approach is only applicable to a small patient population. However, a new approach in regenerative medicine has been developed and now, the dream of a diabetes cure available for the mass population seems achievable through beta-cell replacement. We have initial trials in San Diego with a group using embryonic cells to derive beta-cell therapies in the absence of immunosuppression with the use of a new device, and there are other groups working along the same lines. There will be many clinical efforts on this approach in type I and hopefully type II diabetes in the coming decade.

Ultimately, at DRI and in general, the goal is curing diabetes and all these different approaches work toward this. There are new exciting developments in the biomaterials field as well. These areas – cell biology, biomaterials and immunology – represent our comprehensive and complementary efforts to improve the lives of diabetic patients. Currently, we speak of insulin treatment but the life expectancy of patients with type I diabetes is still twelve years shorter than that of a healthy person, which demonstrates the inadequacy of this mode of treatment. The holy grail is to give patients the same life expectancy and to restore a healthy system of glucose control to diabetic patients.

**We have heard from Dr. Luca Guidotti, the deputy scientific director of SRSI, that translational medicine is at the heart of SRSI's work. As one of the four core institutes within SRSI, how do you promote translational research to ensure that the newest medical advances reach the patient as soon as possible?**

**LP**: Historically, the relationship between the private and public sectors has been very fraught, with one side seeing the other either as too idealistic and naive or too mercenary and calculating. However, we must recognize that the private sector is not our enemy.

One of our most successful projects has included collaboration between the university here, clinicians and Big Pharma, which is our ongoing phase III trial in islet transplantation. This is the first trial of its kind in the world, and we are working with around eight or nine international centers in Europe and the US, targeting for the first time the innate immune response in diabetic patients. We are using a particular anti-chemokine receptor for the first time, which was developed by Dompé, a huge Italian pharmaceutical company. This is a model for translational research: we developed the preclinical aspects of the receptor and then convinced pharma companies to support clinical trials. There have been challenges but overall we are very pleased with this success.

Very practically speaking, industrial collaboration made up 13 percent of our operational budget from 2008 to 2013.

**As you mentioned, you have had very successful projects that brought together diverse stakeholders in the public and private sectors. What have been some of the major challenges of doing this?**

**MB**: Fundamentally, it is the attitudes of the researchers and the academic community. Translational medicine is very complex and demanding on participants. There are three languages we need to be conversant in: science, business and law.

We are scientists by training and we have been taught to focus on publications, data, results and grants. Now, we also need to consider intellectual property (IP), patents, industry collaboration and regulatory assessments. This has increased our workload and mental load immensely, and it has also required a dramatic shift in attitude. For instance, as scientists, we have always thought about open collaboration and sharing, so the idea of a patent and protecting your own IP seems, initially, very conflicting.

We also need more guidance and education on this. For instance, if we want to do phase I trials, we need to interact with regulatory agencies and this is a lengthy process that can take months. Currently, as scientists we have to do this on our own.

**LP**: I agree. We are scientists by training and this is because we enjoy doing science! Now, we have to spend more time in the office and we are learning about regulatory processes and pharmacoeconomics, because it is important that we, as deputy directors of DRI, understand the management of science in addition to science itself. This is unfortunately not the most exciting element of our job but it has to be done, for us.

Another huge challenge is with regulation, both internally and externally, and this is even more applicable to translational medicine. With our trials in pancreatic islet transplantation, we had to deal with the regulatory authorities, both the FDA and the EMA and with different legal teams within the pharmaceutical companies and the Institute. It was complicated because both the FDA and EMA had different sets of requirements and we needed to produce different dossiers and documents for a multitude of stakeholders. A compromise must be reached between these stakeholders and scientific concerns so that there are just one set of issues.

**In France, we 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 academic to collaborate with industry?**

**LP**: There sometimes exists an intrinsic conflict between academia and reality. Even for a doctor, there can be conflicting interests between what is best for a patient and what is better for the healthcare system; the interests are not always aligned. There are ethical and philosophical issues.

But earlier when we spoke about a scientist being a scientist – we want to cure everyone in the world – ultimately it is also undeniable that if scientists are more efficient in these areas like IP, etc., they will be stronger performers in the industry, the processes are more efficient and the outcomes for patients will also be better. Otherwise, as a scientist, you are limited to simply

generating ideas and having someone else take over, you never see them to fruition, and that can also be frustrating.

Part of the issue is that Italy is a complex and heterogeneous country and regional variation exacerbates this matter. If you are in Lombardia or Toscana, you have resources and international companies who are physically present while if you are in Sicily or more rural areas, it is more difficult. The pharmaceutical industry may not want to invest in the underdeveloped areas of Italy either so it becomes a vicious cycle.

**MB**: The reality is still fragmented. We have realized our past mistakes and we are trying to restructure ourselves to overcome this. But in Italy and in Europe more generally, there are still places where academia is seen as a 'pure' environment where IP protection and patents are taboo, commercial topics. Even in Germany, where I was a few days ago, I sensed some suspicion about the fact that I had patented a protocol. It turned out to be very helpful because it built some connection with industry. In Italy, there is a similar reticence and even distrust, especially at smaller and more local universities, which are less exposed to international activity. The truth is that resources are limited and we need to do everything to maximize access to them, but in a responsible and transparent manner.

**LP**: We are very proud that, in some ways, in Italy at least, this is one of the first institutes to take into consideration the full complexities of this issue. For instance, we have started the revolution with the creation of the Office of Biotech Transfer and we have the structures in place to further facilitate translational research. The next step is to revamp our education system to begin introducing and acclimating our students, the next generation of scientific leaders, to this new research environment.

In Italy, the most crucial cultural change that needs to happen is that we must realize that vision alone is insufficient. Vision without funding is an illusion.

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