At this rate of funding, getting a position in an academy will be the “alternative career”

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Juan Manuel González-Rosa gave the Seminar “Humanizing the zebrafish heart: exploring the role of elevated cardiomyocyte ploidy as a barrier to heart regeneration”, at the CNIC, and was invited by Miguel Manzanares.

Juan Manuel González-Rosa currently works at the Cardiovascular Research Center of the Massachusetts General Hospital and Harvard Medical School (USA), but knows the Carlos III National Center for Cardiovascular Research (CNIC) quite well because he worked there from 2008 to 2013. Juan Manuel researches in the field of genetics, molecular biology and cellular biology, especially with the zebrafish model.

- **When did you decide to become a researcher?**

I have always wanted to be a researcher; since I was little I was quite sure of it. My high school teachers tried to talk me out of studying Biology… For some it was frustrating that I didn't want to study Medicine. But, since all of us have to work, the best is to work in something that we are passionate about. And, that is what I try to do, despite the big obstacles that us researchers must sometimes face. .

- **You have been one of the researchers that has benefited from the CNIC's training programs, like Cicerone. What do you think about these types of programs?**

I think they are very useful. In my case, it was my chance to get to know the center. I worked at a laboratory at the University of Malaga and thanks to this summer scholarship I was able to come and research at the CNIC, where I ended up staying and starting my career as a researcher.

- **Did you know right from the beginning which line of research you wanted to follow?**

From the beginning I started working on the zebrafish. In the summer of 2008 I joined Alicia García Arroyo's team with a Cicerone scholarship and, later, I joined Nadia Mercader's team, who at that time was forming her laboratory; I was her first intern. Since then I have been working on cardiac regeneration in the zebrafish model. I have changed my line of research a little, but I still continue in this field.

I think basic research in animals, like the zebrafish, is extremely important in order to understand and design new therapies

- **In this sense, what is the current situation of cardiac regeneration research?**

We still know very little about it. It is very difficult to study the regeneration in mouse or in humans because, in fact, we do not even fully understand how it is produced in the zebrafish, which is a much simpler model. The regeneration of the zebrafish was discovered only 15 years ago and, thanks to this, we now know something more about the cellular and molecular mechanisms that are involved in this process. But, realistically, we are still a long way from understanding how it works. In any case, I think basic research in animals, like the zebrafish, is extremely important in order to understand and design new therapies. Without this work in the field of basic science, we will not get anywhere.

- **What are the main challenges that cardiac regeneration research poses?**

It is an extremely complex task. The heart is one of the organs that, like the brain, does not regenerate after an injury. We know that the heart, which is continuously working, does not have the necessary resources to regenerate after a heart attack. Unlike other tissues, such as the musculoskeletal system, the heart does not have specialized cells for repair and maintenance. What we have learned in the zebrafish is that there are no stem cells in the heart that take care of the regeneration; it is the cardiomyocytes themselves that carry out this process. They enter the cell cycle, divide and regenerate damaged tissue. And why doesn't this happen in humans? What we found out about the zebrafish in the lab in Boston, where I work, gives us some insight. One of the factors that doesn't allow the heart of mammals to regenerate lies in the differences in the cardiomyocytes between both models. Those of mammals are polyploid, that is, they have either two nuclei or a very large nucleus that contains four or more copies of each chromosome. The zebrafish cardiomyocytes are very simple, with a single nucleus and are diploid; they have two copies of each chromosome. If we transform the zebrafish cells into polyploids, the capacity to regenerate is lost. Understanding that this is really very important we can start designing new therapies.

- **How would these therapies be designed?**

What is very interesting is that humans, and mice, have a very small percentage of diploid cardiomyocytes, similar to those of the zebrafish. And if we know that these are the only cells that have regeneration capacity, we will have to expand them somehow. How? It is possible that there are drugs that favor the growth of these cells after a heart attack, or that we can transplant these cells to infarcted hearts.

Mentors are people who are already settled and are generous enough with their time to support the younger researchers

- **Cardiac regeneration has created many expectations that unfortunately have not been fulfilled. What have been the causes?**

It is true that many expectations have been created in the general population about the potential applications of regenerative medicine, and it is true that they are unfulfilled expectations that only generate frustration. And it is also true that us scientists are partially responsible for this. As professionals we must take responsibility for this situation. It is essential that we convey the idea that biomedical research is slow and that we need to invest in basic knowledge before moving on to therapies. When I started my thesis there were many studies focused on the transplantation of stem cells from the bone marrow to the infarcted heart of patients. Obviously it is very important to do this type of studies, in my opinion, but first they must be done in animal models. When they have been done systematically, it has been discovered that the marrow stem cells have a small beneficial effect on the heart, but not the expected one: the cells do not differentiate in muscle, they secrete some signals that attenuate the effects of the infarction, but they do not regenerate the heart.

- **Are you going to continue in this line of research?**

My idea is to continue working with the zebrafish. But in the future, if I can become an independent researcher, I would like to incorporate other systems. Studying only one model will give us a very partial vision. It is important to compare, for example, what happens in mice with what happens in the zebrafish. I would also like to work with other organs, such as the liver, which is a polyploid organ, and its cells are capable of dividing very efficiently. Understanding how other types of cells do it is a possible way to be able to apply it to the heart. Instead of transplanting cells, the goal should be to stimulate the cells that are already in the heart in order for them to be able to divide themselves. That is, use our own modified cells to do the same as those of the zebrafish.

- **How complex is it to become an independent researcher?**

In my opinion, it is becoming a more and more complex process. In principle, those researchers who have completed years of postdoctoral research and who have published several articles in high-impact scientific journals will seek independence. But the truth is that there are a very few number of vacancies and the level of demand is very high. It is a stage of maximum vulnerability for the researcher and, unfortunately, there is very little support for young talent.

- **You´ve spoken about the people at the CNIC that have supported your research. What is the role of the mentor?**

The mentor’s role is critical. And it does not necessarily have to be your director or thesis director, but rather someone with whom you can speak to about the next steps in your career. Nadia Mercader has helped me a lot, but also Miguel Torres and, especially, Miguel Manzanares, all of whom have been a great help to me when making career decisions. Although I have not worked directly with them, they have always had time to talk to me and advise me. Mentors are people who are already settled and are generous enough with their time to support the younger researchers.

We should not promote the idea that the academy is the only option, but rather that there are multiple career prospects.

- **You currently work in Boston. Would you like to come back to Spain?**

I would love to work in my country. Besides, I feel Spain has invested in me, through scholarships, for many years and I would like to give back everything it has given me. I would also like to transmit all the knowledge I have acquired in the USA. However, the economic situation is what it is.

- **What advice can you give researchers who are just starting their career?**

When I was studying Biology I was told what a “traditional research career” was: thesis, post doctorate, and at some point you have your own independent research group. In my opinion, this is a very academic and, nowadays, unrealistic view, which only takes into consideration a part of current research. What were once called 'alternative careers’ that is, non-academic, should not continue to be called that. The problem is that in universities and research centers there is a great lack of information about what can be done outside the academic world. Scientists can also work in the industry or serve as intermediaries between industry and basic science. If I could give some advice to students, I would tell them to explore different alternatives well and to ask themselves without inhibitions what they really want to do. Many people do a postdoc after the thesis because it is what 'must be done' and they do not know that they could do other jobs which they are better suited for. It is at this moment that the role of the mentor is key, because the mentor can guide with knowledge.

- **The general impression is that if you do not do a “traditional” career you are not a good researcher**

It may be that the academy itself generates that kind of stigma. Some of my fellow thesis students, who now work in the industry, tell me that other researchers refer to them as "those who have gone to work for the enemy". And it is a very outdated vision. Not all researchers want to have their own line of research. In the USA, most of us postdocs that continue at the Academy are foreigners. In one of Harvard's doctoral programs, 90% of doctoral candidates opt for positions in industry because they know they have better salaries, better working conditions and that they are really going to work with fantastic equipment. There is much less stigma than in other countries, like in Spain. In my opinion, we should not promote the idea that the academy is the only option, but rather that there are multiple career prospects. As mentors to younger people we must be very respectful of the choices that each one makes. At this rate of funding, getting a position in an academy will be the “alternative career”.

- **And going back to the academy from the industry, is it possible?**

I have little experience in this regard, but I have the impression that, in biomedical research, that return is really infrequent. When this conversation comes up in training talks, I have come to understand that this return is very limited to those researchers who during their time in the industry have acquired really unique technical knowledge that makes them very appealing for certain academic research centers.

- **What differences do you find between researching in the USA and Europe?**

Yes, it is different; neither better, nor worse, but very different. There they are focused on 'selling' their story in the scientific field as if it were unique and the most relevant. Europeans, in general, are more conservative and timid when it comes to 'selling ideas' and 'selling' ourselves. And what is completely different are the resources. Philanthropy does exist in the USA: it is very prestigious to create a chair or a research center with your name. And in Spain, this is very rare.

Another important difference that I have found is the emphasis that is given in the USA to scientific communication, in the transmission of ideas. In the Spanish universities we have a great technical level, but we do not know how to express ourselves very well. Any first-year student from an American university is able to teach a seminar with much more confidence than a Spanish student who is finishing the degree or the thesis. Simply, they are very aware of how important it is to know how to communicate. And that is something they are trained to do.

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