Bertie Göttgens: "Communication between basic and clinical research is complex "

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Dr. Göttgens gave the conference "Cellular States, Differentiation Trajectories and Regulatory Networks of Blood Cell Development" at the CNIC Seminar cycle, invited by Dr. Miguel Manzanares.

Bertie Göttgens' group, of the Cambridge Stem Cell Institute at the University of Cambridge (United Kingdom) uses a combination of experimental and computational approaches to study how networks of transcription factors control the function of blood stem cells, and how the mutations that disrupt these networks cause leukemia. This integrated approach has facilitated the discovery of new combinatorial interactions between key regulators of blood stem cells, as well as experimentally validated computational models for these cells. Dr. Göttgens gave the conference "Cellular States, Differentiation Trajectories and Regulatory Networks of Blood Cell Development" at the CNIC Seminar cycle, invited by Dr. Miguel Manzanares.

- ***What is the main field of your research?***

In our group we are trying to reveal how the blood cells are produced and what goes wrong in the process that causes these cells to be transformed into leukemia cells. Actually, we are trying to discover how the cells make their decisions: the cells in the most embryonic states transform into different types of cells, but they also do it in adult phases and make decisions to maintain a good functioning of the blood -homeostasis-. However, when there are mutations, they are capable of transforming into leukemia cells. That is what we are investigating: which mutations interfere in these decision-making processes that end up producing blood cancers.

- ***And if we know what happens in these processes in their earliest stages could we, in some way, prevent the development of these tumours?***

I don´t think so; I think that this information is most likely to be very useful in managing or treating this type of cancers. The idea is that the balance between normal differentiation and abnormal proliferation is damaged and, if we can find out what controls this balance, we could have a variety of innovative ways to attack the leukaemia tumour cells. Preventing, however, would not be feasible because, in some way, it is a matter of 'bad luck'. How to prevent bad luck? It is very complicated, and in reality, you only have the certainty that you have had bad luck when you have been diagnosed with cancer. But it's true that this information will be useful to improve the treatments. If we know exactly how regulation occurs normally and how it gets out of control, then we will have different routes of therapeutic approach.

- ***Would it be possible to identify these mutations in the earliest phases and in this way apply a direct treatment as soon as possible?***

Like in the rest of the tumours, in leukemias there are a variety of mutations that promote the formation of cancer. That's why it is very important to determine which individual mutations affect this cellular decision-making process and which are the most suitable to be used as targets in a future treatment.

In this sense, we are currently carrying out preclinical trials in a very basic model in order to be able to expand our knowledge in these cellular networks and their interconnections. At the moment we have obtained financing from a pharmaceutical laboratory. This is of course a good sign, because they think that our approach may reach the clinic in the future and have selected it from hundreds of other projects. It is an example of something that has been discovered in my laboratory but that may have clinical implications, especially in the field of diagnosis. And if we finally discover mutations that disrupt cell behaviour, we could screen these mutations and classify patients in different groups. This way, patients could be treated more specifically.

- ***Do you think there is a "gap" between basic and clinical research?***

More than a “gap”, I think that basic-clinical communication is complex. I would classify it as a very narrow “bridge”. Partly because clinical research, especially if a clinical trial is conducted, is very expensive, and requires public funding or funding from a pharmaceutical company. This is part of the problem. But it is also a 'cultural' issue that divides basic researchers from clinical ones. The good thing is that there is a lot of room for improvement. For example, integrating clinical researchers in the basic research groups. That is, make a round trip: 'bench to bedside' and 'bedside to bench'. But in the end, in most cases, it depends on the people. In my case in particular, I collaborate with three different pharmaceutical companies and all of them do it because one of my postdoctoral researchers works in some of them or because I know someone who has put me in contact with someone in their company so that we can work together. What I want to say is that, I am not really convinced that a scientific meeting organized with researchers and industry personnel will be useful to develop joint projects. I think it's more of a personal issue, of friendship. It is not by any means the only way to transfer basic science to the clinic, but in the end, you have to trust the people with whom you are going to collaborate with and, from my experience, this is the way it works best.

- ***How important is mentoring for the younger researchers?***

I see mentoring as part of my work. But I understand the mentoring of young researchers as something that senior researchers do automatically, and not just on issues related to science. That is, we can provide them with very valuable information on various topics: what types of projects can you request? How to advance in the professional career with the difficulties posed by the PhD? ... It is not only about answering scientific doubts, but something more global, more integral. In my case specifically, I go for lunch every Wednesday with two of my junior researchers to discuss aspects related or not to science. We can talk about anything else that they consider relevant (economic aspects, related to the doctorate, etc.). There are many other topics (leading groups, how to organize a budget, how to manage in the academic world ...) that no one usually talks or asks about. And of course, we talk about scientific aspects. I think the best way to be a good mentor is to consider all these aspects, and not just the scientific ones. Otherwise, mentoring would be incomplete.

- ***As director of a lab, do you have any time to do research?***

If I worked 37 hours a week, then no. But no scientist works just those hours, and we try to find time to continue researching. In reality, I don’t have time to do experiments, but I am involved in the process. If I had to take samples, I wouldn’t be able to, because I’d have to leave behind my other obligations, like attending meetings, answering phone calls, creating budgets, etc. But, I am involved in the discussion processes. It is the interesting part of science, the other, writing a job offer, etc. is more boring.

- ***How have the new technologies changed scientific research?***

One of the biggest changes in the field of science has been the incorporation of information technology. You can spend a lot of time with cell cultures, but the interpretation of the results requires bioinformatics. New discoveries in the field of biology are produced with computer science. With genomic technologies it is possible to make great advances. It is increasingly important that the people who design the experiments, in addition to having knowledge of biology, should be good in the field of computer science and in the analysis of results, because, otherwise, they will not make any relevant discovery. Discovering something new is the exciting part of my job. Of course, science has changed, and it will continue to do so, because it is becoming easier and cheaper to perform genomic and proteomic analyses.

- ***Do you remember when you decided to be a scientist?***

I was 19 years old I think. I was in the army, doing my military service. At school I was good at science and mathematics, but I was also good at playing the violin. I was between two possible

career options. But I realized that my talent in violin wasn't exceptional, just normal, so I thought, ok, I'll do the science career then. My older brother was studying an engineering degree and I went to see him at the university and attended some classes, and quickly decided that I wasn't going to study engineering. I chose Biology. But, I continue to play the violin.

- ***What is your opinion of the CNIC?***

Before coming to the CNIC the first time, I asked some of my colleagues about it and they all told me it was a centre of excellence in research. And, I've been collaborating with Dr. Miguel Torres for a long time.

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