

An interview with François Guillemot



François Guillemot heads the Division of Molecular Neurobiology at the MRC National Institute of Medical Research (NIMR) in London. His research focuses on the transcriptional control of neurogenesis, adult neurogenesis and the epigenetic regulation of gene expression in neural development. François recently became an editor for *Development*, and we asked him about his research and career, as well as his lab's future move to the Crick Institute.

When did you first become interested in developmental biology?

I have always been interested in biology, but my first interest was zoology. I spent a lot of time on the French coast, in Brittany, observing little animals at low tide. That was really a great passion of mine when I was young. As developmental biology is closely linked to zoology, the move was quite logical.

What projects are your lab working on at the moment?

My lab's research focuses on neural stem cells and how their fate is regulated at the molecular level. We have two main current directions. One of these is to examine the gene regulatory networks that control neural stem cell decisions: to self-renew, to differentiate into one cell type or another, or to remain quiescent. This work is mostly performed in neural stem cell cultures. Our other focus is on understanding the function of individual genes in neural stem cell fate decisions *in vivo*, either in the developing or the adult brain.

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There has been some controversy as to whether the mouse brain is a good model for the human brain. Do you think it is a good model for the particular questions that you are asking?

The mouse is obviously the closest animal model to humans and the easiest one to work with. It is a good system by default. But it is far from being a perfect model, particularly for the development of the cerebral cortex. Great work has been done looking at the cellular organisation of the human foetal cortex, and there are very striking differences to the mouse. But for other aspects, such as adult neurogenesis, I can't really answer the question of how close the mouse is to the human because there is still so little known

about neurogenesis in the adult human brain. I think that an important future direction of research in the field is to better understand the human brain and to develop tools to achieve this, such as *in vitro* systems that can be used to probe human brain development. Some great progress is being made in that direction at the moment.

You started your career working on the development of the immune system and then moved to developmental neurobiology. Why did you change fields, and what kind of parallels are there between the immune system and the nervous system?

I think I am far from being the only one who changed from an early career in the immune field to neuroscience. My feeling at the end of my PhD was that many of the key discoveries in the immunology field had been made, and what remained to be done was to acquire a deeper understanding of the details, rather than the big picture. At the time, being young and naïve, I wanted to address the big questions that remained unanswered. The neuroscience field seemed to be the most appropriate for this kind of research.

The transition was not that difficult because immunology and neuroscience have in common the fact that the two systems encompass substantial diversity in cell types and cellular responses. You become used to dealing with very complex systems, and in trying to understand where this diversity comes from. However, in practice most of the things that I learned in my PhD and applied later on are maybe more technical. My knowledge of molecular biology (although maybe a bit outdated now!) comes from my PhD work, and I applied that molecular approach to my work in neurodevelopment.

You did your undergraduate and postgraduate studies in France, then you moved to the USA and Canada, and then you came back to Europe. How does the research environment differ between France, North America and the UK?

It is obviously very different and I always try to avoid grading the different systems because every system has its advantages and disadvantages. I think that the British system, where I am now, is very well balanced. I really enjoy the flexibility that it has, giving you the ability to adapt and move on in terms of topics and techniques, probably more than in France. In the UK there is a greater turnover of PhD students and postdocs in the lab than in France, where a larger fraction of the lab is usually considered permanent staff. This stability is great in that it provides continuity, but it is harder to renew, to find new approaches, questions, or to decide to change direction – you need to convince not just yourself and the new people you recruit, but also everyone you are working with already. The British system also provides a good balance between competitiveness and still being collaborative and convivial.

Was it useful for you to move countries?

Certainly, both intellectually and personally. Moving allows you to take a step back and make what you think at the time is the right decision. You are not influenced by earlier decisions that you are obliged to follow because you remain in the same system. By moving countries you start anew, and you can really decide what the question is that you really want to address. Whenever I have the opportunity to recommend something to a young scientist, I encourage them to take full advantage of the great opportunity that scientists have to be able to move around to do research in the best conditions

Did you have a mentor or someone who inspired you or gave you good advice during your early career?

Not a single person. I have taken advice by asking specific questions of the people around me. But Nicole Le Douarin, who was my first thesis supervisor, was a great figure. She was very inspiring, of brilliant intellect and with a real understanding of her system. It made me realise that understanding your experimental model in depth is a great strength, as well as asking the right questions and addressing them with the right techniques. But in terms of career advice, I am more of an improviser: I ask around and then follow my opinion.

How did you find your first months as a *Development* editor?

I was looking forward to it. It was very attractive to work with a great group of colleagues and for a journal that I respect a lot. But I was a little apprehensive of the amount of work, and how much of a distraction it would be to my main occupation. But I have really enjoyed it actually. The volume is manageable and it is different from the daily lab work, so I can easily do it at different times and almost as a diversion from mainstream work. It is quite diverse, and the interactions with authors through their research is something that I enjoy a lot. To see a manuscript, which has real potential but clearly can be improved, to read the diversity of opinions of reviewers and to see the improvements through the revisions: I find this process interesting and most of the time it ends very positively. Another concern I had was how often you have to deal with complicated situations in which people really disagree and you have to arbitrate, but fortunately I haven't encountered this kind of situation yet.

Are there any particular papers that you would like to see submitted to *Development*?

I am fully behind the current effort by the *Development* team to increase the visibility of the journal in the stem cell field. My work is partly brain development, partly stem cells, so I am aware of the

need for *Development* to raise its profile further in the stem cell field, so that it becomes as recognised and important in this area as it is in neural development. Another obvious direction in the mid- to long-term is to move more towards the human as a model of development. Papers that describe human development, such as those using *in vitro* models of organ development, would be very welcome.

Your lab will be moving to the new Crick Institute in the near future. What are your expectations?

My understanding of the vision of the director, Paul Nurse, of how an institute should be run is that you should hire the best scientists and let them decide what they want to work on. I am very happy with this way of thinking. What I am really looking forward to is to have new colleagues. The Crick Institute is a merger of our institute (NIMR) with Cancer Research UK institutes in London together with contributions from three London universities. That will greatly increase the number, but also the diversity, of research that is being done. I look forward to having more contact with cell biology and disease model groups. The NIMR is currently a very interactive place, so it is both our wish and our challenge to make the Crick Institute, which will be at least twice as big, as collaborative as the NIMR is at the moment.

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What advice would you give to young researchers?

I think the best research is done by people who get ideas that other people don't get. So, follow your intuitions and desires, and don't follow advice if it goes against these. And don't hesitate to move, both geographically and in topic, between your PhD and postdoc. Basically, don't be too conservative.

What would people be surprised to find out about you?

Unfortunately, I am not great at cooking which, given that I am French, can sometimes take people by surprise. I love nature and wildlife, and when I moved to the UK I discovered gardening. I have taken my own approach to gardening, and I mostly take care of the weeds that happen to land in my garden. I use my garden as a way to get closer to nature and watch animal behaviour and plant growth – a place for daily observations of wildlife. I enjoy it a lot and it is my way to relax.

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