20 Questions with… Janet Rossant

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20 Questions with 20 Stem Cell Scientists from Across Canada

1. Where were you born? Where did you grow up?

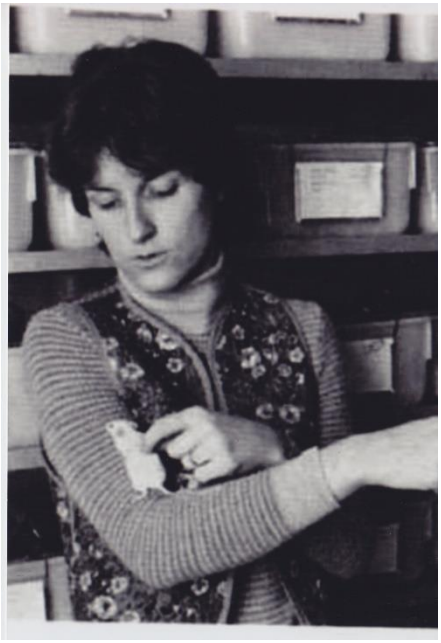
I was born in the United Kingdom in a town called Gillingham in the county of Kent, which is south of London. I grew up there and then went on to university.

2. Where did you go to school?

I did my undergraduate degree at Oxford and then my PhD at Cambridge. I then went back to Oxford and spent of couple of years doing a postdoc.

After that I moved to Canada and married a Canadian, Alex Bain whom I met while we were both attending Cambridge.

I have been in Canada ever since. We first settled on the Niagara peninsula, in St. Catharines and then in Grimsby. I had a job at Brock University and my husband was at various places including McMaster University, at a company in Milton and also at Scarborough Campus of the University of Toronto. So we decided we would put roots there for the moment and head out in different directions.



Janet in the lab at Brock University

3. What did you want to be when you grew up?

I certainly wasn't one of those people who knew exactly what I was going to be when I grew up. I know there are people who say that from the age of eight they knew they were going to the moon. Well, certainly at the age of eight, I did not know I was going to be a scientist.

I was very broadly interested in history and geography, English and science, but I guess I was always leaned into a science for couple of reasons. One, I had a very good science teacher at high school who made biology fascinating, but I wasn't a naturalist. I wasn't out collecting bugs and all the rest of it. I was just interested in the process of how life works. Secondly, I guess was influenced by the sister of my one of my school friends. She was actually a developmental biologist and so she was a sort of role model that exposed me to the idea that there was a career out there where you could do research on interesting things.

But I really didn't know exactly what I was going to do. Even after I finished my undergraduate degree, I was humming and hawing about whether I was going to graduate school or going to teacher's college or even doing something else. I was not sure and I needed pushing. I got pushed by some of the faculty at Oxford to try research, and well, here I am.

4. What are you researching right now?

Early days at Brock University

As you know my research lab is gently declining. I am not declining – my lab is declining.

My brain is still very much fired up with science. While I am beginning to close down my physical lab, I think it's an amazing time to be doing science.

This is an opportune time for younger people to take over. The area of research that I've been interested in over the years, which is really still focused on the very early stages of development: how do you get from an egg to the first cell types of the early embryo and then of course, how do you get stem cells from those cell types. Now more recently people are looking at the same issues directly in human development.

That has always been my interest and that's still my interest and luckily the world is interested in those things as well. This is actually a very popular area of research right now with trainees from my lab and trainees from other labs very active in this space, so I feel that I can step back a little. Hopefully, they will keep me engaged.

5. Why stem cells?

That is an interesting story because it is a Till and McCulloch story.

When I was a graduate student in Cambridge, my supervisor, Richard Gardner, got invited to a meeting in the UK on stem cells. I was thinking, stem cells, what are stem cells? Dr. Gardner invited myself and a postdoc in the lab to write a sort of mini review for the proceedings of the conference. It is no longer the case, but in those days if you went to a conference, people would ask you to write a paper and put it in a book. Conference proceedings were really quite an important thing and you could have a very impactful publication through a conference proceeding. So Ginny Papaioannou and I were tasked with doing a bit of review of stem cells in the early embryo. And it was so early in our understanding or even awareness of stem cells – are there stem cells in the early embryo? What is a stem cell and how do we know if we have a stem cell in the early embryo?

Of course when we started looking at what is a stem cell, that's when the literature led us to Till and McCulloch in Toronto and also C-P Leblond in Montreal. Both of those Canadian groups were really the people leading the way in stem cells.

Leblond was working on the gut and on spermatogenesis using autoradiography to show that there were stem cells, and Till and McCulloch developed their hematopoietic stem cell assay. I read those papers and I was intrigued because the way that they presented and thought about those questions was just so fascinating. Ernest McCulloch actually gave a talk at that conference, so I got a chance to hear him, but not meet him.

When I came to Canada, one of the first things I did was to reach out to a number of other developmental biologists across the country. I was actually able to secure meetings with Leblond and with Till and McCulloch. I had an outstanding meeting the CP Leblond who was an absolute charmer, a gentleman and an amazing person. He was particularly supportive of me in the early days.

That was my entry into Canadian science where I already had Canadian science heroes in hand.

6. Who in your opinion, are the top three Canadian stem cell researchers in history?

What I would say is that obviously we Canadians have particular strength in certain areas of stem cell research. Clearly hematopoiesis (the production of all of the cellular components of blood and blood plasma) and everything associated with it continues to be a major strength in Canada – somehow history carries through.

Canadian work in nervous system and in neural stem cells is also a strength.

And indeed, of course pluripotent stem cells, particularly in driving pluripotent stem cells towards specific pathways for treating degenerative diseases is another area where we have strength.

Top three researchers? No question: Till, McCulloch and Leblond.

7. What is the most significant stem cell discovery or advancement over the last 20 years? The last 60?

Stem cell discoveries by Till and McCulloch, and Leblond are obviously the most significant work of 60 years ago.

For the past 20 years, I do think that the Yamanaka discovery of iPS cells has to stand up there. That would be in mice in 2006 and in human in 2007. I think the impact of that work in terms of discovery is enormous, and in terms of applications, the impact is even bigger. To be able to model disease in a dish, and course as we go forward, hopefully to be able to treat disease as well.

Of course there have been many other important things along the way but if there is one thing that stands out to me, it's iPS cells. If you just look at the citations, the amount of work that has come from that is huge.

8. What are your predictions for stem cell advances in the next 5, 10, 20 years?

In five years, I do believe that we will see some successful clinical trials with cells derived from pluripotent stem cells – think macular degeneration, diabetes, Parkinson's. I think we are going to see some real success there, even within the five-year time frame.

Whether it's at the level where it can get taken up into clinical practice around the world, that's going to be the next 10 years.

20 years? I think that in the stem cell area, we tend to sort of have a laser focus on stem cells. But if you look at the advances in what we call personalized medicine and innovative treatments across diseases and across different areas, then stem cells are only one of many advances. Look at CRISPR; we are looking at amazing potential advances in gene therapy and corrective gene therapy in vivo for genetic diseases. Some of that is going to involve stem cells because you're going to have to make the alterations in stem cells and put them back.

In 20 year's time, the coming together of stem cells and gene therapy is going to be a major approach. Using CRISPR plus stem cells, plus novel molecules that have come out of screens using organoids and stem cell cultures to screen for new drugs to treat disease, we're going to have an armament of innovative therapies. Many will have a stem cell component, either as part of the development or as part of the treatment, but stem cells alone will not be the only treatment. It will be an integrated approach to innovative therapies for disease.

9. What would you describe as the most significant moment in your own research career?

First of all, being able to grow mouse embryonic stem cells, which my lab was not the first to do. Many labs around the world at the time were trying to do this. Two labs in the 1980s, Martin Evans and Matt Kaufman and in the UK and Gail Martin in San Francisco, derived embryonic stem cells. Then Mario Capecchi and Oliver Smithies showed that you could do homologous recombination to make targeted mutations in those stem cells. And if you make a targeted mutation in the stem cell, you can put it back in an embryo and you can make genetically altered mice.

Now this sounds so old fashioned now, because now of course my lab and everybody else is doing those alterations by just taking the CRISPR gene editing tools and injecting them into eggs.

But it was an absolute breakthrough at the time that allowed us for the first time to make targeted mutations in the mouse. And I do remember Alex Joyner and I were working together and we decided, 'well, this is what we're going to have to do' because we were interested in the genes controlling development. All of our Drosophila friends would say, 'Yeah, yeah, you've got all these nice proteins. They look interesting with homeoboxes all over the place, but you don't know what they do because you don't have mutations like we have in the fly.' And it is true of course, you need genetic alterations to prove the function of these proteins.

Tony Pawson, Alan Bernstein, Janet and Alex Joyner

So, she and I started working on her favorite genes which were the engrailed genes. We used PCR (Polymerase chain reaction is a method used to rapidly make millions to billions of copies of a specific DNA sample, allowing scientists to take a very small sample of DNA and amplify it to a large enough amount to study in detail) which had just really come into play, to find those mutations. In fact, we had to get the second PCR machine in Canada to do the experiments. And we ran the gels and…. there is the band that says… we had made the mutation! I think that was probably my most exciting time.

Of course, you look back now and say, 'oh you made a targeted mouse – big deal.' But at the time that was a very important revolution in mouse genetics – no question. And of course, Capecchi and Smithies and Martin Evans got the Nobel Prize for that work.

10. What are you reading right now?

I am working through the 2020 Giller Prize nominees' books at the moment. Right now, I am reading How to Pronounce Knife by Souvankham Thammavongsa. It is very good and I am really enjoying it.

There are different ones for different periods of my life. When I was at school, I used to read a lot. The one that I still remember best and really enjoyed was Anna Karenina. I really liked the Russian literature at that point and that is a beautiful book.

11. Who is your favourite scientist?

This is a difficult one and it is hard not to come up with a cliché.

I admire scientists who are constantly innovative. If you look in the current stem cell arena, one of the people that I admire a huge amount is Hans Clevers. He has managed, obviously not just on his own because he has a big lab and all the rest of it, but he has managed to hit a number of different fields – from signalling to cancer to organoids – in really innovative ways. Every paper is a great paper and his ability to be consistently innovative is something I find very attractive.

We have of course, already talked about Till and McCulloch and Leblond who would all certainly qualify as some of my heroes of science.

12. What in your opinion is the single most important health science or biomedical breakthrough?

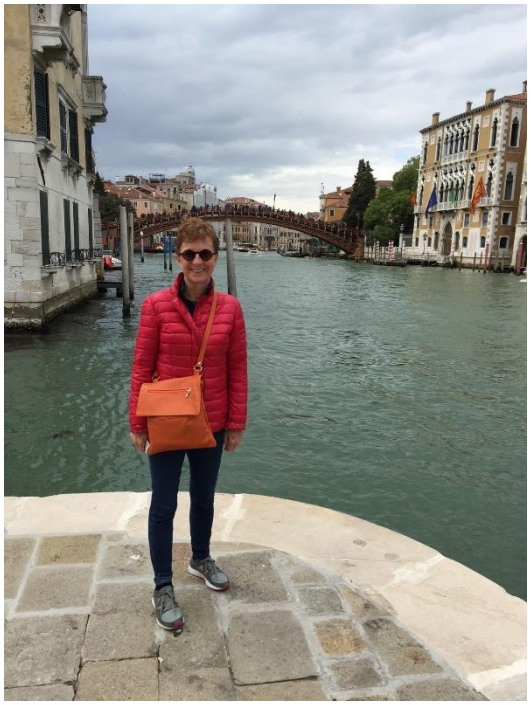
Hygiene – clean water.

Here we are in a pandemic today but think of the pandemics of the past that have not been airborne but have been waterborne. Public health interventions over the last century have really changed the impact of disease on society around the world. That is the most important thing. On top of that, vaccines. What are we doing in the pandemic? Public health interventions and vaccines – they are the two things we need to do now, and they are the two things that have made a big difference in the past and will continue to be important.

13. What is your favourite country to visit? What city would you most like to live in?

Italy. No question on that one, I just love it. I think it would be a very difficult country to live and work there, but it is a fantastic country to visit. It is beautiful, there are layers of history, the food is amazing, the people are so friendly, and the pace of life is more relaxed. It might just be too relaxed, which is why it would be difficult to live and work there.

If I had lots of money and we were not in these ridiculous times in the U.S., I would like to live in New York City. It is just such a vibrant place. You don't need a car; you can walk everywhere. Everybody walks, everybody is fit. There is incredible culture, lots of great restaurants, food, etc. One of my favorite museums in the whole world, the Metropolitan, is there, as well as MOMA. You could spend weeks inside those museums and never come out. And with the Met, when you do come out you are in the middle of Central Park which is the most amazing urban park in the world.



Janet in Venice

14. What are the top three songs in your personal playlist? What is your guilty pleasure song on your playlist?

I am a Springsteen fan. So almost anything that he does - you name it, I like it. I like some of the early Beatles songs. And I actually quite like Drake.

Guilty pleasure? Oh, it has to be ABBA. Every now and again I find myself going around the house singing Mama Mia. Their songs are just so catchy, you have to hand it to them.

15. If not a scientist, what would be your dream job?

I have been asked this before and I have asked myself this and I don't actually know. I enjoy talking and lecturing and putting myself out there, so I think I would probably like to be an actor.

I used to do a bit of amateur acting though I haven't done it for a long time. It is good training for giving lectures. Acting is great for people like me who are introverts because you are now a different person. And in that different personality, you can be totally extroverted or become whatever you want to be, so it is a way of being able to get out of yourself into a new person and have fun.

16. What is the best piece of advice you have ever been given?

Early in my career, when I was deciding whether to do graduate work or not, I was talking to one of the lecturers at Oxford. I was unsure and worried it would be too hard or that it wouldn't work, and the lecturer told me I would never know until I tried.

You just have to try it. If it doesn't work, it's not the end of the earth and there are other pathways.

That's the sort of advice that I now give to people in my lab all the time. When I talk to undergraduates wanting to try research, but they are unsure whether they will be good at it, I tell them nobody knows. I didn't know until I tried it. If it does work, great, and if it doesn't, that is one path that is closed, but other paths will open up. I think that is an extremely important message for people.

17. What is something you think everyone should do at least once in their lives?

I know some people will tell you to do something that is risky and frightens you. I am not going to say that because I won't do that – you're not getting me on a roller coaster or anything like that!

But I do think taking a step where you don't know what the outcome will be – taking some degree of risk – is important.

18. What is your favourite movie?

Casablanca. I know every word and I know all of the things that get misquoted.

19. What is your favourite word? What word do you use too much?

There are some words that are out there, and for a long time you never know how to actually pronounce them. And then I still kind of like them once I've learned how they're pronounced. One of the words that I like is segue, which I thought was pronounced 'seeg' But it is a nice because it has a very specific meaning and there's no other word to replace it.

I like those words that have a very unique meaning. Schadenfreude is another one. We don't even have a word in English for it, but we know what it means, and it is a perfect word.

I think I say "I think" too much.

20. What do you wish you knew more about?

My son, who is an accountant, has very extensive historical knowledge – of medieval history, European history, American history. He even knows about the Haitian revolution.

He once came with me to a reception at the Canadian embassy in Paris. The Haitian ambassador was there, and my son got into a long and erudite discussion with him about the Haitian revolution! I was so impressed but could hardly contribute in a meaningful way to the conversation. I wish I knew more about history – it is so important that we learn from history.