



20 Questions with... Freda Miller

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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 and raised in Calgary with some time spent in Saskatchewan.

2. Where did you go to school?

All of my schooling, except for one year in interior BC, was with the Calgary Public School Board.

I benefitted tremendously from a first-rate public school system in Calgary when I was growing up. I had amazing teachers who really cared, and I was chosen to attend the first gifted children's class in Calgary. I attended the program for two years in junior high school and it had a definite impact on my future.

About a year and a half ago I received the Legacy Award from the Calgary School Board which was one of the biggest honors of my life. I think it should be one of our key priorities as a society to have an amazing public school system so that every child has an equal opportunity to reach their maximum potential.

I started my undergraduate studies in Calgary but then my family moved to Saskatoon and as a consequence I ended up at the University of Saskatchewan. After finishing my undergrad degree, I went back to Calgary to do my PhD in biochemistry and molecular biology, and then moved to San Diego for three years for my postdoc.



Freda and the mountains.



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

One of my favourite things to do growing up was reading and writing. I thought I would end up being a writer.

In grade 9, I had a fantastic chemistry teacher. He had us going into a lab and conducting experiments, which made me excited about science for the first time. That experience completely changed my life and career trajectory.

4. What are you researching right now?

I have always been really fascinated by the concepts of adaptability and plasticity, particularly in the brain. I have had a lifelong interest in how the brain adapts to new

experiences and environments and in the extreme case, injury. In my own case, I work at a cellular level, but at the opposite end of the spectrum these questions go to the core of what it means to be human.

This is where the interest in stem cells arises. They provide one way our tissues adapt to changing environments and they are particularly important following injury. Our own approach to these issues is to understand how stem cells build tissues during development, and then to ask whether the same mechanisms are in play following injury and if so, whether we can learn to recruit them to help the body to repair itself.

5. Why stem cells?

For a long time, I've been interested in adaptation and plasticity, and I started my lab trying to understand how growth factors in the environment regulated these functions during development. It was a logical next step to become interested in stem cells since they are key cellular targets in this regard.

Having said that, I didn't really make the move into stem cells until I had had my own lab for about seven years. At that point neural stem cells had just broken on to the scene and I became convinced that we could make a distinct contribution to the field. And as they say, the rest is history since I have spent the remainder of my career working on stem cells.

My decision to work on stem cells coincided with my move from McGill University to The Hospital for Sick Children (SickKids) Research Institute. In Toronto there's an amazing stem cell community and SickKids is very strong in developmental biology. At the same time, the Stem Cell Network received its initial funding. I was fortunately included in the SCN from the start, and this allowed me to be around people who worked on stem cells in a wide variety of tissues and from many different perspectives. This convinced me that stem cells were where I wanted to be for the rest of my career, and I went from dabbling in them because they were really interesting to making them my major focus.

The Stem Cell Network was very important in that decision.

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

Janet Rossant is the first stem cell scientist that I think of in response to this question. Not only is she an amazing scientist who has made important contributions, but she has had a really important positive influence on my career. She was involved in the initial formation of the Stem Cell Network formation, was my "boss" in her role as Chief of Research at SickKids and she mentored me in many different ways. Janet helped me both scientifically and as a person.

And of course, I have to include **Till and McCulloch** for all of the obvious reasons.

The third person though, is perhaps not as obvious a choice, and is a Canadian who did not work in Canada but instead spent his career in the U.K., **Martin Raff**. I have chosen Martin not only because he did truly creative, big picture science, but also because he gave me some very important advice at a critical point in my stem cell career. We had just discovered skin-derived precursor cells and I was very anxious about this apparently radical discovery. At that point I had a conversation with Martin and he told me that it is a scientist's job to push the boundaries of our thinking, even if in the end that speculation proves to be wrong. In other words, of course publish the most rigorous data possible, but then don't be afraid to use those findings as the basis for speculative big ideas that will push the field forward intellectually. It is then up to you and the community as a whole to critically evaluate and test those new ideas. That conversation made a big difference for me.

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

Definitely the Till and McCulloch discovery from 60 years ago, that our tissues contain endogenous stem cells throughout our lives.

And I would have to agree, probably with the rest of the world, that number two was the definitive evidence of reprogramming and cellular plasticity. This was provided both by the Yamanaka work which ultimately led to iPS cells, and by the body of nuclear transplantation work showing that nuclei from differentiated cells could generate an entire mouse.

These two sets of complementary findings definitively showed that development wasn't a one-way street, and that cells had much more plasticity than we had ever imagined.

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

There are two stem cell research streams that are heading towards the clinic. In one, scientists are manipulating cells outside the body for transplantation back into the body, with the most obvious purpose being cell replacement therapies. There is tremendous progress in this area, but given the nature of the type of manipulation, we are still in most cases many years away from the clinic.

The second involves endogenous stem cells, which is what I work on, and I think we're going to see breakthroughs in the next five years in understanding what makes them tick. And if we can truly understand what regulates them, then it's not going to be as big a step to the clinic. I am very optimistic that in the next 5 to 10 years we will have several approved therapies based on the recruitment of endogenous stem cells for tissue repair.

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

I'm not certain about most significant, but certainly the most exciting was when we discovered skin-derived precursor cells, and showed that we could culture dermal cells and that they were then able to give rise to cells that weren't normally in the skin. This was before Yamanaka, and while in retrospect it seems obvious, at the time it was very surprising.



On the long road to discovery.

10. Who is your favourite scientist?

Newton and Darwin and all those many scientists throughout time who thought out of the box, and paid attention to what they saw even if it wasn't predicted within their current scientific framework.

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

Vaccines. As exemplified by the COVID-19 crisis now, this is the health discovery with the broadest ramifications for the most people. Imagine a world before vaccines when we lived in fear of diseases like polio and smallpox all the time.



Enjoying another mountain range.

12. What are your hobbies outside of the lab?

I love the outdoors and all things associated with that, from hiking to cross country skiing to visiting all of the major mountain ranges.

On a daily basis, I do martial arts, in particular Taekwondo. I teach people in my lab as well.

I've also really been into music. I used to play the piano and lately I've been singing a lot.

13. What are the top three songs in your personal playlist?

This is a tough one to answer. I love different kinds of music.

I've always found anything by Bach to be intellectually stimulating but emotionally calming at the same time. I also listen to a lot of jazz and of course since I come from Calgary, I have a deep affinity for hardcore rock.

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

Writer or owner of a bookstore.

15. What job would you be terrible at?

Medical doctor because I am very squeamish.

16. What is the best advice you have ever been given? What advice would you give to a trainee just starting out?

Like many postdocs and grad students, I went through a period when I didn't know if I could or should be a scientist, particularly since I already had one child as a postdoc. So, the really life-altering advice I received was to just try moving forward in my scientific career, and if it doesn't work well, so be it. I could always do something else at that point. In other words, don't let the fear of failure drive your decisions – it's important to be a risk taker. That genre of advice has been very important for all aspects of my career.

The second key piece of advice I have already discussed above was to think big, to speculate and to push intellectual boundaries while at the same time striving for rigor and completeness in your experiments and the data itself.

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

Everyone should put themselves in the shoes of other people who are less advantaged. Whether that means volunteering in your community or visiting other, less wealthy parts of the world. And once you have that perspective, it changes everything.

18. What skill would you like to master?

I would love to be able to play a musical instrument at a very high level.

19. What is your favourite movie?

The Game of Thrones series.

20. What do you wish you knew more about? What mystery do you wish you knew the answer to?

More about everything – literature, languages, history, etc.

I wish I could understand the giant questions about consciousness. What is the genetic basis of personality? Where is music in the brain? Why do some people have perfect pitch? What is the nature of different kinds of intelligence? My mysteries are all centered around how the brain defines us as individuals.



Enjoying the great outdoors.