20 Questions with… Nika Shakiba

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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 Iran, moved to Canada when I was two and grew up in Toronto. And I have recently moved to Vancouver.

2. Where did you go to school?

I completed my undergraduate degree and PhD at the University of Toronto.

My undergrad was in Engineering Science. This program was probably one of the first that was available at that time in which they blurred the boundaries of what engineering is. You could explore cellular engineering, non-traditional definitions of engineering and get a sense of how engineering principles can be more broadly valuable in biology.

Empire State Building, 1993

I don't think I truly realized the opportunities for engineers to impact biology until I met Peter Zandstra, a chemical engineer who had the audacity to play in a stem cell researchers sandbox. It was so non-traditional and that really excited me. I joined Peter's lab as a grad student. I came in very much on the computational modeling side, and I came out almost entirely experimental. It was a steep learning curve, but Peter had provided such a supportive and collaborative environment that I could pick up that expertise. He was really supportive of that idea exchange across fields and across peers and collaborators.

Through my PhD I explored the underlying rules that shaped the decisions of cells, skin cells as we genetically reprogrammed them back to a stem cell state. Biologists and clinicians were fundamentally driving those quests, so it was a really fun experience to dive in there and work together.

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

Steve Irwin was my Idol growing up. I never missed an episode of The Crocodile Hunter, so I really wanted to be a Zoologist.

4. What are you researching right now?

I just started my new independent lab in the School of Biomedical Engineering at UBC. My lab is interested in understanding the social lives of stem cells. When do they get along? When do they feel they need to bully each other? And we're specifically interested in what are the genetic rules, the genes that lead some stem cells to become bullies, actively killing off their neighbours. It's not a very Canadian attitude for a cell to have.

We're hoping that by better understanding those rules we can then program the rules and give rise to new types of stem cells that are very cooperative or very competitive, and that could be advantageous in some situations. For example, with cell therapies we might want them to be more competitive, so that when we inject them into the body, they can stand their ground and not be eliminated from our bodies, which is oftentimes a barrier to engraftment efficiencies when we transplant blood stem cell therapies.

5. What attracted you to stem cells?

I think part of why stem cells caught my attention was, one, because they have huge potentials for changing healthcare. And as a biomedical engineer, I was definitely motivated by the opportunity to have even just a little impact in that space. It's a powerful type of cell that can self-renew, generate all these specialized cell types in our bodies on demand, which could potentially treat degenerative diseases.

The other part of it was just sheer curiosity. How could it be that this one cell has so many amazing abilities and can transform into different cell types? How can we learn to speak its language? To convince it to become a particular cell for a regenerative medicine application.

And then the last part, which is something that I learned as a Stem Cell Network trainee was that it's part of the Canadian legacy. The first stem cells were discovered in Canada by Drs. Till & McCulloch which gave me more of a push to have this unique opportunity and build on this legacy, contributing to the chain of great Canadian scientists and mentors. And so, I wanted to be part of that.

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

Of course, Drs. Till & McCulloch, they made such a foundational contribution to the field discovering the first type of stem cells, (blood stem cells) and really defining what are the properties of stem cells. Those definitions framed how we understand stem cells. They also did their discovery in such an interdisciplinary way and that inspires me. It was tag team of a clinician Dr. McCulloch, and a biophysicist Dr. Till. That showed the exceptional impact an idea can have when you bring diverse minds together.

And the third person I have always admired and looked up to is Dr. Janet Rossant. Her research contributions to the field have been so profound. For example, discovering the trophoblast stem cell, untangling rules of embryonic development, and she's become a world-renowned leader in the field. She helped to shape the trajectory of the field and has been such an influential mentor to many scientists.

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

I'm somewhat biased. Reprogramming was the core area I studied in my postdoc and in my PhD. It was a big clinical game changer because the 2006 discovery by Yamanaka taught us that by using four genes we can force that specialized cell to undergo a huge transformation and become a stem cell and regain the properties of a pluripotent stem cell that can then produce every cell type. So, now we can derive patient specific cells and we don't have to sacrifice embryos to access these pluripotent cells anymore. It also changed the way we look at cells. They're a lot more plastic than we thought. They can be convinced to completely change their identity and what they do, and that idea really seeded a lot of subsequent cell engineering paradigms. I'm hoping that we can build on this perspective of cells and stem cells as fundamentally programmable units of life. And that is basically the premise my lab is built on.

8. What are your predictions for stem cell advances in the next 5, 10, 15 years?

That's a hard one because as we've seen in the last year, the world can take very unexpected turns, which have huge implications for research and therapies. Barring any other external influences, I can comment on what I hope will happen.

In the next five years, I think a lot of the focus will continue to be around what I call reverse engineering, which is really to understand the molecular rules, the molecular players inside the cell, the DNA, the RNA, and the protein. How do these players interact and shape the decisions of cells and stem cells? To self-renew, to divide to, die, and bully each other. All these elements and decisions that cells and stem cells can make I think we will continue to untangle that inside the cell.

In the next 10 years. I think we'll start to see more examples where these rules can now be forward engineered. That's one of the things the synthetic biology angle is providing, and it's starting to intersect with the stem cell world. I'm hoping we'll see key advances and enabling technologies that make stem cells and cell therapy products more commercializable, scalable, and genetically programmable so that they're behaving in predictable ways in the dish, in our bioreactors, and maybe in the body. I hope that these technologies, these discovery-based pushes, will allow us in the next 15 years to see more cell therapies, including those that have these new kinds of genetic abilities.

9. Who is your favourite scientist?

There's so many of them that have impacted me. One of the more classic scientists that I would pick is Alan Turing. He was a famous mathematician and computer scientist. He also made great contributions to biology and predictions about the chemical basis of morphogenesis. For example, the Turing patterns that are predicted to give rise to stripes in on zebras and different kinds of patterns on animals.

An idea that a simple thought experiment can give rise to a whole field. Being willing to take a risk outside of your comfort zone and make those contributions, as silly as they might seem at the time.

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

University of Toronto Lab, 1996

I would say that my doctoral project that focused on capturing the behavior of individual skin cells as we genetically reprogram them back to a stem cell state. And applying this mathematical modeling approach to dissect the complicated data we generated when we tracked what each individual cell is doing. That led to this prediction that intersected so well with our neighboring lab, the van der Kooy lab. Some of our modeling work and the experimental data we generated made a prediction that they were hypothesising from a different angle and so all of a sudden it felt like fate when our studies kind of intersected. We joined forces and it led to a bigger realization that competition between these reprogramming cells is shaping the outcome of the whole population. This is the first time that we've shown that this type of interaction between cells and stem cells in big multicellular populations have huge implications for what's going to happen to that pool of stem cells, and that the cell population is not a simple sum of their cellular parts.

Our studies were developed in close collaboration with Dr. Jeff Wrana's lab, and they were a main driver on this project. With us as well was Dr. Andras Nagy's lab who had developed a lot of the reprogramming technologies and tools that we used for our studies.

We began to generate the experimental data, we realized we have a lot of information. We should apply very careful mathematical modeling strategies and we started working with Dr. Sidhartha Goyal from U of T, a biophysicist who works on stochastic modeling. It's somewhat reminiscent of the Till and McCulloch team that our project combined biophysics and stem cell biology.

Eventually those models are what generated interesting predictions that intersected with the van der Kooy lab. It was kind of serendipitous, but it was also a product of the very collaborative Canadian stem cell world. The willingness to intersect ideas and what interdisciplinary thinking can do, which empowered me as a biomedical engineer.

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

One of the ones that I was always really excited about was the Human Genome Project. It catalyzed a lot of things. That project was really aimed around reading all of the bases of DNA in human cells. It was a starting point for understanding what those bases mean, how does it encode functions in the human cell.

It was really the first time to be able to sequence DNA at that unprecedented scale. From a technology perspective, it catalyzed all these efforts to reduce the sequencing costs and increase the depth of our sequencing ability. I think it really pushed the next generation sequencing technologies, and now is the basis for whole genome DNA writing efforts as well.

Nowadays so much research involves working with cells and at some point will likely involve DNA sequencing.

12. What are your hobbies outside the lab?

I used to travel whenever possible. I love seeing new places and meeting new people.

I am a bit of a foodie. I really like seeking new flavours, compositions of flavours, and dishes from other cultures. I like seeing the world through the perspective of other people's eyes. I think that's what's common between my travels and being a foodie.

I've also taken up knitting. It's very peaceful, calming, and meditative, which has been helpful being stuck inside through this pandemic.

I've also taken up hiking as a West Coaster. I've really appreciated nature a lot more since moving to Vancouver.

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

I don't know because so much of my life has been connected to science. When I was a little kid, I liked collecting bugs and was interested in marine biology and then ended up in engineering.

I would have to say teaching science and helping others connect with their innate curiosity for the world around us.

14. What job would you be terrible at?

Chef.

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

I was really influenced by my mentors. Peter Zandstra was hugely influential in my professional development and members of my committee continue to be mentors to me like Jeff Wrana, Andras Nagy, and Julie Audet.

I think the common piece of advice that I've kind of learned through those interactions is to find your mentors, your advocates, and allow them to empower you and really appreciate their impact on your trajectory. Finding those people and then paying it forward I think is so important.

Also, balancing expectations as not everyone has all the time in the world to be able to do that detailed level of mentorship. So, knowing who might be appropriate for what question or problem you have and having a roster of people that you can turn to that are wanting to help you get where you want to go.

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

Scuba diving.

17. What skill would you like to master?

I would love to be able to take really complicated scientific concepts, outside of my ability and distill them so simply and elegantly that other people that are way outside of that field can understand it and be inspired by it.

18. What is your favourite movie?

That's hard but I have a recent one that I really loved, My Octopus Teacher. It's a documentary about this guy who scuba dives and befriends this octopus. I was not expecting it out of this documentary, but it became such an emotional rollercoaster.

19. What website do you visit most often?

I'm actually developing a website (Advicetoascientist.com) which is hub for mentorship and outreach in STEM and allows anyone at different career stages to contribute their advice.

We welcome anyone who wants to get involved. It's by scientists for scientists.

20. Who is your favourite Canadian?

Sir Fredrick Banting, a co-discoverer of insulin which had a huge impact on people's lives worldwide.