20 Questions with… Connie Eaves

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20 Questions with 20 Stem Cell Scientists from Across Canada

1. Where were you born?

I was born in Ottawa, but grew up in Kingston, Ontario.

2. Where did you go to school?

Connie Eaves, centre, with Dr. James Till, top left, and trainees at the Ontario Cancer Institute in Toronto.

I went to school in Kingston, first to public school and then to the only high school at the time — the Kingston Collegiate and Vocational Institute (KCVI). I undertook my undergrad and master's degrees at Queen's University also in Kingston. I then went to the United Kingdom where I obtained a PhD in immunology from the University of Manchester based on research I undertook in the Paterson Laboratories of the Christie Hospital and Holt Radium Institute. In the UK, the practice was you could do your PhD research almost anywhere in an academically approved environment. There were no course requirements, no committees and no other oversight, except for the interactions with your thesis supervisor. I worked with Professor Laszlo Lajtha, already a distinguished hematologist interested in stem cells and first Director of the Paterson Laboratories. He also coined the term G_0 to uniquely identify quiescent cells that could still be activated to proliferate. After completing my PhD, I stayed on an extra year to wrap up. I then returned to Toronto in 1970 where I had the good fortune to become a postdoctoral fellow at the Ontario Cancer Institute (OCI) with Dr. James Till.

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

One day in high school, I was listening to a Scottish obstetrician on a "careers day". I was enraptured by his talk and excited by his perspective of the rewards of a profession in medicine. Then and there, I decided I wanted to become a physician — but I also wanted to do research and make discoveries about biological processes that could be important to solving medical problems. Later I found out it might take a decade to complete all the training required to pursue both those goals. So, I left the pursuit of an MD and jumped into research – but always within a cancer hospital environment.

In retrospect, I have come to realize that my upbringing in an academic family with a father who was a highly regarded mathematician also had an early impact on how I have subsequently evolved as a scientist. That critical exposure to basic concepts about the principles of science and logical thinking obviously came early, as well as a desire to be different.

4. What are you researching right now?

Dr. Connie Eaves has made significant contributions to cancer and stem cell research.

We are investigating two different organ systems. In both cases, we want to understand how the cells within them are normally produced throughout life and the nature of the changes they undergo to become malignant. One is the system that makes blood cells and leukemia. The other is the mammary gland that is located inside the breast and source of breast cancer — another commonly devastating occurrence in women and less commonly, but also in men.

In both cases, we obtain normal tissue and manipulate it genetically to see if it then will generate a cancer. Our group has a long history of developing access to discarded human breast and blood-forming cells from normal individuals and, for many years we have now focussed all our research on analyzing these human cells.

Historically we used to undertake parallel investigations of these same cells obtained from mice. That was very instructive because many of the processes of interest are conserved and studies in mice can be more easily controlled. However, now my group is focussed exclusively on analyzing human cells where both the challenges and rewards are greater. Nevertheless, we still use mice in our experiments, as strains of mice that have no immune system but still appear normal and live a normal lifespan are now available. These “immunodeficient” mice are key for our work with human cells because they can support the growth of transplants of both normal and malignant human cells from the two tissues that we study.

We believe many of the important mysteries that remain in cancer are the mechanisms that lead irreversibly to the malignancies that arise in people. To solve these mysteries, we need to be able to trace and characterize how cancers develop from the very first changes that cells acquire to eventually reach a malignant state. This is almost impossible by studying samples of cancers obtained from patients because by the time a cancer is detectable, the process is already much too advanced and the cells too diversified. So, our approach is to first learn as much as we can about the normal cells that can become malignant, and secondly, to then analyze how they change in the course of becoming able to make a human leukemia or breast cancer. The expectation is that we will then be able to identify early changes that may lead to new early detection strategies and methods to prevent them from going further, rather than being forced to wait until they are more advanced and then very difficult to treat.

5. Why stem cells?

I have always been interested in how organisms and tissues grow. In fact, I am really a gardener at heart. Even in cooking, you generate a new dish out of ingredients that simply undergo defined physical and chemical reactions.

The idea of a cell that seems able to grow forever, at least for a lifetime is a very interesting concept. What are the mechanisms that give a single cell this power? What are its unique features? We know all cells in a person have more or less the same genes throughout the life of a person, but some also have to keep diversifying to provide the unique functions of each tissue. So what allows some to just keep growing in the same way?

I worked with James (Jim) Till and Ernest (Bunny) McCulloch, or Bun, a nickname he was given early in life and then stuck, so everyone at work called him Bun. I recall Bun starting a review article with a sentence about the fascination we all have with the concept of origins. That is probably why stem cells are so exciting to people.

However, for me, being brought up by a mathematician, I learned early on this concept like most has limitations. Some things don’t have origins — like a circle, that does not have either origins or ends. That idea has stuck with me forever,

so I entered the pursuit of biomedical research already appreciating that the way we study things can involve a mix of those for which beginnings and ends are meaningful and those that are not. For example, we think of life itself as being finite, and hence the life of a cell as being finite with a beginning and an end. But the components and the energy locked up inside cells that make them viable do not disappear when a cell dies — they just become part of something else. Such apparent dichotomies are very interesting concepts in science.

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

Ernest McCulloch and James Till and Charles Leblond.

Leblond had a different approach from Till and McCulloch. Leblond focussed on histopathological examinations of cells and making inferences based on when and where they divided using autoradiography. He was really the father of the whole stem cell field which then grew up under a protege (Howard Green). Green then went to Boston and later showed that clones of skin cells can be produced in tissue culture. Interestingly, many of the current leaders of the skin stem cell field are former trainees from Green's lab, or are second generation trainees of that scientific lineage. This is an important example of how the expansion of science itself can be seen also to be a clonal expansion process starting from a single individual.

Connie and her husband Allen Eaves circa 1970's.

Till and McCulloch were a similarly important pair but differed because they exemplified the seminal advances that can come from two disciplines coming together. In this case it was the timely combination of thinking both quantitatively and functionally to identify a cell with unique growth properties that can't be identified directly because it just looks like many other cells. Back in the middle of the last century, this was quite a novel concept. Thus, the complementary backgrounds of McCulloch in biomedicine and of Till in biophysics afforded this team a very opportune mixture of expertise. The result was the first experimental evidence of a cell that could "self-renew"; that is a cell able to produce not only fully mature daughter cells, but also undifferentiated daughter cells with the same developmental potential.

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

That's a very difficult question to answer because most so-called discoveries are built on prior work that lead up to a method to reveal something we could not do or understand before. Also, it is difficult to agree on how to measure significance even within the confines of the stem cell field.

But, with these caveats, I would say the most significant discovery in the last 20 years has been the development of a method to create induced pluripotent stem cells — or iPS cells.

In the last 60 years? I would say the Till & McCulloch publication that showed it was possible to identify, quantify and characterize the stem cells of a complex adult tissue based on the properties of their clonal progeny. A close runner up would be the isolation of mouse embryonic stem cells (mESCs) and the demonstration of their ability to produce viable mice from a single mESC that can be genetically manipulated.

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

I'm not very big on making projections. In reality, the biggest advances in science and our society really come from unexpected, unplanned events or findings. COVID19 is a great example. Scientists were aware of the likelihood of a global pandemic many years ago and they talked about it widely. But, as a society, we didn't really understand what it would be like, and did not become very well prepared for it.

Connie speaking at the B.C. Cancer Foundation Cancer Research Centre in 1993.

In addition, when a major advance or discovery is first made it is often difficult to anticipate the future impacts it will have. Thus, it's very hard to make sensible predictions and be on the mark.

CRISPR is probably the biggest technical advance relevant to the biomedical field made in the last decade.

But one can also point to numerous other areas where advances are rapidly emerging. An example, is the impact that mathematical principles are now being used to capture information in ways that revolutionizing the speed and complexity with which enormous pieces of data can be analyzed and used to make predictions. The use of such approaches are already profoundly impacting every aspect of life, including how we can learn about the very complex interacting events that determine how cells work and interact with one another.

In the '60s, '70s and '80s, we thought we could make tidy, high-level descriptions of how cells become specialized. However, what we are now finding is that we were just seeing the tip of the iceberg. We had no idea about how different every cell actually is, nor how complex are their interactions with their immediate tissue environment.

Another area that is rapidly advancing is our ability to engineer cells to alter how they work and then use that approach to build new types of cells, organs, even people, with properties they did not originally have.

Going forward, I think we will have much better ways to make diagnoses and better treatments. We will also have much better and faster ways to understand and analyze information. This will extend to processes that will dramatically change how we as organisms and societies, and as a global, living entity, evolve.

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

Everything is important in the moment. Life is about integrating, sharing and appreciating the value of the moment and investing in the future to try to make it better. I'm a big believer in rationality having a big influence on decision-making.

10. What are you reading right now? What's the best book you've ever read?

I don't read much except for scientific papers and theses. I started reading a fascinating book about the Empress Dowager Cixi who became the person who basically modernized China in the 19th century. It's a great story, but the last time I picked it up was more than a year ago.

I also scan a lot. This gives me the essence. And I do believe to like a book, you really must enjoy how it is written. Among my favourite books are *For Whom the Bell Tolls*, *The Golden Spruce*, the *Clan of the Cave Bear* series, and *Little Women*.

11. Who is your favourite scientist?

I don't have a single favourite. Almost all my friends are scientists and I feel quite close to them. I see them variably; but they are close friends in that we espouse the same fundamental principles.

I am also married to a scientist. He's retired as an active scientist, but still works 24/7 running what he has made into a very successful biotech company. He is a top favourite.

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

Watson and Crick's discovery of the structure of DNA. This led to a breakthrough in our understanding of how life is orchestrated and perpetuated by providing a framework to explain how genes are embodied in DNA sequences.

13. What are your hobbies outside of the lab?

Gardening. I love watching things grow. Making the surrounding area look attractive and natural. I also love music, and am particularly fond of classical — but above all music that has a melody.

14. What is your favourite country/region to visit? Why? What city would/do you most like to visit? To live in?

I'm very fond of many parts of Europe. I spent a year in France when I was young and got to know the UK quite well through my time in Manchester.

My husband and I have been invited several times to be "teachers" in a stem cell summer school that takes place almost every year on a small island in Greece. This has been one of our favourite things to do and places to spend a week in September. This activity has been on hold for two years because of COVID-19; but we've been invited back in 2022 and are hoping to do that. We love history, and Greece is a beautiful place where history also comes alive.

We've also spent time in Alaska, which was just amazing. It's a whole new dimension of more natural and magnificent terrain, wildlife, and vegetation than even British Columbia.

In addition, we had the chance to visit Haida Gwaii a few summers ago. It was one of the most eye-opening trips, we have ever taken. We love the West Coast culture, which goes way back — many thousands of years.

Connie and Allen enjoying the views in Tofino, British Columbia.

15. It's your night to cook. What's your go-to meal?

Because we work all the time, my forte is dinner in 10 minutes. We eat a lot of fish and you can quick-fry most fresh fish in five minutes. We also eat a lot of salad, and vegetables that don't require much cooking. We have salad every night. We also like pasta. I am very partial to ice cream – of which the all-time favorite is "Original Moosetracks."

16. What's the best way to start your day?

We exercise for 45 minutes when we first get up. That's very important, especially as you age. We do a mix of things: exercises to strengthen back muscles and upper body, some balance work, some weights and a lot of stretching.

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

I really like Chopin and Tchaikovsky. Once, I had to pick a piece of music that would be played for the Gairdner Award [for Biomedical Research] as well as an award I received from the Medical Hall of Fame; and for both, I chose the opening lines of "I Have a Dream" sung by Nana Mouskouri.

18. What's the best piece of advice you have ever been given? What advice would you give to a trainee just starting out? To a young kid in primary school?

I don't remember being given much advice, but growing up I was quite close to my paternal grandmother. She was born and raised in a Jewish family in Russia in the late 19th century during the pogroms. Largely self-educated and independent-minded, she decided at the age of 16 to travel alone to North America first to New York City, and then later moved to Canada when she got married. She was big on aspiring to do your best and do something significant. She raised four children who inherited her dream and made it come true. I am sure she had a big impact on me also.

What advice would I give? To identify your passions and pursue them against all odds, but remember life is a never-ending and always changing learning opportunity. Think carefully about your choices and remember the importance of logic when drawing conclusions and making decisions.

19. What do you wish you knew more about?

Many, many things. I really wish I had more training in deep mathematics — so I could analyze data myself, in more sophisticated ways. I do have a deep respect for this basic discipline, but I don't really have much training I can now use to go forward.

I would also love to be able to play a musical instrument, but I think that's also now unlikely.

Connie and the trainees at the Eaves Lab Retreat in Tofino, British Columbia, June 2018.

20. Your work is all about discovery and innovation. What's one thing (personally or professionally) you still like to do the old-fashioned way?

Most of all, I like to see first-hand the trainees I have and have had, and witness their transition from newbies to real professional scientists.