

Melissa Perreault: Thinking big towards a “complexity science” approach in neuroscience – systems, environment, and whole organism research

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Dr. Melissa Perreault, Professor in the Department of Biomedical Sciences at the University of Guelph and member of the College of New Scholars, Artists, and Scientists in the Royal Society of Canada, is participating in the Genomic Press Interview, sharing her unique insights and experiences. As a neuroscientist and citizen of the Métis Nation of Ontario, Dr. Perreault’s work bridges Indigenous perspectives with Western neuroscience, focusing on elucidating sex-specific neurobiological mechanisms underlying neuropsychiatric and neurodevelopmental disorders. Her research aims to identify novel biomarkers and therapeutic targets. At the same time, her advocacy extends to promoting Indigenous representation in STEM fields through initiatives like the Indigenous STEM Mentorship Program at the University of Guelph. Dr. Perreault’s efforts also encompass promoting ethical engagement with Indigenous communities in neuroscience research globally, championing the integration of Indigenous knowledge into brain science through international collaborations. Her multifaceted approach to neuroscience, combining rigorous scientific inquiry with cultural sensitivity and inclusivity, positions her at the forefront of a new era in brain research that embraces diverse perspectives and holistic understanding.

Part 1: Melissa Perreault – Life and Career

Could you give us a glimpse into your personal history, emphasizing the pivotal moments that first kindled your passion for science?

Neither of my parents finished secondary school. I was raised in a one-parent home, and my mother worked odd jobs to supplement being on social assistance. I had a good childhood, though. We rented a small home near a forest, and I spent a lot of time there. I remember wanting to be a medical doctor from a very young age, though I cannot say whether a specific moment or event triggered my passion for the field. But I do remember thinking that as I got older and understood the family situation better, my life would be different from that of my mother’s, and I would grow up to be a financially independent woman. I never expected that trying to achieve that goal would be challenging.

I went into the honors Biology program at McMaster University in Ontario. I loved biology; it was a good program that would get me closer to becoming a medical doctor. It was not easy being a first-generation university student. Still, it was not until I heard the stories and experiences of my classmates that I realized how much I was at a disadvantage. I was unaware of awards or scholarships to apply for, and I did not know whether any academic support was available or how to access them. But I persevered, and I did well, all things considered. In my last year of university, I was first introduced to research in my thesis project. I worked in an evolutionary biology lab focusing on growth and reproductive tradeoffs with Dr. C. David Rollo. It was here that I found my pas-



Figure 1. Melissa Perreault, Ph.D., University of Guelph, Canada.

sion for research. I realized then that although I had thought I wanted to be a medical doctor, I was happiest when I had the opportunity to ask innovative scientific questions and be able to take steps toward finding the answer.

I stayed for an MSc in the same lab but did not receive a stipend, only a teaching assistantship that paid for my tuition, so I supplemented my income by working the night shift on weekends at a donut shop. I loved my lab and project, but when I finished with my degree, I was not sure what to do. I worked for a wildlife removal company for a time, got married, and had my first child. I eventually went into radiation therapy school to treat cancer patients but did not feel I was stimulated enough in such a role. It was excellent timing that my past MSc supervisor reached out to try and coerce me back to graduate school for a PhD as he felt I had a strong aptitude for research. He had a colleague who worked in the Psychiatry and





Behavioural Neurosciences department, Dr. Henry Szechtman, who happened to be looking for a student. It was my first exposure to translational behavioral neuroscience research. I still do translational neuroscience research to this day.

My PhD project used a rat model to study obsessive-compulsive disorder. I had the opportunity to collaborate with excellent scientists including Dr. Philip Seeman and Dr. Jane Foster. Working in Jane's lab introduced me to molecular and cellular neurobiology, and I really enjoyed this mechanistic research. I decided that when I completed my PhD, I wanted to continue to build on these skills.

In my last year of my PhD training, I had my second child and then joined Dr. Susan George's laboratory at the University of Toronto shortly after graduating. Her expertise in neuropharmacology and her focus on dopamine signaling was an excellent fit for me. It was also during my PhD training that my father told me I was Indigenous. I sat with that information for a long time as I was not sure what to do with it.

We would like to know more about your career trajectory leading up to your most relevant leadership role. What defining moments channeled you toward that leadership responsibility?

My postdoctoral training with Dr. George was highly beneficial to my career. I not only had the opportunity to learn about neuropharmacology, I learned what it was like to be part of a team. I had independence and leadership opportunities. She played an important role in the development of the person I am today, and I am grateful for all of the opportunities that she provided. Unfortunately, despite having several high-impact publications and what I believed to be a strong skill set and good ideas, I could not find employment as an independent investigator. It took over eight years.

There were two defining moments in my training, one that gave me an edge toward scientific independence and one that hindered my progress. Through a scholarship from the Canadian Institutes of Health Research, I had the opportunity to spend three weeks in Italy attending the Neuroscience School of Advanced Studies. There, I met Dr. Anthony Grace, an instructor for the course. I subsequently spent some time in Tony's lab learning systems electrophysiology, which provided an additional approach I could use in my program. Tony was also a research mentor for my application for a NARSAD Young Investigator Award, which I was successful in attaining. He had a significant impact on my career progression. He was not only a mentor, but he became a dear friend.

Outside of my research, I began looking into my Indigenous lineage. I spent time at Indigenous events and connected with my Métis culture. I kept this side of myself apart from my work. It was a different time, and being Indigenous was not something you announced. To my knowledge, there was no one like me, which is not surprising given the extremely low representation of Indigenous peoples in neuroscience. As mentioned, I had been applying for faculty positions for years and had yet to get a single interview. I was discussing my frustration with a senior faculty member one day when she asked me if I had my Indigeneity on my applications. I told her I did. She responded that I should remove it. I cannot say conclusively whether removing my Indigeneity from my applications was directly responsible for the interviews I was suddenly able to get. I have thought a lot about it over the years.

I began at the University of Guelph in 2017. I had lost so much time that I had catching up to do. Combining all my technical skills, I was able to develop a successful research program. I excelled at my job and was promoted to Associate Professor with tenure in 2021. However, research was not all I was doing. I developed the Indigenous STEM Mentorship Program and received funding to develop other supports for Indigenous students and to Indigenousize the science building through art and renaming. I found a strong ally in Dr. T. Ryan Gregory, who supported me and my initiatives. My efforts in this domain began to be noticed by people who wanted to learn. I was approached by hospitals, universities, and neuroscience organizations to educate on decolonization, Indigenousization, and Indigenous capacity building. I was also recruited by the Canadian Brain Research Strategy to be on the Indigenous Knowledge Holder's Advisory Group. In this role, I

had (and still do!) the privilege of working with Dr. Judy Illes from the University of British Columbia, who was also Director of Neuroethics Canada and Chair of the International Brain Initiative. Judy allowed me to expand on my initiatives, build collaborations, and start working towards integrating Indigenous knowledge into neuroscience on a global scale.

Today, as a University of Guelph Research Leadership Chair, I balance a full multidisciplinary research program in translational neuroscience with my work in neuroethics and my Indigenous initiatives. It is difficult, but after many years, I believe that I have finally managed to successfully combine the neuroscientist with the Indigenous woman.

Please share with us what initially piqued your interest in your favorite research or professional focus area.

Over the course of my career, I identified important knowledge gaps not only in the neuroscience research we do but also in how we do it. I also experienced a general lack of cultural humility that was particularly pronounced in neuroscience regarding valuing other knowledge and world views. These realizations slowly led to the development of three general research areas that I work on today. The first is the identification of sex-specific biomarkers and therapeutic targets in neuropsychiatric and neurodevelopmental disorders with the goal of moving the field toward more personalized medicine. My second focus is on "complexity science," or holistic research. Though there have been substantial benefits to using reductionistic approaches in neuroscience, there needs to be a better understanding of how neuroscience fits into the broader picture. My final focus is neuroethics, where I educate on ethical Indigenous community research approaches and advocate for integrating Indigenous ways of knowing and doing into neuroscience.

What impact do you hope to achieve in your field by focusing on specific research topics?

I hope scientists will begin to take more real-world approaches to solve real-world problems. This can be achieved through inclusivity in what we study and how we study it. For example, there has been significant growth in whole plant and mushroom use by the public, and this use will only continue to grow in an era of climate change, pandemics, and economic and political uncertainties. These organisms contain hundreds of molecules, many of which are bioactive. As researchers, however, we rarely study the whole organism, with a predominant focus on the major chemical constituents. Entourage effects are overlooked, contraindications with prescription medications are not examined, and the therapeutic value of low-abundance molecules is, for the most part, ignored. Traditional uses for these plants, knowledge acquired over millennia and validated through experience, are also rarely acknowledged. Other examples include the recent widespread acceptance of the need to include sex and gender in neuroscience research or the acknowledgment of the importance of other organ systems on brain health.

From an Indigenous community research perspective, strength-based approaches that are inclusive of communities as research partners instead of research subjects are only now being embraced following a long history of exploitation and stereotyping, and this is by no means restricted to Indigenous communities. We have a long way to go, but perceptions are changing, and alternative views and approaches to our science and how we do it are becoming more accepted.

Please tell us more about your current scholarly focal points within your chosen field of science.

My translational research currently centers around sex-specific biomarkers and therapeutic target identification in depression and autism spectrum disorders, the role of infection in maternal immune activation and its impacts on neurodevelopment, and the neurobiological effects of whole psilocybin mushrooms and other traditional medicines. I also work with Indigenous and non-Indigenous researchers from across the globe on ethical engagement with Indigenous communities in neuroscience research.



Figure 2. Dr. Perreault loves scuba diving in her spare time. Although there are many things to see under the ocean, sharks are among the most exciting creatures. Here, she is diving in the Bahamas with black-tip reef sharks.

What habits and values did you develop during your academic studies or subsequent postdoctoral experiences that you uphold within your research environment?

In academia, rejection is common at all training and career stages. I talk about my rejections with my trainees and how I do not let them affect me. Until we reach such a stage where there are more scientific resources, it is my responsibility to help my trainees develop resilience to rejection and to help them understand that rejection does not equal failure. I have also always been averse to the idea of “imposter syndrome”. Coming from a smaller institution, I always talk to my trainees about academic privilege and how not to compare themselves to those with more resources and support systems.

At Genomic Press, we prioritize fostering research endeavors based solely on their inherent merit, uninfluenced by geography or the researchers’ personal or demographic traits. Are there particular cultural facets within the scientific community that warrant transformative scrutiny, or is there a cause within science that deeply stirs your passions?

Three things require more transformative scrutiny. First, we need to take more time to evaluate impactful science for scholarships, awards, grants, promotions, etc. Only by taking this time can we promote scientific quality over quantity. Second, we need to start expressing cultural humility, recognizing the value of traditional knowledge and world views, and appreciating that embracing multiple perspectives puts us in a better position to develop new connections and ask more innovative scientific questions. Lastly, we need to start studying plants and mushrooms in the way that they are being used in a population. We need to invest in infrastructure to ensure that the relative abundance of the chemical constituents in these organisms is maintained so studies can be replicated and entourage effects can be considered.

What do you most enjoy in your capacity as an academic or research leader?

For me, it is all about building connections with my trainees, colleagues, and those from the community that I have the privilege of meeting. I also

enjoy knowing that my work will make a difference to those who come after me.

Outside professional confines, how do you prefer to allocate your leisure moments, or conversely, in what manner would you envision spending these moments given a choice?

If it were possible, I would spend every free moment on a beach by the ocean in a tropical location. I scuba dive when I am able, and I am somewhat of a shark chaser. I have a motorcycle that I ride to help me unwind in the summer, but I also spend time hiking or at the gym for exercise. I am a fan of science fiction and fantasy books and settle in to read when I have the opportunity.

Part 2: Melissa Perreault – Selected questions from the Proust Questionnaire¹

What is your idea of perfect happiness?

I am still trying to figure that out.

¹In the late nineteenth century, various questionnaires were a popular diversion designed to discover new things about old friends. What is now known as the 35-question Proust Questionnaire became famous after Marcel Proust’s answers to these questions were found and published posthumously. Proust answered the questions twice, at ages 14 and 20. In 2003 Proust’s handwritten answers were auctioned off for \$130,000. Multiple other historical and contemporary figures have answered the Proust Questionnaire, including among others Karl Marx, Oscar Wilde, Arthur Conan Doyle, Fernando Pessoa, Stéphane Mallarmé, Paul Cézanne, Vladimir Nabokov, Kazuo Ishiguro, Catherine Deneuve, Sophia Loren, Gina Lollobrigida, Gloria Steinem, Pelé, Valentino, Yoko Ono, Elton John, Martin Scorsese, Pedro Almodóvar, Richard Branson, Jimmy Carter, David Chang, Spike Lee, Hugh Jackman, and Zendaya. The Proust Questionnaire is often used to interview celebrities: the idea is that by answering these questions, an individual will reveal his or her true nature. We have condensed the Proust Questionnaire by reducing the number of questions and slightly rewording some. These curated questions provide insights into the individual’s inner world, ranging from notions of happiness and fear to aspirations and inspirations.

**What is your greatest fear?**

Starting so late as an independent investigator, I worry I will never be able to afford to retire.

What is your greatest extravagance?

My annual vacation with my adult children.

What are you most proud of?

Against all odds, getting my PhD.

What is the quality you most admire in people?

Authenticity.

What is the trait you most dislike in people?

Dishonesty.

What is your favorite occupation (or activity)?

I have the best occupation.

Where would you most like to live?

I dream about owning a home close to the ocean on a tropical island.

What is your most treasured possession?

My memories and joyful experiences.

When and where were you happiest? And why were so happy then?

I was scuba diving off the coast of Barbados and found myself in a school of small squid. I was diving with two others, but they were not nearby as they were doing training, and so I was alone. It was so peaceful and awe-inspiring, a feeling of pure contentment.

What is your most marked characteristic?

Resilience.

Among your talents, which one(s) give(s) you a competitive edge?

Perseverance. I have overcome many barriers to achieve success. I never give up, and I don't sweat the small stuff.

What do you consider your greatest achievement?

My children.

If you could change one thing about yourself, what would it be?

I would be less shy around new people.

What do you most value in your friends?

That they listen, are honest, and are supportive.

Who are your favorite writers?

Steven Erikson and Brandon Sanderson.

Who are your heroes of fiction?

Not a hero but more someone I admired. Avasarala from the tv show The Expanse. That woman embodied power.

Who are your heroes in real life?

I do not have any real-life heroes.

What aphorism or motto best encapsulates your life philosophy?

Never give up.

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