Genomic Press
BRAIN MEDICINE
From neurons to behavior and better health

INNOVATORS & IDEAS: RESEARCH LEADER

Romina Mizrahi: The crucial role of positron emission tomography (PET) in precision medicine in psychiatry

Mental health and substance use disorders represent a major public health burden worldwide, and current diagnostic methods rarely include objective, quantifiable metrics. In this Genomic Press Interview, Dr. Romina Mizrahi, Professor at McGill University Department of Psychiatry and Principal Investigator, Clinical & Translational Sciences (CaTS) lab at the Douglas Research Center, discusses how positron emission tomography (PET) imaging provides transformative opportunities to study the molecular mechanisms underlying psychiatric disorders. Dr. Mizrahi uses PET to study the pathophysiology of schizophrenia, clinical high risk (CHR) for psychosis, and addiction with a focus on cannabis use. She was the first to investigate *in-vivo* dopamine response to stress in CHR, schizophrenia, and cannabis users. Importantly, Dr. Mizrahi pioneered PET studies with novel radiotracers, including [^{11}C]-(+)-PHNO, [^{18}F]-FEPPA, [^{11}C]-CURB, [^{11}C]-NOP, [^{11}C]SL25.1188 and [^{18}F]SynVesT-1 to image dopamine, neuroinflammation, endocannabinoid, nociceptin expression, monoaminoxidase B (MAO-B) and synaptic density (respectively) in psychosis spectrum, cannabis use, and more recently in suicide phenotypes. These molecular imaging techniques allow for identifying biomarkers related to specific disorders, discovering new treatment targets, early behavioral intervention, and assessing real-time treatment responses. Dr. Mizrahi's research aims to improve individualized treatment decisions and predictions of treatment response in psychiatry by integrating PET data with genetic, clinical, and environmental data. Dr. Mizrahi is a champion for interdisciplinary collaborations aimed at improving the science of mental health, and she has published over 160 papers in high-impact journals. She is highly involved with public health, including extensive media engagement and testimony as a witness at the Canadian House of Commons standing committee on youth marijuana use, an important global priority in the context of cannabis legalization.

Part 1: Romina Mizrahi – Life and Career

Could you give us a glimpse into your personal history, emphasizing the pivotal moments that first kindled your passion for science?
As a psychiatrist, I believe we understand too little about how the brain works; I am curious to understand the brain to find novel treatments for patients. Since I was a resident more than twenty years ago, I felt I could not really answer questions when they asked me, "What is wrong?". Even today, when we discuss cannabis use with young people, there is so little we know. We owe it to our patients and society in general to understand mental illness and substance use disorders.

Figure 1. Romina Mizrahi, MD, PhD, McGill University and Douglas Research Center, Canada.

Please share with us what initially piqued your interest in your favorite research or professional focus area.
I like positron emission tomography (PET) as it allows for direct translation to treatment options for patients. I was fascinated by the work of Dr. Shitij Kapur (My PhD supervisor), who, together with others at the time, revolutionized antipsychotic dosing. This has changed the lives of so many people taking antipsychotic medications.

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 international reputation is underscored by the prestigious ACNP Joel Elkes Award, USA, a distinction I hold as the first-ever female Canadian recipient. My enduring scientific career, marked by resilience in the

face of significant adversity, exemplifies the challenges often encountered by senior female academics.[1,2] These experiences have shaped me to work hard to ensure everyone's contributions are counted. This is what motivates me to deliver, both in academic leadership and scientific discovery.

What is a decision or choice that seemed like a mistake at the time but ended up being valuable or transformative for your career or life?
I stayed too long in a challenging work environment and ended up gaining an unparalleled understanding of work environments. This experience currently drives me to better balance work and personal life and pursue academic leadership—to ensure no one has to endure what I did, that young scientists can focus on advancing science, and that trainees can learn in healthy work environments.

What habits and values did you develop during your academic studies or subsequent postdoctoral experiences that you uphold within your research environment?
I swim almost every day. I use this time to reflect and plan my next steps. I consider my pool routine part of my workday, and I encourage my students to also have a space to decompress.

Please tell us more about your current scholarly focal points within your chosen field of science.
I am interested in identifying molecular targets in vivo using PET for precision psychiatry. I think we need better patient treatment and prevention.

What impact do you hope to achieve in your field by focusing on specific research topics?
I aim to achieve a significant impact in my field by focusing on PET research to identify treatable targets for mental health and substance use disorders. My work has the potential to identify novel treatment targets, enable early detection, objectively measure biological processes, develop personalized treatments, enhance understanding of disease mechanisms, and advance precision psychiatry.

By stratifying patients based on in-vivo brain molecular profiles—similar to advances in cancer care—and identifying distinct molecular signatures associated with different disease presentations, we can develop novel therapeutic interventions that address underlying neurobiological dysregulations more effectively. My research using PET-targeting molecular biomarkers in large-scale clinical trials demonstrates the translation and real impact of this work on patients, ultimately helping me answer all my patients' questions.

What do you most enjoy in your capacity as an academic or research leader?
Mentoring young scientists, especially underrepresented. Above all, I enjoy learning.

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 you feel strongly devoted to?
There is very little diversity at the top, from scientific to academic leadership. Scientific excellence is paramount to demonstrate to wider society the value of science.

Figure 2. Romina Mizrahi during a vacation in the Basque Country, Spain. "I am always happy close to water," she notes, reflecting on her practice of using swimming as a time for reflection and planning—a habit she considers an integral part of her workday and encourages her students to find similar spaces to decompress.

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?
I swim for long periods, as it provides an opportunity to reflect. I also meditate, this is more recent as it helps provide clarity and balance. I have travelled a lot and learned several languages. I think this helps me better understand different cultures, which I believe is essential for academic leadership.

Part 2: Romina Mizrahi – Selected questions from the Proust Questionnaire[3]
What is your most marked characteristic?
Grit.

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

If you could change one thing about yourself, what would it be?
I was too feisty when I was younger, a real advocate for equal opportunities. I understand now that small and persistent changes are required. Like in science, academic culture changes must be made one step at a time. Just like in science, I wish we could go faster. ☺.

[1]Iyer, … Jagsi, Reshma MD, DPhil. Bullying in Academic Medicine: Experiences of Women Physician Leaders. Academic Medicine 98(2):p 255-263, February 2023. | 3
[2]Boivin, N., Täuber, S., Beisiegel, U. *et al.* Sexism in academia is bad for science and a waste of public funding. *Nat Rev Mater* 9, 1–3 (2024). https://doi.org/10.1038/s41578-023-00624-3

[3]In 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.

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What is your current state of mind?
Clarity.

What is your idea of perfect happiness?
Changing all the time.

When and where were you happiest? And why were so happy then?
It has changed over the years; change is a constant variable.

What is your greatest fear?
Perhaps boredom.

What is your greatest regret?
None.

What are you most proud of?
My girls.

What do you consider your greatest achievement?
Everything I achieved, in tandem, including work and family.

What or who is your greatest passion?
Curiosity: learning new things.

What is your favorite occupation (or activity)?
Learning new things.

What is your greatest extravagance?
Perfume.

What is your most treasured possession?
None.

Where would you most like to live?
I am curious about living everywhere. Since I started traveling the world, I have always imagined my life in those places. I could live anywhere on the planet.

What is the quality you most admire in people?
Their weaknesses, being human.

What is the trait you most dislike in people?
Their weaknesses, being human.

What do you consider the most overrated virtue?
Patience.

What do you most value in your friends?
Their presence.

Which living person do you most admire?
Pablo, my partner, he is so unique. My daughters, Tatiana and Nadia, they are so resilient.

Who are your heroes in real life?
All women and underrepresented people who fulfill their dreams, whatever those are. Since I am from the 1970s and perhaps because I also like to dance, I must confess I am a fan of Madonna. As she herself said, "The most controversial thing I've done is to stick around." I admire those who persevere and stick around despite the odds.

If you could have dinner with any historical figure, who would it be and why?
Nothing happens in isolation, so not a single person. I would have dinner (lunch and breakfast) with so many people at so many times in history!

Who are your favorite writers?
Many to cite, but for the last few years, Leonardo Padura has been my favorite. I especially love his novels 'Heretics,' 'The Man Who Loved Dogs,' and 'Personas Decentes.' For those unfamiliar with his work, Padura is one of Cuba's most celebrated contemporary authors – a novelist and journalist whose writing offers a compelling window into Cuban society. Born in Havana, Cuba in 1955, Padura is still actively writing. His detective series featuring Mario Conde has won international acclaim, while 'The Man Who Loved Dogs' brilliantly weaves together the assassination of Trotsky with modern Cuban history. His books portray humanity in such a smart and funny way, balancing sharp social commentary with deeply moving storytelling. I love how his writing never sacrifices human complexity even while addressing significant political themes.

Who are your heroes of fiction?
I like to read literature worldwide, and I cannot think of a single character. Each place and time requires a different hero, so it is hard to choose one.

What aphorism or motto best encapsulates your life philosophy?
Everything changes, be ready!

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