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INNOVATORS & IDEAS: RESEARCH LEADER

Ana Cristina Andreazza: Driven by curiosity – transforming mental health through mitochondrial innovation

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Dr. Ana Cristina Andreazza is a Professor of Pharmacology Toxicology and Psychiatry at the University of Toronto, holding the Thomas C. Zachos Chair in Mitochondrial Research and a Tier II Canada Research Chair in Molecular Pharmacology of Mood Disorders. As the visionary Founder and Scientific Director of the Mitochondrial Innovation Initiative (Mito2i), she leads pioneering research on the role of mitochondrial dysfunction in neurological and psychiatric diseases, organ transplants, and novel therapeutic strategies. Her groundbreaking work has revolutionized our understanding of the relationship between mitochondrial function and mental health disorders, particularly bipolar disorder. Dr. Andreazza's career was inspired by early curiosity, family influence, and a commitment to reduce the stigma surrounding metabolic and psychiatric conditions. Her innovative work bridges multiple disciplines, aiming to discover biomarkers that could enable personalized treatments in mental health. A recipient of numerous prestigious awards, including membership in the Royal Society of Canada College of New Scholars, Dr. Andreazza has published over 200 peer-reviewed papers and is internationally recognized for her contributions to metabolic psychiatry. In this Genomic Press Interview, she shares insights into her remarkable journey from studying wine chemistry in Brazil to becoming a leading force in mitochondrial research while discussing her perspectives on collaborative science and innovation. Driven by a passion for teaching and collaborative science, Dr. Andreazza continues to foster innovation and mentorship in the mitochondrial research community.

Figure 1. Ana Cristina Andreazza, Pharm, PhD, University of Toronto, Canada

Part 1: Ana Cristina Andreazza – Life and Career

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

I began my career as a pharmacist, transitioning to science to explore the antioxidant properties of flavonoids at the Biotechnology Institute at the University of Caxias do Sul, Brazil. This exploration ignited my interest in the redox mechanisms in the brain and propelled me toward graduate studies in Biochemistry. For my doctoral thesis, I investigated how oxidative stress contributes to major psychiatric disorders, such as bipolar disorder and schizophrenia. In 2008, I furthered this research during a postdoctoral fellowship at the University of British Columbia, where I studied oxidative damage to specific mitochondrial proteins in the prefrontal cortex tissue of patients with these conditions. Throughout my education, I was fortunate to learn from exceptional mentors who profoundly influenced my passion for both teaching and discovery, guiding me to cultivate my communication skills through speaking engagements and mentoring others.

However, my interest in science started even earlier. My grandfather's family challenge captivated me: "Why does this wine taste so bad?" This curiosity led me, at a young age, to knock on the door of Professor Mirian Salvador, a local researcher studying resveratrol, with a simple request: "Could I study resveratrol?" Driven by my grandfather's winemaking woes, I wanted to explore the connection between the grape compound and the taste of his wine. Professor Salvador, without hesitation, welcomed me into her lab and exposed me to critical thinking, a deep appreciation for mitochondrial metabolism, and a love for scientific inquiry. This early experience left an indelible mark on my approach to science and leadership.

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?

A defining moment in my career came in 2014 during a webinar where a mother whose son have bipolar disorder—and who had also lost two children to mitochondrial disease—reached out to ask if these two conditions were connected. Her question motivated me to work with her family, which led to discovering similar families worldwide. This marked the birth of a new research area that required extensive collaboration across diverse fields. This experience inspired me to establish the Mitochondrial Innovation Initiative (Mito2i)—a network of researchers, clinicians, patient advocates, and partners committed to transforming our understanding of mitochondrial function in health and disease.

Today, as a Professor in the Departments of Pharmacology & Toxicology and Psychiatry at the University of Toronto, I hold the Thomas C. Zachos Chair in Mitochondrial Research and a Tier II Canada Research Chair in Molecular Pharmacology of Mood Disorders. I am also the Founder and Scientific Director of Mito2i, a Senior Fellow at Massey College, a Member of the Royal Society of Canada College of New Scholars, and serve on the

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Bipolar Scientific Steering Committee for BD2: Breakthrough Discoveries for Thriving with Bipolar Disorder and member of Metabolic Mind. These roles allow me to lead research on mitochondrial function in neurological and psychiatric disease, organ transplant, and novel therapeutic strategies while nurturing an inclusive environment for scientific discovery.

Please share with us what initially piqued your interest in your favorite research or professional focus area.
My family shaped my career path. My mother, a brilliant teacher, devoted her life to public service, empowering those with fewer opportunities. Her dedication inspired me to pursue a career in academia. My father, a mathematician and professor of statistics, possessed an insatiable curiosity but struggled with untreated metabolic psychiatric issues. His journey fueled my commitment to identifying biomarkers that could demystify and reduce the stigma surrounding such conditions. This combination of academic influence and personal motivation solidified my drive to research metabolic psychiatry and the link between mitochondrial dysfunction and mood disorders.

What impact do you hope to achieve in your field by focusing on specific research topics?
My goal is to identify biomarkers that can pave the way for personalized treatments in metabolic psychiatry. Mitochondrial dysfunction is increasingly recognized as a root factor in metabolic syndrome, linking cellular energy regulation with metabolic homeostasis. For example, acetyl-CoA produced by mitochondria initiates cholesterol synthesis, underscoring mitochondria's role in lipid biosynthesis. When mitochondrial function is compromised, cells may shift to anaerobic glycolysis, leading to glucose intolerance and insulin resistance, both prevalent in mood disorders. By uncovering how disrupted metabolism influences disease, I aim to improve treatments, reduce patient suffering, and alleviate healthcare costs associated with ineffective therapies.

Please tell us more about your current scholarly focal points within your chosen field of science.
My research integrates three interconnected areas of mitochondrial science. First, I focus on understanding mitochondrial impairments in mood disorders, particularly bipolar disorder. Using brain organoids derived from patient stem cells, we study the dysregulation of complex I genes, elevated reactive oxygen species, and reduced NDUFS7 expression. This work aims to identify novel therapeutic targets that could restore mitochondrial function and neurotransmission, potentially transforming mood disorder treatment.

In our second research stream, we explore mitochondrial health in organ transplantation, with a particular focus on lung transplants. Our goal is to enhance mitochondrial preservation to improve post-transplant outcomes and reduce complications. We have recently expanded this work to address ischemic and heart injury, taking a multidisciplinary approach to regenerative medicine.

The third area involves a large collaborative network pioneering work in mitochondrial transplantation. We are developing innovative approaches using biomaterials to encapsulate mitochondria for regenerative therapy, and employing organ-on-a-chip platforms to create stable mitochondrial transplants. One exciting direction is our work on developing a mitochondrial donor biobank, which holds promise for advancing translational and clinical applications of mitochondrial transplantation.

As Founder and Director of Mito2i, I work to create a collaborative environment that bridges these research themes, facilitating a holistic understanding of mitochondrial health and contributing meaningfully to patient care and scientific advancement.

What habits and values did you develop during your academic studies or subsequent postdoctoral experiences that you uphold within your research environment?
An open-minded approach to data interpretation, coupled with a readiness to learn from diverse perspectives, has been central to my work. I emphasize critical thinking and foster a collaborative environment where my team feels encouraged to bring fresh insights that often lead to breakthroughs.

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?
Absolutely. I am passionate about promoting inclusion and equity and encouraging the integration of diverse perspectives into scientific inquiry. Barriers tied to one's background, training location, or cultural heritage often limit one's voice in science. I advocate for an environment where critical thinking benefits from varied perspectives, fostering a more comprehensive understanding of complex issues. Through this approach, we can create a more inclusive, effective, and impactful scientific community.

What do you most enjoy in your capacity as an academic or research leader?
Teaching is a true passion of mine. I enjoy sharing knowledge and learning from brilliant colleagues and students who inspire me immensely.

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 cherish time with my family, whether playing board games, going for nature walks with our dog, or building lasting memories with my daughter. These moments provide a refreshing balance to my professional life and are a constant source of joy.

Part 2: Ana Cristina Andreazza – Selected questions from the Proust Questionnaire[1]

What is your idea of perfect happiness?
To live fully in the present and embrace every moment along the way.

What is your greatest fear?
Failure to positively impact the lives of those who depend on our research.

Which living person do you most admire?
My mom. She dedicated her life to public service, uplifting individuals from underprivileged backgrounds in southern Brazil with unwavering compassion and commitment.

What is your greatest extravagance?
Enjoying the occasional dinner at a Michelin-starred restaurant.

What are you most proud of?
My daughter—her growth and resilience inspire me daily.

[1] 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.

Figure 2. Science in collaboration and joy. The Andreazza Lab cultivates a nurturing environment where collaboration and leadership flourish, often brightened by visits from Skater, our beloved lab mascot (center) – a four-year-old Keeshond/American Eskimo mix who reminds us to take restorative breaks in nature. Top right, then going clockwise: the Andreazza Lab team featuring (back row) Daniel, Jaeyoung Choi, Timofei Chernanga, Pavel Powlowski, David Bodenstein, Tiago S. Silva, Thisha Ravindran, (front row) Erika Beroncal, Lauren Pappis, Kassandra Zachos, Dana El Soufi-El-Sabbagh, Anna Gimenez, Angela Kwak, and special guests Skater and Isabela. Top right adjacent: connecting with courageous and brilliant minds, such as Thomas C. Zachos. Above bottom right: witnessing the field's growth, we collaborate with visionary leaders like Kirk Nylen and Franco Vaccarino at Metabolic Mind. Bottom right: my family's unwavering support and inspiration – Marles and, in loving memory, Armando Andreazza. Bottom left: having good times with Michael Berk in Crans-Montana, Switzerland. Above bottom left: with my beloved family, James and Isabela Pierlot. Middle left: MITO2i (Mitochondrial Innovation Initiative) represents our commitment to fostering innovation, as shown with Sonya Brijbassi. Top left: the joy of traveling, sharing knowledge, and building collaborations and friendships is evident in partnerships with esteemed colleagues such as Marion Leboyer, here on an e-scooter in the urban landscape.

What is your greatest regret?
I consciously try to live in the moment and learn from each experience.

What is the quality you most admire in people?
Fairness.

What is the trait you most dislike in people?
Dishonesty and discrimination.

What do you consider the most overrated virtue?
Listening—when it is done superficially without truly understanding or engaging with others.

What is your favorite occupation (or activity)?
Walking or hiking in nature.

Where would you most like to live?
Wherever my family is, that is my actual happy place.

What is your most treasured possession?
My family.

When and where were you happiest? And why were so happy then?
The day my daughter was born. It began an indescribable journey of joy, love, and growth.

What is your current state of mind?
Optimistic. I feel a sense of hope as mitochondrial research gains recognition as a critical factor in many diseases, bringing us closer to innovative therapies.

What is your most marked characteristic?
Passion. I am enthusiastic, expressive, and wholeheartedly committed when believing in a cause or helping someone in need.

Among your talents, which one(s) give(s) you a competitive edge?
My openness to listening to diverse viewpoints and synthesizing them into a cohesive understanding.

What do you consider your greatest achievement?
My family—their support and presence are invaluable to me.

If you could change one thing about yourself, what would it be?
I would ease my tendency to overthink.

What do you most value in your friends?
Their readiness to support when needed.

Who are your favorite writers?
My husband. His ability to synthesize knowledge and captivate his audience through his writing deeply inspires me.

Who are your heroes of fiction?
Monica is a Brazilian cartoon character—a fierce and passionate seven-year-old girl who always stands up for herself and others.

Who are your heroes in real life?
Mitochondria—these tiny structures are essential to life, driving energy and function in our cells.

What aphorism or motto best encapsulates your life philosophy?
Keep going; good things will happen.

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