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Yogesh Dwivedi: Pre-clinical and translational research focusing on gene regulation through epigenetic and epitranscriptomic mechanisms and their implications in mood disorders and suicidal behavior

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Dr. Yogesh Dwivedi is the Elesabeth Ridgely Shook Endowed Chair and Professor in the Department of Psychiatry and Behavioral Neurobiology at the University of Alabama at Birmingham (UAB). He joined UAB in 2013 after working at the University of Illinois at Chicago for about 20 years, where he rose to tenured Professor. He is the Vice Chair for Faculty Affairs and Faculty Development, Co-Director of the UAB Depression and Suicide Center, Director of Translational Research of the UAB Mood Disorder Program, and the Director of the Alabama Brain Bank. He has published over 160 papers in peer-reviewed journals and serves on the editorial board of several scientific journals. He leads multiple National Institute of Mental Health-funded studies and has also edited a book entitled *The Neurobiological Basis of Suicide*. The recipient of several national and international awards, Dr. Dwivedi is a member of the Scientific Council of the American Foundation for Suicide Prevention and a Fellow of the American College of Neuropsychopharmacology (ACNP), International College of Neuropsychopharmacology (CINP), and International Neuropsychiatric Association. His research broadly elucidates the molecular and cellular mechanisms associated with early-life stress, mood disorders, and suicidal behavior by integrating basic and clinical neuroscience. More specifically, his studies focus on gene regulation through epigenetic, epitranscriptomic, and non-coding RNAs and whether these mechanisms play a role in mood regulation and suicidal behavior. He is also working on translating these findings into biomarkers for depression, suicidality, and treatment response. Dr. Yogesh Dwivedi kindly agreed to engage in the Genomic Press Interview, sharing his distinctive blend of personal and professional narratives.

Figure 1. Yogesh Dwivedi, University of Alabama at Birmingham (UAB), USA.

Part 1: Yogesh Dwivedi – 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 was born and educated in a small town in northern India. I first discovered organic chemistry in high school, and my passion for science was kindled. My Chemistry teacher taught the subject with reference to day-to-day life in such a relatable manner that by the end of my first year in high school, I had a makeshift Chemistry lab of my own in the shed of my home. After school, this is where I could be found, mixing solvents and replicating the lessons learned in school with the materials I could access at home. The real fascination lay in the application of the subject to human life. Chemistry was my major in BS, and I secured the highest marks in my graduating class. My interest in Chemistry took me away from my small town since advanced degrees were unavailable, and I had graduated early. During those days, only five universities in India offered a Master's program in Biochemistry. The selection was highly competitive due to the limited number of seats; I was fortunate to secure a seat, and the education was transformative. I committed to biochemistry during my MS degree. My passion for Biochemistry and its application to humankind led me to pursue my Ph.D. at the Central Drug Research Institute, a prestigious research organization in India focusing on drug discovery. This is where my love for Neuroscience was born; one of my mentors was an internationally renowned neuroscientist and neuropharmacologist. With his recommendation and support, I joined a postdoctoral position at the Illinois State Psychiatric Institute (ISPI), Chicago, which was at the forefront of research in biological psychiatry.

My passion for science took me farther and farther away from my small town until finally; everything came together during my postdoctoral research at ISPI; in the challenging new domain of mental disorders, I could utilize my education in Biochemistry and Molecular Biology to make a difference. While working in Chicago, I came in contact with several prominent researchers at the National Institute of Mental Health, which further shaped my ideas and became instrumental in establishing my lab as Principal Investigator. The journey from the shed that housed my first Chemistry lab to establishing my own lab as a faculty member in a different country was arduous. However, such was my commitment to science that no boundaries could restrict me.

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Figure 2. A patch of Drift Roses embellishes Yogesh Dwivedi's garden in Birmingham, Alabama.

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?
As a faculty member at the University of Illinois at Chicago, I was content with the space and responsibility I was given where I was engaged in harnessing my ideas and making my way into the field of biological psychiatry. While I had envisioned leadership in the field of research in the distant future, I had not anticipated a leadership role in academic psychiatry until I was given a chance to help establish the Depression and Suicide Center when I joined UAB. It gave me an excellent opportunity to translate my ideas into expanding the basic and translational research arena within the confines of the Center. This led to other opportunities for leadership both within UAB and in the larger scientific community. As the director of the Behavioral Neuroscience Division at UAB and the director of translational research of the UAB mood disorders program, I had the opportunity to mentor and collaborate with a wide range of faculty and impact the future course of research. These roles prepared me for my position as Vice Chair for Faculty Affairs and Development and Director of the Alabama Brain Bank. These leadership opportunities have provided me with a sense of fulfillment in making a difference and evolving by listening to other people's ideas.

Please share with us what initially piqued your interest in your favorite area of research or professional focus.
While working in the area of gene regulation, I became highly interested in the field of non-coding RNAs. Not only do non-coding RNAs occupy most of the genome, but they also allow venturing into a territory with many unknowns. I was primarily interested in microRNAs, a specific class of small non-coding RNAs whose mode of action is unique, where multiple miRNAs could regulate a single gene or multiple genes could be regulated by a single miRNA, more so in a highly coordinated fashion. This has led me to deeply explore other non-coding RNAs, their contribution to epigenetic modifications, and, ultimately, their relevance to psychiatric illnesses.

What kind of impact do you hope to achieve in your field through your focus on your specific research topics?
I hope that my work will help in understanding the biological basis of depression and suicide, which will not only lead to identifying the causal factors but also help in developing targeted therapies. I also hope to develop CNS-based biomarkers to help clinicians accurately diagnose patients and gauge the treatment response.

Could you tell us more about your current scholarly focal points within your chosen field of science?
Currently, I am working to understand the role of non-coding RNAs in gene regulation at multiple levels for their contribution to psychiatric illnesses, particularly depression and suicidal behavior. These include the role of non-coding RNAs in epigenetic and epitranscriptomic modifications of genes using the human postmortem brain, rodent models, peripheral cells from human blood samples, and human induced pluripotent stem cells (iPSCs). Simultaneously, I am researching if these modifications can be used as biomarkers for diagnosis and treatment response, particularly using extracellular vesicles derived from the brain.

What habits and values did you develop during your academic studies or subsequent postdoctoral experiences, that you uphold within your own research environment?
Through my academic studies and postdoctoral training, the habits I developed and the values that shape my research environment are those of persistence, patience, constant questioning, and preparedness for challenges and failures.

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 you think warrant transformative scrutiny, or is there a cause within science that deeply stirs your passions?
I am passionate about science being free of all political or sociocultural restraints and deriving only from facts.

What do you most enjoy in your capacity as academic or research leader?
I love to discuss new ideas and how to implement them with innovative techniques that can transform the field.

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?
Gardening is what I cherish most in my leisure moments. My wife and I are habitual gardeners, always planting, replanting, pruning, fertilizing, and, more than all else, growing with our plants.

Part 2: Yogesh Dwivedi – Selected questions from the Proust Questionnaire[1]

What is your idea of perfect happiness?
Perfect happiness for me is being at peace with myself, knowing that I have done my bit and am cherished by my loved ones.

[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.

What is your greatest fear?
My greatest fear is the sudden loss of a loved one.

Which living person do you most admire?
There are several people I admire from various spheres.

What is your greatest extravagance?
Planning trips with my wife as we constantly seek new adventures; our latest adventure was a trip aboard the Arctic Circle to see the Aurora Borealis in Abisko.

What are you most proud of?
I am most proud of my son—not just of his achievements but also of the sensitive and kind person he is and the wonderful man he is becoming.

What is your greatest regret?
Apart from the small ones littered across my lifespan, I have done my best to live without significant regrets.

What is the quality you most admire in people?
Honesty and integrity.

What is the trait you most dislike in people?
Pretentiousness.

What do you consider the most overrated virtue?
Virtues are virtues—I try not to overthink them but focus on trying to be a good human being.

What is your favorite activity (physical or intellectual)?
At the top of the list are gardening and reading.

Where would you most like to live?
Mukteshwar is a small town nestled in the Himalayas in India. I have tried to recreate this setting in my home in the hills of Birmingham, Alabama.

What is your most treasured possession?
My father's watch, which he gave to me when I left home to pursue my education at the age of 19, has been a constant reminder of his presence even after he was gone.

When and where were you happiest? And why were so happy then?
Thankfully, there have been many such instances; it is hard to choose one specific moment.

What is your current state of mind?
Calm: I do my best to stay balanced.

What is your most marked characteristic?
I am highly driven.

Among your talents, which one do you think gives you a competitive edge?
Gardening has instilled in me the values of hard work, persistence, and patience, which give me an edge in science.

What is a personality/characteristic trait you wish you had?
We are who we are, but we can constantly better ourselves. I would like to cultivate a sharper sense of humor.

What do you consider your greatest achievement?
That I have played a small part in the field of depression and suicide studies.

What do you most value in your friends?
Openness and trust are what I value most in my friendships.

Who are your favorite writers?
I read extensively in English and Hindi, as well as fiction and nonfiction, so it is not easy to choose favorites. My favorites are Indian-American writers: Amartya Sen, Jhumpa Lahiri, Siddhartha Mukherjee, Ashwini Sanghi, Chitra Divakaruni, and others.

Who are your heroes of fiction?
My heroes of fiction are primarily humans who are often flawed but heroic in their efforts to survive.

Who are your heroes in real life?
People who inspire me daily are always at it, trying their best to live meaningfully, one day at a time.

What aphorism or motto best encapsulates your life philosophy?
Never give up!

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