

Psychedelics

OPEN

INNOVATORS & IDEAS: RISING STAR

Michael A. Wheeler: Psychedelics and neuroimmune circuits—what a strange trip, indeed

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In a thought-provoking Genomic Press interview, Dr. Michael Wheeler emerges as a brilliant scientific innovator at the intersection of neuroscience and immunology. As an Assistant Professor at Harvard Medical School and an investigator at Brigham and Women’s Hospital, Wheeler’s groundbreaking research explores how brain-immune communication shapes our behaviors and emotions. His innovative laboratory weaves together genomic screening, single-cell technologies, and behavioral studies to unravel the fascinating dialogue between peripheral immune cells and brain function. Most remarkably, Wheeler’s NIH-funded research has shown that psychedelics like psilocybin can reverse stress-induced fear behaviors by targeting a previously hidden neuroimmune pathway connecting inflammatory cells in the meninges to critical brain regions controlling emotions and rewards. This groundbreaking work has just been further validated in a *Nature* article (23 April 2025, DOI: [10.1038/s41586-025-08880-9](https://doi.org/10.1038/s41586-025-08880-9)) showing how psychedelics regulate the complex interplay between brain and immune cells in fear responses. By revealing how psychedelics modulate not just neurons but also immune responses, Wheeler’s paradigm-shifting research opens exciting new therapeutic possibilities for depression, addiction, and stress-related disorders. Through his warm, authentic scientific approach and deep curiosity about mind-body connections, Wheeler represents a new generation of researchers redrawing the boundaries between psychiatry and immunology to transform our understanding of mental health.

Part 1: Michael Wheeler – Life and Career

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

My community growing up did not have a lot of resources, so I was not exposed to bench research until I went to college. But I had incredible teachers and mentors as a kid that exposed me to important ideas. In particular, I think the moment that inched me closer toward a career in science rather than the humanities (which I loved) was during my Psychology class in high school thinking about consciousness; both its essence and subjectivity and thinking about the lack of control we have over our conscious experiences. That early fascination with the involuntary nature of thought eventually shaped my interest in how external forces—like stress or trauma—can reshape our inner world. I also loved math. Therefore in college, I pursued both the humanities and science/engineering, and really had trouble selecting a path. I did internships in preparation for law school, medical school, and graduate school. My first exposure to basic science was as a college freshman. I was privileged to join the lab of Hongjun Song at Johns Hopkins, training under Michael Bonaguidi, who

now runs his own lab at USC. Besides the techniques, I took 2 major lessons from my time as an undergraduate in that lab. The first is that you cannot do great science alone, everyone needs a great team. The second is how to strategize building a scientific story from the ground up, which is probably the aspect of science that most captivated me.

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

Counterintuitively, when I decided to pursue a PhD in Neuroscience was during my internship at the Public Defender’s office in the Baltimore City Capital Defense Division. I felt that the actions of the people we defended were so inextricably linked with their environmental circumstances, inclusive of physical or emotional abuse beyond their control, that I was desperate to understand the inner workings of their minds. Since that experience, my long-term goal has always been to get at the environment-brain interplay to try and, naively, remediate some of the socially inflicted human suffering that I witnessed there. However, I am more optimistic that we can begin treading that path as I have learned more about neuroimmune mechanisms in a laboratory setting.

We would like to know more about your career trajectory leading up to your current role. What defining moments channeled you toward this opportunity?

I have been super fortunate to work in a Department that values developing and retaining former trainees and facilitating their independence. Choosing mentors who care about me as a person and a scientist has been the most career-defining factor. Whether it is the Song lab taking in an undergraduate with zero knowledge of science, my graduate school mentors Chris Deppmann and Ali Güler, who fostered my growth, or my postdoctoral mentor Francisco Quintana helping me during my transition to independence, or even my excellent bosses now like Vijay Kuchroo, Howard Weiner, and Tracy Batchelor, I feel fortunate to have had these mentorship experiences.

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?

One of the most intimidating choices I made was joining the lab of an Immunologist during my post-doc. I only trained in Neuroscience at that point, so when I looked at Francisco’s papers on dendritic cells and T cells, I was nervous about what I was getting into. However, I lucked out by having extraordinary lab mates from different fields. Francisco allowed us to connect and work together, allowing us to do some exciting things. This experience ultimately allowed me to learn a new scientific language. Moreover, now, I am a faculty member of the Gene Lay Institute of Immunology and Inflammation, contributing to Neuroimmunology while continuing to learn from some of the most respected figures in immunology.





Figure 1. Michael A. Wheeler, PhD, Harvard Medical School, Brigham & Women's Hospital, USA.

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

Most important is to read, read, and read the literature to stay current with the latest work, as you are never the first to find something. Related to this, I also love incorporating new methods and analytical frameworks to study problems I am interested in. It is crucial to use orthogonal (and novel) methods to validate conclusions, perform time courses, and analyze independent variables through screening platforms. These types of designs are what we like to do in my lab. On a personal level, it is important to make every team member realize how much they offer and to emphasize everyone's unique skill sets. I have drawn this principle from every lab I have trained in.

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

We are deeply interested in establishing links between the brain and immune system to uncover whole-body therapeutic targets in psychiatry and inflammatory diseases. Just this week, we have published new findings in *Nature* on 23 April 2025 (DOI: [10.1038/s41586-025-08880-9](https://doi.org/10.1038/s41586-025-08880-9)) that really tie into this goal. We found that astrocytes in the amygdala use a specific receptor called EGFR to limit stress-induced fear. When chronic stress disrupts this signaling, it leads to a cascade involving brain-resident cells and immune cells that ultimately increases fear behavior. What is fas-

cinating is that psychedelic compounds can reverse this entire process: they reduce the immune cell accumulation in the brain meninges coincident with reducing fear behaviors. It is part of our broader effort to map these brain-body communication circuits, almost like creating that wiring diagram I mentioned earlier. I am particularly excited about the clinical validation aspects of this work. Altogether, this work suggests that the immune system also controls psychedelic-induced brain plasticity. It suggests psychedelics could be therapeutic not just for neuropsychiatric conditions, but potentially for other inflammatory diseases as well.

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

I am excited about the prospect of identifying brain-body communication loops as a fundamental feature of physiology. Often, we think of mental health disorders based on their behavioral symptoms. However, we are likely leaving much underlying biology on the table by focusing solely on the brain. I am hopeful that we can bring structure to the field of Neuroimmunology and define the topology of neuroimmune interactions—almost like charting a wiring diagram for how mind and body stay in dialogue, which we can do through many of the sensitive single-cell approaches now available, some of which we helped develop. I hope that this leads to a revolution in thinking about therapeutic agents to treat neuropsychiatric disorders.



Figure 2. Members of the Wheeler lab are out having dinner in Boston in early 2024.

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

As a PI, my favorite part is bringing people into the lab and onto our team with completely different scientific (and personal) backgrounds to have everyone work together. This facilitates cross-pollination between ideas that could only happen on the organizational level. Importantly, everyone makes significant contributions, grows as a scientist, and drives us in new directions. There is way too much for me to learn or know individually, so relying on such a skilled and motivated team is exciting.

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?

Now, as ever, one of the most important things we scientists must do is engage with non-scientists about our work and explain how scientific consensus is distinct from something akin to belief. We need effective communicators to relay complex scientific findings authentically and groundedly: What was done? What are its limitations? What is next? What are the real-world implications? When "science" the discipline is presented as a monolithic, dogmatic enterprise, it may evoke suspicion. And that is understandable—scientists thrive on skepticism, and we should expect the same from the public.

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 learned to love movies from my mom and have been a regular at the Coolidge Corner Theater in Brookline for years. I even have a personalized seat there. I love watching movies that introduce avant-garde ideas or new filmmaking styles.

Part 2: Michael Wheeler – Selected questions from the Proust Questionnaire¹

What is your most marked characteristic?
Openness to change.

Among your talents, which one(s) give(s) you a competitive edge?
Resilience in the face of failure.

If you could change one thing about yourself, what would it be?
To be more spontaneous.

What is your current state of mind?
Excited for the future.

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 idea of perfect happiness?**

I learned about a Japanese practice called “forest bathing,” which involves spending time in nature. I love “city bathing,” which involves taking long walks in Boston (and other cities), particularly in busy areas, to feel how alive everything is.

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

When my wife and I first visited Paris in the springtime, we wandered through the streets, found a fantastic restaurant called La Mascotte, and ate outside amidst the bustle. It was Hemingway’s “moveable feast,” Godard’s *Breathless*, just dynamic bliss.

What is your greatest fear?

Not savoring the present.

What is your greatest regret?

I try not to regret anything—mistakes tend to be good teachers.

What are you most proud of?

My two kids it is the first thing I have done that will outlive me.

What do you consider your greatest achievement?

I am hopeful I have not done it yet, though building a thriving, collaborative lab is something I am deeply proud of.

What or who is your greatest passion?

My family.

What is your favorite occupation (or activity)?

I love going out to nice restaurants.

What is your greatest extravagance?

It would not hurt if the restaurant adjoined a nice hotel.

What is your most treasured possession?

An autographed UFO drawing from Bob Lazar.

Where would you most like to live?

Paris.

What is the quality you most admire in people?

Grit and altruism.

What is the trait you most dislike in people?

Cruelty and hubris.

What do you consider the most overrated virtue?

The solitary genius.

What do you most value in your friends?

Authenticity.

Which living person do you most admire?

Werner Herzog – his work is bold, creative, and feels deeply human.

Who are your heroes in real life?

Santiago Ramón y Cajal. He was such a meticulous scientist and dominant thinker whose observations are still alive today.

If you could have dinner with any historical figure, who would it be and why?

Socrates—a deadly combination of brilliant and fun.

Who are your favorite writers?

I am enthralled by Robert Caro’s biographies of Lyndon Johnson and am waiting impatiently for the fifth and final volume. I also just read *The Sellout* by Paul Beatty, which is so densely brilliant that its only comparison is *Infinite Jest*. Two other books I recently read that I found profound and unique were *Barracoon* by Zora Neale Hurston and *The Twilight World* by Werner Herzog, both about how environments profoundly shape identity.

Who are your heroes of fiction?

I have always been a Sherlock Holmes fan, and for that matter, Dr. House.

What aphorism or motto best encapsulates your life philosophy?

A jug fills drop by drop.

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