Fourth Issue, 6 March 2025

Welcome to *Science Prism*—your gateway to exploring the brilliance of science and discovery. Like a prism dispersing light into a spectrum of colours, we distil complex scientific ideas into clear, engaging, and thought-provoking insights. Delivered monthly, Science Prism is designed for students, researchers, and curious minds, bringing you the latest breakthroughs, timeless questions, and actionable ideas to fuel your curiosity and drive innovation. Guided by our tagline, "*Illuminating Science, Empowering Minds,*" we aim to inspire fresh perspectives and connect the transformative power of science with the world around us. Join us each month as we explore knowledge, spark curiosity, and celebrate discovery, one insight at a time.

Happy International Women's Day!

As International Women's Day approaches on March 8th, we at *Science Prism* are thrilled to present this special edition of our newsletter. This issue is a tribute to the extraordinary contributions of women researchers who have shaped our understanding of microglia, the brain's immune sentinels. Their pioneering work has been instrumental in unraveling the complexities of microglial function in health and disease, offering invaluable insights that continue to propel neuroscience forward.

For this special occasion, we've combined our *Science Spectrum* and *Science Shaper* sections to spotlight the women whose dedication, passion, and discoveries have left a lasting impact on microglial research. While we recognize the immense contributions of men and other researchers across neuroscience, this issue focuses on celebrating women in the spirit of International Women's Day. *We also acknowledge that many more remarkable women scientists, both within and beyond the microglia field, deserve recognition* — and while it's not possible to highlight everyone in a single issue, we extend our deepest respect and admiration to them.

Our goal with this special edition is not only to inspire but also to emphasize the importance of continued support and equal opportunities for women in science. Progress is built on collaboration, and this issue serves as a testament to how women researchers, alongside their male colleagues, are collectively shaping the future of neuroscience.

We proudly dedicate this edition to all women — especially to those in science — honoring their resilience, brilliance, and unwavering pursuit of discovery.

Wishing all our readers a thoughtful and empowering International Women's Day!
Warm regards,
Team, *Science Prism*.

Science Shapers + Science Spectrum: Celebrating the Women in Microglia Science

March is a time of celebration, a moment dedicated to recognizing the strength, resilience, and brilliance of women across all fields. Particularly in science, where women have historically fought for recognition, we encounter an inspiring group of researchers whose groundbreaking work on microglia— the brain's resident immune cells—has transformed our understanding of neuroscience. These extraordinary women scientists have made significant discoveries that highlight the multifaceted roles of microglia, from their involvement in neurodevelopment and neurodegeneration to their roles in brain tumors and psychiatric disorders. No

longer seen merely as "janitors" of the brain, microglia are now understood to be master regulators of brain function. Their perseverance in balancing rigorous research with the challenges of family and professional life not only advances our knowledge in the field but also paves the way for future generations. In this special feature, we honor these pioneering women, delving into their innovative research and its profound impact on our understanding of brain health and disease. Through this endeavor, we are not only celebrating individual researchers but also tracing the evolution of our understanding of microglia — cells once thought to be mere brain janitors or agents of neuroinflammation. Over time, research has revealed their multifaceted roles as dynamic regulators of neural circuits, guardians of homeostasis, and critical players in both health and disease. Each discovery has been a stepping stone, gradually unmasking the intricate and essential nature of these cells and propelling the field forward with renewed curiosity and wonder.

Dr. Monica Carson: Pioneering Microglial Diversity and TREM2 Research

In 2002, **Dr. Monica Carson** made a significant breakthrough in our understanding of microglia, the immune cells of the brain. She was the first to discover that **TREM2 (Triggering receptor expressed on myeloid cells-2)**, a key receptor for microglial function, doesn't have a uniform presence throughout the brain. Instead, its expression varies between different brain regions. This was a groundbreaking revelation, especially at a time when microglia were generally seen as a single, uniform type of cell.

Dr. Carson's findings laid the groundwork for years of research into how these microglia regional differences influence brain health and disease. Fast forward nearly 20 years, and TREM2 continues to be a focus of intense study, particularly in the context of Alzheimer's disease and other neurodegenerative conditions. Her pioneering work has helped shift the scientific community's attention to the diversity and specialization of microglia, which are now seen as essential for proper brain function.

Reference: *Schmid et al. J Neurochem. 2002 Dec;83(6):1309-20.*

Dr. Beth Stevens: Microglia as the Sculptors of the Brain

In 2007, **Dr. Beth Stevens** made a groundbreaking discovery that transformed our understanding of brain development. Her research revealed that microglia do more than just clear cellular debris—they actively **prune and refine synapses**, shaping neural circuits during development. This study was the first to show that microglia recognize and eliminate weak or unnecessary synapses, much like sculptors chiseling away excess material to reveal a masterpiece. Her work fundamentally changed the way scientists viewed microglia, shifting them from passive immune responders to **active architects of the developing brain**.

This discovery had profound implications for **neurodevelopmental disorders** like schizophrenia and autism, where disruptions in synaptic pruning are now believed to play a role. Dr. Stevens' research bridged the fields of **neuroscience, immunology, and psychiatry**, highlighting the deep connection between the brain's immune system and cognitive health. Her pioneering work continues to inspire new therapeutic strategies for brain disorders, proving that understanding microglia is key to unlocking the mysteries of neurodevelopment.

Reference: *Stevens et al. Cell. 2007 Dec 14;131(6):1164-78.*

Dr. Bahareh Ajami: Settling the Debate on Microglial Origins

For decades, scientists debated whether microglia, the brain's resident immune cells, continuously replenished from circulating monocytes or

maintained their own self-renewing population. In **2007 and 2011**, **Dr. Bahareh Ajami** provided the definitive answer—microglia are largely **self-sustaining and do not derive from blood monocytes**, challenging previous assumptions (Ajami et al., 2007, 2011). Using elegant genetic fate-mapping techniques, her work showed that microglia maintain their numbers **independently within the brain**, a critical insight that reshaped our understanding of their biology and long-term function.

This discovery impacts how we understand neuroinflammation, brain injury, and neurodegenerative diseases, where monocyte infiltration and microglial activation are often confused. By clarifying microglial origins, Dr. Ajami's work provided a foundation for targeted therapies that distinguish microglial responses from peripheral immune cell infiltration. Her research resolved a long-standing controversy and remains a cornerstone in microglial biology, emphasizing the **unique identity and lifelong persistence of these vital brain cells**.

References:

Ajami et al. Nat Neurosci. 2007 Dec;10(12):1538-43.
Ajami et al. Nat Neurosci. 2011 Jul 31;14(9):1142-9.

Dr. Ania Majewska: Unveiling Microglia's Role in Synaptic Remodeling and Brain Plasticity

Dr. Ania Majewska has been at the forefront of microglia research, unraveling their critical role in sculpting neural circuits during development and in response to experience. She is a pioneer in using **advanced in vivo imaging techniques to track microglial behavior, revealing their dynamic role in the brain**. Her groundbreaking research demonstrated that microglia are not passive cells but **active participants in synaptic plasticity**. In a landmark 2010 PLOS Biology paper, co-authored with **Dr. Marie-Ève Tremblay**, she provided the first live imaging evidence of microglia monitoring and remodeling synapses, solidifying their role as key players in synaptic plasticity. This discovery transformed the understanding of microglia as dynamic regulators of brain function, showing how their surveillance and remodeling of synapses influence learning, memory, and sensory processing.

More recently, **Dr. Monique Mendes** and Dr. Majewska's work has shed light on microglial self-renewal and maturation in the adult brain. In a 2021 eLife study, her team used chronic in vivo two-photon imaging to reveal that under basal conditions, microglia exhibit limited turnover and migration, but following depletion, they rapidly repopulate through local division. This **rapid self-renewal was shown to occur largely independently of the P2Y12 receptor,** challenging previous assumptions about microglial signaling. Her findings demonstrated that **newly born microglia take on mature roles within days, bypassing the prolonged maturation typically seen during development.** This work highlights microglia's remarkable adaptability and their essential role in maintaining brain homeostasis, further cementing Dr. Majewska's legacy as a leader in unraveling the complexities of microglial biology.

References:

Tremblay et al. PLoS Biol. 2010 Nov 2;8(11):e1000527.
Mendes et al. Elife. 2021 Jul 12:10:e61173.

Dr. Marie-Ève Tremblay: Unveiling Microglial Surveillance and the Mystery of Dark Microglia

In 2010, **Dr. Marie-Ève Tremblay** revolutionized microglial research with a pioneering **PLOS Biology** study along with **Dr. Ania Majewska** that combined **high-resolution electron microscopy** and **live two-photon imaging** to directly visualize microglia interacting with synapses. This groundbreaking work provided the first concrete evidence that microglia continuously **survey and shape neuronal connections** rather than acting solely as immune responders. Her research shifted the field's focus toward **microglial-neuronal interactions**, opening new avenues for understanding how these cells contribute to both **healthy brain function and neurodevelopmental disorders**.

Beyond this foundational discovery, **Dr. Tremblay, alongside Dr. Kanchan Bisht**, co-discovered **dark microglia**, a unique and enigmatic microglial phenotype, first described in their **2016 Glia** paper. These highly electron-dense microglia appear under conditions of **chronic stress, aging, and neurodegeneration**, displaying a distinct morphology suggestive of **hyperactive synaptic remodeling**. Their discovery highlighted previously unrecognized microglial heterogeneity, suggesting a critical role for dark microglia in **synaptic pruning and brain plasticity**. This work has since inspired a wave of research into microglial subtypes and their roles in brain health and disease, cementing **Dr. Tremblay's** legacy as a trailblazer in the field.

References:

Tremblay et al. PLoS Biol. 2010 Nov 2;8(11):e1000527.
Bisht et al. Glia. 2016 May;64(5):826-39.

Dr. Miriam Merad: Unraveling the Embryonic Origins of Microglia

Dr. Miriam Merad, a pioneering immunologist, played a pivotal role in reshaping our understanding of microglial ontogeny. In her landmark 2010 study, alongside Dr. Florent Ginhoux and colleagues, she demonstrated that adult microglia originate from primitive myeloid progenitors arising in the yolk sac before embryonic day 8 — a discovery that settled long-standing debates about the developmental origins of these enigmatic brain-resident macrophages. This seminal work not only established microglia as ontogenetically distinct within the mononuclear phagocyte system but also opened new avenues for exploring their lifelong maintenance and resilience against hematopoietic turnover.

Dr. Merad's research continues to influence the field, highlighting the evolutionary conservation of microglia and their crucial role in maintaining central nervous system homeostasis. Her work laid the foundation for understanding how early-life events shape microglial function, with profound implications for neurodevelopment, disease susceptibility, and potential therapeutic strategies for neuroinflammatory and neurodegenerative disorders.

Reference: *Ginhoux et al, Science. 2010 Nov 5;330(6005):841-5.*

Dr. Amanda Sierra: Microglia as Silent Caretakers of the Neurogenic Niche

In 2010, **Dr. Amanda Sierra** uncovered a fascinating and often overlooked aspect of microglial function—**their active role in clearing apoptotic cells in the neurogenic niche, even in the absence of injury**. Her study introduced the elegant **"ball-and-chain" phenomenon**, where microglia tether and engulf dying newborn neurons in a highly orchestrated process. This discovery shattered the long-held notion that microglial phagocytosis is primarily a response to damage, instead revealing their **constant surveillance and maintenance of brain homeostasis** under normal conditions.

Dr. Sierra's work fundamentally **redefined the relationship between microglia and neurogenesis**, showing that these cells do not simply remove cellular debris but **actively shape the survival and integration of newborn neurons**. Her study provided some of the most stunning images of microglial-neuronal interactions, inspiring a deeper exploration of how these brain-resident immune cells sculpt neural circuits. This work continues to be a cornerstone for understanding microglia's role in brain plasticity, development, and neuroprotection.

Reference: *Sierra et al. Cell Stem Cell. 2010 Oct 8;7(4):483-95.*

Dr. Rosa Paolicelli: The Landmark Discovery of Microglial Synaptic Pruning

In 2011, **Dr. Rosa Paolicelli** published a **groundbreaking study** that provided the first **direct evidence** of microglia actively pruning synapses in the developing brain. While microglia had long been recognized for their immune functions, their role in **shaping neural circuits** remained largely speculative. Her study elegantly demonstrated that microglia identify and eliminate weak or excessive synapses, ensuring the proper refinement of neuronal connections. This work was pivotal in shifting the focus of the field, showing that **microglia are essential sculptors of the brain during development**.

Dr. Paolicelli's discovery was very crucial, transforming microglia from obscure immune cells into **key regulators of neurodevelopment**. This study not only cemented microglial synaptic pruning as a fundamental process but also opened new avenues for understanding **how disruptions in this process may contribute to neurodevelopmental disorders such as autism and schizophrenia**. Her work remains a cornerstone in microglial research, inspiring a generation of neuroscientists to explore their role beyond immunity.

Reference: *Paolicelli et al. Science. 2011 Sep 9;333(6048):1456-8.*

Dr. Dorothy Schafer: Expanding the Synapse to a "Quad-Partite" Model

In 2012, **Dr. Dori Schafer** published a landmark study demonstrating that **microglia prune synapses in the developing visual system through complement signaling**. This discovery not only solidified the role of microglia in synaptic refinement but also introduced a new perspective on how **the immune system actively shapes neural circuits**. By showing that complement proteins tag weaker synapses for elimination by microglia, she revealed a precise mechanism by which these cells sculpt brain connectivity, transforming our understanding of synaptic maturation.

Dr. Schafer's work extended beyond pruning—she fundamentally altered the way neuroscientists think about synapses. Traditionally, synapses were viewed as tripartite structures involving **pre- and postsynaptic neurons and astrocytes**, but her research added microglia as an essential fourth component, redefining it as the **"quad-partite synapse"**. This conceptual shift positioned microglia as **active modulators of synaptic function**, rather than mere immune sentinels, and continues to influence studies on neurodevelopmental and neurodegenerative disorders today.

References:

Schafer et al. Neuron. 2012 May 24;74(4):691-705.

Schafer et al. Glia. 2013 Jan;61(1):24-36.

Dr. Kathryn Lenz: Microglia and the Origins of Sex Differences in the Brain

In 2013, **Dr. Katy Lenz** pioneered research revealing that **microglia contribute to sex differences in brain development**. Her study provided the first clear evidence that these immune cells are not only involved in synaptic pruning and neural circuit formation but also play a crucial role in **shaping sex-specific brain organization**. This breakthrough sparked a wave of research investigating how microglial activity differs between male and female brains, **shedding light on why certain neurodevelopmental disorders, such as autism and ADHD, display sex-biased prevalence**.

Dr. Lenz's work **challenged the long-standing notion** that sex differences in the brain arise solely from hormonal influences. Instead, she demonstrated that **microglia act as key mediators**, responding to hormonal signals in a way that influences brain wiring and function. Her research continues to be instrumental in **bridging neuroimmunology,**

developmental neuroscience, and psychiatry, offering crucial insights into how sex differences emerge in the brain and how they may contribute to neurological and psychiatric disorders.
References: *Lenz et al. J Neurosci. 2013 Feb 13;33(7):2761-72.*

Dr. Soyon Hong: Microglial Synaptic Pruning in Neurodegeneration
In 2016, **Dr. Soyon Hong** made a **game-changing contribution** to the field by extending the concept of **microglial complement-dependent synaptic pruning** from the developing brain to **neurodegenerative diseases**, particularly Alzheimer's disease (AD) (Hong et al., 2016). Her work demonstrated that microglia, in addition to their developmental role in synaptic refinement, **actively contribute to synaptic loss** in the context of neurodegeneration. By showing that microglia use complement proteins to eliminate synapses in Alzheimer's, she **highlighted a pathological mechanism** that could contribute to cognitive decline in AD and other neurodegenerative diseases.

Dr. Hong's discovery was revolutionary because it bridged the gap between **neurodevelopment** and **neurodegeneration**, showing that the same mechanisms responsible for sculpting healthy brain circuits during development could also **drive disease progression when dysregulated**. Her work has opened new therapeutic possibilities, where modulating microglial activity and complement signaling may offer strategies to slow or even reverse synaptic loss in Alzheimer's and related diseases.
Reference: *Hong et al. Science. 2016 May 6;352(6286):712-716.*

Dr. Kanchan Bisht: Dark Microglia and Capillary-Associated Microglia
In 2016, **Dr. Kanchan Bisht** made a groundbreaking contribution to our understanding of microglial heterogeneity with the discovery of **dark microglia**, a unique subset of these immune cells identified through **electron microscopy**. In collaboration with **Dr. Marie-Ève Tremblay**, Dr. Bisht revealed that dark microglia, which exhibit distinct morphological features, are closely associated with **neurodegenerative conditions**, such as Alzheimer's disease and aging. This discovery challenged the previous views of microglia as uniform cells and demonstrated that these cells **exist in a variety of functional states**, some of which may be **pathologically activated** in the brain's response to disease.

In 2021, Dr. Bisht continued her pioneering work by identifying **capillary-associated microglia (CAMs)**, a new subset of microglia that form intimate associations with **brain capillaries** and play a key role in **neurovascular function**. This discovery opens up new avenues for understanding the **neurovascular unit**, **blood-brain barrier integrity**, and how disruptions in these processes may contribute to diseases like stroke, glioblastoma, and Alzheimer's. Through these revolutionary findings, Dr. Bisht has reshaped our understanding of microglial roles in **brain homeostasis and disease**, offering exciting new directions for future research.
References:
Bisht et al. Glia. 2016 May;64(5):826-39.
Bisht et al. Nat Commun. 2021 Sep 6;12(1):5289.

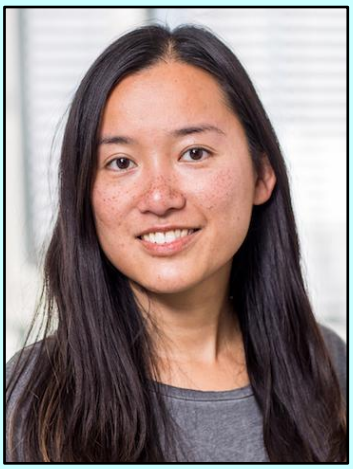
Dr. Mariko Bennett: Advancing Microglial Targeting Tools with Tmem119
In 2016, **Dr. Mariko Bennett** made a significant advancement in microglial research by developing new tools for the **specific identification and targeting of microglia**, particularly through the use of **Tmem119**, a protein uniquely expressed by these cells. Her groundbreaking work enabled **more precise isolation** of microglia,

which had been a major challenge in studying these cells. By using Tmem119 as a marker, she facilitated **advanced genetic manipulation techniques**, allowing for the first time specific targeting and modification of microglial cells in vivo, with **unprecedented accuracy**.

Dr. Bennett's research **paved the way** for the development of **novel Cre and EGFP reporter lines**, tools that are now widely used to study microglia in various contexts, from development to neurodegeneration. This work has been transformative, providing the **research community with essential resources** to explore microglial functions more effectively, and it continues to support a deeper understanding of their role in the brain's immune responses and neuronal health.

Reference: *Bennett et al. Proc Natl Acad Sci U S A. 2016 Mar 22;113(12):E1738-46.*

Dr. Tuan Leng Tay: The "Microfetti" Mouse Model and Microglial Turnover



In 2017, **Dr. Tuan Leng Tay** introduced the **"Microfetti" mouse model**, a revolutionary tool that enables the visualization of **microglial turnover** dynamics in both the **healthy and diseased brain**. Through a **multi-coloured cell labeling system**, Dr. Tay's model allows researchers to track microglial **proliferation and apoptosis** across different brain regions, revealing a **complex and dynamic process** of microglial turnover. This innovative model showed that, in a healthy brain, **microglial turnover** is coupled with **regional heterogeneity**, but following brain injury, specific brain areas exhibit **localized expansions** of microglia, highlighting the cells' ability to adapt to **pathological conditions**.

Dr. Tay's **"Microfetti" model** has had a profound impact on microglial research by offering both a **visually striking and scientifically insightful approach** to studying microglial behavior in real time. It has opened up exciting new possibilities for exploring microglial responses in **neurodegenerative diseases, injury models**, and other **neurological disorders**, providing invaluable insights into how the brain's immune cells respond to both **health and disease**. This work is a testament to Dr. Tay's creativity and expertise in advancing tools that push the boundaries of **neuroscience research**.

Reference: *Tay et al Nat Neurosci . 2017 Jun;20(6):793-803.*

Dr. Anna Molofsky: IL-33 Signaling Between Microglia and Astrocytes in Synapse Remodeling

In 2018, **Dr. Anna Molofsky** made a pivotal contribution to the field of neuroimmunology with her discovery of the signaling mechanism between **microglia and astrocytes** that orchestrates synapse remodeling during brain development. In their **Science** paper, Dr. Molofsky's lab revealed that **IL-33**, a key cytokine, acts as a critical signal for communication between these two glial cell types, facilitating the **reorganization and maturation of synaptic connections**. This finding provided a deeper understanding of the **immune interactions** that are essential for synaptic plasticity and brain development.

Dr. Molofsky's work highlighted the importance of **glial-immune signaling** in shaping the brain's structure and function. By uncovering how microglia and astrocytes work together through IL-33 to regulate synaptic remodeling, her research has opened up new avenues for understanding developmental neurobiology and **synaptic diseases**, including autism and schizophrenia. This discovery bridges the gap between **neuroscience and immunology**, demonstrating how glial cells are not only structural components of the brain but also active participants in its developmental and functional processes.

Reference: *Vainchtein et al. Science. 2018 Mar 16;359(6381):1269-1273.*

Dr. Valerie Wittamer: Zebrafish Microglia and Species-Specific Differences in Microglial Turnover

In 2018, **Dr. Valerie Wittamer's** lab made an exciting discovery about microglial turnover that challenged previous assumptions in mammalian models. Her study revealed that, unlike mammals, **zebrafish microglia undergo full turnover in adulthood**, replacing embryonic microglia with new **adult microglia**. This

groundbreaking work highlighted **species-specific differences** in how microglial populations are maintained throughout life and provided fresh insights into **vertebrate microglial dynamics**. Dr. Wittamer's research opens the door to understanding how different species have evolved to manage microglial function, which could have profound implications for our understanding of **neuroinflammation, neurodegeneration**, and **developmental diseases**.

By using the zebrafish model, Dr. Wittamer is shedding light on the **identity, dynamics**, and **maintenance** of microglia, while also clarifying the **conserved and divergent features** of microglial biology across vertebrate species. Her work has been critical in broadening our perspective of **microglial diversity**, offering valuable comparative data that could lead to **novel therapeutic strategies** for **neurodegenerative diseases** in humans. Dr. Wittamer's contributions are a key step in unraveling the complexities of **microglial function** and how it differs across species.

Reference: *Ferrero et al. Cell Rep. 2018 Jul 3;24(1):130-141.*

Dr. Staci Bilbo: Microglia, Sex Differences, and Neurodevelopmental Disorders

Dr. Staci D. Bilbo has made significant contributions to neuroscience research by revealing the role of microglia in the sexual differentiation of the brain and their impact on susceptibility to **neurodevelopmental disorders such as autism spectrum disorder (ASD)**. Her research revealed that **sex differences in microglial number, morphology, and function during critical developmental windows** could explain the male-biased prevalence of ASD. By bridging immunology and neurobiology, Dr. Bilbo's work highlighted how systemic factors, such as **immune signaling and the gut microbiota, influence brain development in a sex-specific manner**, reshaping how scientists approach sex differences in brain research.

Dr. Bilbo's research also redefined birth as an inflammatory event, identifying **oxytocin as a key modulator of neuroinflammation**. This paradigm-shifting discovery provided crucial insights into the early-life origins of neurodevelopmental disorders and potential therapeutic interventions. Her pioneering studies have not only expanded our understanding of microglia's multifaceted roles in brain health and disease but have also paved the way for more inclusive research practices that account for sex as a biological variable, leaving an enduring impact on the field.

References:

Bilbo et al. Exp Neurol. 2018 Jan;299(Pt A):241-251.
Kingsbury and Bilbo. Front Neuroendocrinol. 2019 Oct:55:100794.
Block et al, Cell Rep. 2022 Aug 2;40(5):111161.

Dr. Ashley Kopec: Microglia, Dopamine Receptors, and Sex-Specific Adolescent Behavior

In 2018, **Dr. Ashley M. Kopec** made a groundbreaking discovery linking **microglial activity to sex-specific differences in adolescent social behavior**. Her study revealed that microglia in the nucleus accumbens (NAc) eliminate dopamine D1 receptors (D1rs) through complement-mediated phagocytosis in male, but not female, rats during adolescence. This receptor pruning was found to be **crucial for the natural maturation of male social play behavior**, establishing that microglia shape NAc development in a **sex-specific manner**.

By identifying immune-mediated receptor elimination as a driver of sex differences in social behavior, Dr. Kopec's research provided **novel insights into the role of microglia in adolescent brain plasticity**. Her work

underscores the importance of considering **sex as a biological variable** in studies of brain development and behavior, with broad implications for understanding neuropsychiatric disorders with sex-biased prevalence. This research has opened new avenues for exploring how **microglial activity influences reward circuitry, social interactions, and mental health across the lifespan**.
Reference: *Kopec et al. Nat Commun. 2018 Sep 25;9(1):3769.*

Dr. Li Gan: Microglial Renewal and Its Implications for Neurodegenerative Diseases

In 2019, **Dr. Li Gan** made a significant discovery about microglial self-renewal in the adult brain, showing that **newborn microglia emerge from existing microglial populations without contributions from non-microglial lineages**. Her research demonstrated that these **newborn microglia initially exist in an immature state**, gradually maturing through distinct transcriptional programs that guide them back to a steady-state homeostatic phenotype. Microglial recolonization occurs through proximal expansion, with newly formed microglia creating stable territorial clusters to restore brain microglial density. This process relies on NF-κB signaling for maturation and apoptotic egress of excess microglia, highlighting the delicate balance required to maintain microglial homeostasis.

These findings offer profound insights into **microglial resilience and regeneration**, suggesting that **targeting microglial renewal and maturation pathways** could inspire novel therapeutic strategies for **neurodegenerative diseases like Alzheimer's and Parkinson's**, where microglial dysfunction is a key factor. Dr. Gan's work has opened new avenues for exploring how **manipulating microglial self-renewal** might restore brain health and combat neurodegeneration.
Reference: *Zhan et al. PLoS Biol. 2019 Feb 8;17(2):e3000134.*

Dr. Erin Gibson and Dr. Michelle Monje: Microglial Activation in Chemotherapy-Induced Cognitive Dysfunction

In 2019, **Dr. Erin Gibson** and **Dr. Michelle Monje** identified a key mechanism underlying chemotherapy-induced cognitive impairment, or "chemo brain." Their study revealed that **methotrexate chemotherapy induces persistent activation of microglia**, which triggers downstream **astrocyte activation and disrupts oligodendrocyte lineage dynamics**, leading to **white matter dysfunction and impaired myelination**. Notably, the researchers demonstrated that depleting microglia restored oligodendroglial function, normalized myelin microstructure, and reversed cognitive deficits in their mouse model (Gibson et al., 2019).

This discovery is groundbreaking because it highlights **inflammatory microglia as a therapeutic target** for mitigating chemotherapy-related cognitive impairment. By manipulating microglial activity or promoting their depletion, researchers may be able to **alleviate the neurological side effects of chemotherapy,** offering new hope to cancer survivors suffering from long-term cognitive dysfunction. Dr. Gibson and Dr. Monje's work paves the way for future interventions aimed at **preserving brain health during and after cancer treatment**.
Reference: *Gibson et al. Cell. 2019 Jan 10;176(1-2):43-55.e13.*

Dr. Ana Badimon and Dr. Anne Schaefer: Microglial Regulation of Neuronal Activity via ATP Hydrolysis

In 2020, **Dr. Ana Badimon** and **Dr. Anne Schaefer** uncovered a fundamental mechanism by which **microglia safeguard neural networks by regulating neuronal activity**. Their research demonstrated that microglia **sense extracellular ATP released during neuronal activation** and convert it to adenosine via the enzymes CD39 and CD73. Adenosine then acts on A1 receptors to **suppress excessive neuronal firing, functioning as a negative feedback loop to prevent network hyperexcitability**. Strikingly, the ablation of microglia in their mouse model led to heightened neuronal synchronization and spontaneous seizures, highlighting the essential role of microglia in maintaining neural stability (Badimon et al., 2020).

This discovery not only reveals a new layer of **microglial control over brain circuits** but also underscores the **therapeutic potential** of targeting microglial ATP-adenosine signaling in **epilepsy and other neurological disorders** characterized by hyperactivity. By acting as non-neuronal modulators of synaptic activity, microglia emerge as pivotal players in preserving brain homeostasis and present promising avenues for innovative interventions aimed at restoring circuit balance in disease states.

Reference: *Badimon et al, Nature. 2020 Oct;586(7829):417-423.*

Dr. Monique Mendes: Unraveling the Dynamics of Microglial Self-Renewal and Maturation

In a pivotal 2021 *eLife* study, **Dr. Monique Mendes** illuminated the remarkable self-renewal capacity of microglia, the brain's resident immune cells. Using chronic in vivo two-photon imaging in awake mice, she demonstrated that under normal conditions, microglia exhibit **limited turnover and migration**, but following depletion, they rapidly repopulate the brain through local division of surviving cells — a process surprisingly **independent of P2Y12 receptor signaling**. Through mathematical modeling, Dr. Mendes showed that the observed division rates could fully account for the speed of repopulation, challenging prior assumptions and underscoring microglia's intrinsic ability to sustain brain homeostasis without external cues.

Her research further revealed that newly generated microglia acquire **mature morphological characteristics** within days, bypassing the slow, developmental-like maturation once thought necessary. This rapid adaptation allows microglia to quickly reintegrate into neural circuits, maintaining structural and functional stability in the brain. By capturing microglial dynamics in real time, Dr. Mendes's work has redefined our understanding of microglial resilience, opening new avenues for exploring how these cells might be harnessed as therapeutic targets in neurodegenerative diseases and brain injury.

Reference: *Mendes et al. Elife. 2021 Jul 12:10:e61173.*

Dr. Astha Dheer: Microglial Dual Functions in Epilepsy.

In 2024, **Dr. Astha Dheer** and colleagues explored the intricate **roles of microglia in seizure dynamics**, uncovering their dual functions in epilepsy (Dheer et al., 2024). Using chemogenetic manipulation in a kainic acid-induced seizure model, they demonstrated that the **acute activation of microglial** Gi-DREADDs **reduced seizure severity** by enhancing microglia-neuron interactions and dampening neuronal hyperactivity. However, prolonged activation over several days pushed microglia into a homeostatic-like state, impairing interferon-β signaling and microglial proliferation, ultimately increasing neuronal loss after seizures.

This research provides crucial insights into how **microglial plasticity shapes seizure outcomes**, highlighting the **delicate balance between the beneficial and detrimental effects of microglial activation**. By showing that microglial responses evolve over time, Dr. Dheer's work opens new therapeutic avenues, suggesting that precise temporal modulation of microglial activity could improve long-term outcomes for epilepsy patients.

Reference: *Dheer et al. Brain Behav Immun. 2024 Jan:115:406-418.*

As we reflect on the remarkable women whose research has illuminated the intricacies of microglia and transformed our understanding of brain health and disease, we also extend our deepest gratitude to the many other women researchers in the field whose names may not appear on this list but whose contributions are equally invaluable. This list is by no means exhaustive, and we wholeheartedly appreciate the collective efforts of all women and men researchers who continue to push the boundaries of neuroscience, shaping the future of discovery one insight at a time.

Through Science Prism, we remain committed to highlighting the contributions of exceptional researchers across all scientific disciplines. By sharing their stories and breakthroughs, we aim not only to honor their tireless pursuit of knowledge but also to inspire the next generation of scientists to dream boldly and pursue research with passion and perseverance. After all, science is a shared global endeavor — a collective pursuit of knowledge that holds the power to change lives and illuminate the unknown for the betterment of humanity. To all those pushing the boundaries of knowledge, we extend our heartfelt gratitude and admiration.

ABOUT THE TEAM:



***Dr. Kaushik P. Sharma** and **Dr. Kanchan Bisht** are neuroscientists at the Department of Neurology, Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Dehradun. With over a decade of extensive research experience across renowned institutions in India, Europe, Canada, and the USA, they are dedicated to making science accessible and inspiring the next generation of thinkers, innovators, and problem-solvers.*

***Dr. Shreesh Raj Sammi**, an Assistant Professor in the Department of Translational Neuroscience at Michigan State University, USA, brings his expertise in neurotoxicology and neurodegenerative disorders to the team. In addition to his research pursuits, Dr. Sammi is deeply committed to training the next generation of researchers and making science accessible to diverse audiences.*

This newsletter is an effort to empower individuals with the latest updates on scientific breakthroughs and provide a foundational understanding of health-related scientific aspects. It aims to ignite scientific curiosity and support students and young researchers in their academic and professional journeys.

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