

Unlocking the Secrets of Multiple Sclerosis Progression: Brain-Immune Cell Communication



Interview conducted by Danielle Ellis, B.Sc.

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Thought Leaders

Dr. Cameron McAlpine

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To commemorate World Multiple Sclerosis (MS) Day, we spoke to Dr. Cameron McAlpine, an Assistant Professor of Medicine and Neuroscience at the Icahn School of Medicine at Mount Sinai, about his latest research that sought to understand better the proteins and signals that act as messengers between brain and immune cells in MS.

Please can you introduce yourself and tell us about your professional background?

I am Dr. Cameron McAlpine, an Assistant Professor of Medicine and Neuroscience at the Icahn School of Medicine at Mount Sinai in New York City. I completed my Ph.D. at McMaster University in Canada and postdoctoral training at the Massachusetts General Hospital and Harvard Medical School in Boston, USA. My lab studies inflammation in the brain and how the brain talks to the immune system in neurodegenerative diseases.

Multiple sclerosis is a lifelong condition affecting the brain and the spinal cord. What is the pathophysiology of multiple sclerosis, and what was previously known about the immune-mediated nature of this disease?

Multiple sclerosis is an autoimmune and inflammatory disease of the central nervous system, including the brain and spinal cord. It is characterized by inflammatory lesions in the brain and spinal cord composed of immune cells

that have migrated to these locations from the blood and other sites in the body. Although we know that both brain and immune cells are important to the progression of multiple sclerosis, the ways in which these cells communicate with one another is poorly understood.

What questions remained around the pathways or proteins implicated in this disease that you sought to answer?

The role of various types of brain and immune cells has been studied extensively in MS. However, we did not know how these cells talk or communicate with one another to coordinate their function and biology. We sought to understand better the proteins and signals that act as messengers between brain and immune cells in MS.



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Please could you briefly detail how you conducted your research and describe your main findings?

We studied the brains of patients with MS and used mouse models of the disease. We discovered that an inflammatory protein called interleukin-3 (IL-3)

was elevated in the brains of people with MS relative to healthy controls, and when we blocked IL-3 signaling in mouse models of MS, the clinical symptoms, inflammation, and spinal cord lesions in the mice were improved. We then discovered that IL-3 was being produced by brain cells called astrocytes and immune cells called T cells.

Moreover, we found that IL-3 signals, or talks, to other brain and immune cells called microglia and macrophages, reprogramming them to be more inflammatory and worsening disease. Our work identified IL-3 as a key messenger between brain and immune cells that worsens MS by provoking inflammation.

Your work identified IL-3 signaling as a potentially promising new therapeutic target. What could this mean for the future of MS treatment?

MS currently has no cure. Our data suggest that future studies should test if blocking IL-3 signaling is an effective therapeutic strategy to curtail clinical symptoms and pathology in MS.

IL-3 has also been associated with multiple disorders, such as Alzheimer's disease. How could your findings influence the medical understanding and treatment of other diseases?

We are learning that IL-3 plays many roles in the brain. Our lab has shown previously that IL-3 has an important role in Alzheimer's disease, and we now reveal its function in MS. Further study is needed to fully understand how IL-3 and inflammation impact the brain and how we can modulate IL-3 signaling to improve neurodegenerative diseases.

The theme for World MS Day 2020-2023 is 'connections,' which aims to build community connection, self-connection, and connections to quality care. As a researcher, how important is it to connect with those communities your research and discoveries will directly impact?

It is critical for researchers and scientists to connect to people and communities. Many exciting discoveries are being made, and it is important to communicate and explain those discoveries to everyone impacted by MS. The theme 'connections' is particularly appropriate for the research being done in my lab. We study the connections between cells and how they communicate with one another. It is important to understand and foster connections – from cells to communities!



World MS Day aims to raise awareness for those affected by MS. What are some common misconceptions about MS, and what do you wish people better understood about this disease?

MS is a complex disease involving many cell types, organs, and systems. Studying and understanding how cells outside of the brain, like immune cells in the blood and other organs, contribute to disease is important. Part of this is studying how these cells and organs communicate and talk to one another.

What is next for you and your research?

We are continuing to study the role of IL-3 in the brain. We are performing further studies to test new therapeutics that target IL-3 to treat MS and other disorders that involve brain inflammation.

Where can readers find more information?

- You can read our paper here: [https://www.cell.com/immunity/fulltext/S1074-7613\(23\)00177-2](https://www.cell.com/immunity/fulltext/S1074-7613(23)00177-2)

- You can find out more about the McAlpine lab here: <https://labs.icahn.mssm.edu/mcalpinelab/>

About Dr. Cameron McAlpine

I am an Assistant Professor of Medicine and Neuroscience and a Principal Investigator in the Cardiovascular Research Institute and the Friedman Brain Institute at the Icahn School of Medicine at Mount Sinai. My lab studies the brain and immune system connections in cardiovascular and neurodegenerative diseases. My lab is funded by the National Institutes of Health, the Cure Alzheimer's Fund, and the Alzheimer's Association.



Written by

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Danielle graduated with a 2:1 in Biological Sciences with Professional Training Year from Cardiff University. During her Professional Training Year, Danielle worked with registered charity the Frozen Ark Project, creating and promoting various forms of content within their brand guidelines. Danielle has a great appreciation and passion for science communication and enjoys reading non-fiction and fiction in her spare time. Her other interests include doing yoga, collecting vinyl, and visiting museums.