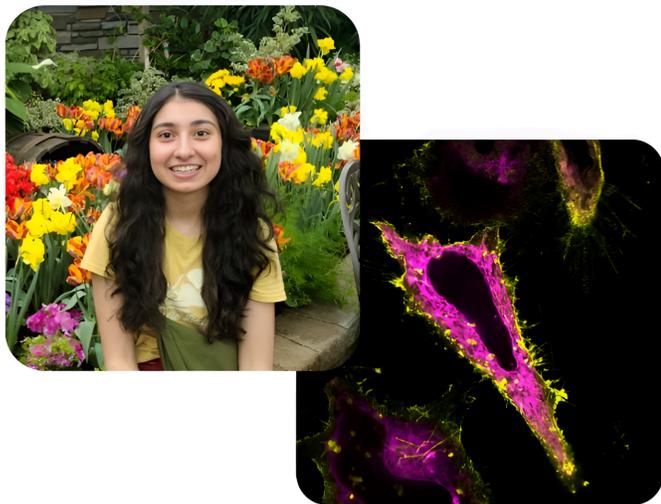


Ehlam Iftikhar is an undergraduate student in the Faculty of Science. In her physiology program, she is researching sphingomyelinases' role in extracellular vesicle production in Parkinson's disease under her supervisors, Dr. Julie Jacquemyn and Dr. Maria S. Ioannou. Her image titled *Sphingomyelinase: The Hidden Trigger of Parkinson's Progression* is featured on the front cover of the issue.



“While it’s important to choose a research topic that excites you, I believe the most crucial factor is finding the right team to work with.”

What can you tell us about your research image?

Sphingomyelinases (SMase) are enzymes involved in converting sphingomyelin into ceramide and phosphorylcholine on membranes. Their activity has been linked to various neurological disorders, where altered lipid metabolism may contribute to disease progression. However, their role in Parkinson's disease (PD) remains unclear. By utilizing various model systems that mimic PD, focusing on the most common risk factor for PD mutations in *GBA1*, and extracellular vesicles (EVs), I am investigating how SMases contribute to disease progression. This is because understanding the role of SMases in EV subtypes that potentially carry toxic proteins in PD can reveal novel therapeutic targets to slow disease progression.

The image highlights immunostained HeLa cells treated with conduritol-beta-epoxide, an irreversible inhibitor of GCase, the enzyme encoded by *GBA1*. HeLa cells were transfected to overexpress nSMase (yellow) and an ER marker (mCherry-sec61b, magenta). The nSMase contains a C-terminal FLAG-tag, allowing detection with a FLAG M2 primary antibody and an anti-mouse secondary antibody. Results show nSMase outside the ER, potentially on the inner leaflet of the plasma membrane.

Why is your research important?

Exosomes have been extensively studied as potential carriers of pathological α -synuclein in PD, and their inhibition with certain drugs has been explored as a strategy to mitigate disease progression. However, targeting exosomes may inadvertently promote other vesicle subtypes that potentially carry α -synuclein. This highlights the need for a broader approach. By elucidating the role of SMases in EV production, our research aims to identify a novel therapeutic target(s), potentially offering a complementary approach to current treatments to slow disease progression for over 9 million Parkinson's patients worldwide.

Have you made any interesting findings in your research?

One subtype of sphingomyelinase, known as acidic sphingomyelinase (aSMase), is associated with lysosomal membranes and can be secreted to the plasma membrane under certain stressful conditions. This secretion process is thought to contribute to changes in membrane composition and extracellular vesicle formation. While increased levels of aSMase have been reported in several neurological disorders, its specific role in PD remains unclear. In a PD model system, we observed changes in aSMase activity using a biochemical assay alongside alterations in extracellular vesicle release. Additional imaging experiments revealed that inhibitors of sphingomyelinase activity reduced vesicle formation under these conditions, suggesting that aSMases may play a role in membrane dynamics and vesicle biogenesis in disease contexts.

What specific advice would you give to younger students who are interested in scientific research?

While it's important to choose a research topic that excites you, I believe the most crucial factor is finding the right team to work with. Research is inherently collaborative, and the people around you will shape your experience in profound ways. Take the time to meet the supervisor and lab members before committing to a lab to ensure the environment fosters growth.

For me, joining Dr. Ioannou's lab has been an incredibly rewarding experience. I'm deeply grateful for her guidance - her kindness, patience, and encouragement have made me mature both as a researcher and as a person. My lab mates have also been invaluable by always helping me troubleshoot experiments and brainstorm ideas. Being part of such a collaborative and supportive team has made my research journey rewarding.

If you could work in any laboratory in the world, what would you choose? What field of research would you want to be involved in?

I am passionate about innovative research that combines environmental sustainability with ecological health. As someone who practices/teaches worm composting and urban beekeeping, I am eager to explore two key areas: worm metabolism and bee population health.

For worms, I aim to study the organic waste they process most efficiently, focusing on how diet influences their reproductive rates and composting effectiveness. This research could offer insights into addressing urban and agricultural waste challenges. In the realm of bees, I would love to research environmental factors driving the decline in bee populations. Investigating the impact of pollutants, pesticides, and climate change could lead to strategies that support bee recovery and enhance their vital role in pollination and food production.

Both areas of research are crucial in combating environmental challenges, and I would be grateful to contribute to solutions that foster sustainable ecosystems.

In regards to your research, who has influenced you the most?

In my research journey, no one has influenced me more than my supervisor, Dr. Julie Jacquemyn. She embodies resilience,

intelligence, and dedication. Her unwavering positivity inspires me every day. Her innovative research techniques and profound knowledge have enriched my learning, but what stands out most is her emotional intelligence - she recognizes when I feel overwhelmed and provides thoughtful guidance that empowers me to persevere. Her ingenuity and perseverance in tackling challenges leave me in awe, and her motivation drives me to strive for excellence. I am incredibly grateful and honoured to learn from such an inspiring role model, and I hope to emulate her passion and strength in my own career.