JEFFREY ATKINSON

NSERC DISCOVERY GRANT RECIPIENT - 2017 COMPETITION

"Phosphatidylinositol-based probes of membranes, proteins and enzymes"

professor
CHEMISTRY

How would you describe the creativity and/or innovation in the heart of your research?

Our work uses synthetic organic chemistry to make molecular tools that allow the investigation of proteins and membranes. In the last decade, we have been successful at making fluorescent forms of vitamin E (tocopherol) that allow us and others to follow where it goes in membranes and cells. More recently, lipid transfer proteins that move lipids around cells have been discovered to have a much more complex role in cell biology than previously thought. The new NSERC Discovery Grant will support us in making complex reactive phospholipid analogues that will test the function of several lipid transfer proteins and associated enzymes in key cell signaling systems.

What does receiving this grant mean to you?

The work described in this grant cannot be done "on the side." It needs the full attention of all the students I can afford to have in my lab. This is a significantly new area for us and I am excited that NSERC approved of our ideas and plans and that they saw fit to fund the proposal.

What is the aim of your research?

We aim to uncover the molecular level details of how proteins move water-insoluble compounds around the cell. The proteins somehow have to know what to pick up (and where) and where to take it. Maybe even more importantly, what look like simple proteins (they act like suitcases, holding on to a molecule that doesn't like to be in the water filled cell interior) might work with other proteins and enzymes to regulate lipid biosynthesis and many other phenomena.
In our work, a protein that is known to move a common membrane phospholipid around the cell, may also control the enzyme mediated synthesis of critical lipids called "phosphoinositide phosphates (PIPs), that take part in a huge number of regulatory processes within cells. We aim to unravel the details of this process, showing not only how it happens in a test tube, but also where it happens in a cell.

What is/ will be the impact of your research?

The molecules that we are making and the tests we will do with them, will test a hypothetical mechanism of action for a family of proteins that have been known for many years, but lack biochemical details in support of the hypothesis.
While we are looking at a specific family of proteins, the general mechanism is likely to be applicable across many other proteins that do their job close to biological membranes.
This has ramifications for understanding disease mechanisms, cell cycle and cell death. We have designed our molecules so that we can use them as bait to go fishing for unknown proteins that interact with ours. This is discovery at its purest.

What courses do you teach at Brock University?

BTEC/CHEM 3P93: Proteins and Nucleic Acids
BTEC 3P09: Bioreactor Processes
BTEC/CHEM 4P27/5P27: Enzyme and Co-enzyme Mechanisms
BTEC/CHEM 5P25: Medicinal Chemistry

Best advice for students wanting to be successful in your class?

Attend the class. Sounds silly, but it directly correlates with passing.

R E A D.

Read the text book if you have one, the scientific literature in your area and beyond. Then read it again.

Who has influenced you the most in your career and/or research?

Great teachers/mentors and proud, supportive parents. I've found that the students' high school experience has a tendency to beat interests out of them. Sometimes it is comforting to know that there are real people who do science for a living and who get excited about some of the weirdest details they come across in nature.
It's OK to be smart.
And it should be understood that even the smart people have to work hard. Few things are easy. I had excellent teachers at all levels of my schooling and also people who could listen and direct me through tough times and important decisions.
Scientific research is amazing, but one does have to live a life as well. I've had a few mentors who, whether in their teaching or by example, showed me how to do my best at both.

What are your most important publications?

Our first measure of molecules that bind to the tocopherol transfer protein.
C. Panagabko, S. Morley, M. Hernandez, P. Cassolato, H. Gordon, R. Parsons, D. Manor, J. Atkinson, Ligand specificity in the CRAL-TRIO protein family, Biochemistry, 42 (2003) 6467-6474.

Our most recent fluorescent vitamin E analogue.
M. Ghelfi, L. Ulatowski, D. Manor, J. Atkinson, Synthesis and characterization of a fluorescent probe for a-tocopherol suitable for fluorescence microscopy, Bioorg Med Chem, 24 (2016) 2754-2761.

How the tocopherol transfer protein recognizes phospholipid membranes.
W.X. Zhang, V. Thakur, A. Lomize, I. Pogozheva, C. Panagabko, M. Cecchini, M. Baptist, S. Morley, D. Manor, J. Atkinson, The contribution of surface residues to membrane binding and ligand transfer by the a-tocopherol transfer protein (a-TTP), Journal of Molecular Biology, 405 (2011) 972-988.

What do you see yourself doing in 10 years?

Sippin' sarsaparilla in the moonlight.

What do you enjoy most about your research?

Research gives you the opportunity to be incredibly creative.

Many people think scientists blindly follow some arcane set of rules for research.
In our case, my students and I design molecules and experiments to test these very rules.
When do things work as expected? • When do they not? • Why do they not? • What if we do this...?
It is very rewarding to watch young scientists develop and feel the spark of discovery, the pride of problem-solving.