Families of SMA Canada Awards $140,000 Grant to Joceyln Côté, PhD, University of Ottawa

FSMAC has awarded a $140,000 research grant to Joceyln Côté, PhD, at The University of Ottawa, for his project, "Investigating the mechanism by which SMN regulates translation: identification of novel therapeutic targets.”

Understanding the function of the SMN protein is vital to understanding SMA and serves to aid in the development of therapeutics. In this grant, Dr. Côté and his team plan to build upon their prior work which describes a new function for SMN in the regulation of protein production, called translation. They propose to perform experiments to gain a better understanding of how SMN goes about doing this new function, and also to determine what might be the consequences of losing this function in cells from SMA patients.

This work will provide crucial insights into a novel function for SMN that is misregulated in SMA. This will lead to a more complete understanding of disease mechanism. In turn, identification of the molecular mechanisms and the various players/regulators involved in this process may yield novel therapeutic targets for the treatment of SMA.

This grant was funded by Families of SMA Canada.

Meet Dr. Côté

Who are you?

I am a biochemist and molecular biologist by training with specific expertise in the field of RNA metabolism. I obtained my PhD from the University of Sherbrooke in the province of Quebec, Canada. I then pursued my training as a postdoctoral fellow at Washington University in St. Louis, Missouri and at McGill University in Montreal, Quebec, Canada.I started my independent research group at the University of Ottawa in 2004 and I am now a Full Professor in the Department of Cellular and Molecular Medicine.

How did you first become involved with SMA research?

Coming from a biochemical background, I initially started working on SMA because I identified SMN, or more specifically a part of the SMN protein called the Tudor domain, as a domain capable of 'sensing' arginine methylation in proteins. Following this discovery, we reasoned that these 'methylated' proteins might represent a major subset of proteins that would stop functioning normally in the absence of SMN in SMA patients, and that studying these proteins might help us gain a better understanding of what SMN does in spinal cord motor neurons and how loss of these activities leads to SMA. Although it started primarily as a scientific question, after I first attended the Annual FSMA Research Conference back in 2002 and met SMA kids and their families, it became clear to me that I was going to do my best to contribute my expertise towards increasing our fundamental understanding of this disease in the hope that it would help one day in the elaboration of novel therapeutic strategies.

What is your current role in SMA research?

My lab uses biochemical, molecular and cell biology approaches, working with various models of SMA, in order to gain a better understanding of the precise function that SMN plays in spinal cord motor neurons, and how loss of that function leads to the disease. For example, we are trying to identify the other proteins and RNA molecules that SMN interacts with and controls in motor neurons. Doing so should give us some insights into what SMN is actually doing in this cell type. Then, we assess if these SMN interacting partners could represent valid targets that might be easier to manipulate than SMN itself to improve disease.

What do you hope to learn from this research project?

From this project we hope to learn about a new function for SMN in the regulation of protein production. We want to gain a better understanding of how SMN goes about doing this new function, and how loss of this function in motor neurons contributes to SMA.

How will this project work?

We propose to use a series of biochemical, molecular and cellular approaches that will allow us to:

1. determine the composition of the regulatory complex(es) in which SMN functions to regulate protein production in motor neurons;
2. identify the subset of messenger RNAs that are regulated by SMN at the level of protein production and determine whether these are misregulated in SMA; and
3. explore the therapeutic potential of increasing the levels and/or activity of regulators of SMN function in SMA cells in order to compensate for loss of SMN. For these experiments we are using cell culture and mouse models of SMA, but also validating our results using SMA patient cells to insure that our findings are relevant to the human condition.

What is the significance of your study?

The current proposal will provide crucial insights into a novel function for SMN in spinal cord motor neurons. Identification of the targets that are misregulated due to loss of this novel SMN function in SMA should lead to a more complete understanding of disease mechanism and has the potential to identify new therapeutic targets.