MS Research

Spring/Summer 2018

FEATURE STORY

Bridging the gap: Going from discovery research to treatments for MS

contents

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@Dr_KarenLee

Scientists are constantly thinking of ways to connect their research to the scientific field. During my PhD, I used to ask questions like how my protein of interest, or my target compound is connected to and alters MS. The connections made by researchers in the lab are key to future clinical trials. However, much of the research performed on the bench stops there! Why you ask? The next phase of the drug discovery pipeline, called translational research, is a high-risk iterative process which results in few successful compounds transitioning to clinical trials.

Over the last few decades, funding for translational research has declined, resulting in a critical gap that has caused the translation of new research discoveries into treatments to fall behind. The MS Society of Canada is connecting with organizations like the U.S. National Multiple Sclerosis Society (NMSS) and Centre for Drug Research and Development (CDRD) to address this gap by designing new programs aimed at advancing the discovery of treatments for MS. In this issue, you'll read about two projects that are funded in collaboration with CDRD that could lead to the development of new disease-modifying therapies for people living with progressive MS. Dr. David Granville's research team (The University of British Columbia) is working on ways to inhibit molecules that are known to cause neurodegeneration in progressive MS and Dr. Rebecca Spain's research team (Oregon Health and Science University) is working on a formulation of an antioxidant supplement, called Lipoic Acid, to see if it is more easily tolerated while maintaining or even improving its efficacy.

You will also learn about our collaboration with Fast Forward, a non-profit subsidiary of NMSS that connects academic and clinical researchers with private sector drug development in order to develop and advance innovative MS therapies. With Fast Forward, we are co-funding Dr. Fang Liu (Centre for Addiction and Mental Health), who is optimizing a series of compounds that contributes to nerve cell death. Having already funded her earlier discovery work in the lab that uncovered these unique drug properties, the MS Society continues to support Dr. Liu as she attempts to transform these molecules into effective drugs for MS.

Even though I am no longer in the laboratory, I'm still thinking of ways to make connections but from a different angle. An area of focus for me and the research team at the MS Society is how we can connect and engage the MS Community—researchers, clinicians and people affected by MS. One way we do that is through our community representative program. You can read about our community representative program, an initiative we launched in 2012 to involve people affected by MS in our research review process, in this issue. Through connecting the community in this process, we provide a venue for those impacted by MS to have their voices heard in research while learning about the latest research happening in Canada. I encourage you to stay connected to the MS community and the MS Society. So, connect with me by visiting my blog at **DrKarenLee.ca** or follow me on Twitter **@Dr_KarenLee**.

Sincerely,
Dr. Karen Lee
Vice-president, research

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Progression & therapies

Bridging the gap

Going from discovery research to treatments for MS

Dr. Rebecca Spain, Oregon Health and Science University

“This back and forth process between the laboratory experiments, translation to clinical practice, and having that practice inform the next set of experiments and treatments is critical for the development of even more effective treatments, and ultimately, a cure.”

Three important steps are required when taking an idea from the research laboratory into a viable treatment. The first step is the discovery phase (also known as basic science) where researchers aim to identify new targets, such as a protein, that may be contributing to a disease. Promising results from the discovery phase are then explored further in the translational phase which requires developing a compound that can alter the behaviour of that protein (target) and doing a series of tests that determine if the compound could act as a drug that modulates the disease. Finally, the last stage is a clinical trial, where the drug is tested in people to determine if it will truly be safe and effective.

Translational research is an iterative phase that involves a lot of trial and error to assess if the drug will be safe and produce a beneficial effect in animal models of the disease. Once the target for a potential therapy is identified, the next step in the translational phase, called lead identification, is to identify a lead compound that will interact with the target in some way. The last step in translational research is called lead optimization. Lead optimization is the process of finding compounds that are similar to the identified lead, but have a better interaction with the target, or are less likely to interact with other cells or proteins in the body—which is important for decreasing side effects of treatments. Key questions are answered about a potential drug in translational research: How quickly is it absorbed? How is it distributed to different tissues? How is it metabolized and excreted? At what dose is the drug toxic? These are all crucial questions researchers must answer to ensure that their compound will be both effective and safe in humans.

Here, we feature two translational research projects that are funded in collaboration with Centre for Drug Research and Development (CDRD) that could lead to the development of disease-modifying therapies for people living with progressive MS.

Dr. David Granville

(The University of British Columbia): Granzyme B inhibitors to protect nerve damage in progressive MS

One of the weapons that certain immune cells use to destroy harmful invaders is an enzyme called granzyme B. In the MS brain, granzyme B mistakenly targets the body's own nerve cells by programming them to self-destruct. Additionally, granzyme B stops young nerve cells from functioning properly, thereby preventing them from replenishing the pool of injured nerve cells and repairing the damage. Dr. David Granville and his research team have identified an inhibitor of Granzyme B called VTI-1003. This inhibitor has already shown to impact disease-like behaviour and promote repair in an animal model of MS. However, more research is needed to characterize this inhibitor. "Before advancing into humans, it is essential that we determine if the drug is safe, how the body clears the drug and if there are any potential side effects that we should be aware of," says Dr. Granville. The research team will also identify the optimal dose that the drug is effective while still maintaining its efficacy. These studies will help guide drug development as the team hopes to move the drug forward towards testing in the clinic.

Read more about these two projects:
https://mssociety.ca/research-news/article/ms-society-supports-two-new-translational-projects-on-progressive-ms-in-collaboration-with-centre-for-drug-research-and-development-cdrd

Dr. Rebecca Spain

(Oregon Health and Science University): Improving the tolerance and efficacy of supplement, lipoic acid, for treatment of progressive MS

A natural substance produced by our own bodies and found in foods, called Lipoic Acid (LA) is an over the counter antioxidant supplement which has been shown to reduce inflammation and disability in mice that have an MS-like disease. A pilot clinical trial, led Dr. Rebecca Spain and her colleagues, showed LA reduced brain volume loss suggesting the supplement had a beneficial, protective effect on MS brains. However, many of the participants experienced upset stomach and related side effects to the LA. From blood samples, the team also discovered that not everyone absorbed equal amounts of LA. Therefore, working with CDRD, Dr. Spain will develop a form of LA that does not cause unpleasant side effects but will more uniformly be taken up into the bloodstream between people. "Better oral tolerance will allow more people to easily take lipoic acid, and it's likely that more uniform absorption of the supplement will allow for a more uniform treatment effect," says Dr. Spain.

The MS Society, together with CDRD, has risen to the occasion of overcoming challenges in the drug discovery pipeline by funding translational research. "While many targets show promise at the cell or animal stage, it is important to identify the most promising therapies for humans and to translate such findings into the clinic," says Dr. Granville. By tapping into the infrastructure and expertise in drug development and commercialization offered by CDRD, highly promising targets such as those being investigated by Dr. Granville and Dr. Spain can be taken to the next level and nudged into the treatment pipeline. Dr. Spain expresses the importance of the drug discovery pipeline, "This back and forth process between the laboratory experiments, translation to clinical practice, and having that practice inform the next set of experiments and treatments is critical for the development of even more effective treatments, and ultimately, a cure."

Representing the community in MS research

Community Representatives

“ Being a community representative taught me a lot about MS research and changed my perspective on research. ”

Six years ago, the MS Society of Canada launched an initiative to involve people in the MS community in the research review process. Termed Community Representatives, this group is made up of people who have a personal connection to MS, some even living with the disease themselves.

So, what do Community Representatives do? Community Representatives work with leading researchers to review grant proposals submitted from all across Canada. Community Representatives review parts of grant and award applications and provide ratings and comments on various aspects of research proposals. This includes commenting on the relevance of the research to the challenges faced by people affected by MS, and the capability for the project to yield outcomes that will improve the health and quality of life for people affected by MS.

“It was very humbling,” says Shannon Bachorick, a Community Representative for the past two years, “to interact with the scientists who have dedicated their career to MS research and to read the grant proposals from people who have no connection to MS, yet wish to work toward finding a cure.”

Community representatives offer a unique perspective to the research review process and a crucial one, because they can comment on how research could impact their day-to-day living, and what the outcomes of research could mean not only to themselves, but to the broader MS community. Community Representatives represent the voices of those affected by MS in the research sphere. Not only that, but these individuals have the opportunity to better understand the ongoing research that is happening in Canada.

“Being a community representative taught me a lot about MS research and changed my perspective on research,” says Sarah Flohr, a Community Representative in 2017. “The projects varied in topics but were all driven with the purpose of improving the lives of those impacted by MS, understanding the disease and finding a cure.”

To learn more about Community Representatives and to see if you may be eligible to apply, visit our webpage: ***https://mssociety.ca/participate-in-research/community-representatives***

Translational research

Fast Forward

from basic research to life-saving outcomes

Dr. Fang Liu, Centre for Addiction and Mental Health (CAMH) pictured here with Dr. Karen Lee

Moving findings from laboratory into life-saving outcomes for people living with MS as quickly as possible is a priority for the MS Society of Canada. This is possible by investing in translational research, which aims to test and validate early stage discoveries in order to make them viable for clinical trials.

The MS Society is aiming to address the need for translational research by designing and funding new programs aimed at advancing the discovery of treatments for MS. Through a collaboration with a non-profit subsidiary of the National Multiple Sclerosis Society (U.S.) called *Fast Forward*, the MS Society will co-fund a new research project that will target the neurodegenerative process that is thought to contribute to progression in MS. The project will be led by Canadian MS researcher Dr. Fang Liu from the Centre for Addiction and Mental Health (CAMH) in Toronto, Ontario.

Dr. Liu's project builds on preliminary findings from her MS Society-funded project launched in 2012. The operating grant she received from the Society six years ago enabled her research team to demonstrate the interaction between specific proteins in the brain that can lead to the destruction of nerve cells that are required for proper functioning. This form of nerve cell death, called neurodegeneration, is a hallmark of progressive MS and is an important contributor to the accumulation of neurological disability. Dr. Liu found that, by interrupting the activity of these proteins, there was a noticeable reduction in symptoms in mice with an MS-like disease.

Building off of this work, Dr. Liu has developed two series of drug-like compounds that could be used to halt the neurodegenerative process in MS. Her translational project involves an extensive list of research experiments, which ultimately aim to determine if these compounds have drug-like properties and to test if the compounds are effective and have the potential to improve neurological function in animals with an MS-like disease.

Dr. Liu herself reiterates that there is a need for the development of novel therapeutics, as only 55 per cent of individuals with relapsing-remitting MS have effective disease-modifying therapies. Drugs for progressive MS are scarce with only one approved therapy for this form of the disease. There is an important unmet need for treatments that disrupt the processes that contribute to progression in MS, specifically neurodegeneration and we're taking an important step forward by funding translational projects like Dr. Liu's.

Read more about Dr. Fang Liu's study: ***https://mssociety.ca/research-news/article/ms-society-funds-new-translational-research-project-for-progressive-forms-of-ms***

Trending in MS Research

Noteworthy advancements

Canada has one of the highest rates of multiple sclerosis in the world. It's because of our donors, event participants, and volunteers that we are able to fund some of the best MS research in the world, right here in Canada. To read more about the studies mentioned below and the latest in MS research, visit **mssociety.ca/research-news**, and follow **@Dr_KarenLee** & **@MSSocietyCanada** on Twitter.

MS Society of Canada @MSSocietyCanada · Jan 25
Is diet related to progression in MS? A new study suggests that individuals with MS with a healthier diet had better outcomes #Wellness

MS Society of Canada @MSSocietyCanada · Dec 7
The approval of oral Mavenclad™ for the management of relapsing-remitting MS means that there are now 15 disease-modifying therapies for individuals living with RRMS

MS Society of Canada @MSSocietyCanada · Nov 13
In the 20 years since interferons were introduced to treat MS, how are they being used? Canadian researchers have published a study on how individuals are using DMTs for #MS

MS Society of Canada @MSSocietyCanada · Aug 29
MS Society funded postdoctoral fellow uncovers new information about the genetic make-up of microglia immune cells implicated in #MultipleSclerosis

“My hopes for MS research are for a cure and for prevention of MS. I hope that strides continue to be made for better treatments for people with MS.”

PETER, RESEARCH PARTNER SINCE 2005

“People living with multiple sclerosis need hope – and I want to help provide that.”

AGNES, RESEARCH PARTNER SINCE 2004

“I believe researchers will find a cure for multiple sclerosis – for me, for everybody, in my lifetime. Supporting research is an expression of hope, my expression of hope.”

KEN, RESEARCH PARTNER SINCE 2002

MS Research Partners

MS RESEARCH PARTNERS

This year we are recognizing 70 years of breakthroughs, progress, and hope through MS research funding. In that time, the Multiple Sclerosis Society of Canada has invested over $175 million dollars into research. This is only possible through the generosity and leadership of donors investing in a future without MS.

Each year, people like Ken, Peter, and Agnes directly support MS research through the Research Partners program, a dedicated group of donors committed to ending MS. Research Partners receive updates on current research projects, and invitations to attend MS research events. Many Research Partners, like Ken, are personally affected by multiple sclerosis. Others, like Agnes, are simply committed to a cause they believe in — ending MS.

Together, Research Partners are funding important research into the cause and cure for MS, to learn more about MS, find new treatments and therapies, and provide hope to Canadians and their families who are affected by this disease.

We are extremely grateful to this community of donors and would like to invite you to join them with a minimum annual donation of $1,000.

Become a Research Partner Today

Contact Yurixhi Giacinti, Development Officer Annual Giving, Leadership Giving at 1-800-268-7582, or yurixhi.giacinti@mssociety.ca or visit our website https://mssociety.donorportal.ca

BECAUSE OF YOU
MS SOCIETY-FUNDED RESEARCH MILESTONES

2000 Multiple Sclerosis Scientific Research Foundation (MSSRF) launches study to determine whether transplanting bone marrow stem cells in people with MS can manage disease

2004 Published study in *Nature* reveals important information about the role of viruses in the development of MS

2007 University of Calgary researchers discover pregnancy-related hormone that encourages the rebuilding of myelin

2010 Research reveals more about the impact of other health conditions and lifestyle factors on quality of life of people affected by MS

2011 MSSRF funds a multi-centre study on progressive forms of MS

2012 Study points to sleep apnea as a major contributor of fatigue in people living with MS

2013 MSSRF funded stem cell study from 2000 advances understanding of risky but effective bone marrow transplantation as a treatment for MS

2017 Minocycline clinical trial demonstrates delay in MS onset in people with early signs of the disease who received this safe and inexpensive acne treatment

2018 Ocrevus (ocrelizumab) conditionally approved by Health Canada as the first disease-modifying therapy available for early primary progressive MS