Celebrating a pioneer of MS research

University of Chicago neurologist receives the 2014 John Dystel Prize for pioneering work in the field of neuroimmunology.

by Donna Shryer

Every story has a beginning. When it's a great story, we yearn for more. And more is precisely what neurologist Dr. Barry G. Arnason has delivered with his prolific, ongoing investigation into T cells, a type of white blood cell that develops in the thymus gland and impacts the immune system. Dr. Arnason played a pivotal role in discovering how dysfunctional T cells affect the development of multiple sclerosis, which led him to breakthrough studies that influenced drug management therapies, ultimately affecting how people with MS manage the disease. He has also studied what happens—or does not happen—during MS attacks in order to further advance therapies that may not involve T cells at all.

In recognition of his pioneering accomplishments, Dr. Arnason received the 2014 John Dystel Prize for Multiple Sclerosis Research. The $15,000 prize, awarded jointly by the National MS Society and the American Academy of Neurology, was delivered during the Academy's 66th

annual meeting in May 2014. Each year, the John Dystel Prize recognizes a significant contribution to research in the understanding, treatment or prevention of MS.

“The more we learn about how certain neurotransmitters may be involved in the development and progression of MS, the higher the possibilities for finding new treatments and prevention methods for this disease,” Dr. Arnason said in a release from the Academy after he was honored. “I am very much pleased, honored and humbled to be receiving this award.”

T-time

Dr. Arnason’s career began in 1959 as a fellow for the National MS Society, which he says makes the Society’s participation in awarding him the Dystel Prize “even more meaningful.”

From the start, Dr. Arnason focused on T cells, establishing their role in the development of MS.

Today, we now know that T cells fall into three broad categories, with each kind playing a role in the immune system. These categories are:

- **T helper cells**, including one subset of a T cell called CD4, send signals to activate the body’s immune response when foreign substances, such as viruses or bacteria, are detected.
- **Cytotoxic or “killer” T cells**, also called CD8 T cells, destroy cells bearing antigenic material, a toxic substance that triggers an immune response in the body.
- **Regulatory T cells** (also called Treg cells), which include different subsets of CD4 and CD8 T cells, direct other immune cells and, if necessary, turn off the immune response.

All T cells develop at birth in the thymus gland, but their role was initially a mystery. While still a fellow, Dr. Arnason thought to remove the thymus gland from rats, and then inject them with experimental autoimmune encephalomyelitis (EAE), an MS-like disease that occurs in animals. “These rats had no lymphocytes, which subsequently came to be called T cells, and no disease,” Dr. Arnason recalls.

This study on the immunological role of the thymus began in March 1961 at the Harvard University Department of Bacteriology and Immunology in Boston, and soon proved that T cells play a role in the development of MS. This established Dr. Arnason as a founding father of neuroimmunology, a field that combines the study of the nervous system and the immune system.

Identifying the link between different types of T cells and MS spurred Dr. Arnason to lead clinical trials for treatments that would modify the immune system’s reaction to dysfunctional T cells. Several of Dr. Arnason’s studies focused specifically on interferon-beta, and these study results played a pivotal role in interferon-beta-1b (marketed as Betaseron, and later, also as Extavia) becoming the first non-steroidal FDA-approved therapy for relapsing-

remitting MS drug management therapy.

The ripple effect

Receiving the Dystel Prize is by no means a lifetime achievement award, since Dr. Arnason remains active in "molding virtually every element of modern MS care," stresses Dr. Elizabeth Hartman, board-certified neurologist and MS specialist at the Center for Neuroscience, Orthopaedics & Spine in Dakota Dunes, South Dakota. Dr. Hartman nominated Dr. Arnason for the Dystel Prize, and she also did her clinical MS fellowship at the University of Chicago under Dr. Arnason. "We wouldn't be where we are in terms of advancements in treatment and management of MS without Dr. Arnason's involvement," Dr. Hartman says.

Dr. Anthony Reder, a neurologist and professor of neurology at the University of Chicago who teaches alongside Dr. Arnason, believes that Dr. Arnason's unique way of thinking triggers worldwide ripples in research. "He is a rare conceptual leader who rethinks things, questions the herd mentality and is always creatively looking at ideas from a new perspective."

Turning ripples into waves

"Discovering the T cell was no trivial thing and it hugely impacted our thinking about MS over the years," Dr. Arnason says, although he quickly adds that T cells are only part of a larger story.

He next focused on genetics and found one gene that encodes CD4 T cells, which predisposes a person to MS and may also make the disease worse. Dr. Arnason's research also found another gene that encodes CD8 T cells and protects against MS.

"When we first discovered these genes, we put all our emphasis on CD4 T cells, to see if we could find a way to stop the disease from getting worse. That may have been an error, because it turns out that the CD8 cell's function crashes during MS attacks. That prompted us to look instead at ways to augment the CD8 cells and thus protect against MS," Dr Arnason says.

Coming from this new angle, Dr. Arnason and his team are currently investigating immunoglobulin-like transcript 3, a protein that signals CD8 cells to shut down the immune response when it should be on. "This protein isn't there when people have an MS relapse, so the immune response turns off. There are various drugs, like albuterol, that can regulate the protein, but we're the first to test these drugs on people with MS," Dr. Arnason stresses.

A new target

Another investigation that currently has Dr. Arnason energized concerns steroids. For severe MS exacerbations, most neurologists recommend a short course of high-dose corticosteroids. "For those with relapsing-remitting MS, we know that steroids make symptoms better during the attack because they bind to a steroid receptor. However, steroids don't delay the onset of

progressive MS. None of the drugs used to treat MS work in progressive MS—because we now believe that progressive MS does not depend on the T cell. If it doesn't depend on the T cell and it does involve the immune system, then it must depend on parts of the immune system that are not T cells, and that, we think, is the monocyte."

Monocytes are another type of white blood cell with receptors that respond to external stimuli and transmit signals to sensory nerves. In people with progressive MS, these receptors are resistant to steroids now in use. "Studying this theory might offer new ideas to treat progressive MS and possibly add a few twists to the steroid story."

A deeper understanding

At this point in his five-decade career, when others of his stature might hang the "gone fishing" sign, Dr. Arnason says he's having "too much fun to quit." So the story continues, which Dr. Hartman says benefits everyone. "He has this brilliant mind, with a much deeper understanding of the immunology of MS than the vast majority of people. On top of that he's a really nice guy, so whether you're working with him, learning from him, or are his patient, it's a phenomenal experience."

Donna Shryer is a Chicago-based freelance writer.

Learn more about the John Dystel prize for Multiple Sclerosis Research. It is awarded jointly by the National MS Society and the American Academy of Neurology.

Read about last year's John Dystel Prize winner, Dr. George C. Ebers, in "The Ebers effect: Unraveling the MS and vitamin D connection."