Beautiful melody

Robin Franklin, PhD, is pioneering research in myelin repair to reverse damage associated with progressive MS.

by Susan Worley

Robin Franklin, PhD, has been named the fifth recipient of the National Multiple Sclerosis Society's Barancik Prize for Innovation in MS Research for his pioneering research focusing on regenerating myelin to halt or reverse damage associated with progressive MS.

Franklin is a professor of stem cell medicine at the Wellcome Trust-MRC Cambridge Stem Cell Institute and director of the MS Society Cambridge Centre for Myelin Repair in Cambridge, England.

"Professor Franklin continues to make significant advances in myelin repair, offering real hope that solutions will be found that restore function to people living with MS," notes Bruce Bebo, PhD, Society executive vice president of research.

The Barancik Prize, funded by the Charles and Margery Barancik Foundation, is the world's largest award created exclusively for the recognition of MS research. Major supporters of MS research for more than 20 years, the Baranciks established the $100,000 international prize to reward exceptionally innovative scientific research geared toward treating or curing MS.

Early career

The many intriguing facets of Franklin's research career began with an intense scientific

curiosity about cells in the brain, including those that play a significant role in the repair of damage caused by multiple sclerosis.

“Two things have interested me most during my career as laboratory scientist,” Franklin says. “One is the brain, which is by far the most interesting and most complex of all the organs in the body. And the other is tissue regeneration, a property of biology that is unique to living organisms. These two primary interests led naturally to a focus on regenerative processes in the brain.”

The focus of Franklin’s earliest research on the brain was oligodendrocytes, the cells that produce myelin—the protective sheath that surrounds neurons in the brain and enables them to successfully transmit signals. It is damage to myelin and the underlying nerve fibers that is responsible for a variety of MS symptoms, which range from visual problems to difficulties with movement and balance.

A unique approach

Jonah Chan, PhD, the first recipient of the Society’s Barancik Prize who also focuses on myelin repair, commented on the originality that characterizes Franklin’s exploration of the remyelination process.

“It would be nearly impossible for me to highlight a single achievement from professor Franklin’s tremendous body of work. I can only say that his work, which has recently resulted in an ongoing clinical trial, is transformative. I feel truly fortunate to have Robin as a colleague, an example and a friend.”

—Jonah Chan, Rachleff professor in the Department of Neurology at UCSF School of Medicine

“Before the 1980s, scientists were taught that cells in the brain couldn’t regenerate,” Franklin says. “But from the early 1980s onward, it became apparent that while this was generally true, it was not true of oligodendrocytes. My PhD supervisor at the University of Cambridge, Bill Blakemore, was a real pioneer in describing the process by which myelin was regenerated in the brain, and in demonstrating that myelin was actually a component of the brain that can regenerate very well.”

For the past 20 years, Franklin has continued the work of his first mentor—deepening his examination of oligodendrocytes and taking a closer look at the stem cells (known to scientists as oligodendrocyte progenitor cells) that produce them. These stem cells are especially important because when oligodendrocytes are lost or damaged during MS relapses, or episodes involving myelin damage, they must be replaced.

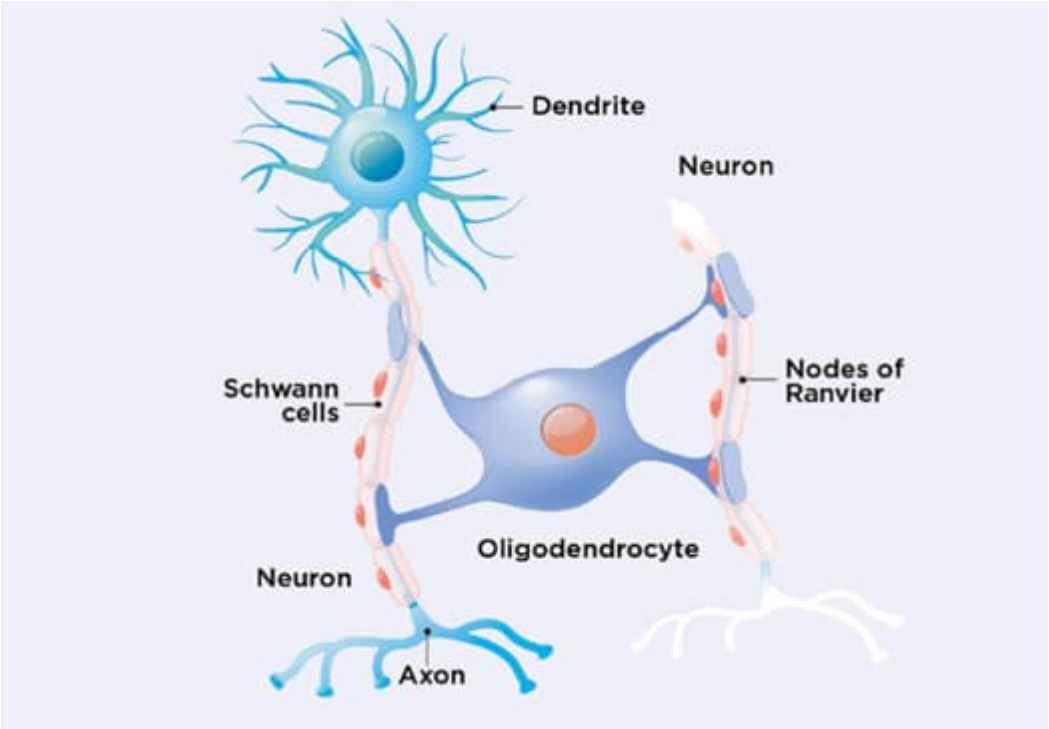
“The general belief used to be that it was necessary to transplant stem cells in order to regenerate tissue in any part of the body,” Franklin explains. “But my work has helped

advocate the idea that in fact you don't have to transplant stem cells, because there are plenty of them already in the brain. If you understand what controls those stem cells and what they do, you can design drugs to control the behavior of stem cells in a way that is helpful to the regenerative process."

The effect of aging on myelin repair

Franklin was the first scientist to describe the impact of aging on the formation of new oligodendrocytes and to clearly establish the connection between aging and secondary progressive MS.

"Remyelination is a beautiful and exquisitely orchestrated process that occurs spontaneously and works efficiently after injury in the early stages of MS," Franklin notes. He explains that after stem cells are activated in the area of injury, they migrate and undergo cell division so that they become abundant in the vicinity of injury. Finally, they undergo a change that allows them to become myelin-forming cells.



The Society is supporting research looking at key molecules that are important to the cells that make myelin (oligodendrocytes) and that may serve as targets for promoting myelin repair.

"When this process is working correctly, it is like a great symphony orchestra, with all the instruments playing in tune and producing a beautiful melody," he explains, "But as you get older, this very complex and highly regulated process gets a bit tired, and after a while the instruments don't necessarily all play at the right time. Or they may begin to play the wrong notes, or play certain notes too softly or too loudly, so that the music they play becomes unrecognizable."

In individuals with MS, the process of remyelination becomes less well-regulated and less well-orchestrated with age. Eventually it results in an inability to produce myelin, which coincides with the onset of secondary progressive disease.

“Nearly all people with MS eventually reach this phase where the regenerative process is so inefficient that it can’t prevent the loss of nerve fibers,” Franklin says. “It is necessary to find a way to put myelin back on the nerve fibers to stop them from degenerating, because once nerve fibers degenerate, they are lost forever.”

Developing a therapy to promote remyelination

For Franklin and his colleagues, the road to developing a therapy that encourages remyelination began with defining the key stages of the regenerative process and understanding the molecules involved.

“One of the things that we have tried to do is identify who the key players are in each movement of the symphony—that is, who the key players and the conductor are during the regenerative process,” Franklin says. “And a few years ago my colleague Charles ffrench-Constant and I discovered that there is a receptor, called RXR, which is critically important in the final step of making a stem cell into a new oligodendrocyte.”

Franklin and his colleagues also discovered that a drug called bexarotene, which has the ability to activate that receptor, already exists and is used in the clinical treatment of a type of lymphoma. One advantage of studying a drug currently in clinical use is that it already has undergone significant testing. Thanks to Franklin’s discoveries, a clinical trial examining the use of bexarotene to regenerate myelin is underway.

“What is most exciting now is that we are gaining a deeper understanding of how age affects the defects in stem cells that occur as you get older.” Franklin says. “And, as a result of that deeper understanding, we are beginning to identify ways to rejuvenate stem cells and make them work as efficiently in the older person as they do in young people. Our future goals are to refine that understanding and enable the development and implementation of highly effective drugs to treat secondary progressive MS.”

Susan Worley is a freelance medical writer in Bryn Mawr, Pennsylvania.

Learn more about the Barancik Prize for Innovation in MS Research.