# Creative approaches

## Barancik Prize winner Francisco J. Quintana’s research targets progressive forms of MS.

**by Mary E. King, PhD**

Francisco J. Quintana is a professor of neurology at the Ann Romney Center for Neurologic Diseases at Brigham and Women’s Hospital, Harvard Medical School. He created a new model for studying MS, developed two types of therapies that are entering clinical trials, identified new types of cells that are important in MS, and is advancing our understanding of how cells inside the brain that are involved in MS autoimmune processes talk to each other.

**Francisco J. Quintana, PhD, is the 2020 recipient of the Barancik Prize for Innovation in MS Research for his groundbreaking work that could lead to new treatments for people with progressive forms of multiple sclerosis.** Photo courtesy of Francisco J. Quintana, PhD

“Professor Quintana collaborates on a global scale to apply creative approaches to very complex questions about what triggers brain inflammation in multiple sclerosis and to find ways to stop it,” says Bruce Bebo, PhD, executive vice president at the National Multiple Sclerosis Society, which administers the award. “He has earned the Barancik Prize for being highly resourceful in applying advanced technologies to make progress toward developing new treatment approaches, especially for progressive forms of MS.”

Two leading MS researchers who supported Quintana’s nomination also praised his work.

Quintana is “an incredibly talented young scientist whose highly significant contributions have already generated novel hypotheses, identified important immunoregulatory mechanisms and opened new areas of research in MS,” says Howard L. Weiner, MD, co-director at the Ann Romney Center for Neurologic Disease at Brigham and Women’s Hospital and the Robert L. Kroc professor of neurology at Harvard Medical School.

Dr. Lawrence Steinman, MD, Zimmermann professor of pediatrics, neurology and neurological sciences at Stanford University, says that Quintana’s findings “have important implications for our understanding of the pathogenesis of MS and other neurologic disorders, while they also identify candidate targets for therapeutic intervention.”

“I’m humbled, honored and happily surprised,” Quintana says. “It is one of the biggest awards you can dream of as a scientist working in MS. I couldn’t be more thankful.”

Quintana adds: “While it is great that I got this prize, the biggest accomplishment I can dream of is if anything we are doing ends up improving the lives of patients with MS.”

Quintana also credits the extremely supportive environment at his institution. “I have been lucky to be surrounded and mentored by people who are so passionate about MS. I am very thankful about receiving this prize, but the real prize will be helping patients.”

**Roots of research interest**

Quintana points to his grandfather as a key reason for the direction his research has taken.

“Growing up, one of my role models was my grandpa, the father of my mom,” he says. “I was very close to him, but eventually, he came down with a neurologic disease. It was very sad for me because he went from being this very big, strong, tall energetic man into someone who was completely lost. Although he didn’t have MS, this experience pushed me toward the world of neurologic diseases, including MS, as I began my research.”

Quintana emphasizes that the National Multiple Sclerosis Society has played a central role at multiple stages of his career. “The very first grant I got as a principal investigator was from the Society. It allowed me to start my laboratory and form my research group,” he says. “Later, they awarded me the Harvey Weaver Scholar award faculty grant, which allowed me to put resources and lots of thought into new areas of research in MS.”

**Outstanding research contributions**
Quintana says his research group’s efforts are focused on mechanisms of MS disease and its treatment. One major project, he explains, began with basic science investigations of an important protein called aryl hydrocarbon receptor (AHR). This protein is involved in many important cell functions. When specific small molecules bind to it (a process called activation), AHR travels to the nucleus of the cell, where the DNA that makes up our genes resides. AHR can alter how DNA is read in the nucleus, changing how genes behave.

Quintana says that AHR interested him in part because the types of small molecules that can activate it come from a number of sources. The sources include bacteria in our guts, the food we eat and even pollutants, all factors that are of increasing interest to researchers wondering about their impacts on MS.

Quintana’s wide-ranging work in this area demonstrates his unique talents for investigating basic science questions.

He broadens the work to multiple avenues of research that may produce real clinical impact for people with MS. His research has resulted in groundbreaking publications in some of the foremost science journals, including Cell, Nature and Nature Medicine.

Quintana’s research showed that genetic changes produced by AHR include significant effects on T cells. AHR can reduce the activity of a particular type of disease-promoting T cells while making another type of T cell, one that is helpful in immune diseases, more active.

## What is the Barancik Prize?

The Barancik Prize for Innovation in Research was created in 2013 by the Charles & Margery Barancik Foundation and is administered by the National Multiple Sclerosis Society.
As major supporters of MS research projects for more than 20 years, the Baranciks developed the Barancik Prize to recognize exceptional scientists who have demonstrated outstanding innovation and originality in MS research. Barancik Prize winners receive $100,000 that can

be used at their discretion.
Charles and Margery Barancik passed away in 2019, and the National Multiple Sclerosis Society joins their family in mourning their loss.

Quintana is interested in how AHR can affect autoimmune diseases like MS and diabetes. His investigations led to the development of very tiny, synthetic spheres called nanoparticles as a potential therapeutic agent. These tiny particles have been designed to trigger AHR's positive effects in autoimmune diseases. The nanoparticles have been licensed by a pharmaceutical company that will begin clinical trials, first in people with type 1 diabetes, by the end of 2020.

(The exact composition of these nanoparticles is proprietary information, but other types of nanoparticles have been made out of metals like gold or types of fats. They have been used to deliver medicine to tumor cells as one example of their increasing use in medicine.)

His team is also developing probiotics, which we all carry in our intestines — the live yeasts in yogurt, for example. For this research, however, the probiotics developed by Quintana's team suppress inflammation. The hope is to create a therapeutic probiotic that will be helpful in MS. However, the research is still in the early phases and is further away from reaching clinical trials.

Quintana's work in AHR then led his team to identify some of the specific small molecules produced by gut bacteria that also activate AHR. The team also investigated the effects of these molecules on two types of glial cells important in MS research, astrocytes and microglia. "And that led us to deeper questions about what controls these cells and how they communicate among themselves," Quintana adds.

Quintana and his group have also looked more closely at astrocytes, which were once thought to be all alike. However, they identified different types of astrocytes, including one type that may play a key role in MS progression. These discoveries led the team to think of new ways to help people with MS. One of these involves taking an existing drug for another disease and seeing if it will help treat progressive MS, an area Quintana describes as one of the biggest unmet clinical needs in MS.

In addition, Quintana has developed new models for studying MS, including using zebrafish, to screen many different kinds of environmental chemicals, like pesticides, fire retardants and preservatives, to see their impact on neurodegeneration.

**Future directions**
Looking to the future, Quintana says: "We are just really starting to understand how the astrocytes and microglia are regulated. We want to know more about the different populations of these types of cells and the T cells in the brain and how they communicate — who talks to whom and which mechanisms do they use to do it. We are developing a whole

new set of tools to study these interactions in human and animal cells. Understanding those cells, their diversity, how they communicate and how they are regulated is a basic and important question for neuroimmunology.”

**Mary E. King, PhD, is a medical writer in Boulder, Colorado.**

Learn more about MS research.