

The Edmond J. Safra Fellowship in Movement Disorders

*Bridging the Gap in Parkinson's
Research and Care*



THE MICHAEL J. FOX FOUNDATION
FOR PARKINSON'S RESEARCH

“Medical science has proven time and again that when the resources are provided, great progress in the treatment, cure, and prevention of disease can occur.”

–Michael J. Fox

Foreword

Seeing a movement disorder specialist — a neurologist with extra training in treating Parkinson’s and other movement disorders — is key to living well with Parkinson’s.

These physicians have the knowledge and experience to balance complicated medication regimens, integrate the latest therapies and round out one’s care team with other experts. When also skilled as researchers, movement disorder specialists can use insights from their patients to inform studies toward improved understanding of disease and treatments. People with Parkinson’s who see specialists typically report feeling better.

To meet an ongoing and growing need for movement disorder specialists, The Edmond J. Safra Fellowship in Movement Disorders is building a network of movement disorder clinician-researchers across the globe. Launched in 2014, this collaboration between the Edmond J. Safra Foundation and The Michael J. Fox Foundation (MJFF) bridges the gap in funding to train movement disorder specialists. Annually, the program awards five academic institutions the financial resources to teach and mentor a new specialist over a two-year period. By the year 2021, this program will graduate 20 physician-scientists around the world who can connect the dots between their patients and discoveries in the lab. This publication introduces the five fellows who pioneered the first class and are now moving on to esteemed next steps in their illustrious careers.

The Michael J. Fox Foundation is grateful for the vision of the Edmond J. Safra Foundation in enabling this program, one of our many partnerships supporting pivotal and far-reaching work in Parkinson’s research and care.



by Rachel Dolhun, MD

➤ *A Field of Medicine on the Move*

There's a myth that there's little to be done for patients with movement disorders like Parkinson's disease. The fact is, the field is on the cusp of a treatment revolution.

Here's why.

Depending on whom you ask, a physician who chooses a career in movement disorders — treating patients with conditions such as essential tremor, Parkinson's disease (PD) and dystonia — is either in for a rewarding experience or one that's utterly discouraging. As a movement disorder specialist myself, I happen to be in the first camp. Those actually in the field generally are. I believe there's no better time to be a movement disorder specialist.

Why? Research and drug development in Parkinson's are producing real results, meaning that doctors have substantial and growing options to help our patients. Don't get me wrong — for decades, we've been able to do a great deal, thanks to the drug levodopa, around since the late 1960s, and to deep brain stimulation (DBS), approved for PD in 1997. These treatments have been life-changing for many. But we don't yet have a cure — that is, a “disease-modifying” therapy, meaning anything that could slow or stop the progression of PD. For a long time, that persistent gap has been partly to blame for some physicians' reluctance to pursue a career in movement disorders.

But now, that too is changing. Here are some recent developments that give reason for great optimism:

- + **Several disease-modifying therapies are in varied stages of clinical trials.** A handful of drugs targeting different disease pathways are in Phase II and III trials, which means they are moving through the development pipeline with promise and potential. We're nearing the day when we can offer our patients a therapy to change the course of their Parkinson's.
- + **Genetic research is revolutionizing our understanding of PD.** This research laid the groundwork for many of these therapies, and is now building a foundation for precision medicine in PD. The boom in genetic research and greater ease of genetic testing are helping to unlock the mysteries of disease mechanisms and subtypes, as well as leading toward biomarkers to diagnose and track disease.
- + **New and better motor and non-motor symptomatic therapies are on the horizon.** A number of desperately needed rescue therapies, for when Parkinson's symptoms suddenly return, are expected to come to market within the next one to two years. And a variety of interventions to ease once under-addressed non-motor symptoms, such as dementia, depression and constipation, are now in clinical trials.
- + **Deep brain stimulation is advancing.** Soon, the technology may be applicable to broader populations of people with Parkinson's, and alleviate a wider range of symptoms. Researchers are working to create the next generation of DBS — specifically, a system able to interpret a person's brain signals and deliver electrical stimulation only when needed rather than continuously. DBS is already tailored to each patient, but this is a huge step toward more individualized and precise Parkinson's therapy.
- + **Other promising technologies are booming.** Think smartphone apps and wearable devices, which allow patients to track their symptoms and log medication and its effects. These offer some of our best chances at taking an objective measure of a patient's lived experience with PD; many of these devices are now being evaluated and validated in clinical trials. What this means for movement disorder specialists is that it will soon be possible to use data from patients' wearable gadgets to adjust medication or perhaps even differentiate a Parkinson's tremor from an essential tremor, speeding the time to diagnosis and reducing errors. In addition, telemedicine is bringing the house call into the 21st century — in virtual form. Health care providers can now more easily reach remote patients or those who have difficulty traveling.

These advances are rapidly moving PD patients toward a better future. But movement disorder specialists also can promise patients a better today, thanks to the continued investment of time, manpower and money into research and development. As a result of this investment, more drugs than ever before are available to target motor and non-motor symptoms and improve patients' and families' quality of life. As of this writing, seven new therapies have come to market since 2014: a drug for orthostatic hypotension; two unique formulations of carbidopa/levodopa; a medication for PD psychosis; a new MAO-B inhibitor; an anti-dyskinetic; and a long-acting amantadine for motor symptoms. In addition, there are now three DBS systems on the market instead of the one device that dominated for years, which means patients and doctors have a wider array to choose from. More therapies equal more options for patients — an undeniable sign of progress.

As the population grows older and more people develop Parkinson's and other age-related movement disorders, such as essential tremor, there is a growing need for specialists in the field. Those who choose movement disorders as a specialty will care for our parents and eventually, our own generation, with new, even more effective tools in hand — tools that will cure Parkinson's and other movement disorders and prevent our children from living with these diseases. That's a remarkable promise, and it's closer to being achieved than ever.

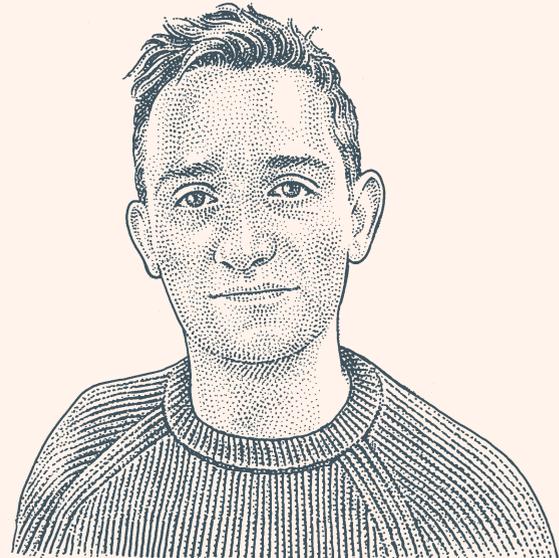
Rachel Dolhun, a fellowship-trained movement disorder specialist and MJFF's vice president of medical communications, leads The Edmond J. Safra Fellowship in Movement Disorders program at The Michael J. Fox Foundation.

Class of 2018 Fellows

David Breen,
BSc (Hons), MBChB,
MRCP (Neurol), PhD

Toronto Western Hospital
Toronto, Canada

*Making a Meaningful Difference,
One Step at a Time*



Movement disorder specialists can have a big impact on patients' ability to live the way they want to. I'm not an adrenaline guy — I like the slow burn of figuring out the right diagnosis and treatment and making the tweaks that lead to small gains that add up to a lot. The Edmond J. Safra Fellowship in Movement Disorders has given me the time to get to know my patients and find out the symptoms and problems that matter to them. Alongside the diagnostic challenge of movement disorders, I enjoy this aspect of my job.

Solving the Parkinson's Disease Puzzle

My research touches on several important pieces of the Parkinson's disease (PD) puzzle. First, we have just contributed to The Michael J. Fox Foundation-funded Systemic Synuclein Sampling Study (S4), which is evaluating the best biofluids and tissues to measure alpha-synuclein (the protein that clumps in the brain cells of everyone with PD) as a potential diagnostic marker. Second, we are recruiting patients for a trial to evaluate a new drug for PD dementia. Third, I'm leading a few projects to investigate how other pathologies (such as vascular or Alzheimer's-type pathology) contribute to PD progression.

In July 2018, I will return to Edinburgh, Scotland (where I went to medical school). There, I will look after patients and

help build the movement disorders program, as well as lead research to better understand the genetic and environmental risk factors for PD. In particular, I am interested in how sleep and circadian rhythm disruption influence brain health.

A Friend for Life

Our clinic strives to provide the best care for every patient we see, no matter their duration of disease or level of impairment. My boss, Professor Anthony Lang, has known some of his patients for over 20 years, and likes to say that when you diagnose someone with PD, you have a "friend for life." I like that continuity and working with patients and their families to make a meaningful difference in their lives.

*As told to Paula Derrow
Illustrations by Nancy Januzzi*

Marissa Dean, MD

University of Alabama at Birmingham (UAB)
Birmingham, Alabama

*Looking at Parkinson's Disease
through Patients' Eyes*



During my residency, I had a one-month fellowship in movement disorders, and immediately, felt this was where I should be. I love the continuity of care, and that you don't just treat neurologic symptoms, but also issues with mood and behavior, and other aspects of primary care.

Recently, I was taking a history of a new patient with Parkinson's and he asked, "Why do strange things happen when I'm asleep?" I realized that he probably had REM Sleep Behavior Disorder, where people act out their dreams — common in those with PD. When I explained, he was relieved, and I was reminded that it's important to step back and see the world from the patient's perspective. There's a huge opportunity to educate patients and provide support.

Parkinson's Disease — Nature or Nurture?

I'm interested in the genetics behind PD. My opinion is that the disorder is most likely due to a complicated interplay of environment and genetics that we don't yet fully understand. If we can see how genetic modifiers and various risk factors interact with environmental factors like viruses and bacteria,

we might be able to find a way to avoid the interactions — and the development of PD.

Reaching Underrepresented Populations

I'm intrigued by PD in the African American population — there's not a lot of data there, and African Americans tend to be underrepresented in clinical trials. That makes me wonder if there is a decreased prevalence, and if so, if that's due to a difference in symptoms brought on by gene-environment interactions. I'm starting a project at UAB to study these issues — and staying on here as an assistant professor. There's the potential to discover much about gene-environment connections in the next decade, and I'm in a great place to make that happen.

Class of 2018 Fellows

Lenora Higginbotham, MD

Emory University
Atlanta, Georgia

*Helping People with Atypical
Parkinsonism Get an Earlier Diagnosis*



My grandmother was diagnosed with Parkinson's disease when I was in medical school. My aunt and I did a lot of caring for her — taking her to doctor's appointments — which is what sparked my interest in movement disorders. But even more, I was inspired by watching her medical team care for someone with a progressive disease with such enthusiasm. It made me want to be like that.

A Tricky Diagnosis

My first year as a fellow, I discovered how tough it was to distinguish between patients with PD and atypical parkinsonism. There are still no specific treatments for the latter, but there is a benefit to being able to target patients earlier. We can give them advice at an earlier stage, and even steer them toward clinical trials that might change the course of their disease. With that in mind, I've focused my research on finding a biomarker that could make identifying atypical parkinsonism easier.

We know that certain EEG (brain wave) markers exist that may help differentiate PD patients from those who don't have the disease. But no one has compared these markers in

patients with PD to those with atypical parkinsonism to see if the latter has any characteristic features. Our initial results suggest that there may indeed be distinct differences.

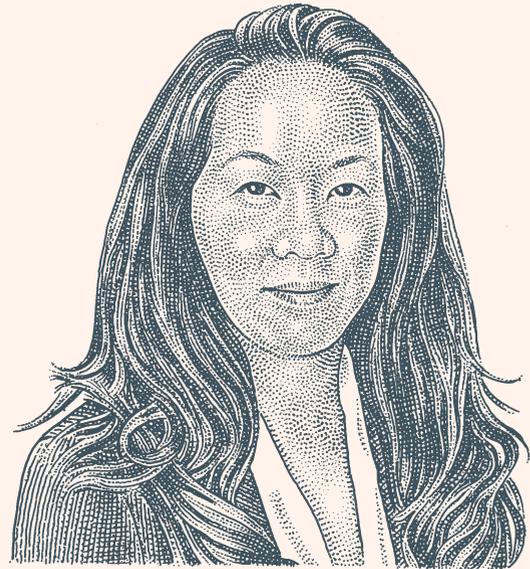
A Measure of Hope

From my experience with my grandmother, I learned how crucial it is for people with chronic, degenerative diseases to have caring physicians who are always trying to improve their quality of life. Moreover, if we find a biomarker for atypical parkinsonism, that biomarker could become a target for treatment; we could potentially use medication to change certain brain waves, and make an impact on patients' lives. That would be amazing.

Christine Kim, MD

Columbia University
New York, New York

*Helping Patients Pursue
Their Passions*



I fell in love with the clinical aspects of movement disorders during my residency at New York Presbyterian/Columbia University Medical Center. Practicing movement disorders relies more on your understanding of a patient's history and examination rather than on many diagnostic tests. Personally, I find that satisfying.

A Family Affair

Caring for patients with Parkinson's disease is a team effort — not just the medical team, but also the patient's family and caregivers. Family is so crucial in helping us figure out how best to help patients, and in identifying the issues that impact them most we can come up with more individualized treatment plans. For example, one of my PD patients is an avid gardener; we focus on optimizing his mobility, but also on avoiding dehydration and low blood pressure due to working outdoors in the heat. He regularly sends us photos of his beautiful garden!

Analyzing What Happens When Movements Go Awry

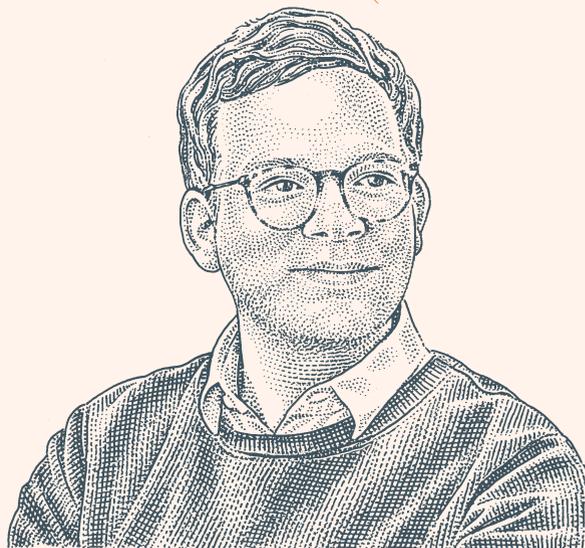
My research centers on focal task-specific dystonia — a movement disorder characterized by excessive muscle contraction affecting one specific body part; one common example is writer's cramp. I am a professional musician and am particularly interested in musician's dystonia, which affects up to two percent of professional musicians and can be career ending. Secondary dystonia also is very common in people with PD. It can be painful and debilitating, and the treatments often have many side effects. Learning more about primary dystonia — the kind that affects musicians — is a good starting point to get to the bottom of the causes and underlying circuitry of dystonia in PD. Our understanding of the pathophysiology of the disease is growing so fast right now; it is truly an exciting time to be entering the field.

Class of 2018 Fellows

Gerrit Machetanz, MD

University of Tübingen
Tübingen, Germany

*Developing a Partnership
with Patients*



With the population growing older, we need more physicians who are familiar with Parkinson's disease and other movement disorders. That's one reason I've started my own outpatient clinic for atypical parkinsonian disorders here in Tübingen during my Edmond J. Safra Fellowship. This is an important step to improve specialized care. I'm booked through September 2018.

Digging into the Causes of PD

Research-wise, I'm separating out the underlying mechanisms of PD — genetic and non-genetic. One differentiation is between damaged mitochondrial versus lysosomal systems. I'm evaluating methods to detect the major drivers of Parkinson's in a single patient, in the hope of developing more individualized treatments. Say there are two people with PD, but one has mitochondrial problems, while for another the underlying issue is protein sorting. Evaluating patients this way — on a biochemical as well as a clinical level — could lead to a variety of new, more precise therapies.

A Matter of Trust

What I find really rewarding is how, with PD and atypical parkinsonian syndromes, you see patients again and again, over the course of many years. And while my primary task is to give advice on medical and other therapeutic treatments, many other issues come up that result in our forming quite intimate relationships. Sometimes, I'll help patients find a way around their symptoms so that they can continue to work — for instance, helping a watchmaker who has run his own business and now has a tremor continue his livelihood in a satisfying way. Or I'll write a series of letters to an insurer who has declined to cover a patient's prescription. To do all this, an enormous amount of trust has to be established. It's a partnership that forms over many years of continuous contact.

Class of 2018

Fellowship Directors

Stewart Factor, DO

Emory University
Atlanta, Georgia

Stewart Factor is professor of neurology, director of the Movement Disorders Program and Vance Lanier Chair of neurology at Emory University School of Medicine. He has held committee memberships for many organizations, including the Movement Disorder Society, the American Academy of Neurology and the Parkinson Study Group. Stewart has edited three textbooks and authored numerous peer-reviewed articles on Parkinson's and other movement disorders. His research centers on Parkinson's biomarkers, freezing of gait, Huntington's disease, dystonia and tardive dyskinesia. Stewart co-directed three MDS-PAS Movement Disorders Schools for Neurology Residents.

Susan Fox, MBChB,
MRCP, PhD

Toronto Western Hospital
Toronto, Canada

Susan Fox is a professor of neurology at the University of Toronto and a staff neurologist at the Toronto Western Hospital. She also is a clinical investigator. Her research includes pre-clinical studies investigating disease mechanisms, particularly neuropsychiatric problems of Parkinson's, as well as Phase II and III clinical trials of new treatments for Parkinson's disease (PD) and other movement disorders. Susan is secretary of the Movement Disorder Society and past chair of the Movement Disorder Society Evidence-Based Medicine Committee.

Thomas Gasser,
MD, PhD

University of Tübingen
Tübingen, Germany

Thomas Gasser is professor of neurology, chairman of the Board of Directors at the Center of Neurology, and dean of research of the medical faculty at the University of Tübingen, Germany. He also is director of the Department of Neurodegenerative Diseases at the Hertie-Institute for Clinical Brain Research and coordinator for clinical studies at the Tübingen partner of the German Center for Neurodegenerative Diseases. His research focuses on the genetic and molecular underpinnings of Parkinson's disease, dystonia and other movement disorders. Thomas currently serves as a scientific advisor for The Michael J. Fox Foundation (MJFF).

Class of 2018 Fellowship Directors

Un Jung Kang, MD

Columbia University
New York, New York

Un Jung Kang is the H. Houston Merritt Professor of neurology and chief of the Division of Movement Disorders at Columbia University. His research concentrates on understanding the mechanisms that cause PD and how the basal ganglia, a circuit of cells involved in Parkinson's and other movement disorders, change over time with Parkinson's and in response to dopaminergic therapy. He also works on PD biomarkers, as the principal investigator of the MJFF-sponsored Fox Investigation for New Discovery of Biomarkers (BioFIND) and as a member of MJFF's Parkinson's Progression Markers Initiative (PPMI) biospecimen review committee.

David Standaert, MD, PhD

University of Alabama
at Birmingham (UAB)
Birmingham, Alabama

David Standaert is the John N. Whitaker Professor and chair of neurology, senior member of the Division of Movement Disorders, and director of the Bachmann-Strauss Dystonia and Parkinson's Disease Center of Excellence at UAB. He is chairman of the American Parkinson Disease Association's Scientific Advisory Board and director of their Advanced Center for Parkinson Research. He also is associate editor of the journal *Movement Disorders*. David studies causes of PD-related neurodegeneration, particularly neuroinflammation and mechanisms of dyskinesia. He oversees several PD therapeutic and biomarker clinical trials. He co-directed two MDS-PAS Movement Disorders Schools for Neurology Residents and previously served as an MJFF scientific advisor.

Classes of 2019 and 2020 Fellows

Ten additional movement disorder specialists are receiving vital training with support from The Edmond J. Safra Fellowship in Movement Disorders.

2019

Katherine Amodeo, MD

University of Rochester
Rochester, New York

Fellowship Director: Irene Richard, MD

Sarah Horn, MD

University of Pennsylvania
Philadelphia, Pennsylvania

Fellowship Director: Nabila Dahodwala, MD, MS

Katherine Leaver, MD

Icahn School of Medicine at Mount Sinai
New York, New York

*Fellowship Directors: Susan Bressman, MD, and
Rachel Saunders-Pullman, MD, MPH, MS*

Jessica Weinstein, MD

University of California San Francisco
San Francisco, California

Fellowship Director: Nicholas Galifianakis, MD, MPH

Natalie Witek, MD

Rush University
Chicago, Illinois

Fellowship Director: Katie Kompoliti, MD

2020

Juliana Coleman, MD

University of Alabama at Birmingham (UAB)
Birmingham, Alabama

Fellowship Director: David Standaert, MD, PhD

Grace Crotty, MB, BCh, BAO, MRCPI

Massachusetts General Hospital
Boston, Massachusetts

Fellowship Director: Alice Flaherty, MD, PhD

Eric Jackowiac, MD

University of Michigan
Ann Arbor, Michigan

Fellowship Director: Praveen Dayalu, MD

Greg Kuhlman, MD, MBA

Toronto Western Hospital
Toronto, Canada

*Fellowship Director: Susan Fox, MBChB,
MRCP, PhD*

Kimberly Kwei, MD, PhD

Columbia University
New York, New York

Fellowship Director: Oren Levy, MD, PhD

Class of 2021

Fellowship Centers

The Michael J. Fox Foundation is proud to announce the academic centers that will host the fourth class of The Edmond J. Safra Fellowship in Movement Disorders.

Emory University

Atlanta, Georgia

Northwestern University

Chicago, Illinois

Radboud University

Nijmegen, The Netherlands

University of Lübeck

Lübeck, Germany

University of Pennsylvania

Philadelphia, Pennsylvania



THE MICHAEL J. FOX FOUNDATION
FOR PARKINSON'S RESEARCH

As the world's largest nonprofit funder of Parkinson's research, The Michael J. Fox Foundation is dedicated to accelerating a cure for Parkinson's disease and improved therapies for those living with the condition today. Funding more than \$800 million in research to date, the Foundation pursues its goals through high-impact research efforts coupled with an active global engagement of scientists, Parkinson's patients, business leaders, clinical trial participants, donors and volunteers.

www.michaeljfox.org



EDMOND J. SAFRA
PHILANTHROPIC FOUNDATION

Edmond J. Safra, one of the 20th century's most accomplished bankers and a devoted philanthropist, established a major philanthropic foundation to ensure that individuals and organizations would continue to receive his assistance and encouragement for many years to come. Under the chairmanship of his beloved wife Lily, the Edmond J. Safra Foundation draws continuing inspiration from its founder's life and values, and supports hundreds of organizations in more than 40 countries around the world. Its work encompasses four areas: Education; Science and Medicine; Religion; and Humanitarian Assistance, Culture and Social Welfare. The Foundation has provided significant funding for Parkinson's disease research and patient care at dozens of hospitals and institutes in places as varied as Natal (Brazil), Toronto, New York, Grenoble, Paris, London and Jerusalem.

www.edmondjsafra.org



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