



2021 in Review and What's Next






Where the
Power of Science
Meets the Power
of Community



THE MICHAEL J. FOX FOUNDATION
FOR PARKINSON'S RESEARCH

The Michael J. Fox Foundation (MJFF) devotes philanthropic capital to promising science with the goal of bringing new treatments and cures to people with Parkinson's disease (PD). Even in the face of a global pandemic, the momentum in Parkinson's research continues — from microscopic discoveries in the lab to thousands of individuals contributing to progress in meaningful ways. Today, the power of science meets the power of community.

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Section 1



Transforming the Drug Development Landscape

In a year dominated by the biggest science story in a century, major milestones in Parkinson's research nonetheless continued to make headlines with significant deals in the therapeutic industry, game-changing clinical trials and groundbreaking partnerships. Today, it is fair to say that The Michael J. Fox Foundation (MJFF) plays an irreplaceable role in the field and its future trajectory.



Alpha-synuclein: Major Deal Pushes Vaccine Further in Testing

A long-watched Parkinson's vaccine is advancing in testing after a major deal between two biotech companies — both of which received early-stage funding from MJFF — puts more resources behind the program.

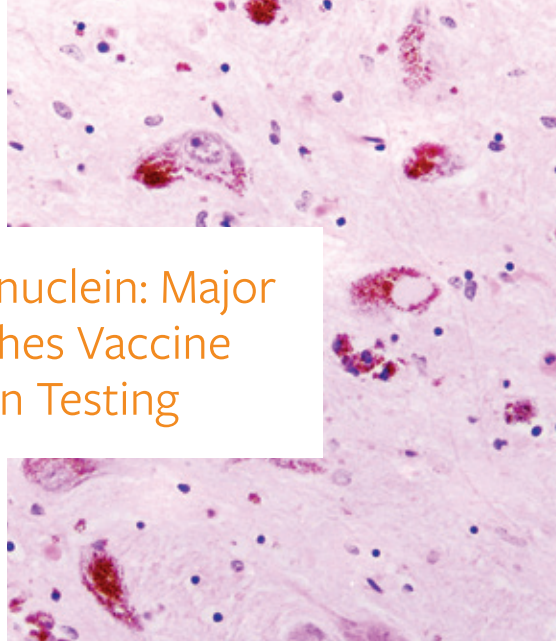
The therapy prompts the body's natural immune response to neutralize alpha-synuclein by using a synthetic protein to elicit antibodies (like how the flu vaccine works). Alpha-synuclein is a key Parkinson's protein known to form harmful clumps in the cells of people with the disease, similar to beta amyloid in Alzheimer's.

With MJFF support, Austrian biotech AFFiRiS AG launched the earliest trials of the vaccine in 2012. The work took a significant step forward in 2021 as Swiss biotech

AC Immune acquired the AFFiRiS portfolio in a deal valued at \$59 million. AC Immune is preparing to launch a Phase II human study of its now-optimized vaccine.

This hand-off (from a smaller company to a larger one with deeper pockets) is a textbook example of the Foundation's "de-risking strategy." MJFF supports early, risky projects to help drugmakers build data and attract partners that can usher the most promising therapies through larger, more expensive later-stage trials. The Foundation wears multiple hats in de-risking: financially supporting early-stage projects, orchestrating troubleshooting and follow-on work to keep promising science moving forward, sharing open-access data to

Continued on page 7



Tracing Parkinson's

An imaging tracer is a long-sought tool for drug development. MJFF is a lead funder in efforts to validate tracers for alpha-synuclein and other targets.



What:

Historically, researchers have relied on post-mortem studies to understand the roles of various proteins in the brain. Imaging tracers are groundbreaking research tools that allow scientists to visualize proteins in the living brain.

How:

A small, radioactive tracer compound, injected in the arm, travels to the brain and "tags" itself onto the targeted protein. A brain scan is then done to measure the tracer and thereby visualize the protein.

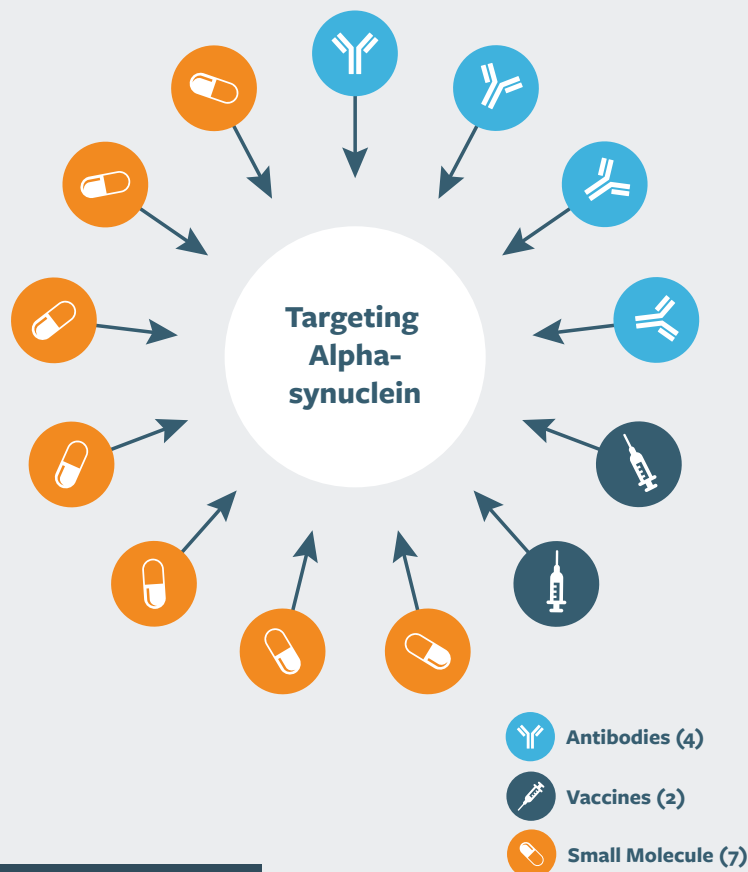
Why:

Measuring levels and location of a protein in the brain can help scientists understand its role in disease, track progression, select study volunteers and assess a drug's efficacy. An Alzheimer's therapy was recently approved based on imaging tracer data (see page 17).

When:

Backed by philanthropist and Citadel CEO Ken Griffin, MJFF granted millions to three teams currently racing to develop Parkinson's tracers. Results from AC Immune's latest trial of a tracer compound are expected in 2021.

Thirteen Therapies in Trials



In biomedical research, we expect the majority of ideas — even promising ones — to fail. MJFF embraces calculated risk and funds a wide range of therapeutic approaches in any given area to increase “shots on goal” and the likelihood of success.

accelerate progress at key inflection points, making key introductions in the field and generally doing whatever it takes to ensure no promising science languishes for lack of funding or focus.

For example, the Foundation has granted more than \$5 million to AC Immune since 2015 for its pursuit of a tool to allow scientists to visualize alpha-synuclein in the living brain — something that has never been possible in Parkinson’s before

and has proved game-changing in Alzheimer’s research. An imaging tracer would speed development and testing of new treatments by allowing more nuanced selection of study participants and faster assessment of therapeutic impact on underlying disease biology. (See “Tracing Parkinson’s,” page 5.)

Read more on this deal and the 12 other ongoing human studies in alpha-synuclein at michaelfox.org/asynpipeline.

What’s Next for Alpha-synuclein

- + **Recruiting critical volunteers:** Many alpha-synuclein trials will continue recruiting participants in 2022. MJFF is working hard to educate and engage potential research volunteers in support of more efficient studies, faster results and future testing. (To learn more, visit foxtrialfinder.org.)
- + **Harnessing our natural immunity to speed new treatments:** Immunotherapy has yielded tremendous results in cancer research over recent decades. The body’s defense system could similarly hold potential to drive next-generation Parkinson’s treatments. Pharmaceutical firms AstraZeneca and Takeda are leading this field with an ongoing alpha-synuclein antibody trial. Their approach introduces antibodies engineered to try and clear out the problematic protein. Results from the trial are expected in 2022.
- + **Visualizing success in imaging:** As AC Immune’s imaging tracer trial nears results, other MJFF grantees plan to enter human testing in the coming 12 to 18 months. More shots on goal means more chances to achieve this game-changing tool.

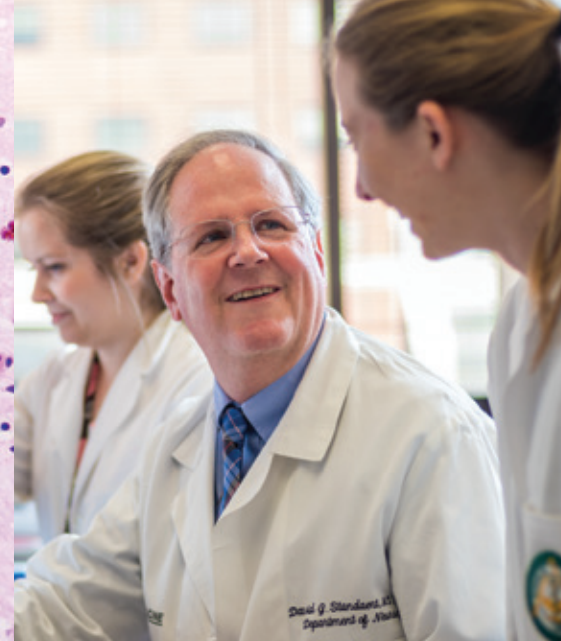
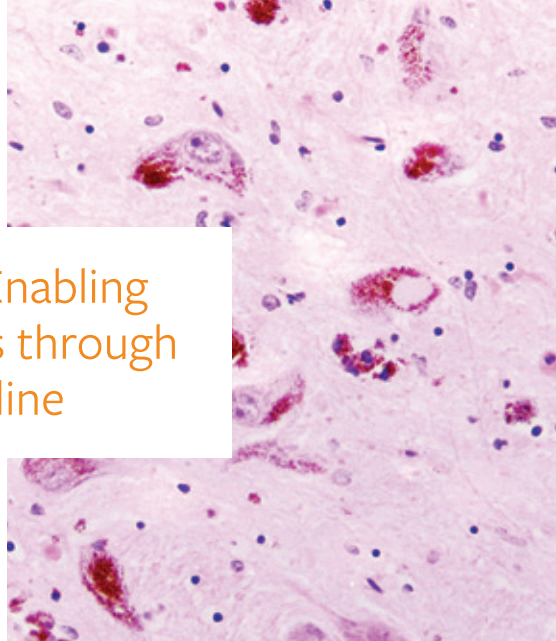


LRRK2: Enabling Progress through the Pipeline

Mutations in the LRRK2 gene cause a small minority of Parkinson's cases, but the biological changes found in these individuals yield critical clues for the development of better Parkinson's treatments that would benefit everyone with the disease — genetic mutation or not.

In 2020, two major players in Parkinson's drug development — San Francisco biotech Denali and Cambridge pharmaceutical firm Biogen — announced the launch of a late-stage trial of their therapy targeting the LRRK2 protein. As this report goes to press, the highly anticipated results from this trial are expected by year-end 2021. Additionally, Biogen is testing a separate approach targeting this same high-priority pathway.

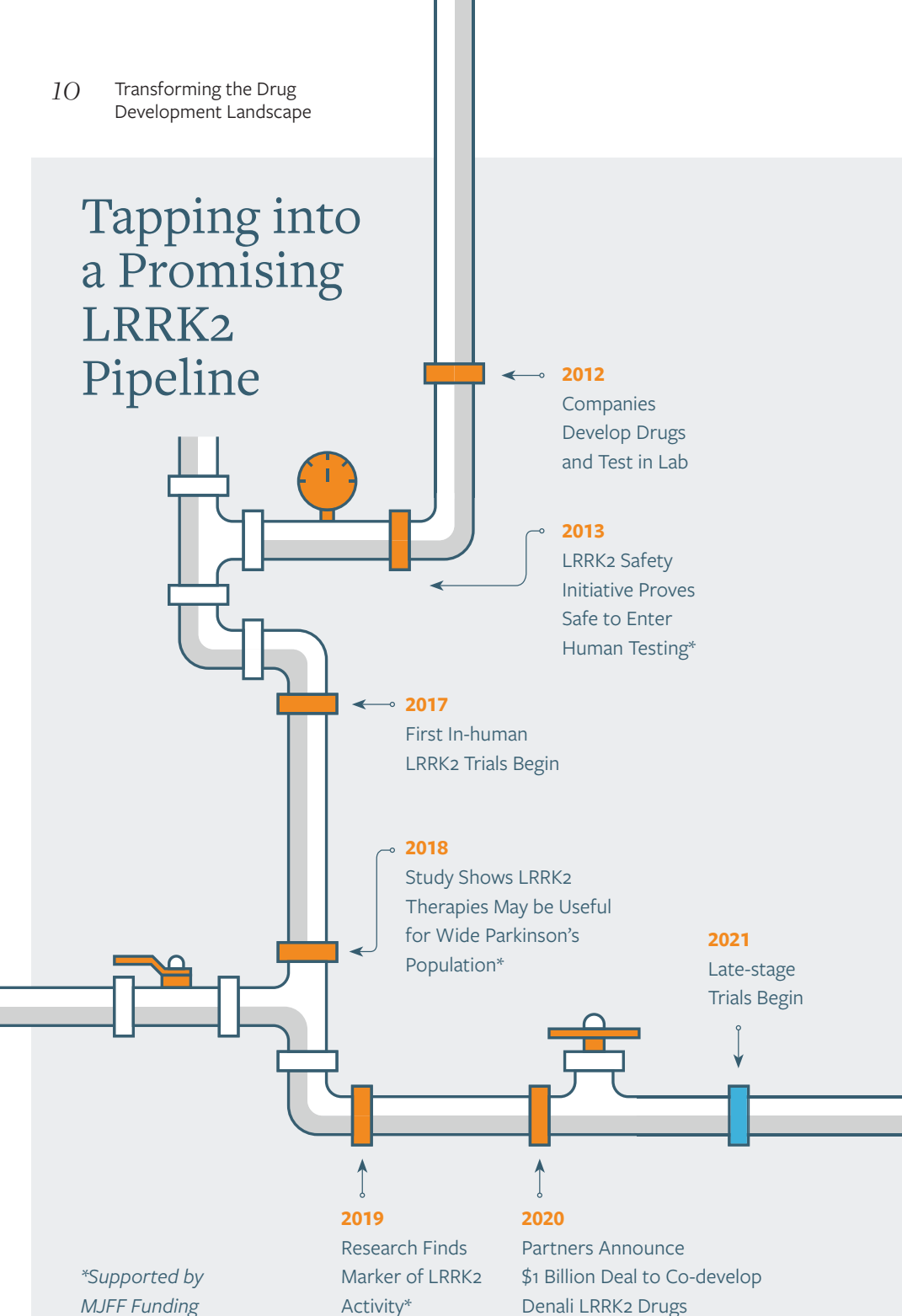
LRRK2 was discovered in 2004 and quickly emerged as one of The Michael J. Fox Foundation's most important areas of focus. (One of the first major studies of LRRK2 was funded at the pharmaceutical firm Wyeth through our Therapeutics Development Initiative program in 2006.) Today, as LRRK2 continues its steady march toward market, it is fair to say that the entire field as it exists today could only have been achieved through key findings and interventions conceived and financially enabled by MJFF. (See "Tapping into a Promising LRRK2 Pipeline," page 10.)



“Denali and Biogen now have the information that will help them pick the doses for their next trials that will hopefully be safe and may be successful in slowing disease. This is an exciting step.”

— Marco Baptista, PhD,
Vice President of Research Programs,
The Michael J. Fox Foundation

Tapping into a Promising LRRK2 Pipeline



What's Next for LRRK2

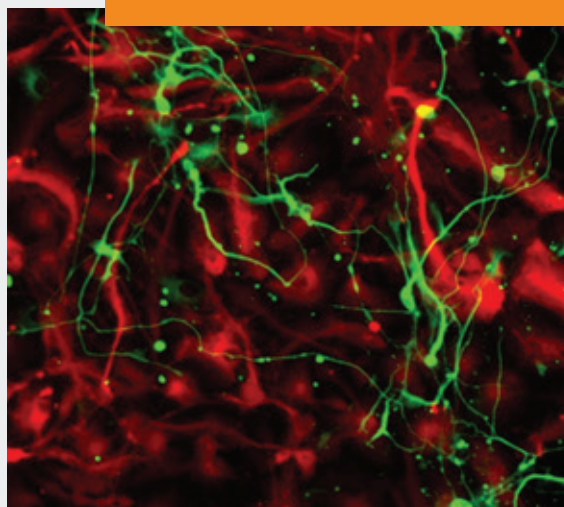
- + **Prevention on the horizon:** MJFF's landmark study PPMI (read more on page 16) is expected to recruit LRRK2 mutation carriers with and without Parkinson's throughout 2022 and 2023. Learnings from studying these individuals are considered critical for LRRK2 therapies to move into preventive trials.
- + **A revolution in Parkinson's genetics:** Intense study of LRRK2 requires MJFF to financially support an ongoing campaign to identify other cellular players with roles in the LRRK2 pathway that gives rise to Parkinson's. In 2021, Foundation-supported research uncovered another gene, CORO1C, that may increase likelihood of Parkinson's in conjunction with a LRRK2 mutation. In 2022, Foundation grantees will continue to study this emerging genetic target and its potential for drug development.



Also Heading to the Clinic

Novel Stem Cell Trial Begins

A trial implanting dopamine cells created from engineered stem cells began in June. MJFF funded original studies to create dopamine cells — which are lost in Parkinson's — from this type of stem cell.



Troublesome Symptoms the Focus of New Trials

In 2021 MJFF allocated nearly \$11 million in grants funding new approaches to ease some of the most troubling symptoms of Parkinson's, including constipation, depression, dyskinesia, gait freezing, speech issues, sleep problems and tremor.

\$11M
to symptomatic therapies

Positive Phase III Results



MJFF partner Amneal Pharmaceuticals in New Jersey announced positive Phase III results from their carbidopa/levodopa extended-release compound. The extended-release capsules worked better than immediate-release tablets at reducing “off” time in people with advanced Parkinson's and motor fluctuations. They plan on submitting a New Drug Application to the FDA mid-2022.


New App Makes DBS Adjustments More Accessible

Abbott, maker of Infinity deep brain stimulation (DBS) devices, now allows patients to receive stimulation adjustments remotely through an app. This technology can help if you live far from your doctor or have issues with travel. MJFF successfully advocated for insurance coverage of this service during the COVID-19 pandemic.



“I’m quite encouraged about the momentum in drug development led by MJFF in partnership with the PD community.”

— Jeff Keefer, Vice Chairman, MJFF Board of Directors



Section 2



Understanding the Biology of Parkinson's

The biology of Parkinson's disease (PD), and its many symptoms and subtypes, is complex. Genetics, environment and aging interact to cause disease. But not everyone with a genetic mutation linked to Parkinson's will develop the disease, nor will everyone exposed to an environmental risk factor be diagnosed.

Today, thousands of researchers worldwide are partnering with The Michael J. Fox Foundation (MJFF) to understand the triggers and cascade of cellular changes that lead to Parkinson's so we can find ways to slow, stop or prevent it.



PPMI: A United Effort to Predict and Prevent Parkinson's

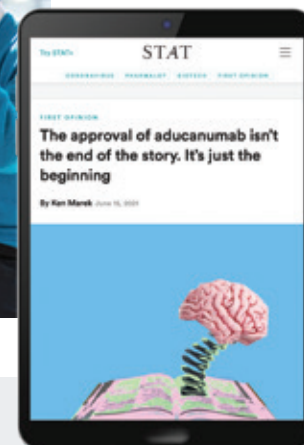
For the past decade, thousands of patients, scientists and volunteers have contributed to MJFF's landmark Parkinson's Progression Markers Initiative (PPMI) study.

A cornerstone of our efforts to increase biological understanding of the disease and its symptoms, PPMI is a peerless endeavor to funnel insights, practical tools and data directly into today's drug development environment. In turn, human studies of the disease increase our understanding of biology and open new avenues of scientific inquiry to speed next-generation strategies to eradicate the disease once and for all.

In 2021, PPMI entered its next phase: enrolling people newly diagnosed with Parkinson's as well

\$102.2M
*invested in
PPMI
since 2010*

as those who may be at risk for the disease. By growing the study from 1,500 to 4,000 participants, taking part at nearly 50 sites in 12 countries, and enrolling as many as 100,000 people online, we hope to gain critical information about who gets the disease, who doesn't, and why.



Brain Biology in the News

A new Alzheimer's drug made headlines after receiving FDA approval in 2021. Aduhelm (aducanumab) is the first Alzheimer's disease therapy to be approved since 2003 and the first that targets the disease process, rather than merely treating symptoms.

When MJFF launched PPMI in 2010, the study was modeled after the Alzheimer's Disease Neuroimaging Initiative (ADNI), a public-private partnership in Alzheimer's that gave rise to the biomarkers supporting aducanumab's development. Ken Marek, MD, MJFF's scientific advisor and co-principal investigator of PPMI, penned an op-ed in leading research outlet STAT about the implications for the PD field:

"The aducanumab story should redouble our commitment to develop and test biomarkers for Parkinson's that will provide a clear understanding of the biology of this disease. This is the only way to efficiently test whether drugs slow the disease process and ultimately slow Parkinson's-related disability. Researchers need to work with pharmaceutical teams to give them these tools to ensure that their studies will meet every standard that's required, so when encouraging data emerge, they can move forward effectively...The best way to put the approval of aducanumab into perspective is to see it as just the beginning of a pipeline of therapies that target the underlying biology of brain disease."



“We certainly all share the desire to slow down symptoms and progression, and to be as resilient as possible in the face of neurological disease. I am hopeful that my participation in studies like PPMI can serve as my contribution to this vitally needed research and can hopefully over time lead to true scientifically proven cures and prevention strategies.”

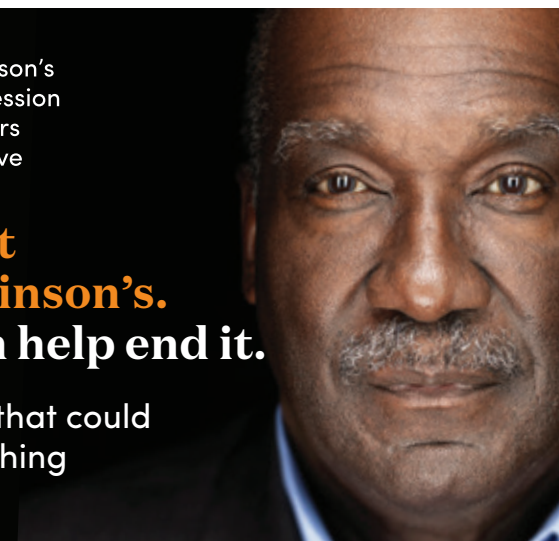
Brian Duggan, 67, lives with REM sleep behavior disorder, which is when you act out dreams while asleep. It's a risk factor for Parkinson's disease, and many people experience it after diagnosis with Parkinson's. PPMI is now recruiting people with risk factors including individuals who act out their dreams while asleep.



Parkinson's
Progression
Markers
Initiative

**He doesn't
have Parkinson's.
But he can help end it.**

Join the study that could
change everything



What's Next for PPMI

PPMI is powered by you. As of this writing, over 67,000 individuals have completed an online screening form. If you...

- + have been diagnosed with Parkinson's in the past two years and are not yet taking Parkinson's medication
- + have a parent, brother or sister, or child with Parkinson's (and you are over age 60)
- + act out your dreams while you sleep
- + would like to join as a control volunteer with no known history of brain disease

learn more and get started today at michaeljfox.org/ppmi.



Environmental Exposures: Uncovering their Role in Parkinson's

The Michael J. Fox Foundation explores cures from all angles, including toxic factors in the environment or in lived experience that may contribute to Parkinson's risk.

Such information is critical in advocating for regulations to limit these exposures and the risk of Parkinson's and other diseases. (MJFF leads much of this advocacy as the founder of the Unified Parkinson's Advocacy Council, an alliance of more than 20 partner organizations.) Additionally, these connections provide the basis for biological studies that may point scientists to novel intervention approaches.

In 2021, MJFF announced grants supporting studies to investigate

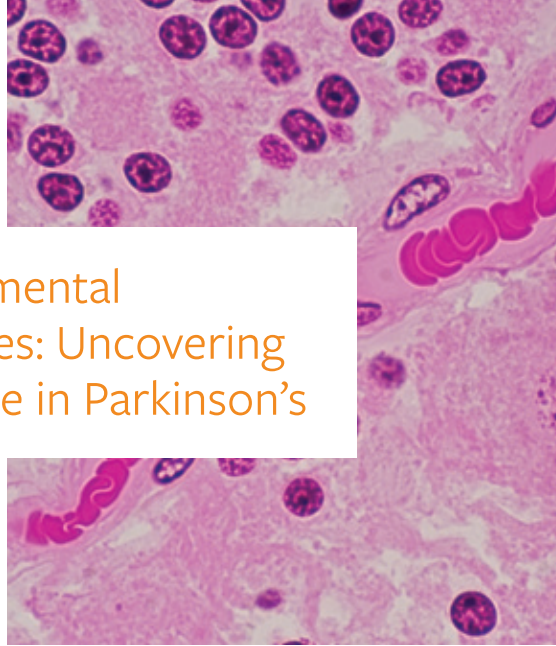
the connection between exposure to factors in the environment (e.g., pollution and pesticides) and disease. These include:

Exposures during Military Service

Service at some military bases and deployment sites is linked to greater risk of Parkinson's. This study out of University of California, San Francisco will review data from over 200,000 service members on a range of health and environmental toxicants encountered during military service and deployments.

Profiles of Geographic Parkinson's Clusters

Geographic areas where more people develop Parkinson's than expected can provide clues about environmental causes. Researchers



California Funds Its Parkinson's Disease Registry

In July 2021, California Governor Gavin Newsom signed the state's Fiscal Year 2022 budget, which includes \$8.4 million over four years for the California Parkinson's Disease Registry (CPDR), and a four-year provision to expand the CPDR to include other neurodegenerative diseases. The CPDR exists to acquire, record and analyze epidemiological data of the incidence and prevalence of disease that can identify Parkinson's "hot spots" in the state. The registry will soon make its de-identified data open to the scientific community, which could be useful

for studies on environment and PD.

An estimated 117,000 Californians live with Parkinson's — the highest state-based number of people with the disease in the country. In addition to helping fund the CPDR, MJFF organized a neurological disease coalition to encourage expansion of California's data collection effort to other neurodegenerative diseases, which inform one another when it comes to discovering better treatments and cures.

at Washington University in St. Louis, Missouri will use data from over 22 million Medicare recipients to find clusters of people with Parkinson's and identify potential environmental exposures in that area.

Influence of Today's Pesticides on Disease

A team at University of California, Los Angeles will review data on pesticide use in California from 1974 to 2018 (more than 200 pesticides) and compare it with home and job address histories from volunteers in a large PD study. They will also

study how those exposures may change biology, which could help better understand disease even in people without exposures.

Air Pollution's Impact on Parkinson's

Some studies have shown increased risk of PD with exposure to air pollutants, but more evidence is urgently needed. A study from University of Eastern Finland will compare data from over 22,000 people with PD and 148,000 control volunteers with exposure to 16 different pollutants (e.g., smog, gases).



What's Next for Environmental Risk Factors

+ Combing Fox Insight data for answers:

Two studies will use data from MJFF's Fox Insight, an online study that collects information from people with PD and their loved ones about the lived experience of the disease, to learn about the impact of environmental factors on PD. One study will pull from questionnaires on smoking/tobacco use, caffeine consumption, anti-inflammatory medication history and pesticide exposure to assess if there are links to age of disease onset and progression. Another team will look at data to determine the association between environmental exposure, genetic variants, and motor and cognitive symptoms. Their goal is to understand how the environment and genes interact to influence both symptom severity and progression.

+ Keeping harmful pesticides off store shelves:

Alongside several petitioners ranging from environmental advocates to other disease groups, MJFF has joined a lawsuit against the Environmental Protection Agency (EPA) to challenge its latest registration review of paraquat. Exposure to paraquat increases Parkinson's risk by 320 percent and more than 30 countries have already banned paraquat — including China, where the chemical's manufacturer is headquartered. Every 15 years, the EPA reviews all herbicides and pesticides to confirm they are safe for use. This review process takes several years and has many steps. The latest round of pesticide review finalizes the EPA's assessments of human and environmental impact and allows the pesticide to be bought and used until it is reviewed again.



Also Heard
around
the Lab



Aligning Science
Across Parkinson's

The Aligning Science Across Parkinson's (ASAP) initiative is a basic science initiative that counts MJFF as its implementation partner. With the Foundation's support, ASAP is fostering collaboration and resources to better understand the underlying causes of Parkinson's disease.

The critical importance of basic research

Fourteen research teams will begin deep research studies into brain networks and brain-body connections in Parkinson's with \$131 million in ASAP support announced this year. MJFF has lent our field view and grantmaking infrastructure to help select projects and manage grants.

Making Parkinson's genetics inclusive

ASAP's Global Parkinson's Genetics Program (GP2) has gathered data from almost 78,000 people toward its goal of studying gene changes in more than 150,000 volunteers with and without Parkinson's. With an emphasis on participants from underrepresented populations, GP2 aims to paint a fuller picture of Parkinson's genetics, which traditionally has focused on people of European descent.

Do men get Parkinson's more often?

A new study is looking at dark pigment (melanin) in cells of men versus women. Men may build up the pigment faster, harming cell function. More data could lead to a new strategy to stop Parkinson's. Meanwhile, some experts question if biology or diagnosis trends — perhaps dismissing women's symptoms — are responsible for skewing Parkinson's more male. Efforts to train the workforce toward more equitable care may impact that ratio. MJFF is funding both initiatives.



“We’re now at a point that we have therapeutics in the clinic that can address the underlying biology of disease. For me this is a really exciting time to be in the field, to be driving the understanding of these discoveries and applying them to patient therapeutics.”

— *Carole Ho, MD, Chief Medical Officer and Head of Development at Denali Therapeutics*

Section

3

Creating
Momentum
with Our
Community

No one becomes part of the Parkinson's disease (PD) community by choice. But once here, many find the community to be a source of comfort and friendship. The Michael J. Fox Foundation (MJFF) strives to foster those connections at scale and welcome everyone to play an active role in ending the disease for good.

The next five to seven years are critical for people and families living with Parkinson's. The explosion of science, coupled with the passion of the global PD community, positions us to achieve a new level of acceleration in addressing decades of unmet medical needs and, ultimately, finding a cure.



Inclusiveness in Research: A Parkinson's Cure for All

Our understanding of the cause, progression and treatment of Parkinson's is growing, but remains far from complete.

To date, most research has not been inclusive of the broader community of people with Parkinson's. As a result, we have an incomplete picture of how PD affects individuals and families across racial, ethnic, socioeconomic, gender, sexuality and geographic spectrums.

To address this critical knowledge gap, The Michael J. Fox Foundation launched Promoting Diversity,

Equity and Inclusion in Parkinson's Disease Research (DEI-PD) in 2021, a program specifically seeking investigator-initiated research to engage Black, Latino, Asian, Indigenous groups, and LGBTQ+ communities, as well as individuals from underprivileged socioeconomic circumstances. Broadening research participation will provide a more holistic view of the causes of disease and lead to new treatments for more people.

Parkinson's 360, The Michael J. Fox Foundation's guide for patients and families living with Parkinson's, is now available in Spanish as well as English. You can find it and other Spanish-language resources at michaelfox.org/parkinson360-espanol.



What's Next for Increasing Inclusiveness in Research

- + **Partnering with local communities:** Since 2018, MJFF has partnered with the Community Access, Recruitment and Engagement (CARE) Research Center at Massachusetts General Hospital and Harvard Medical School on FIRE-UP PD (Fostering Inclusivity in Research Engagement for Underrepresented Populations in Disease) to develop culturally relevant messaging and materials in four cities nationwide to increase diversity and inclusion in PD research.
- + **Expanding diversity in PPMI:** Phase II of FIRE-UP PD will include 10 research sites and encourage enrollment in MJFF's PPMI (see page 16), to bring together a larger, more diverse group. The goal is to provide meaningful data on which strategies work to engage underrepresented populations in research.
- + **Uncovering genetic links:** As part of its mission, GP2 (see page 24) has launched the Black and African American Connections to Parkinson's Disease (BLAAC PD) study, which aims to recruit 10,000 Black and African American people to help better understand genetic connections to Parkinson's in this population.



Parkinson's Buddy Network: Cultivating Connections

Meeting others who share similar circumstances is crucial for building a support system that can help people living with Parkinson's manage day-to-day realities, overcome challenges and take control of their disease. But finding others living with Parkinson's and building new relationships isn't easy.

To help meet this need — especially with increased urgency amidst the pandemic — MJFF launched the Parkinson's Buddy Network in 2021. The online platform is designed for people with PD, their loved ones and caregivers to connect with others based on shared interests, backgrounds and experiences with the disease. Users can search for people in their area, exchange private messages, post to discussion boards, and join groups focusing on specific topics.

Beyond the Buddy Network, the Foundation continues to offer many paths to interact with the Parkinson's community, including participating in research, advocating for Parkinson's-related policies, fundraising and learning about the latest advances — all of which can lead to new contacts and a broader support system.



What's Next for the Buddy Network

In its first year, the Parkinson's Buddy Network attracted over 5,000 active users. In early 2022, the platform will launch to a broader community to expand its reach and also, its offerings. New features in 2022 will include:

- + Mentorship opportunities to pair those seeking advice with those willing to provide help.
- + More group options for different stages of your Parkinson's journey.
- + Increased accessibility across devices and a refreshed look and feel.

You don't have to wait to start making connections today. The Buddy Network welcomes:

- + People living with Parkinson's
- + Parkinson's caregivers
- + Friends and family of someone who has/had Parkinson's

More buddies mean more connections and a richer experience for you and your loved ones. To join, visit michaelfox.org/buddynetwork.





Also Seen
in the
Headlines

Recognized as a woman creating social change at scale, Debi Brooks, CEO and Co-Founder of The Michael J. Fox Foundation, was named to *Forbes* “50 Over 50: Impact List.”



PD Avengers

The PD Avengers, a global alliance of Parkinson’s disease advocates, took over MJFF’s podcast for a special two-part episode highlighting the many organizations and resources for people living with PD and their families.

“The truth is we can never have enough people helping people with Parkinson’s live a better life and search for a way to end this disease.”

— Soania Mathur, MD, MJFF Patient Council
Co-Chair and PD Avengers Co-Founder



MJFF’s Limited Series COVID-19 Podcast won a Webby Award and People’s Voice Award for best in science and education podcasts. Honoring the best of the internet, The Webby Awards are presented annually by the International Academy of Digital Arts and Sciences.

“I have a passion for moving the dial with philanthropy capital and doing whatever it takes.”

— Debi Brooks, CEO and Co-Founder,
The Michael J. Fox Foundation

“The need around COVID manifested itself into a real desire and energy to create something new. If we wanted a vaccine, we got a vaccine. When we wanted to go to the moon, we went to the moon. If we want to cure Parkinson’s, we’ll cure Parkinson’s. We’re not just dreaming about these things. We’re envisioning them and making them real.”

— Michael J. Fox on the power of science and community to impact change.



THE MICHAEL J. FOX FOUNDATION
FOR PARKINSON'S RESEARCH

**Here. Until
Parkinson's isn't.**

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