PMDF

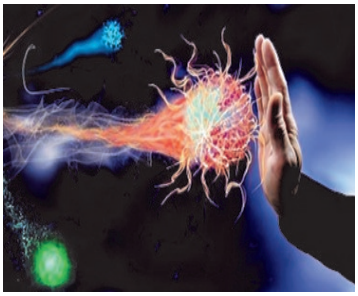
THE PARKINSON'S AND MOVEMENT DISORDER FOUNDATION

Newsletter ☙ Spring 2017

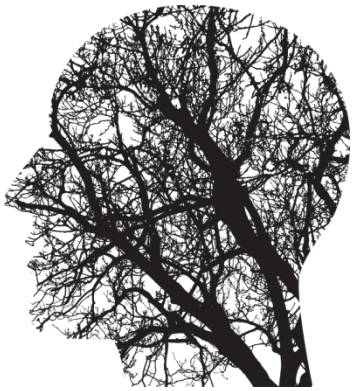
PMDF Grant Winners for 2017

by Mary Ann Chapman, PhD

The Parkinson's and Movement Disorder Foundation (PMDF) is pleased to announce its grant award winners for 2017. Thanks to your generous donations and attendance at our 2016 fundraiser, we were able to award $5000 to each of two researchers.



One of this year's award winners is Dr. Carlos Barcia, a distinguished researcher and professor at the Autonomous University of Barcelona in Spain. Dr. Barcia and his colleagues are studying immunotherapy for the treatment of Parkinson's disease. Brain immune cells known as microglia are a hot topic of research in Parkinson's disease. These cells possess membrane proteins that signal them to engulf and eliminate neurons. In fact, the cells are a type of phagocyte, which comes from the Greek word *phagein* meaning "to eat." Dr. Barica's group is trying to determine whether blocking membrane proteins with an immunotherapy (i.e., an antibody that specifically binds to the proteins) might help preserve neurons in the brain. The first hurdle that the researchers face is trying to get the immunotherapy through the brain's protective defenses. If the immunotherapy is able to get into the brain, they will then determine whether it protects nerve cells in an animal model of Parkinson's disease. We are eagerly awaiting the results of these studies and hope that the immunotherapy will be a success.



Another of this year's award winners is Dr. Bradley Groveman, a Research Fellow at the National Institutes of Health at the Rocky Mountain Laboratories in Colorado. Dr. Groveman is working on a method to identify misfolded proteins in small samples of urine, blood, and cerebrospinal fluid—the liquid that surrounds the brain and spinal cord. In Parkinson's disease, the protein alpha synuclein is known to misfold and act like a template for other molecules of alpha synuclein, which then build up into insoluble masses in the brain. Many people believe these protein masses prevent nerve cells from working properly and cause them to die. Some of the misfolded protein clumps find their way into blood and other tissues. It is possible that if these masses of misfolded protein could be detected at extremely low levels, Parkinson's disease could be diagnosed earlier. This, in turn, would allow people to receive earlier treatment, which may help prevent the neurons from dying and the disease from progressing. We believe that the method Dr. Groveman is testing is a promising technique and look forward to his results!

The Parkinson's and Movement Disorder Foundation

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President's Letter

Dear friends of PMDF,

As a person with Parkinson's disease, I tend to pay attention to news about progress in our understanding and treating of that disease. But at PMDF, "Movement Disorder" is our middle name. Although Parkinson's disease research receives the greater part of our grants, we also fund studies on other movement disorders. Many movement disorders are unknown to those who aren't directly affected by them, and our foundation is an important source of research funding for these conditions. We have sponsored studies on multiple system atrophy, blepharospasm, and dystonia. You can see the projects we have supported on our web site at http://pmdf.org/ResearchAwards.php.

In addition, we publish articles about a variety of movement disorders in out newsletter. For example, in this issue we have an article on the genetics of dystonia. Past newsletters have featured articles about spasmodic dysphonia, restless leg syndrome, essential tremor, and many other conditions. You can search the newsletter archives on our web site at http://pmdf.org/newsletters.php.

Our job at PMDF is to enable people who want to support research in these areas to make contributions to projects that are well thought out, aimed at achieving important results, and likely to be performed successfully. We hold two fundraisers every year. The first, the 5K Zent-a-Thon, is coming up on June 10. The second, the fall fundraiser, is still in the planning stages. You can support PMDF, and the research that's important to you, by attending these fundraisers. Additionally, you can contribute directly to PMDF.

Thank you for your support.

Sincerely,

Mark Wadsworth
President

What Your Genes Can Tell You and Others about Dystonia?

by April Ingram and Mary Ann Chapman, PhD

Dystonia is a complex and variable neurological movement disorder. Muscles receive abnormal instructions from the basal ganglia, a deep part of the brain that helps control coordination of movement. Our muscles and brain seem to be key the pieces, but where do our genes fit into the puzzle of dystonia?

Most cases of dystonia are idiopathic, meaning that the cause is unknown. However, at least 27 genes have now been associated with various forms of dystonia,[1] so we know that genes play a role. Changes, or mutations, in most of these 27 genes can predispose people to dystonia, but do not guarantee that they will develop the disease. The mutations must interact with unknown environmental factors, life events, or other genes in order for the disease to be expressed. For example, some individuals develop dystonia following an injury to the neck, brain, or spinal cord, whereas others do not. Researchers are trying to determine whether the people who develop dystonia after such injuries have a genetic predisposition that makes them vulnerable and, alternately, whether individuals who do not develop dystonia despite such injuries have some sort of protective factor.

Researchers are also trying to determine the relationship between genetics and clinical symptoms. It may seem logical that people with exactly the same mutation would develop the same type of dystonia, but this isn't always the case. With the same mutation, some people show only mild dystonic symptoms affecting one part of the body, whereas others develop a much more severe and generalized dystonia. Still others never develop dystonia at all. The mismatch between dystonia genes and symptoms is also sometimes seen in identical twins, who by definition have the same genetic makeup. Despite the same genetic mutation, one twin may develop dystonia and the other may not. Alternately, the dystonia may appear differently in identical twins, such as one documented case in which one twin's neck twisted one way and the other twin's neck twisted the opposite way.[2]

One of the biggest challenges in determining which genes are linked to dystonia is that these studies require tissue samples from thousands of people in order to reach scientifically valid conclusions. Because dystonia is a rare disorder, it can take individual researchers decades to collect enough samples for study. Collectively, many researchers can agree to gather and share the precious genetic material from their patients to make research progress more quickly, provided patients agree to having their genetic material shared in this way. These large collections of genetic samples, stored at a central site to share among many researchers doing genetic studies, are called biorepositories, or biobanks. The information collected and stored within a biorepository is an incredibly valuable resource for scientific research now and for generations of future re-

searchers.

For people with dystonia who participate in a biorepository study, the type, extent and severity of dystonia is evaluated and a blood sample is collected and sent to the central repository location. Samples are not labeled with individual names, but rather with unique barcode identifiers. A biospecimen repository for primary dystonia has been established by researchers from Washington University School of Medicine in St. Louis Missouri and Emory University in Atlanta Georgia, and they are currently recruiting participants. Ultimately, this biorepository is expected to be critically important for finding genetic alterations or other biomarkers responsible for the development of different forms of dystonia. Additionally, the information collected will also look at the natural history of dystonia (patterns of progression over time).

Most of the dystonias for which genetic mutations have been identified are dominantly inherited, meaning that only one parent needs to have the mutation for a child to inherit the gene. It is important to remember, though, that not everyone who inherits a "dystonia gene" will develop symptoms. This is referred to as *reduced penetrance*. The following table lists some of the dominant genes that are associated with dystonias. Most of the gene names are scientific abbreviations used by researchers to identify the gene and the protein it encodes. Researchers are now trying to determine what role the various genes play in nerve cells and how mutations in them might be involved in dystonia. The PMDF is proud to have funded work related to some of these genes, including TorsinA and THAP1. For a more complete list, see Reference 1 at the end of this article.

Genetic tests are available for selected mutations associated with dystonias. However, many people with dystonia do not have any of the mutations discovered thus far. It is possible that these people may have a mutation that has not yet been discovered, or that the cause of their dystonia is not genetic at all. Researchers simply do not yet know. Recently, a commercial genetic test and health risk report was approved by the United States Food and Drug Administration. This test can tell if you have a certain mutation that is associated with a rare form of early-onset dystonia. However, dystonia itself is rare, and any given mutation rarer still. Additionally, we don't yet have any means to prevent or cure dystonia. Therefore, it is important for all of us to weigh the benefits and drawbacks of genetic testing. Importantly, a positive result from genetic testing is not a diagnosis. Even if you have a genetic predisposition for a disease such as dystonia, it doesn't mean you will develop symptoms. Nevertheless, people who obtain a positive result for a serious disease like dystonia should speak to their family physician or genetic counselor.

Examples of Some Dominant Genes Associated With Dytsonias[1]

Locus and disease	Gene
DYT1: Oppenheim's torsion dystonia	TorsinA
DYT5: Dopa-responsive dystonia	GCH1
DYT6: Craniocervical dystonia (Mennonite/Amish)	THAP1
DYT11: Myoclonus-dystonia	e-SG
DYT12: Rapid-onset dystonia-Parkinsonism	ATP1A3
DYT25: Cervical dystonia	GNAL

The reality is that the genetics of dystonia are complicated and there is no single gene responsible for all cases or types of dystonia. Genetic tests are not available for every form of dystonia. Most people who are diagnosed will not test positive for a currently known dystonia-causing mutation, and only a percentage of those who do will ever develop symptoms. The good news is that global scientific research efforts are ongoing to try to improve the understanding of origins of dystonia, and move toward more optimized, individualized treatments.

References

1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5237827/pdf/fneur-07-00241.pdf

2. https://medicalxpress.com/news/2012-03-id-gene-primary-cervical-dystonia.html

Zent-A-Thon 5K Walk/Run Fundraiser

The Parkinson's and Movement Disorder Foundation and The National Spasmodic Torticollis Association are hosting the 7th Zent-A-Thon 5K Walk/Run Fundraiser to raise funds and help spread awareness of Parkinson's and other movement disorders. The fundraising event will take place at Mile Square Park in Fountain Valley, California, on Saturday, June 10, 2017. This is a great opportunity to get outdoors with family and friends, support the two organizations, get some health benefits, and raise awareness. This will be a fun and friendly family event that everyone can enjoy. Kids under 12 do not need to pay the registration fee.

Prizes will be awarded to the 1st, 2nd and 3rd persons to cross the finish line. Prizes listed on next page.

All participants who paid the registration fee will automatically be entered in a raffle and have the opportunity to win gift card prizes ranging from $79.99 to $5. There are over twenty-five prizes being raffled off! In addition to winning prizes, registered participants will also receive lunch catered by Katella Deli Restaurant and Bakery located in Los Alamitos, a T-shirt, and beverages.

This year we are adding activities for kids, including a coloring and drawing area, and "beach volleyball" for kids. If there is an activity you would like us to add please contact us and we will see if it is feasible. This is a family event so we welcome any suggestions to make it more fun and entertaining for everyone.

We would like to give special thanks to the following companies for their generous sponsorships: Katella Deli Bakery and Restaurant, AbbVie, ACADIA Pharmaceuticals, Lundbeck Worldwide, Merz Inc., and US WorldMeds. We would also like to thank our new Treasurer, Gianni Truong in helping us to secure funding to continue this fun family event.

If you are in Orange County, LA County, or San Diego County, bring your family and friends and participate in the Zent-A-Thon! You can walk the 5K, run the 5K, or both. Street parking is available around Mile Square Park, meter-free. If you park your car on the grounds, parking is $5 per vehicle. You can register online by visiting http://www.pmdf.org/events.php or by mail using the form on the last page in the newsletter. If you are bringing a child (or children) under 13, please let us know so we can make sure food arrangements can accommodate everyone attending. Due to park regulations, registration cannot be processed at the park. Please register by June 5.

If you are unable to attend the event please consider helping us to promote the event and raise more awareness by promoting it on Facebook by liking the page and/or sharing the

page with your friends. The link is https://www.facebook.com/events/201581527015817/.

Zent-A-Thon 5K Walk/Run Fundraiser

Mile Square Park
Fountain Valley

Saturday, June 10, 2017
8:30 am: Sign-In
10:00 am: Race Start Time
11:00 am: Lunch Available

First Place Prize - 2 Disneyland Park Hopper Tickets
Second Place Prize –JumpSport Trampoline
Third Place Prize - 2 Knott's Berry Farm Tickets

Chance to win a prize in raffle drawing. Raffle prizes include: Complimentary Six Flags Magic Mountain Ticket, Katella Deli Gift Card, Amazon Gift Card, Starbucks Gift Card, iTunes Gift Card, Target Gift Card & More

$20 – per person to register
$5 – parking inside the park
Free – street parking
Lunch, T-shirt and beverages are provided for participants

Register online at: http://www.pmdf.org/events.php

Sponsors

5K Run/Walk
Saturday
June 10, 2017
8:30 a.m.

Movement Disorders
ZENT-A- THON

Mail-in registrations must be postmarked by June 5, 2017

Registration Form

NAME: _____

ADDRESS: _____

CITY: _____STATE:_____ZIP:_____

EMAIL: _____PHONE: _____

5K T-SHIRT SIZE (Circle One) Adult: M L XL Minimum age of entry 13

How many child/children you will be bringing under 13: _____ (free)

IN CASE OF RAIN: The race will proceed as planned. We reserve the right to change the date under extreme circumstances.

ADDITIONAL DONATIONS

Donations are tax-deductible and an acknowledgement letter will be sent to the donor for tax purposes

Contributor Information			
First Name	Last Name	Mailing Address	Amount

ENTRY FEE(S) OR DONATION

Entry Fee: $_____ ($20)

Donation: $_____

Total: $_____

My Employer has a Matching Gift Program: $_____

Please make check payable to NSTA

Visa ( ) MasterCard ( )

_____
Credit Card No.

_____
Expiration Date

_____
CVV Code (last 3 digit on the back of your card)

Mail Entry Form & Payment to:
NSTA
9920 Talbert Street
Fountain Valley, CA 92708
For more information call: 714-369-7426

RELEASE FORM (all registrations must be signed)

I hereby waive any and all claims against NSTA, PMDF, event sponsors, personnel, and all other persons, firms, corporations and/or entities or anyone associated with this event, their respective or successors, for any injury or claims for damages that I may suffer from participation in this event. I grant full permission for organizers to use photographs, videotapes, recordings or any other record for this event.

_____
Signature

_____
Date

_____
Signature of parent or guardian (if under 18 years old)

_____
Date

THE PARKINSON'S AND MOVEMENT DISORDER FOUNDATION
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OUR MISSION

To support basic and clinical research into the causes, treatments and cures for Parkinson's disease and other movement disorders such as dystonia, myoclonus, spasticity, and tremor.

The Parkinson's and Movement Disorder Foundation is committed to working with other organizations that have similar philosophies in an effort to bring together expertise from both basic and clinical science perspectives.

We are dedicated to enhancing the quality of life for those who suffer from movement disorders and their families, through research, education, and community outreach.