Dear WPC friends,

In April of this year we launched the WPC Blog and can see that clearly there was a need for this new facet of the WPC. Each weekly post, written by a past WPC presenter, committee member, or delegate, showcases the variety of work being done and ideas that are out there about Parkinson's research, care, and advocacy.

To date, we have had posts by basic scientists on c-Abl, LRRK2, genetics, and prevention of PD with some of our clinical experts choosing to write about personalized medicine and cell therapy. A few PwP authors have written pieces about resiliency and coming to grips with the reality of having PD. Just like the WPC, we believe there is value in diversity of opinions from all areas of the community, with strong representation from men and women who have been working in the field for many decades. We also like to highlight our up and coming experts who we hope will stay committed to the Parkinson's community for many years to come.

If you haven't visited the WPC Blog yet, take a sneak peak below at the post by Matthew Farrer, PhD on genetics and Parkinson's and be sure to sign up to get notified each time we put up a new blog post. 2019 These posts are designed to keep you "in the know" on some key Parkinson’s topics and to wet your appetite for the kinds of sessions we will offer at the WPC in Kyoto, Japan in June 2019.

We hope you will be inspired to join us in Kyoto!

Kind regards,

Elizabeth "Eli" Pollard
Executive Director

WPC Blog Highlight

To Predict And Prevent
When you have a problem, it’s best to remedy the cause rather than the symptoms....otherwise any fix will be temporary and could lead to more problems. In Parkinson’s disease (PD) we currently have medications for ‘symptomatic benefit,’ but none that slow or halt disease progression. Clinical trials of new medications, largely informed by toxin-induced models of disease, have failed. Dopamine replacement therapy remains the best drug to help with movement initiation, but many motor and non-motor features remain. Its benefits are also temporary; increased doses of medication are required to prevent ‘wearing off’ and can result in dyskinesias.

So how can genetics help? Consider a car’s engine as an analogy for PD enabling the car’s motion. When the engine doesn’t start, or fails to work optimally, it’s best to do some diagnostics. Is it the distributor, the battery, the spark plugs etc? Although the physiology of cortical-striatal-midbrain (nigral) circuits in PD is well described, our knowledge of underlying cellular and molecular problems...the smaller parts of the engine...and why some get PD and others are spared...is rudimentary. Genetic research can fill this gap.

Although funding agencies/industry invest huge amounts in clinical trials in PD, given the promise of great return, they had scant knowledge of its molecular cause(s). Nevertheless, to predict and prevent disease i.e. for pharmaceuticals to be neuroprotective, they should target the cause. In early 1997, when I started my career, ‘prevailing wisdom’ suggested genetic analysis in PD was a futile endeavor. It had long been described as a sporadic disease, due to environmental exposures rather than genes, despite ~14% of patients having an affected first-degree relative. Disease concordance in monozygotic twins was quite low/negligible. Nevertheless, health and disease are biological traits and must have some genetic contribution.

At that time I had just joined Mayo Jacksonville where Dr. Manfred Meunter, formerly Chair of Neurology at Mayo Scottsdale, told me of a family with multi-incident parkinsonism-dementia, first seen at the Clinic in the early 1920’s. With a little reading I became aware of many other families in which PD appeared as a heritable trait, passed from one generation to the next. In 1880, 1883, Charcot, the grandfather of French neurology, encouraged and supported two of his students to study familial ‘paralysis agitans’. Allen, 1937, working in the Carolinas, identified and published many pedigrees with multi-incident PD. In 1940, Henry Mjones documented familial parkinsonism throughout Sweden etc.
Thus, one dark, rainy winter’s evening, I came to meet members of the Spellman-Meunter kindred, (named after the neurologists who had first described the family’s plight). I wanted the family's blood for DNA studies, their clinical data and most importantly their approval to find the gene I thought may be responsible for their disease. Anguished sobbing came from within the house as a couple of biker’s swiftly answered the door. The ‘angels’ barked at me to go out back where I learnt they had been running from parkinsonism-dementia, ‘the bug’, for generations. They had been told the cause was environmental. Their mum was crying, helping to care for her ~30 year old son while his young children...the next generation... played on the floor. She had lost her husband in the same circumstance, to the same malady, 30 years prior. It was tragic. In this family, parkinsonism starts in the fourth decade and leads to dementia and ultimately death within about a decade. That night I made a first promise to find the cause and figure out a remedy.

It took several more years of painstaking research, fieldwork to track down relatives throughout the US, genotyping and linkage analysis. Finally, despite the early pessimism of the field and grant funding agencies, we discovered alpha-synuclein (SNCA) multiplication as the cause. Most people have 2 copies of the gene (human beings are diploid, one set of chromosomes from Dad, one set from Mum) whereas clinically affected members of this family had 4 SNCA copies. We discovered more families with parkinsonism due to 3 SNCA copies, albeit with a less aggressive, later-onset phenotype. Indeed, in work begun by Henry Mjones in the 1930s, in the best described SNCA multiplication family, we found patients with 4 copies who developed early-onset parkinsonism and those with 3 copies who had late-onset parkinsonism. In human brain we showed SNCA genomic copy number, gene and protein expression levels were correlated. We also appreciated that common variability throughout SNCA is a modest a risk factor for sporadic PD, for its motor progression and for subsequent dementia.

**Where is Parky?**
by Kirk Hall, WPC 2019 Blogger

Hi everybody! This is Parky the Raccoon comin’ at ya’ from the “Far Out!” west! I am lovin’ tent camping with my new family and their collection of little critters (they call them grandchildren) in the many scenic campgrounds, state and national parks (or parkies, as I like to call them). However, I do NOT like the bears! They are totally rude, plus they smell awful! I can see why so many people are high on life (and other things) out here! We have been going to church quite a bit (I have been prayin’ that I will see many of you at the 5th World Parkinson Congress in Kyoto, Japan, also known as the WPC 2019.

**Did you know you could subscribe to the WPC Blog?**

In between our triennial Congresses we are constantly searching for new ways to keep the Parkinson’s community connected and give everyone access to the latest research. As we looked around at the Parkinson’s blogosphere we realized that we had a unique perspective to offer. By approaching a number of presenters and committee members from past World Parkinson Congresses and asking them to write about the topics that inspire them and which they feel are the most important to the community, we can present to you insights from the front lines in the fight against Parkinson’s.

Since the blog was launched, we have had posts from:
My favorite hymn is “Little Brown Church in the _____ (sorry, you are going to have to fill in the blanks). Can you guess what state I’m in? Any of you Parkies who guessed confusion, my new Parkie buddy here in ________ says he knows “whence you speak”.

By the way, any of you “farm animals” who think I should have included “from” before “whence”, see http://grammarist.com/usage/whence-from-whence/.

. . . . just to name a few.

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