

Australian researcher outlines an integrated approach for studying Parkinson's

By Simone Otto

So often in science, researchers are limited by knowing only one piece of a much larger puzzle, such as Parkinson's disease (PD). Even if it is a fascinating piece, it rarely reveals how the whole picture may look.

In his Keystone Science Lecture Nov. 4 at NIEHS, Australian clinical neuroscientist [George Mellick, Ph.D.](http://www.griffith.edu.au/professional-page/associate-professor-george-mellick), (<http://www.griffith.edu.au/professional-page/associate-professor-george-mellick>)

discussed his work with "The Queensland Parkinson's Project: An Interdisciplinary Approach to Studying Parkinson's From the Population to the Lab," outlining a method for investigating Parkinson's that promises to put the pieces together. "It's very hard to model the entire human picture," he said, pointing to the value of integrating the strengths of human, animal, and cell-line models.

Mellick, an associate professor at Griffith University in Australia, has spent more than 10 years studying PD. Over this time he helped establish Parkinson's Queensland, a non-profit organization that oversees a study with more than 4000 participants, approximately half of whom have been diagnosed with PD, and also funds research, with a vast representative cohort for population studies.

Mellick began his presentation with a little history, referring to descriptions of a shaking palsy disease called *Kampavata* seen in Ayurveda texts dating back to 2000 BCE and earlier, which clearly described Parkinson's disease many hundreds of years ago. Interestingly, ancient plant-based treatments included seeds that contain *leva-dopa*, which is still the mainstay of PD motor symptom management, pointing to the value of understanding nature and valuing the insights of older and different medical systems.

Mellick's talk was hosted by Jonathan Hollander, Ph.D., a program administrator in the NIEHS Genes, Environment, and Health Branch.

Creating feedback loops to advance research

Eskitis Institute, where Mellick is deputy director, is home to Nature Bank, a repository for thousands of optimized natural product fractions; Compound Australia, which stores some 600,000 compounds from Australian chemists; and Neuro Bank, which maintains human cell lines. These resources afford researchers the opportunity to screen a vast number of compounds with omics testing and understand their relationship to PD.

When this knowledge feeds back into population analysis via the Queensland Parkinson's Project, it creates a positive feedback loop in Mellick's research, with lab experiments informing



Shunning the podium, Mellick entered the audience space to deliver a more intimate presentation on his work. (Photo courtesy of Steve McCaw)



Hollander, center, said he was grateful for the opportunity to hear more about the Queensland Parkinson's Project. He took advantage of Mellick's visit to NIEHS for the large PD meeting Nov. 3-4 to schedule the talk. (Photo courtesy of Steve McCaw)

population studies and data from clinical and population studies refining lab experiments. This bidirectional process supports studies in how genes and the environment interact with the aging process and how this interaction leads to the disease.

Mellick gave listeners many interesting examples of the value of this approach. Population research includes gene-hunting for rare forms of inherited PD, which directs research through unbiased discovery of genes linked to Parkinson's of which there had been no *a priori* knowledge, as well as genetic risk factor analysis for cases with no clear genetic link.

Building on genome-wide analysis to drive cell-line experiments

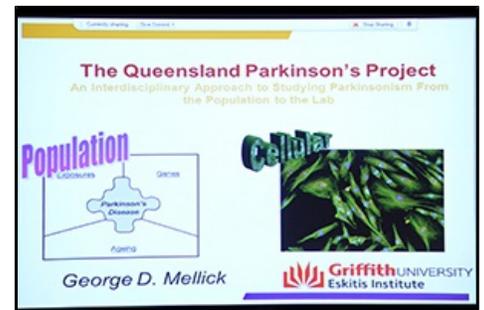
Once genetic analysis has connected a gene to the disease, Mellick uses pharmacology to study the protein in human olfactory neurosphere-derived cells (hONS) obtained from people with monogenetic PD in the Queensland Project. Because neurons in PD patients display an aberrant response to stress and toxins unique to these cells, hONS cells provide a human neural-specific way to quickly and effectively study proteins suggested by genomic studies.

This integrated research has led to the discovery of several interesting molecules that are currently being researched, including alpha-synuclein, leucine-rich kinase 2, vacuolar protein sorting-associated protein 35, and nuclear factor (erythroid-derived 2)-like 2, and will likely continue to generate a plethora of clues to how genes and environment interact with small molecules within the cell, ultimately leading to PD.

(Simone Otto, Ph.D., is an Intramural Research and Training Award fellow in the Ion Channel Physiology Group at NIEHS.)



A number of Hollander's colleagues in the NIEHS Division of Extramural Research and Training (DERT) turned out for the talk, including Mike Humble, Ph.D., and DERT Deputy Director Pat Mastin, Ph.D. (Photo courtesy of Steve McCaw)



Mellick's opening slide was a graphic representation of his integrated approach to studying PD. (Photo courtesy of Steve McCaw)

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