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Van Andel Research Institute expands into new areas of Parkinson's research

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Van Andel Research Institute (VARI) is continuing the expansion of its neurodegenerative disease research program, which aims to answer fundamental questions about diseases such as Parkinson's and Alzheimer's, with the addition of two outstanding scientists.

Gerhard (Gerry) Coetzee, Ph.D., and Viviane Labrie, Ph.D., will join the Center for Neurodegenerative Science in November and March, respectively. They will utilize cutting-edge techniques to uncover the molecular underpinnings of Parkinson's and Alzheimer's, helping to pave the way to new therapies that slow, stop or reverse disease progression. Their expertise in molecular biology, genome-wide association studies (GWAS) and epigenetics offer novel insight for investigating these diseases and augmenting research already underway at the Institute.

Epigenetic marks play an important role in determining whether a gene is switched "on" or "off," and can contribute to disease development and progression. Neuroepigenetics, or epigenetic modifications in the brain, have been linked to functions such as learning, memory and stress responses, and have been implicated in several neurodegenerative diseases.

"There is great potential for epigenetics to revolutionize our understanding of how neurodegenerative diseases occur and progress," said VARI's Research Director Peter Jones, Ph.D., D.Sc. "This knowledge is critical for the development of new treatment options. We are thrilled Dr. Coetzee and Dr. Labrie are joining our team."

Shifting the paradigm

It's still not clear why people develop Parkinson's. Scientists know genetics play a role in less than 10 percent of Parkinson's cases. The remaining majority of cases occur sporadically with no known cause, although scientists suspect a combination of genetic, epigenetic and environmental factors may be involved.

Neuroepigenetics offers a new approach to uncovering the origins of Parkinson's, a key step in developing better ways to diagnose and treat the disease and improving the quality of life for the seven to 10 million people around the world with Parkinson's.

"There is a strong sense in the global Parkinson's community that we're on the edge of a paradigm-shifting change in how we diagnose and treat the disease," said Patrik Brundin, M.D., Ph.D., director of VARI's Center for Neurodegenerative Science. "When it comes to the 10 percent of cases that are inherited, we largely know which genes are involved. The addition of Dr. Coetzee and Dr. Labrie's expertise will significantly strengthen our existing multidisciplinary team and help us understand how genetic risk factors play a role in the remaining 90 percent of cases, and why some people develop Parkinson's disease while others with a similar genetic makeup do not."

Linking pieces of genetic code to Parkinson's

Genome-wide association studies, or GWAS, is a method that links pieces of the genetic code to physical traits, allowing scientists to narrow down regions of the genome that may be associated with a particular disease. Although dozens of these pieces of code variations —called SNPs—are linked to Parkinson's, it is difficult to know precisely how they influence disease risk. It also is challenging to define exactly which

gene each SNP influences; although it's easy to assume a particular SNP affects a nearby gene,it is possible that the culprit actually is a gene that is located farther away.

As a VARI professor, Coetzee will use GWAS and post-GWAS functional characterization to determine which SNPs truly are associated with the risk of developing Parkinson's and how they are linked to disease onset. Much of this work will utilize FunciSNP and motifbreakR, computer software tools developed by Coetzee's team that integrates GWAS data along with other genomic and epigenomic information to differentiate functional SNPs from non-functional ones. Coetzee's work could provide a roadmap for the development of genomically based diagnostics for Parkinson's as well as more targeted and effective therapies.

"Genome-wide genetic associations with complex diseases are at the forefront of modern genetics," Coetzee said. "This has become topical after the human genome was sequenced and the unexpected realization was made that most of our genome does not code for proteins but rather how their expression levels are regulated. The uncovering of such regulatory genetic lesions in the genomes of people with Parkinson's will not only lead to a better understanding of the etiology of the disease but also to the development of therapies slowing or halting the disease."

Coetzee has more than 30 years of experience in molecular biology and human genetics and most recently served as a professor at University of Southern California's Norris Comprehensive Cancer Center. He has made several discoveries in the fields of prostate and breast cancer, and has contributed significantly to functional characterization of GWAS data and the understanding of how cancer risk factors actually operate. He plans to continue this work in parallel with his Parkinson's disease research.

Linking faulty gene regulation to Parkinson's and Alzheimer's disease

Labrie will study epigenetic processes involved in healthy brain function as well as in disease, and explore the complex interplay between genetic and epigenetic features by integrating GWAS and epigenome-wide association studies (EWAS). She aims to identify abnormally regulated regions of the genome and investigate how these contribute to the two most common neurodegenerative diseases—Alzheimer's and Parkinson's. These studies will provide a better understanding of the underlying causes of these diseases and reveal new opportunities for early diagnosis and treatment.

"Epigenetics may be an important crossroad for both genetic and environmental risk factors for Alzheimer's and Parkinson's diseases," Labrie said. "We know that epigenetic marks are central to the function of healthy brain cells, yet do change within an individual over time and in response to environmental triggers. The accumulation of these changes with age could be important in Alzheimer's and Parkinson's, both of which occur later in life."

She currently is an assistant professor at University of Toronto and a project scientist in the Krembil Family Epigenetics Laboratory at the Centre for Addiction and Mental Health. Labrie was among the first to characterize the role of a novel neurotransmitter in the brain and its role in schizophrenia. She also created a new method for mapping epigenetic marks, and has contributed extensively to the field's understanding of a particular mark called 5-hydroxymethylcytosine and its impact on brain function.

Provided by Van Andel Research Institute