manitoba neuroscience network

# Investigating pathogenic human CDK19 variant functions in Drosophila reveals insight into normal and disease mechanisms of Cdk8/19 family proteins.

SEMINAR & VISITING SPEAKER SERIES

DATE

Tuesday, June 27th, 2023

TIME

2:00 PM to 3:00 PM

LOCATION

Basic Medical Sciences: Theatre B

SPEAKER


## Esther Verheyen, PhD

Professor, Department of Molecular Biology and Biochemistry, Simon Fraser University. Co-Director, Centre for Cell Biology


BIO

Dr. Esther Verheyen, is a Professor in the Department of Molecular Biology and Biochemistry, Simon Fraser University and Co-Director of the SFU Centre for Cell Biology, Development & Disease. She is also Chair of the CIHR Institute of Genetics Advisory Board. Dr. Verheyen earned her BA at Cornell University, and completed her PhD in Genetics at Yale University School of Medicine with Dr. Lynn Cooley studying profilin function in Drosophila development. She carried out postdoctoral studies with Dr. Spyros Artavanis studying Notch signaling. She joined the faculty at Simon Fraser in 1998. In 2016 she was awarded the 'Grant and Moens Award of Excellence in Genetics' from the Canadian Society for Molecular Biosciences (CSMB).


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ABSTRACT


My research involves studying how cells grow and differentiate to form properly patterned organs and tissues and how these tissues are maintained through the life of the organism. We study proteins that are highly conserved between humans and model organisms. Our research has focused on using Drosophila and mammalian cell culture to elucidate molecular mechanisms controlling signal transduction and cellular homeostasis. The protein interactions and cellular processes we investigate have direct parallels in humans and are implicated in human diseases, such as cancer, developmental disorders and neurodegenerative diseases. Research in the fruit fly has been at the root of many key discoveries that have led to medical breakthroughs and to understanding human disease etiology. In my research program I have adapted to the shifting paradigm in research priorities by guiding my research into the study of human proteins implicated in disease.

We have extensively studied the function of the Homeodomain-interacting protein kinase (Hipk) in development, signaling and in a Drosophila tumour model. In our studies of Hipk in tumorigenesis we gained valuable skills in characterizing mitochondrial dynamics and regulation. Recently we have also used Drosophila to identify distinct functions of the four human HIPK orthologs. We also described that loss of Hipk can affect the neuromuscular function in Drosophila. Investigating a genetic link between Hipk and other kinases led to our discovery that the Cyclin-dependent kinase 8 (Cdk8) plays a critical role in neuromuscular health and that loss of Cdk8 causes abnormal motor skills (failures in flight and climbing assays) and that this is accompanied by changes in mitochondrial form and dynamics and muscular degeneration.

These effects have not been previously reported and provide a compelling link between Cdk8 and Parkinson's Disease (PD). We found that expression of Cdk8 in flies carrying a mutation in Pink1, a gene implicated in familial early onset PD, reversed the locomotor impairment, muscle degeneration and mitochondrial defects found in PD flies. We also have preliminary data that suggest a mechanistic link between lipid droplet formation and mitochondrial defects and neuromuscular degeneration in PD, which we seek to investigate. The strength of our approach is that we can use the genetically tractable and well characterized Drosophila system to investigate new areas of research that are directly relevant to PD. Our past track record highlights that we can gain valuable and impactful insight into biology of development and disease using these approaches and that we have the molecular, cell biological and biochemical tools to investigate genetic interactions in depth. Drosophila studies into PD mechanisms, in particular the role of mitochondrial dynamics, have shaped our understanding of PD and we believe our work linking Cdk8 to PD mechanisms will open new areas of research and therapeutics.


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