# BBB Seminar (BMED382)

SCAN ME

Thursday, February 12. 14:30 at the BBB, Auditorium 4

## Human iPSC-based models for understanding disease and developing new therapies

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Mitochondrial dysfunction underlies many human diseases, especially neurodegenerative and metabolic disorders. Of these, POLG-related disease is one of the most common hereditary mitochondrial disorders, caused by mutations in the gene encoding mitochondrial DNA (mtDNA) polymerase, the enzyme responsible for mtDNA replication and repair. Defective POLG activity leads to mtDNA depletion, OXPHOS complex deficiency, and progressive bioenergetic failure, with devastating effects on energy-dependent organs such as the brain, muscles, and liver. Yet the reasons for this selective vulnerability and the mechanisms of disease progression remain unclear, partly due to the lack of suitable human disease models.

In this talk, I will describe how human iPSC-based models can be used to study POLG-related mitochondrial dysfunction and identify treatment strategies. By using patient-derived neural stem cells, dopaminergic neurons, and brain organoids, we can recapitulate critical aspects of the human disease, including mtDNA instability, defects in OXPHOS function, increased oxidative stress, and alterations in the stress response. Human cell-based models allow mechanistic studies to be performed in disease-relevant cell types and can also assess genotypic specificity of the disease phenotype.

Finally, I will present how iPSC-derived cellular systems can be combined with functional readouts and drug screening strategies to identify compounds that improve mitochondrial function and neuronal cell survival. Together, these approaches demonstrate the potential of human iPSC-based models to connect fundamental studies of mitochondrial biology with impactful studies aimed at identifying therapies for mitochondrial and neurodegenerative diseases.

Chairperson: Karl Johan Tronstad, Department of Biomedicine