

BCHM 421/422 Project – 2023-24

Project 2 Outline: Parkinson's disease (PD) is a common neurodegenerative condition that involves protein aggregation and loss of dopaminergic cells in the brain. Most commonly alpha-synuclein aggregates and accumulates in lipid vesicles in PD. We are studying how this aggregation can be controlled in vitro and in cell cultures. We will grow human cells as well as induced pluripotent stem cells, differentiate them to neurons and then treat them with aggregated alpha-synuclein and various lipids in lipid vesicles. Cell degeneration will be assessed, and growth factors will be used to regenerate cells. These studies are hoped to identify specific lipids involved in protein aggregation and to develop methods to prevent neuronal degeneration.

Supervisor: Inka Brockhausen

Project Title: Role of lipids in alpha-synuclein aggregation

Project Goals: To define factors that lead to protein aggregation in Parkinson's disease

Experimental Approaches: Protein analysis, alpha-synuclein aggregation, stem cell cultures, cell differentiation, preparation of lipid vesicles, transfection of neuronal cells, assessment of cell proliferation, degeneration and regeneration.

References:

Brockhausen I, Schutzbach J, Wang J, Fishwick B, Brockhausen J. Glycoconjugate journal special issue on: the glycobiology of Parkinson's disease. *Glycoconj J*. 2022 Feb;39(1):55-74. doi: 10.1007/s10719-021-10024-w.

Tanudjojo B, Shaikh SS, Fenyi A, Bousset L, Agarwal D, Marsh J, Zois C, Heman-Ackah S, Fischer R, Sims D, Melki R, Tofaris GK. Phenotypic manifestation of α -synuclein strains derived from Parkinson's disease and multiple system atrophy in human dopaminergic neurons. *Nat Commun*. 2021 Jun 21;12(1):3817. doi: 10.1038/s41467-021-23682-z.

Doi D, Magotani H, Kikuchi T, Ikeda M, Hiramatsu S, Yoshida K, Amano N, Nomura M, Umekage M, Morizane A, Takahashi J. Pre-clinical study of induced pluripotent stem cell-derived dopaminergic progenitor cells for Parkinson's disease. *Nat Commun*. 2020 Jul 6;11(1):3369. doi: 10.1038/s41467-020-17165-w.

Galvagnion C. The Role of Lipids Interacting with α -Synuclein in the Pathogenesis of Parkinson's Disease. *J Parkinsons Dis*. 2017;7(3):433-450. doi: 10.3233/JPD-171103.