

Project 1.10. Comparative analysis of synaptic architecture in human neurodegenerative disorders

Supervisor: Dr. Oleg Glebov

Laboratory: Synaptic Plasticity and Disease

Background:

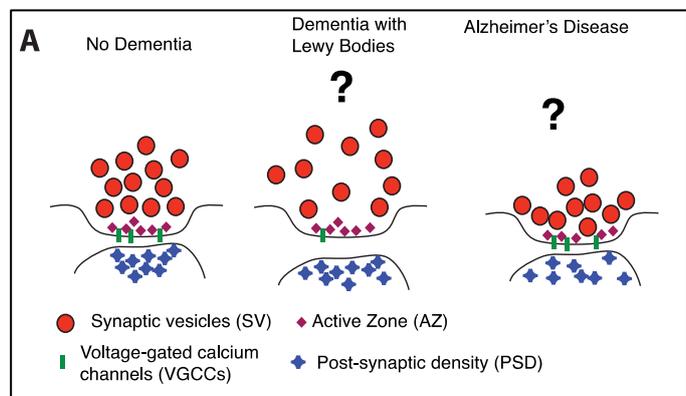
Synapses are complex specialized contact zones between neurons, which allow neurons to transmit information across the central nervous system. Although dysregulation of synapses is strongly implicated in neurodegenerative disorders such as dementia in its various forms^{1,2}, the synaptic molecular events associated with neurodegeneration remain poorly understood.

Aim:

This project will take advantage of a unique resource of human post-mortem brain samples available from the UK Brain Banks Network³. Preliminary data shows that the two most prevalent forms of dementia – Alzheimer’s disease (AD) and dementia with Lewy bodies (DLB) – may be associated with gender-specific and disease-specific changes in the nanoscale synaptic structure in the human brain (see Figure). Accordingly, the 1st aim of this project will be a detailed comparative investigation of synaptic architecture comparing healthy controls and subjects with AD and DLB, using advanced light microscopy and biochemistry.

Furthermore, one or more of the following secondary aims may be considered:

- 1) Analysis of synaptic architecture in animal models of human neurodegeneration;
- 2) Investigation of synaptic dysregulation in other human disorders of the central nervous system, i.e. developmental disorders, psychiatric disorders, and addiction;
- 3) Analysis of human synaptic architecture to identify age-dependent synaptic changes.



Requirements:

Essential:

- fluent English,
- ability to work independently,
- general laboratory skills,
- previous experience with light microscopy and image analysis.

Desirable:

- good grasp of statistical methods, Programming skills.

References:

1. Sheng, M., Sabatini, B. L. & Südhof, T. C. Synapses and Alzheimer's disease. *Cold Spring Harb. Perspect. Biol.* 4, (2012).
2. Berezki, E. et al. Synaptic markers of cognitive decline in neurodegenerative diseases: a proteomic approach. *Brain* 141, 582–595 (2018).
3. UK Brain Banks Network - Research - Medical Research Council. Available at: <https://mrc.ukri.org/research/facilities-and-resources-for-researchers/brain-banks/>. (Accessed: 9th July 2020)