Project Title: Developing single-stranded DNA sequencing technologies using unique molecular barcoding	**Code: CCS1**

Host School / Institute: Central Clinical School

Address: 100 Mallet St, Camperdown, NSW, 2006

Certificates & Clearances required: No

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Co-Supervisor/team: Neurogenetics and Epigenetics Research Group consists of a mixture of wet-lab based molecular and cellular biologists as well as dry lab based bioiformaticians

Project Type: Laboratory based; Data Analysis

Project Category: Genetics; Molecular biology

Skills / Attributes of a successful student: Students having some wet-laboratory experience and fundamental understanding of genetics would be advantageous but not essential.

Project Keywords: DNA; Dementia; Neurodegeneration; Genetics; Epigenetics

Project Description: Next generation sequencing (NGS) technology produces enormous amounts of single-molecule data that is theoretically capable of detecting rare nucleic acid differences, such as the detection of somatic mutations or rare fragments of cell-free DNA (cfDNA). However, due to intrinsic errors within NGS data production such applications are prohibitive. However, using uniquely barcoding (UMI) of single-stranded DNA (ssDNA) molecules enables sequencing error correction and analysis of rare DNA molecules in large background.

This project aims to develop techniques to produce ssDNA UMI sequencing libraries that are capable of investigating rare genetic and epigenetic (DNA methylation) events such as somatic variation and cell-free DNA methylation analysis. The project aims to produce ssDNA UMI sequencing libraries from Frontotemporal Dementia patients positive/ negative for the C9orf72 repeat expansion, that has been shown to exhibit somatic variation, as well as the analysis of cfDNA methylation within these patients to identify brain-derived cfDNA (cell-of-origin detection).