### Research Theme

*Neuroscience and Mental Health*

### Research Project Title

Evaluating somatic mosaicism in diseased brain tissue

### Principal Investigator

Foo Jia Nee

### Project Description

There is increasing evidence to suggest that somatic mutations that occur during post-zygotic cell division may predispose to neurological disorders. Moreover, age-related somatic mutations have been shown to influence cancer and aging, and have also been postulated to play a role in neurodegeneration. Such mutations may disrupt genes that are crucial during the early stages of embryonic development and hence may never be seen in the germline because of negative selection. The degree of mosaicism may also underlie variation in disease severity and age of onset.

In collaboration with the Imperial College Parkinson’s disease brain bank and the upcoming LKCMedicine/National Neuroscience Institute brain bank, we will analyze post-mortem brain tissue from deceased patients that have previously been diagnosed with neurodegenerative diseases such as Parkinson’s disease, Alzheimer’s disease and Lewy Body Dementia as well as from healthy controls. We will attempt to detect somatic mutations at high sensitivity using the latest single-cell genomic technologies at the Genome Institute of Singapore, A*STAR. With this data, we will test the following hypotheses:

1. Are there genes being recurrently disrupted by mosaic mutations that are enriched in the site of pathology of patients but are undetectable (or only detectable with much higher sequencing coverage) in the blood? Newly-identified genes will be followed up functionally in animal and cell models.

2. Are there age-related somatic mutations and other genomic insults that have accumulated at the site of pathology of patients, that may be associated with disease development?

### Contact Us

If you have questions regarding this project, please email the Principal Investigator.

Foo Jia Nee, PhD
Nanyang Assistant Professor
+65-6808-8259
jianee.foo@ntu.edu.sg