**Research Theme** (Please indicate as appropriate)

| ☐ | Dermatology & Skin Biology | ☐ | Family Medicine & Primary Care |
| ☐ | Health Systems & Population Health | ☐ | Infection & Immunity |
| ☐ | Metabolic Disorders | ☒ | Neuroscience & Mental Health |
| ☐ | Medical Education | ☐ | Others (Please specify): |

**Research Project Title:**

**Distinguishing early mechanisms of ApoE4 contributions to risks of late life neurodegeneration**

**Project Description:**

The brain’s structure and function distinguish individually distinctive “fingerprints”, but also change throughout life in ways that reflect disease risk. Brain structural features are highly heritable. Differences in functional magnetic resonance imaging (fMRI) measures are found in many diseases, but have been more difficult to relate to genetic variation because of their complexity. However, with integration of data from both imaging (MRI, fMRI) and electrophysiology (magnetoencephalography, electroencephalography) distinct contributions from the ways in which the brain’s vascular structures respond and neuronal activity can be distinguished and related to differences in brain structure. This may allow genetic correlations to be discovered. The advanced facilities at LKC Medical School provide an internationally competitive environment for supporting this still very novel research.

The project will involve developing a memory testing paradigm that can be used for studies of both fMRI and MEG (or EEG) in healthy volunteers. Volunteers who carry protective or Alzheimer's risk apolipoprotein E genes (heterozygotes and homozygotes) will be studied serially with the three methods. Previous work from co-supervisor Matthews' laboratory found significant fMRI signal differences with ApoE4 gene carriers that appeared to be due in large part to differences in the functions of brain blood vessels (neurovascular coupling). By comparisons of fMRI studies conducted under different conditions and the electrophysiological measures, this can be tested directly.

The project will provide excellent training in a broad range of advanced clinical biomedical imaging methods and in their quantitative analyses. It will test a novel potential mechanism of Alzheimer’s disease risk and explore new ways in which treatments addressing similar disease mechanisms might be targeted. The PhD training could suit an individual with a psychology, bioengineering, physiology or biomedical background.
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<th>Brief summary of main Methodologies and/or Techniques to be learned during the proposed PhD (experimental or analytical):</th>
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<td>Keywords:</td>
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### Supervisor(s)

#### Primary Supervisor
- **Name of Supervisor:** Balazs Gulyas  
  **Designation:** Professor  
  **Email:** balazs.gulyas@ntu.edu.sg

#### Co-Supervisor *(need not be determined at this time)*
- **Name of Supervisor:** Paul Matthews  
  **Designation:** Professor, Imperial College London  
  **Email:** p.matthews@imperial.ac.uk

### Main Location of Research Work *(Please indicate as appropriate)*

- ☒ LKCMedicine Experimental Medicine Building @ Yunnan Campus  
- ☐ LKCMedicine Clinical Sciences Building @ Novena Campus  
- Others *(Please specify)*: Imperial College London

### Other Information

1. Does the proposal need IRB’s approval?  
   - ☐ Yes  ☐ No
   - If “Yes”, is the IRB’s approval in place?  
     - ☐ Yes  ☐ No
2. Does the project involve contact with patients?  
   - ☐ Yes  ☐ No
3. Is there a potential for overseas academic exchange as part of this research project?  
   - ☐ Yes  ☐ No
   - If “Yes”, please specify: ____________________________________________