PI profile

## Zameel Cader

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|  | **Professor Zameel Cader**  **Titles**: Head of Translational Molecular Neuroscience Research Group, Consultant Neurologist, Lead for IMI IM2PACT  **Location**: Weatherall Institute of Molecular Medicine  **Department**: Nuffield Department of Clinical Neurosciences  **Group**: Cader  **Webpage**: <http://im2pact.org/>  <https://www.ndcn.ox.ac.uk/research/translational-molecular-neuroscience-group>  **Email**: zameel.cader@ndcn.ox.ac.uk |

### GMS themes:

[Please retain any that describe your research, deleting others:]

* Genomic and –omic technologies
* Functional genomics
* Genome biology (genomes and genetic variation)
* Genomics of disease
* Genomic analysis (bioinformatics and statistical genetics)
* From genes to clinic (target discovery, structural biology, medicinal chemistry)
* Application of genomics in the clinic (diagnostics and therapeutics)

### Research Overview

The Cader laboratory focuses on target discovery and therapeutics in neurological disorders using human-centric approaches. We work extensively with human cellular disease models derived from induced pluripotent stem cells (iPSC) and complement this with mouse models. Our major disease areas of interest are migraine and pain, autism and dementia. These are major diseases of our time for which drug therapies are limited and drug discovery in this field is very challenging due to lack of access to human cells. We have developed unique methods to generate human cell types and investigate disease relevant phenotypes. Recently we have been investigating circadian mechanism in pain and as an opportunity to develop ‘chrono-medicines’.

We have conducted compound and CRISPR/Cas9 cell phenotypic screens with iPSC disease models to identify currently available that might be repurposed as therapeutics and to reveal disease mechanisms. This has been combined with single cell RNA sequencing of iPSC models and human neuronal tissue to discover cell types relevant to neurological disease processes. Using advanced chemo-proteomic methods such as photo-affinity probe pull-downs, our lab is identifying novel drug targets.

The development of a successful central nervous system therapy requires penetration across the blood-brain-barrier. A major program in our lab is to develop better models of the blood-brain-barrier and understand how this might be disrupted in disease. We are using transcriptomics and proteomics to interrogate the barrier in human surgical and post-mortem brain tissue. We are also developing novel iPSC protocols to produce brain endothelial cells.

Project areas: Human iPSC disease models, phenotypic screens, single cell RNA sequencing, CRISPR/Cas9 technology, target discovery and validation

### Specific project proposals:

* ‘The role of the mTOR pathway in neurological disease. The mTOR pathway is a major cellular signalling pathway regulating cell cycle, protein translation, response to inflammation and for neuronal function. We have completed a CRISPR/Cas9 screen and have identified important regulators of this pathway that now need deeper exploration in our iPSC neuronal tissue models. The project will involve investigating candidate mechanisms in depth using further genetic and pharmacological manipulation and assessing the effect on cellular and molecular phenotypes using single cell omics approaches and electrophysiological assays such as calcium imaging and multi-electrode arrays.’

Please contact directly for further information.

*These pages were reviewed/updated:* ***[insert date]***

Project proposal

# **Title**: **[Project title here]**

Supervisors: [name and title of relevant individuals]

Wet/dry lab mix (approx): X% wet lab, X% dry lab

### Description:

[Write a ~ half-page page description of the project here].

### Training Opportunities:

[Write a brief description of the training opportunities the project will provide].

### Background reading / references:

Please include references as desired. Suggested format:

* [Surname] [Firstname], [other authors]… **(year in bold)** . [Title]. [Journal name], [other details]. Available at: [link]

Insert any additional project description(s) on subsequent pages if applicable. Please use the same template and use separate pages for each project.