Title: *Experimental and computational modelling of hippocampal neurogenesis and neuronal maturation using human induced pluripotent cells*

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The hippocampal dentate gyrus is one of two areas in the CNS where neurogenesis occurs throughout life. Defects in neurogenesis have been implicated in the pathogenesis of epilepsy, dementia, and mental illness.

Long-lasting neural progenitor cells in the subgranular zone (SGZ) of the DG generate new neurons (granule cells) which progressively mature as they migrate away from the SGZ, acquire greater dendritic complexity and integrate into existing hippocampal circuitry. This integration is critical to their role in learning and memory. Recently, hippocampal neurogenesis in the DG has been modelled *in vitro* using human induced pluripotent stem cells (hiPSCs).

We have identified genes that regulate neuronal maturation in the DG, which influence neuronal migration and dendritic complexity in other model systems (mouse, worm) and regions of the CNS (cortex). The aim of this project is to model human hippocampal neurogenesis using iPSCs and determine how these genes influence neuronal maturation, migration and dendritic complexity. We will create computational models from experimental data of dendritic outgrowth versus branching, and generate predictions of the impact of genetic mutations that can be tested experimentally.

This project is uniquely cross-disciplinary and capacity building at the interface between stem cell and molecular biology, computational neuroscience and clinical medicine. It will capitalize on the internationally renowned expertise of stem cell biologists and computational neuroscientists at the Universities of Bristol and Exeter. The University of Bristol's Bioimaging Facility has state-of-the-art live cell imaging facilities to record neurite outgrowth and migration of cultured neurons in real-time combined with unbiased automated computational analyses of neurite length and dendrite complexity, which we have successfully applied to hiPSC-derived cortical neurons. Once established, our experimental and computational models are ideally suited to test novel therapies for epilepsy, dementia and mental illness, in collaboration with industrial partners and clinicians.

Subject areas:

1. Medical/Clinical Science
2. Neuroscience/Neurology
3. Molecular biology
4. Genetics
5. Applied Mathematics
6. Data Analysis
7. Mathematics
8. Bioinformatics
9. Cell Biology/Development
10. Health Sciences