

Ph.D. Proposal Presentation

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Division: Department of Stem Cell Biology

Title of the project: Delineating the Role of SHANK3 on Oxidative Stress in Autism Spectrum Disorder: Insights from iPSC-derived Neurons

Date & Time: 14th October 2025, Dr Shanta Rao Auditorium at 10.30 am.

Abstract

SHANK3, a critical scaffolding protein associated with autism spectrum disorder (ASD), is essential for synaptic function and neuronal homeostasis. Mutations in SHANK3, which occur in approximately 1–2% of individuals with ASD worldwide, have been previously linked to neuronal dysfunction. However, the precise molecular mechanisms underlying SHANK3-related neuronal impairment remain unclear. In this proposed study, we aim to investigate the effects of SHANK3 mutations using patient-specific induced pluripotent stem cell (iPSC)–derived neurons. We hypothesize that SHANK3 deficiency disrupts the interaction with STIM1, leading to its accumulation and subsequent impairment of the Nrf2 associated antioxidant pathway. This dysregulation is expected to reduce Nrf2 phosphorylation and nuclear translocation, downregulate antioxidant genes such as NQO1, HO-1, and SOD, and increase oxidative stress and neuronal dysfunction. By characterizing the cellular and molecular impact of SHANK3 mutations in a patient-specific model, this study will provide novel insights into the mechanisms of neuronal dysfunction in ASD and identify potential targets for therapeutic intervention.