جامعة حمد بن خليفة
HAMAD BIN KHALIFA UNIVERSITY
عضو في مؤسسة قطر
Member of Qatar Foundation

HBKU Flagship Research Grant Program 3rd Cycle– Project Highlight

Project Title: A cell line multi-omics AI based approach to screen for the effects of a Qatari RGS4 gene mutation on G protein stabilization in Autism.

Research Team:

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Executive Summary

This project addresses autism spectrum disorder (ASD) heterogeneity by investigating a novel homozygous RGS4 mutation (c.100G>C) identified in a Qatari patient. This mutation, within a highly conserved regulatory region, disrupts RGS4's critical inhibitory function on Gαo/i proteins, key regulators of brain function and neurodevelopment implicated in ASD. We propose a novel, integrated approach combining CRISPR-Cas9 to engineer isogenic cell lines (mutant vs. control) with biochemical/cellular assays to dissect the mutation's impact on G-protein signaling. Crucially, we will leverage AI-driven analysis to interpret complex multi-omics data (proteomics, epigenetics, transcriptomics) from these limited-sample, high-dimensionality datasets.

Aligned with the HBKU Flagship call, this project pioneers a rapid, standardized workflow for evaluating ASD-linked mutations at QBRI. It uniquely integrates precise cellular modeling with advanced AI to overcome challenges in translational ASD research. Beyond understanding this specific mutation's molecular pathology, the project establishes foundational capacity at QBRI for future high-throughput screening (cell lines, organoids) and complex data analysis. It fosters significant cross-institutional collaboration, driving innovation in Qatar's biomedical research landscape for ASD.

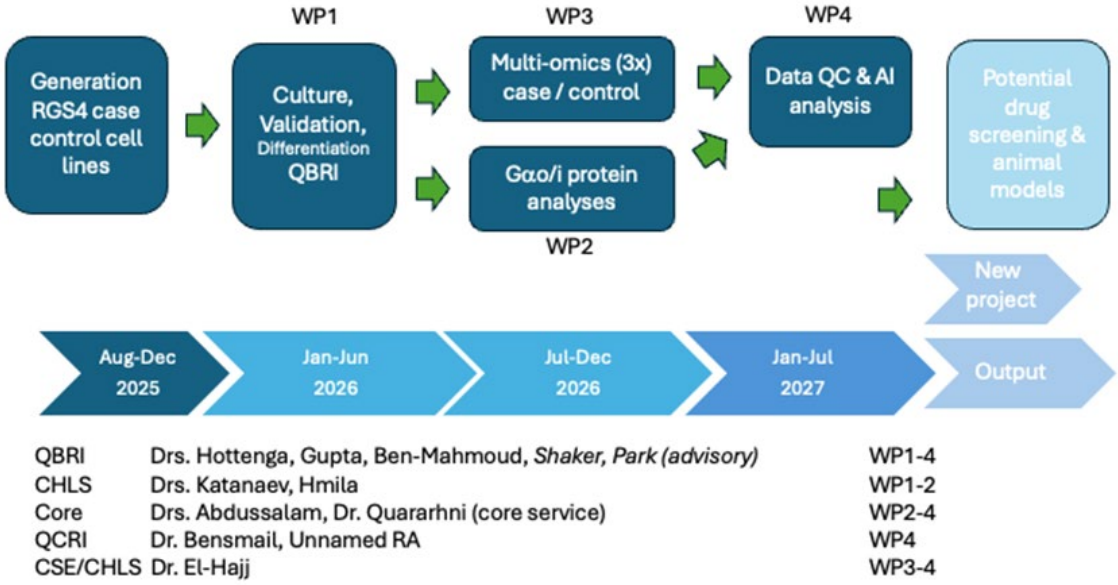
Expected Outcome

This project will deliver: (1) Validated molecular pathology of the RGS4, E34Q mutation via biochemical/cellular characterization of Gαo/i signaling defects in CRISPR-engineered cell lines; (2) An established rapid screening workflow at QBRI for ASD mutations, integrating CRISPR engineering with multi-omics profiling (proteomics/epigenetics/transcriptomics); (3) Developed AI analysis protocols to resolve high-dimensionality translational datasets; and (4) A foundation for high-throughput screening (HTS) using validated cell models and analytical frameworks, enabling future drug discovery and mechanistic studies.

Keywords:

Autism Spectrum Disorder; RGS4 Mutation (E34Q); G-protein Signaling; CRISPR-Cas9 Engineering Multi-omics Analysis; AI-driven Data Analysis; Translational Neuroscience; High-Throughput Screening (HTS); QBRI Neuroscience; Personalized Autism Therapy.

Figure: project work packages (WP), timeline and contributing teams



Flgship Area

Autism: Causes, Diagnosis and Intervention

- Autism genetics, molecular pathology, and cellular mechanisms.

Generative AI and Applications

- Applying AI for multi-omics data analysis and protocol development.