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

HBKU Thematic Research Grant 2nd Cycle– Project Highlight

Project Title: Dissecting the role of uncontrolled neural stem cell division in cortical neurogenesis and glioma genesis

LPI: Dr. Fadel Tissir

Executive Summary

Neurogenesis and brain tumorigenesis share signaling molecules that underlie cell proliferation, differentiation, migration, and survival. Self-renewal of neural stem cells (NSCs) and their differentiation are tightly regulated processes that secure accuracy of cell division accuracy and production of correct numbers of neurons and glial cells. Abnormalities in the molecular mechanisms that control these processes lead to devastating neurodevelopmental diseases (e.g., microcephaly, intellectual disability, autism, attention deficit hyperactivity disorder, and epilepsy) with considerable economic and societal impact. They also cause aneuploidy and genome instability leading to neoplastic transformation and emergence of cancer stem cells. We reported that Diaphanous 3 (DIAPH3) is expressed in NSCs and safeguards their division. Its loss weakens the mitotic checkpoint leading aneuploidy and loss of NSCs. Cortex-specific ablation of DIAPH3 impairs neurogenesis and causes microcephaly and behavioral deficits. Our preliminary results show that DIAPH3 loss fosters glioma initiation and recurrence in mice and humans. In this proposal, we will investigate the effect of deregulated mitotic division of NSC on neurogenesis and glioma genesis in humans. We will develop ex vivo models to enable identification of markers for cell cycle -associated neurodevelopmental disorders, and control glioma progression and recurrence.

Expected Outcome

The project should enable us to:

- Identify novel predictors of survival of GBM patients.
- Characterize targetable molecules that impede glioma stem cell survival and restrict tumor progression.

-

Collaborating HBKU entities:

Dr. Mohamed Aittaleb - College of Health and Life Sciences (CHLS), HBKU

Dr. Lawrence Stanton - Qatar Biomedical Research Institute (QBRI), HBKU

Schematic: