

HBKU Thematic Research Grant 2nd Cycle– Project Highlight

Project Title: Engineering a high affinity peptide combining computational and experimental methods towards precision medicine applications



LPI: Dr. Kabir H Biswas

Executive Summary

Breast cancer remains a major health challenge in Qatar (and the world at large) with the maximum number of malignant cancer incidences. The latter is primarily due to the metastasis of the cancer cells to other organs in the body. In this regard, breast cancer cells in a subset of patients utilize E-cadherin (E-cad)-based cell-cell adhesion for migration and 'homing in' to other organs, thus making it an attractive target for therapeutic interventions. Specifically, E-cad adhesion is mediated by the interaction between E-cad extracellular domain (ECD) on the extracellular side and through the formation of a complex between E-cad intracellular domain (ICD), β -catenin, α -catenin and the actin cytoskeleton on the intracellular side. Further, cytoskeletal force-mediated activation of α -catenin, which is required adhesion assembly and reinforcement through the recruitment of other proteins, requires it to interact with β -catenin. In this project, we will develop a precision biomaterials engineering pipeline combining computational, biochemical, and biophysical approaches and live cell assays to generate a high affinity α -catenin binding peptide. The engineered peptide can be used for modulating β - and α -catenin interaction as well as targeted degradation of α -catenin, and thus, enabling restriction of metastatic cancer cell adhesion capacity.

Expected Outcome

Successful execution of the project will lead to the design of a high affinity, α -catenin binding peptide (and a biosensor). The intellectual property (IP) generated will be patented through QF-IDKTO. Research results will be published in a high impact, international journal. Additionally, it will contribute knowledge to the fields of precision medicine, synthetic protein design, cell adhesion and targeted protein degradation.

Collaborating HBKU entities:

Dr. Prasanna Kolatkar - *Qatar Biomedical Research Institute (QBRI), HBKU*

Dr. Henning Horn – *College of Health and Life Sciences, HBKU*

Schematic: *illustration of the project workflow.*

