Indian Institute of Science
Centre for BioSystems Science and Engineering

BSSE Seminar

19th August 2019, 4:00PM, Monday, MRDG Seminar Hall, 1st floor, Biological Sciences Building

Differential Regulation of Signaling Pathways in a Novel Colorectal Carcinoma Cell Line

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ABOUT THE SPEAKER

Dr. Monideepa Roy is a founding member of Akamara Therapeutics, a startup geared toward developing novel therapeutics in the oncology space. Following her Ph.D. in JNU, Delhi, she trained in the Department of Pathology, Brigham and Women's Hospital and Harvard Medical School and received a fellowship from the US Department of Defense. Her innovative work has earned her several accolades including the first Thomas Gill Prize for Research Excellence at Brigham and Women's Hospital, Boston and a Career Development Award from Leukemia Lymphoma Society, USA. She established and has led the R&D laboratory at Invictus Oncology in New Delhi since 2011 and aims to develop a pipeline of novel supramolecular anticancer compounds and is an inventor of several patents.

ABSTRACT

Colorectal cancer (CRC) is the third most common cancer across the globe with the highest trends worldwide reported in Asia for both incident (51.8%) and mortality (52.4%) rates (all genders and ages) per 100,000 population. The rise in CRC can be attributed to dietary changes, aging population, smoking, physical inactivity, obesity and other risk factors. The emergence of new therapies, although promising, have had a limited impact on long-term survival due to the great disparity in resource availability and screening infrastructures among countries with varying levels of economic development. Toward making attempts in curbing this rising trend, countries such as Japan, South Korea, Singapore, and Taiwan have launched population-based screening programs. The CRC trends in Asian countries are well mirrored in India with high incidence and mortality rates, poor sensitivity to conventional therapies and a dearth of early diagnostic parameters posing a huge challenge in CRC management. In India, another layer of complexity is added to the already existing unmet need due to the high level of genetic diversity present among the Indian population. In order to have a better understanding of the etiology of CRC in India, we have characterized a novel cell line derived from an Indian CRC patient and shown that suppression of E-cadherin expression, concomitant with overexpression of epithelial-mesenchymal transition (EMT) related molecules, manifested in the form of highly migratory and invasive cells. Loss of membrane-tethered E-cadherin released β-catenin from the adherens junction resulting in cytoplasmic and nuclear accumulation and consequently, upregulation of *c-Myc*. These cells also showed dramatic transcriptional enhancement of β-catenin expression along with a substantial increase in proteasome activity. The differential regulation of these pathways in CRC have the potential to be harnessed for developing either as molecular markers or targeted therapeutics that could be more effective in certain populations.