# Indian Institute of Science
## Centre for BioSystems Science and Engineering
## BSSE Seminar

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# The CEBPD transcription factor in Breast Cancer: "not so simple"


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**ABSTRACT**

Inflammatory breast cancer (IBC) is the rarest but deadliest form of breast cancer. "Despite major international efforts to understand IBC biology, genomic studies have not led to the discovery of distinct biological mechanisms in IBC that can be translated into novel therapeutics". A unique characteristic of IBC is high expression of E-cadherin and the frequent formation of emboli within the cancer parenchyma and dermal lymphvasculature. E-cadherin can contribute to cancer cell survival under hypoxia, establishment of metastasis through collective cell migration, and chemotherapy resistance. Thus, a detailed understanding of the molecular pathways that lead to E-cadherin expression and emboli formation may provide unique insights into IBC cell biology as well as other highly aggressive BC subtypes. IBC cells can form emboli-like structures in vitro when cultured in viscous suspension with gentle agitation, which mimics conditions within the lymphatics. This assay showed that emboli are distinct from tumor spheres because non-IBC cell lines form spheres but not emboli. We found that a C/EBPδ-COX-2/PGE2-GSK3b(inhibition) pathway is important for stabilization of E-cadherin-mediated cell-cell adhesions and formation of emboli- like structures by IBC cell lines. In addition, reconstitution of this pathway in a non-IBC cell line such as MCF-7 can promote clustering as well as formation of emboli-like structures. This result suggests that the emboli culture assay may also be informative for the study of pathways that promote clustering of circulating non-IBC tumor cells. PGE2 signaling may explain other features that are prominent in IBC such as high degree of lymphangiogenesis and invasiveness. Intriguingly, PGE2 signaling can be autocrine or paracrine. Stroma-derived PGE2 or other inhibitors of GSK3b would in part explain the importance of the tumor microenvironment in IBC pathology. COX-2/PGE2 also promotes migration and invasions, which stands in some contrast to enhancing cell-cell adhesion through E-cadherin except for E-cadherin's role in collective cell migration.


**BIOGRAPHY**

Dr. Balamurugan Kuppusamy obtained his PhD from the University of Madras, Chennai, India. Dr. Kuppusamy pursued his postdoctoral studies at the University of Zurich, Switzerland and at the National Cancer Institute. Since March 2015, he serves as a staff scientist in the Laboratory of Cell and Developmental Signaling (NCI/CCR). Dr. Kuppusamy is a recipient of NCI Cancer Genetics and Signaling Fellowship. In 2011 and 2012, Dr. Kuppusamy received the NIH "Fellows Award for Research Excellence" and NCI Fellows and Young Investigators "Outstanding Achievement in Science Award", respectively. In 2015, Dr. Kuppusamy was awarded a research grant from the METAvivor Foundation to study the role of the CEBPD-FBXW7 signaling pathway in inflammatory breast cancer, an aggressive subtype of breast cancer. His areas of expertise include Hypoxia, Signal Transduction, Cancer Stem Cells, Mouse Models, Breast Cancer, CEBPD transcription factor, FBXW7, and Inflammation.