COX-2 elevates oncogenic miR-526b in breast cancer by EP4 activation and this miRNA is a promising biomarker for monitoring and personalizing breast cancer therapy

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Micro RNAs (miRs) are small regulatory molecules emerging as potential biomarkers in cancer. Previously, it was shown that COX-2 expression promotes breast cancer progression via multiple mechanisms including induction of stem-like cells (SLC), owing to activation of the prostaglandin E2 receptor EP4 (PTGER4). Over expression of COX-2 also up regulates micro RNA-526b (miR-526b) in association with aggressive phenotype. We tested functional roles of miR-526b in breast cancer and the mechanistic roles of EP4 signaling in miR-526b up regulation were examined. A positive correlation was noted between miR-526b and COX-2 mRNA expression in breast cancer cell lines. Stable over-expression of miR-526b in poorly metastatic MCF7 and SKBR3 cell lines resulted in increased cellular migration, invasion, EMT phenotype and enhanced tumor sphere formation \textit{in vitro} and lung colony formation \textit{in vivo} in immunodeficient mice. Conversely, knockdown of miR-526b in aggressive MCF7-COX-2 and SKBR3-COX-2 cells reduced oncogenic functions and reversed the EMT phenotype \textit{in vitro}. Furthermore, it was determined that miR-526b expression is dependent on EP4 receptor activity and downstream PI3K/AKT and cyclic AMP (cAMP) signaling pathways. Additionally inhibition of COX-2, EP4, PI3K/PKA in COX-2 over expressing cells down regulated miR-526b and its functions \textit{in vitro}. Finally, miR-526b expression was significantly higher in breast cancer tissues and associated with reduced patient survival. This study presents novel findings that miRNA 526b is a COX-2 up regulated, oncogenic miRNA promoting stem-like cells, the expression of which follows EP4 receptor-mediated signaling. Micro RNA (miR526b) expression correlates with breast cancer patient survival and is a promising biomarker for monitoring and personalizing breast cancer therapy.

Biography

Mousumi Majumder has completed her PhD in 2009 from Human Genetics Unit of Indian Statistical Institute, Kolkata, India. Soon after she joined as a Postdoctoral fellow in the Anatomy and Cell biology Department at the University of Western Ontario, Canada. She published 16 peer-reviewed publications and received several national and international awards as a graduate and Postdoctoral fellow. Her expertise is in the field of cancer genetics and epidemiology, cancer stem cell biology and microRNA genetics.

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