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## 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 *in vitro* and lung colony formation *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 *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 *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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