Audrey Claing, Madridge J Cancer Stud Res. 2016
http://dx.doi.org/10.18689/2640-5180.a1.002

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International
Cancer Study & Therapy Conference

April 4-6, 2016 Baltimore, USA

# ARF proteins are key molecular switch controlling breast cancer invasiveness

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Triple-negative breast cancers (TNBC) are a highly invasive type of breast cancer and associated with poor prognostic. The Epidermal Growth Factor Receptor (EGFR)is overexpressed and regulates cellular proliferation as well as invasiveness. Drugs inhibiting its activity have however shown limited effects mainly due to the development of resistance. There is therefore a need to identify new therapeutic targets for the design of alternative therapies.We and others have shown that the Ras-related ADP-ribosylation factors (ARF) are another class of small GTPases regulating key features of cancer cells. Here, we report that ARF1 is highly expressed in cells and tumor tissue of the most aggressive and advanced subtypes of breast cancers. Knock down of ARF1 expression impairs the ability of breast cancer cells to proliferate, migrate and degrade the extracellular matrix. Furthermore, growth of primary tumors as well as lung metastasis is reduced in a murine xenograft model when expression of the GTPase is inhibited. To understand how ARF1 contributes to invasiveness, we used a poorly invasive breast cancer cell line, MCF7 ($ER^+$), and examined the effects of overexpressing ARF1 to levels similar to that found in invasive cell lines. Our findings demonstrate that increased levels of ARF1 lead to the epithelial-mesenchymal transition (EMT). Mechanistically,ARF1 controls cell–cell adhesion through ß-catenin and E-cadherin. In addition, this GTPase promotes oncogenic Ras activation and expression of EMT inducers such as snail and slug. We further show that ARF1 overexpression enhances MCF7 cell invasion, proliferation and even resistance to treatment with the chemotherapeutic agent, etoposide. *In vivo*, ARF1 overexpressing MCF7 cells are able to form more metastases to the lung. Overall, our results identify ARF1 as a molecular switch of cancer progression and thus suggest that limiting the expression/activation of this GTPase could help improve outcome for breast cancer patients.

**Biography:**

Dr. Claing received her PhD in Pharmacology from the Université de Sherbrooke, in Canada. She then joined the laboratory of Robert J Lefkowitz at Duke University as a post-doctoral fellow where she began to be interested in the function ARF proteins plays in mediating receptor-mediated cellular responses. She is currently professor of Pharmacology at the Université de Montréal. Her research team studies the molecular basis of cell migration and proliferation, with emphasis on the basic mechanism by which ARF proteins controls intracellular signaling. She is recognized for her pioneering research aimed at unraveling the function of ARF1 in breast cancer.