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Dissecting the role of EIF5A signaling in breast cancer

Marie Therese Rached
The Institute of Cancer Research, UK

Triple negative breast cancer (TNBC) is a highly recurrent subtype of breast cancer with the worst prognosis, potentially attributed to the presence of cancer stem cells within these tumors. The elongation initiation factor 5A (EIF5A) is a protein with a unique amino acid, hypusine, synthesized post-translationally from the polyamine spermdine through step wise enzymatic reactions. This hypusination crucial for EIF5A activity and cell proliferation has been reported in multiple cancers; however, its function in breast cancer requires further understanding. We showed increased expression of EIF5A mRNA and protein as well as its hypusinated form in a subset of TNBC cell lines compared to non-TNBC lines using gene expression and western blot studies (n=12). To better understand how inhibition of EIF5A hypusination influences TNBC, we inactivated EIF5A pathway with inhibitors targeting the hypusine forming enzymes. We confirmed that loss of EIF5A hypusination was associated with alteration in cell cycle progression, reduced proliferation and survival in a subset of TNBC cell lines using flow cytometry and cytotoxicity assays. At the molecular level, cell cycle alteration among subtypes was associated with changes in CDK2 activity. The stem cell associated transcription factor c-MYC showed potential differential regulation following drug treatment in a subset of TNBC cell lines suggesting its potential role in EIF5A pathway activity. These studies suggest a distinct role of the polyamine/hypusine pathway during cell cycle progression and proliferation of a subset of TNBC. Targeting this pathway using anti-tumor therapeutic agents might provide means to effectively combat the aggressive TNBC subtype.

Biography

Marie Therese Rached has completed her PhD in Metabolic Signaling in 2014 at Imperial College, London. She is currently pursuing Postdoctoral training at The Institute of Cancer Research in Sutton, United Kingdom. Previously she worked as a Research Staff Associate at Columbia University, New York, where she published multiple papers on the role of the skeleton as an endocrine organ regulating energy metabolism.

marietherese.rached@icr.ac.uk

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