

Translational regulation in breast cancer and the cancer stem cell – from protein synthesis to therapy

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Because mRNAs encoding proteins with oncogenic and angiogenic properties have greater requirements for specific factors in the protein synthesis apparatus than most mRNAs, targeted inhibition of specific mRNA translation is a promising new area for drug development in human cancer therapeutics. Our research in locally advanced, inflammatory and metastatic breast cancers has identified several translation initiation factors that are specifically hyper-activated and/or upregulated, along with hyper-activated mTOR, which promote breast cancer metastatic progression and resistance to therapy. Research will be presented which shows that high levels of components of the translation initiation complex as found in late stage breast cancers facilitates selective translation of mRNAs encoding proteins involved in the DNA double strand break repair and cell survival pathways, as well as resistance to DNA damage chemotherapies in the cancer stem cell population. Cancer stem cells are thought to underlie breast cancer recurrence, metastasis and resistance to treatment. This work begins to elucidate previously unknown translational control pathways of the breast cancer stem cell, providing a novel understanding of the role of the regulation of mRNA translation in human cancer and promising clinical treatment strategies that will be discussed.