MicroRNA: A New Target for Breast Cancer Research

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Have the women in your life been screen for breast cancer recently? If not, perhaps they should. Breast cancer is the most common form of cancer and the leading cause of cancer-related mortality in women worldwide. There were approximately 2 million new breast cancer cases in 2018. Research over the past decades has helped improve our understanding and treatment of breast cancer. However, despite the improvement in understanding and treatment, breast cancer recurrence and metastasis remain a major clinical problem. Researchers at the University of Liverpool may have found biomolecules that predict patient survival in their study published in *Nature*.

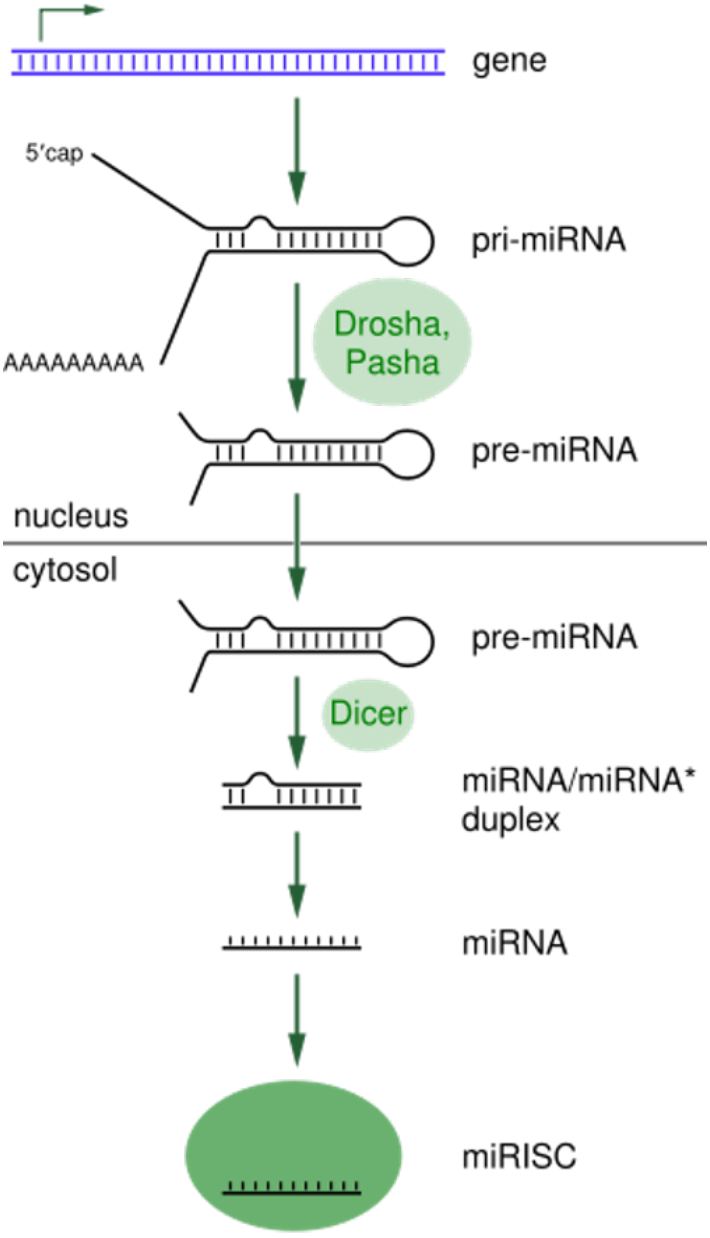
During metastasis, cancerous cells develop stem-cell characteristics, evade the immune system, and travel to different organs to seed another cancer. Recent studies suggest that microRNA (miRNA) plays a critical role in breast cancer metastasis by modulating gene expression. By analyzing miRNA expression profiles, Athina Giannoudis and her team identified four profiles that may be responsible for breast cancer metastasis to the brain.

MiRNA are short RNA molecules, composed of roughly 20-24 nucleotides, that regulate virtually all pathways in mammals and other animals. MiRNA function by physically base-pairing with messenger RNA (mRNA) molecules and silencing them, preventing the production of proteins, large molecular machines that are reasonable for carrying out the fundamental processes in cells.

MiRNA comprise roughly two percent of the human genome and are maintained in similar forms in many organisms, such as mice and worms. Due to abundance and ubiquitous presence, MiRNA have evolved to regulate many processes from cell growth to cell death.

The stability of hundreds of mRNA can be affected by misregulation of a single miRNA resulting in profound implications for cells. This includes “transformation” during which cells change from a normal to a cancerous. Genes that promote and suppress growth are regulated MiRNA. As a consequence, miRNA misregulation has been linked with multiple types of cancer, including brain cancer. Similarly, in breast cancer, miRNAs have been observed to be acting as tumour promoters and suppressors.

Hypothesizing that miRNA may play a role in the development of metastatic brain cancer after breast cancer, the researchers first compared the total miRNA in breast cancer patients in which the tumour relapsed and developed into breast cancer to patients who did not relapse, and found over 100 differentially expressed miRNA. The miRNA appeared to be regulating pathways involved in cell to cell signalling, growth, and metastasis, processes that explain the development of secondary cancer.



To assess which of the miRNA play a role in brain cancer development, the researchers compared total miRNA in BC patients in which the tumour relapsed and developed into brain cancer to patient breast cancer relapsed into just

breast cancer. They found four miRNA that regulates roughly 150 genes involved in metastatic transition, growth, and cell death, among other processes.

One of the major targets of these miRNA appears to be cMET, a protein overexpressed in brain tumours. Interestingly, the researchers suggest that cMET may also promote brain colonization in recurring breast cancer patients. Therefore, inhibition of cMET through available drugs may patients that secondary brain tumor patients.

MiRNA as Biomarkers for Breast Cancer

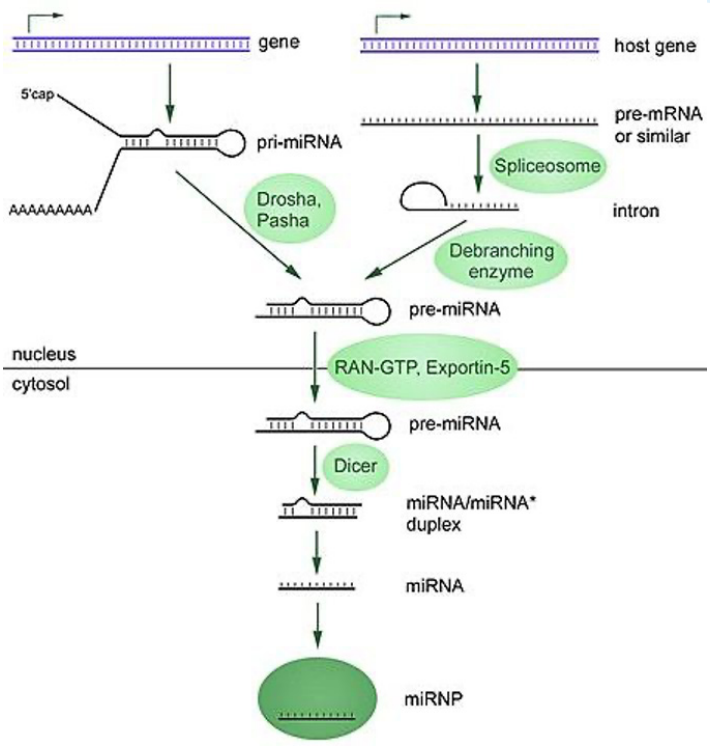
Breast cancer patients often have aberrant miRNA expression and, as a consequence, the use of miRNA as diagnostic biomarkers is the focus of the current research in the field. For example, researchers at Zhejiang University studied whether miRNA-55, a miRNA highly abundant in breast cancer patients as a potential tool for breast cancer diagnosis. Their results suggested that miRNA-55 had was able to accurately identify breast cancer patients compared to non- breast cancer patients. Further studies found that other miRNA could be utilized to distinguish patients at different breast cancer stages and predict breast cancer development in women with familial risk.

MiRNA analysis may now have the potential to identify patients who may be at risk to relapse to develop breast cancer or brain cancer. Early intervention is one of the major factors that increases survival rate thus the development of a sensitive and selective test is important to guide treatment.

Targeting miRNA for Therapeutic Intervention

The role of miRNA in promoting breast cancer has sparked interest in miRNA-based cancer treatment. Currently, researchers are using drugs to block miRNA that causes cancer or express miRNA that may cause cancerous cells to die. For example, researchers at the Medical College of Southeast University found that targeting miRNA in a mouse model inhibited tumour growth and metastasis. Likewise, targeting miRNA may prevent breast cancer patients from relapsing into breast or brain cancer. Although there are no miRNA-based therapeutics in the clinic, the early signs from basic science research are quite promising.

In this paper, the role of miRNA in breast cancer metastasis into brain cancer has been highlighted. The researchers highlight that breast cancer patients who relapsed to develop brain cancer have four miRNA, in particular, differentially expressed. Studies have revealed that differential miRNA expression is correlated with the patient's condition and tumour stage. However, a comprehensive understanding of the network of miRNA associated with breast cancer will elucidate the molecular mechanisms by which they promote cancer. Furthermore, future studies on larger and heterogenous populations will translate into practical application for clinical settings to improve diagnosis, develop therapeutics and impact patient survival.



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