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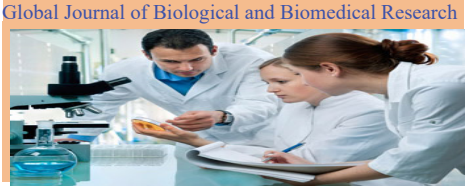

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Significance of novel secretory markers upregulation using mir526b

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ABOUT THE STUDY

Breast cancer was diagnosed more frequently than lung cancer in 2021, making for 11.7% of all cancer cases. Additionally, there was an increase of 9.3% between 2018 and 2020 in the number of breast cancer-related fatalities worldwide. Breast cancer patient survival is 99% when diagnosed in the localised stage, therefore adding accessible, non-invasive, and cost-effective technologies to routinely screen for breast cancer with current procedures is one strategy to deal with the rise in cases and fatalities from the disease.

The complexity of breast cancer has resulted in the development of customised treatment plans that depend on the tumour grade, stage, and presence or absence of hormone receptors (HR, including the ER, PR, and HER2 receptors for oestrogen and progesterone). 73% of breast tumours that have been diagnosed are of the luminal A subtype (HR+/HER2-), followed by 12% triple-negative (HR-/HER2-), 11% luminal B (HR+/HER2+), and 4% HER2-enriched (HR-/HER2+) tumours. Precision medication and individualised therapy can increase patient survival. However, in most nations, standard mammography screening for breast cancer detection begins around age 50. Finding early detection biomarkers is a major focus of breast cancer research due to rising rates of breast cancer in younger populations.

Growth factors, ligands, and other chemicals are secreted by cells in order to interact and communicate with nearby cells. During oncogenic transformation, the makeup of these secretions varies, creating a distinct Tumour Microenvironment (TME) that could affect the outcome of metastasis. The collection of proteins that cells secrete into extracellular space is known as the secretome. It contributes significantly to the human proteome (13%–20%) and is crucial for cell motility, cell signalling, and cell-cell communication. Additionally, secretory proteins control a variety of cancer characteristics, and as more secreted proteins are present in physiological fluids close to tumours, they can be found in blood. The secretome therefore contains a variety of regulatory mechanisms that affect cancer and carcinogenesis.

Short non-coding RNAs called miRNAs control the expression of genes after transcription. Nearly every element of cancer genesis and progression in breast cancer is correlated with miRNA dysregulation. The inflammatory enzyme Cyclooxygenase-2 (COX-2), which is overexpressed in poorly metastatic luminal Two oncogenic miRNAs, miR526b and miR655, are upregulated in the MCF7 breast cancer cell line. miR526b and miR655 overexpression in weakly metastatic luminal Breast cancer characteristics such Epithelial to Mesenchymal Transition (EMT), cell migration, invasion, activation of Cancer Stem Cells (CSCs), tumor-associated angiogenesis, lymphangiogenesis, oxidative stress, and hypoxia responses were increased by the breast tumour cells MCF7 and SKBR3.

In addition, miRNA-overexpressed cell secretions and metabolites increased the angiogenic potential of primary endothelium Human Umbilical Vein Endothelial Cells (HUVECs) and caused oxidative stress, tumor-associated angiogenesis, and lymphangiogenesis in poorly metastatic MCF7 cells. High miR526b and miR655 expression is linked to poor breast cancer patient survival, and both miRNAs were significantly more expressed in human breast cancers than in disease-free reference tissues. Both pri-miR526b and pri-miR655 can be found in patient blood plasma, and pri-miR526b is a sensitive blood-based breast cancer biomarker that can detect the disease as early as stage I. New miRNA regulators affecting the TME will be discovered by examining the impacts of these oncogenic miRNAs on the composition of the secretome. Therefore, a better comprehension of oncogenic miR526b- and miR655-high tumour secretions could lead to the discovery of new biomarkers and a better understanding of miRNA tumour biology.

Oncogenic miRNAs including miR526b and miR655 encourage aggressive breast cancer characteristics and change cells in the TME. We have discovered that the phenotypes of cells present in TME are altered by cell-free miRNA and miRNAhigh tumour cell secretory proteins. It may be possible to understand the methods by which miRNA regulate TME and find potential biomarkers by analysing the cell secretomes of miR526b and miR655 in ER-positive breast cancer cell lines. Large-scale secretome analyses can be challenging since many extracellular proteins are signalling molecules that are detected at low levels and may not be chosen because of a higher threshold.