INTRODUCTION TO EXOSOMES AND CANCER

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Abstract

Cancer research has found a novel foothold in studying exosomes, the 40–140 nm membrane-bound vesicles secreted by cells as molecular messengers. These secreted vesicles of endocytic origin act as signaling conveyors between cells by shuttling molecular cargo in the form of proteins, mRNA, miRNA, and lipids. The many roles of exosomes in normal physiology and disease are becoming clearer as they are increasingly studied. Their role in cancer is being found to range from sending protumorigenic messages between cancer cells and to no cancer cells to aid in the growth and spread of tumor. Tumor exosomes are implicated in angiogenesis, metastasis, drug resistance, immune evasion, and even more processes involved in the pathophysiology of cancer. As we begin to uncover these roles, researchers are discovering the importance of understanding exosomes, as they pertain to cancer, as a means of discovering much-needed biomarkers, elucidating the mechanisms of cancer biology, identifying therapeutic targets, and using exosomes themselves as a mode of therapy against cancer.

Keywords: Proteins, mRNA, exosomes, Tumor, technology.

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CANCER

Globally, cancer is the second most common cause of death. Overall, there has been a rise in the frequency of cancer; by 2014, there were over 1,665,540 cancer patients in the United States alone, and 585,720 of them had passed away from the illness 1. Consequently, cancer is a major issue that has an impact on everyone's health in human cultures. Regretfully, the illness exhibits tissue-level variability, which poses significant challenges to its precise identification and therapeutic effectiveness [2, 3]. The prostate, lung and bronchus, colon and rectum, and urinary bladder have the largest percentages of cancer types in males, correspondingly. The breast, lung and bronchus, colon and rectum, uterine corpus, and thyroid are the areas in women where cancer incidence is highest. ..According to this statistics, the majority of cancers in men and women, respectively, are prostate and breast cancers 4. Blood cancer and malignancies of the brain and lymph nodes account for the largest percentage of cancer cases in children, respectively 5, 6. A sequence of progressively occurring gene mutations that alter cell activities cause cancer. It is evident that chemical substances have a role in the formation of cancer cells and gene alterations. Moreover, smoking contains a number of chemical components that cause cancer and cause lung cancer. 7. Fascinatingly, chemicals found in the environment that have the potential to cause cancer affect cells' cytoplasm and nucleus either directly or indirectly, resulting in genetic abnormalities and gene mutations. 9, 10, 11, 8, 9. Other carcinogens include radiation, germs, and viruses. components, making up around 7% of all cancer cases 12. Cancer generally causes cellular relationships to break down and essential genes to stop working. This disruption causes aberrant proliferation and has an impact on the cell cycle 13, 14. Under normal circumstances, proto-oncogenes promote cell division and development; nevertheless, when a genetic mutation occurs, they transform into oncogenes, which are most hazardous to a cell's ability to survive 15. In addition, unchecked cell division is brought on by the absence of tumor suppressor genes. 16. Normally, repair genes encode proteins and enzymes with repairing capabilities; around 30 different types of repair proteins have been identified. 17. Eliminating uracil from DNA circumvents DNA damage and eliminates the primary lesions caused by UV radiation, which are basically the roles of repair genes to effectively fix the DNA 18.

The study of cell destiny and epigenetic changes, such as DNA methylation, histone modifications, and nucleosome location, which are crucial in the development of cancer, makes epigenetics a dynamic field 19, 20. A significant decrease in DNA methylation (about 5-6% drop in the overall quantity of 5-methyl cytosine) 21 is a characteristic of cancer cells. The bulk of histone changes in cancer cells are caused by an overall decrease in mono-acetylated H4K16 22. The majority of the time, the molecular processes behind the actions of all families of chromatin-modifying proteins are still unclear, but they are all linked to cancer 23. To get a deeper understanding of cancer, we examined the disease from a molecular standpoint in this work.

EXAMINE THE PROCEDURE

Using terms like "cancer and molecular process," "cancer and treatment," and "molecular aspects," we first looked for research publications. The publications that met these word criteria were then thoroughly evaluated, and the results were appropriately reported.

FROM A MOLECULAR PERSPECTIVE, CANCER

Chromosome translocation (gene Bcr and oncogene Abl in chronic blood cancer), point mutation (Ras gene in colon cancer), deletion (Erb-B gene in breast cancer), amplification

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(N-myc in neuroblastoma), and insertion activation (C-myc in acute blood cancer) are genetic alterations that result in oncogene generation and genetic disorders. An interchange of genetic material between chromosomes 9 and 22 is the reason why older people are frequently diagnosed with chronic blood cancer. Ph1 is a biomarker produced by this illness that is present in 95% of patients and can help with accurate diagnosis. A novel gene combination that translated into a protein with kinase activity was created as a result of the Bcr gene's link to the Abl oncogene 24, 25, 26, 27.

A p53 gene mutation results in the production of an odd protein that plays a significant part in disrupting the p53-related biological pathway. It has been revealed that p53 anomaly occurs in 60% of cancer cases. since a result, the p53 gene has a complicated relationship with cancer, since abnormalities in these molecular and biological processes result in the production of cancer cells. Under normal circumstances, angiogenesis, differentiation, senescence, cell division, and DNA metabolism are all significantly impacted by p53. Furthermore, the majority of p53-related mutations affect the DNA-binding location, and p53 regulates the replication-related impairment of genes. Cancer cells are maintained in the G1 and G2 stages of the cell cycle by p53's cooperation with CDK1-P2 and CDC2. 28, 29. In actuality, p53 either stimulates or inhibits the growth of cancer cells. The p53 protein attaches itself to DNA following damage inflicted by other genes, which activates the WAF1 gene 30, 31. This process connects p53 to CDK2, which in turn prevents p21 from having an influence on the subsequent phase of the cell cycle. The three pathways by which p53's anti-cancer effect is active are stimulation, for DNA-repairing proteins, activation of apoptosis, and cell cycle arrest in G1/S phase 16, 32, 33, 34, 35, 36, 37, and 38.

All things considered, hypomethylation mostly affects repetitive regions and causes chromosomal instability, gene loss, and increased gene mobility 21, 39. One of the best examples of hypomethylation is L1 from the LINE family, which has been linked to bladder, lung, and breast malignancies 40. Oncogenes with ectopic expression can be activated by hypomethylation in certain promoters; MASPIN, a tumor suppressor gene, exhibits this situation in breast and prostate cancer. Additional instances include DPP6 and MAGE in melanoma 41, SNCG in breast and ovarian cancer, and S100P in pancreatic cancer. In contrast to general hypomethylation, hypermethylation is limited to a particular CpG site. Hypermethylation of the promoter causes transcription inactivation that affects genes involved in repair (Hmlh1, WRN, and BBRCA1), vitamin response (CRBP1, RARB2), modulation of the cell cycle (P16INK4b, P16INK4a), and programmed cell death (TMS1, DAPK1, and WIF-1). These occurrences are crucial in the development of cancer. 42. Because most research focuses on the CpG regions of promoters, hypermethylated promoters may thus be regarded as new biomarkers for the diagnosis and prognosis of cancer. Furthermore, it is noteworthy that aberrant methylation, such as hypermethylation in the CpG region, commonly takes place during cancer (45–65%). 43, 44. The overall disruption of DNA methylation patterns may be caused by DNMT's poor regulation; in fact, it has been found that DNMT1 and DNMT3b are highly expressed in a variety of tumor types. Furthermore, miRNA controls the expression of DNMT, and it has been discovered that the The MIR-29 family directly and indirectly lowers the expression of DNMT3a, DNMT3b, and DMNT1 45.

Tumor suppressors BRG1 and BRM, which are ATPase subunits linked to the SWI/SNF complex, are identified as playing a crucial role in 15–20% of cases of lung cancer. It's interesting to note that BRG1 has been shown to control local gene expression and to destabilize the p53 and SWI/SNF complex. Through its interactions with RB, p53, MYC, MLL, and BRCA1, the SWI/SNF complex plays a role in the development of several

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malignancies. As a result, blocking the SWI/SNF complex prevents cells from growing. Moreover, promoter hypermethylation caused by nucleosome positioning alterations suppresses transcription. Nucleosomes occupy TSS due to promoter hypermethylation; this problem has been linked to MLH1 in colon cancer. Encoding genes for components of chromatin-changing complexes, such CHD5, are the primary site of CpG hypermethylation in cancer. Its expression is decreased in this circumstance, and the regular structure of chromatin 52 is disrupted. Histone variations, such as an increase in MacroH2A expression during the senescence process, are also linked to cancer in addition to the nucleosome positioning problem. Consequently, lung cancers with elevated MacroH2A expression have a better prognosis because of a decrease in the quantity of cell proliferation 53. (6-10)

CONCLUSION

Over the last thirty years, a significant amount of data about the functions of genes and proteins in the development of cancer cells has been documented by researchers. Actually, one of the most significant findings was the function of altered genes in cancer cells. Environmental variables linked to genetic mutations have been discovered recently. We can identify new cancer biomarkers and assess the strength of gene expression and faulty proteins with the aid of various molecular techniques. These discoveries may help treat cancer and lessen its side effects. Furthermore, several investigations into the role of epigenetic pathways in the onset and advancement of diverse medical conditions, including cancer, are ongoing. Furthermore, it appears that several facets of epigenetic stay a mystery. On the other hand, by pinpointing all relevant genes and environmental variables, this provides us with a thorough blueprint for future attempts to prevent cancer.

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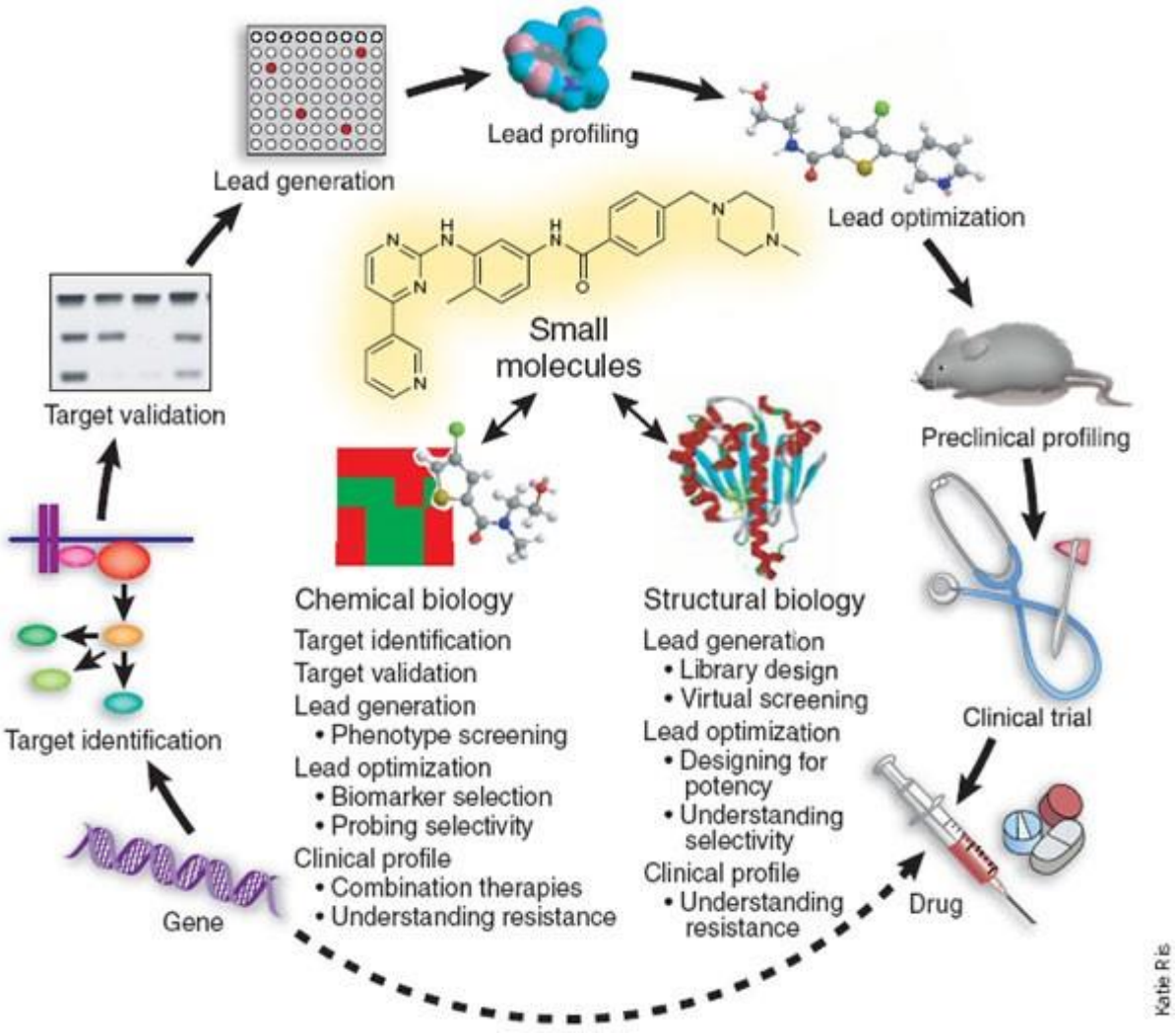

Fig. 1: Exosomes and Cancer

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