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Cancer Metastasis and its Suppressor Genes

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Abstract

Cancer is type of disease involves abnormal growth of cell. It can easily transmit & forms tumors to one organ to another organ. Metastasis is the spread of a cancer or other disease from one organ or part of the body. Metastasis is the spread of cancer cells to new areas of the body. Through metastasis the cancer cells are spreading to the different parts of the body through the blood and lymph nodes. Tumors formed from cells that have spread are called secondary tumors. The cancer may have spread to areas near the primary site is regional metastasis and to parts of the body that are farther away is distant metastasis. So it is also called as the 4th stage of the cancer.

Keywords: Metastasis; Tumor; Suppressor genes; Breast cancer

Introduction

Metastasis is a complex process, which spread the cancer from one organ to another without any direct contact. It requires the regulation of both metastasis-promoting and metastasis suppressor genes [1-5]. Firstly lymph node are affected early, then for the lungs, liver, brain and bones are the most common metastasis locations. It shows some symptoms and also cause pain but it is not the first symptom. Sometimes the effected person do not show any symptoms but the effected organ begin to shrink until its lymph node undergo lysis or burst [6-12].

Metastasis can spread through blood or lymphatic system or both routes.

Spreading routes:

1. Lymphatic Spread: Through lymph nodes and it is most common route for carcinomas.
2. Hematogenous Spread: Typical route for sarcomas, originating from kidney – renal cell carcinoma.
3. Transcoelomic: It is through penetrating the surface of peritoneal, pericardial, pleural and subarachnoid spaces. Ovarian tumors can spread to the surface of the liver.

After the tumor cells come to rest at another site and they penetrate into another vessel and multiply forming another tumor. This new tumor is known as a metastatic (or) secondary tumor. Metastasis is one of the "Hallmarks of Cancer". Metastasis cancer is also called as 4th stage of cancer because its spread regionally to lymph nodes, tissues or organs and it can also

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spread to distant parts of the body [13-19]. We cannot cure the cancer but we have the potentiality to reduce the fatality rate of the effected person. Major methods are of surgery, radiation and chemotherapy.

People can gain the knowledge and know the information thorough Open access journals. It provide more information and accessibility to the readers in gaining the required information [20-26].

To create awareness among the people, researchers and scientists together form a society. The main aim of these societies is to visualize and create awareness to people and also sharing the knowledge to the world.

Open access journals in Cancer share the recent and scientific research publications to the society. Journal of Cancer Science & Therapy provides information on recent therapeutic techniques used to reduce the cancer. Chemotherapy: Open Access is a open access journal which publishes high quality articles to improve the knowledge and provide chemotherapy techniques which are used in the present world. Cancer Surgery, Advances in Cancer Prevention, Breast Cancer: Current Research, Cancer Medicine & Anti-Cancer Drugs, Journal of Cancer Science & Therapy, Journal of Cancer Diagnosis gives more information globally, sharing preventive and diagnosis methods. Some upcoming conferences are going to discuss their ideas on cancer therapy which is 19th Euro Congress on Cancer Science and Therapy on July 17-19, 2017. Some are aimed to sharing the information and debate in conferences through Cancer Therapy, Biomarkers & Clinical Research. Some of the speakers explored new ideas and motivate the conference in young researchers through their speech in 25th World Cancer Conference. Some of the journals have high prowess members they are actively participating as Editor-in-chief are Maria Jose Molina Garrido and Steven D Wexner are having high importance their research work. High professional people will share the knowledge and their ideas to visualize the young researchers in the world through the journals [27-33].

Metastasis Suppressor Genes

Metastasis Suppressor is a protein that helps to prevent metastases. It is one of the lethal cancer process. Metastasis suppressors were first identified using a microcell-mediated chromosome transfer (MMCT) [34-39]. It is a technique to transfer a chromosome from a donor to recipient cell line. When compared with tumor suppressor, metastatic suppressor act by different mechanisms. However it do not affect the primary tumors. Chromosomes 1, 6, 7, 8, 10, 11, 12, 16, and 17 were found to harbor metastasis suppressors [40-46]. The discovery of metastasis suppressor genes is helps to understanding the metastasis mechanism and provide prognostic markers and therapeutic targets to cure the cancer clinically.

MicroRNAs (miRNAs) are a class of gene regulators that bind the 3′ untranslated regions of target messenger RNAs, leading to either suppression of their translation or acceleration of their degradation. In the cell MDA-MB-231 (established from a pleural effusion of a 51 year old woman with metastatic breast cancer) and its metastatic variant, contains 6 miRNAs. In that miR-335 and miR-126 suppress metastasis without effecting the primary tumor growth. miR-335 targets multiple pathways (SOX4), which helps the metastatic suppression [47-53]. But in breast cancer – miR-335 expression is correlated to metastasis free survival.

Genes

Metastasis-suppressing genes (proteins) are identified in humans and other animals, including BRMS1, CRSP3, DRG1, KAI1, KISS1, NM23 and various TIMPs [54-59]. Most act by altering aspects of signal transduction. Decreased expression of the suppressor gene is the key parameter determining metastatic potential and may occur by a variety of mechanisms. nm23 (NME1) and KAI1 are the best characterized metastatic suppressor genes [60-68].

NM23

NME\NME1 nucleoside diphosphate kinase 1 is an enzyme which is a metastatic suppressor. It was identified in 1988 as the first metastatic suppressor due to its reduced mRNA transcript levels in highly metastatic cells [69-76]. It exists as a hexamer composed of 'A' (encoded by this gene) and 'B' (encoded by NME2) isoforms. Mutations in this gene have been identified in aggressive neuroblastomas.

NM23 is a suppressor active in melanoma, breast and colon cancers and apparently inhibits the functioning of a kinase enzyme that promotes cell division. It is having eight family members NM23-H1 – NM23-H8 [77-82]. Among this NM23-H1 and NM23-H2 suppress metastasis in multiple tumor types. NM23 expression can serve as a potential prognostic marker for survival in breast, ovarian, melanoma, gastric, hepatocellular and non-small cell carcinoma. It affects the MAPK (Mitogen-activated protein kinase) and cytoskeleton-organizing cellular pathways [83-88].

Most of the metastasis supressors are downregulated in clinical tumor samples ratherthan mutated. Metastasis suppressors have potentiality to block metastasis and improve the survival of the affected person when the suppressor genes are activated. NM23 promoter region contains glucocorticoid response elements that can elevate the NM23 expression [89-95]. Dexamethasone medroxyprogesterone acetate (MPA) can have the ability to increases NM23 expression. It is using in treating human breast cancer.

KAI1

KAI1 is a metastatic suppressor gene located on human chromosome 11, belongs to the family of cell surface glycoproteins. It is found in prostate and breast cancers [96-99]. It forms complexes with proteins called integrins and it will link cells together. The complex formation may inhibit detachment and migration of cancer cells.

Decreased KAI1 expression has been observed in several common solid epithelial tumors, including prostatic, pancreatic, lung, hepatic, colorectal, ovarian, and esophageal cancers. In recent study observed that by using immunohistochemical technique we can know the frequent loss of KAI1 expression in a number of squamous cell carcinomas [100-102].

Conclusion

Metastasis is always coincide or depends on the primary cancer i.e., where the tumor is started from a cancer cell. Different types of metastasis suppressor genes are identified in both humans and animals. Those genes are only suppress the metastasis process in a limit time but not the entire time. Methods such as radiotherapy, chemotherapy, anticancer drugs can only increase the life span of the effected person but not to decrease the cancer cells.

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