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A Review on Targeted Cell Therapy for Breast Cancer, Colon Cancer and Lung Cancer

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Abstract

Cancer mainly defined as a group of diseases lead to growth of abnormal cells anywhere in the body. Anything that potentially leads to the growth of abnormal cells in the body is called cancer. Cancer cells grow with potential to invade or spread in any parts of the body. Cancer can be caused by various agents and factors depending upon the type of cancer developed in the particular region. Chemical and toxic substance exposure, ionizing agents and genetic factors are majorly responsible for developing cancer cells in the body state or degree of disease is determined by medical uses such as biopsy which helps in diagnosis of cancer and determining its types and extent of cancer cells spread throughout the body. The molecular targets such as VEGF, oestrogen, protease activated receptor, BRAF has become major innovations towards drug discovery both naturally and chemically.Symptoms of cancer varies according to the types and extent of disease developed in body symptoms like fatigue, weight loss, change in bowel and bladder function, cough and skin tone are some of the early signs of developing cancerous cells in the body. In this study, we focussed the targets of leading cancers among male and female like breast cancer, lung cancer and colon cancer in drug discovery and development.

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INTRODUCTION

Millions of people globally are affected by cancer, it is not defined as particular diseases but consist of group of diseases which make it more complex and difficult to diagnose the state of disease and its types (Calnan, 1987). Cancer is of various types depending upon the site where the growth of abnormal cells developed. However, once cancer is diagnosed correctly can be treated and cured but still the chance of intermittent is possible (Evans *et al.*, 2014). There are two types of treatment mainly preferred in such cases-chemotherapy and targeted cell therapy. Target cell therapy has advantages over chemotherapy that it only attacks and destroys cancerous cells (targeted cell) in site of disease where chemotherapy destroys normal cells also present at site of disease which may later affect normal functioning of the system (Devita *et al.*, 1975). Target cell therapy is preferred for some types of cancer cell treatment where patient may have to go for chemotherapy, radiation therapy, or hormone therapy yet, target cell therapy consists of very minor sides effects such as skin problems, GIT problem compared to chemotherapy or hormone therapy (Schally and Nagy, 2004). Vascular Endothelial Growth Factor is type of protein which is pro-

duced by various cells including tumour cells, particular targeted cells in case of cancer. VEGF plays an important role in normal physiological function in the body such as formation of bone cells, haemostasis. Inhibition the actions of VEGF lead to up regulation of physiological function in the body (Mattern *et al.*, 1996).

Cancer is found to be one of the most leading causes of death Worldwide. Over 9.6 million deaths are estimated Worldwide in 2019 by WHO (World Health Organisation). The data chart prepared by tallying with the records of most common cancer that arises worldwide in million versus Death in million due to cancer was given in Graph 1 and Table 1 . (REFERENCE WHO RECORDS- PUBLIC DOMAIN)

Breast Cancer

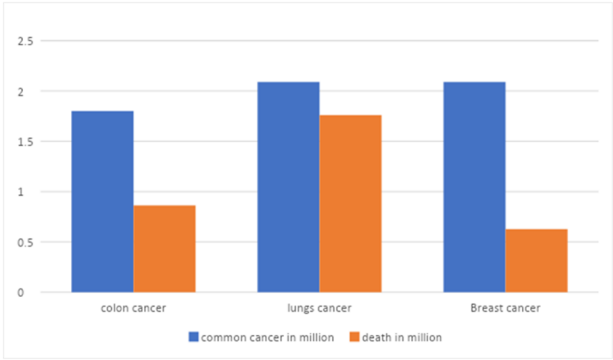
Breast cancer is formed in the breast due to the development of the abnormal cells. In United States, breast cancer is diagnosed for women after skin cancer (Gage *et al.*, 2012). Breast cancer grows or spreads when the breast cell passes the other parts of the body or when the abnormal cells which present in the other parts of the body to the breast. The common types of breast cancer are invasive, non-invasive, ductal carcinoma situ, invasive ductal carcinoma, lobular carcinoma situ, metastatic breast cancer, triple negative breast cancer, breast cancer which occurs during the pregnancy etc (Lochter and Bissell, 1995). Stages involved in breast cancer ranges from 0-4 i,e stage0, stage1, stage3, stage4. These stages are caused by the characteristics like size, the type of the cancer i.e non- invasive or invasive, due to the presence of the cancer in lymph node of the body than the breast (Davidson and Hancock, 2007).

Etiology of Breast Cancer

Changes in the shape of breast cancer, itching, occurs nipple change, chunk feel in the breast, changes in bladder, inflammation etc , Breast cancer are caused by the oncogenic virus. Epstein Barr virus, mammary tumour virus, Human papillomavirus, are the candidate viruses (o). The main cause of breast cancer is still unknown (Joshi and Buehring, 2012). Age is one of the main causes for breast cancers where women are above 60 are affected more. Increase in age leads to risk of breast cancer. Family history such as mother, daughter may also cause (McPherson *et al.*, 2000). A greater risk factor takes place for the women who have never been pregnant also. Early stage of menstruation i,e before age 12. Consuming more alcohol also leads to an increase in risk factor. Obesity or overweight is also one of the reasons to cause breast cancer. The women who gave birth to the 1^{st} child after the ages can also increase the risk factor of breast cancer (Kwan *et al.*, 2010).

Targets For Breast Cancer

The targets for breast cancer used to block the growth of cancer in the breast. Oestrogen receptor is the main therapeutic target in breast cancer. In breast cancer the agents that target oestrogen receptor have been the most used therapeutics (Bange *et al.*, 2001). Oestrogen and oestrogen receptors are used as key drivers. It is used to inhibit the oestrogen signalling pathway in women (Grevitt, 2018). The recombinant antibody trastuzumab targets HER2. In biosynthesis of oestrogen the aromatase catalyses the rate limiting steps. The inhibitors are the most effective targets. Breast cancer is a complex heterogeneous compound. The potential therapeutic targets are P13K/AKT signalling pathway, microRNAs (Cooke *et al.*, 2003).



Graph 1: Number of deaths in millions due to Colon Cancer, Lung Cancer and Breast Cancer

Drugs Approved (Usfda) To Treat And Prevent Breast Cancer

Some of the drugs are (Nab-paclitaxel) used to suppress microtubules, (Everolimus) act as immunosuppressant, (pamidronate disodium)-inhibition of bone resorption suppressant, (doxorubicin)-inhibitor of topo –isomerase, (Darbepoetin alfa)- stimulator of erythropoietin, (pamidronate disodium)-inhibition of bone resorption, (Exemestane)-steroidal aromatase inhibitor, (Tamoxifen) - inhibit proliferative action, (Raloxifene)- act as selective oestrogen receptor modulator

Colon Cancer

It is the third leading type of cancer in males and the fourth place in females. The growth of colorectal cancer on the lining of the intestine is called polyps. There are two types such as adenomatous polyps, hyperplastic polyps and inflammatory polyps (East *et al.*, 2008).

Table 1: Types of Cancer, Estimated death and Death caused by Colon, Lung and Breast Cancer

Types of Cancer	Estimated Figure in Millions	Death Caused by Cancer in Millions
Colon Cancer	1.80 million cases	862 000 deaths
Lung Cancer	2.09 million cases	1.76 million deaths
Breast Cancer	2.09 million cases	627 000 deaths

Etiology of Colon Cancer and Its Clinical Manifestation

The symptoms vary based on the size and stages of the cancer present in the large intestine (Majumdar *et al.*, 1999). Presence of blood in the stool, rectal bleeding, sudden weight loss, diarrhoea, changes in the consistency of the stool that last more than four weeks. Most of the patients don't have any of the symptoms in early stage (Hall *et al.*, 2015). By the growth of Polyps colon cancer are caused. The risk factors of colon cancer are elder age i.e more than 50yrs, consuming more alcohol, using excess tobacco, over smoking, active inflammatory bowel disease etc (Smith *et al.*, 2001).

Targets For Colon Cancer

Colon cancer is mostly diagnosed in early stage itself. The main two targets are Vascular Endothelial Growth Factor drugs and Epidermal Growth Factor which targets the specific protein (Khorana *et al.*, 2003). The key targets for anticancer treatment are RAS, a protein family. The novel protein causes the normal cells in the lining of the colon to become malignant, grow and spread. The mitogenic signalling pathway in gastrointestinal mucosa was triggered by EGFR (Satelli and Li, 2011). SATB2 is a novel transcription factor. It is a protein SWITCH that controls which genes are turned on or off inside the cell of the cancer. Cytochrome P450(CYP) is an enzyme which increases colon cancer and it is a monooxygenase. And it forms the fatty acids called EPOMES (epoxy octadecenoic) (Wang *et al.*, 2019a).

The EPOMES are very dramatically increasing the producing enzymes of EPOMES are CYP monooxygenases are more expressed in colon cancer, in mice. When the CYP monooxygenases are removed from the mice then the tumour growth was suppressed by blocking the enzyme the colon cancer can be reduced (Bruno and Njar, 2007). EPOMES are the metabolites which are found in the vegetable oil and red meat which are called as linoleic acid. It increases the tissue concentrations by consuming more linoleic acid (Wang *et al.*, 2019b).

Vascular Endothelial Growth Factor

Vascular Endothelial Growth Factor and VEGF-R (Vascular Endothelial Growth Factor Receptor) for colorectal cancer treatments. VEGF or VEGF-Receptor blocks the tumour directly of anti-angiogenic effect. Angiogenesis is the reason for the growth of tumour or malignancy. VEGF plays a major role in angiogenesis which is used to fix the VEGF expression (Okita *et al.*, 2009).

Protease Activated Receptor

The G-protein coupled receptor contains protease activated receptor. Protease activated receptor is lacking in physiology than the other G-protein coupled receptor family (Trejo, 2003). PAR consists of four types such as PAR1, PAR2, PAR3and PAR4. The PAR1 is the similar structure assertion of protein.

The PAR2 was induced by thrombin. Aortic vasodilation and MAPK signalling activation (Shea-donohue *et al.*, 2010). Without the proteolytic cleavage the exogenous synthetic agonist peptide binds on the second extracellular loop (ECL2). Biased downstream signalling activation induced after the convincing of the protease cleaving the N terminal domain (Gieseler *et al.*, 2013).

They make the availability for the future activation by synthetic agonist peptide. The BRAF mutation is one of the parts of signalling pathway or route of communication. BRAF V600V is effective when the drugs inhibit BRAF (Platz *et al.*, 2008).

Lung Cancer

Lung cancer is also called as lung carcinoma and it is a malignant tumour in the lung by uncontrolled growth of cells in the lung tissue (Bremnes *et al.*, 2011). And this growth can spread other side of the lung by process of metastasis in other parts of the body and tissue nearby lungs.

There are two principle subtypes of lung cancer, small cell lung carcinoma and non – small cell lung carcinoma (NSCLC), representing 15% and 85% of all lung malignant growth, individually (Brambilla *et al.*, 2001).

NSCLC is additionally arranged into three: squamous cell carcinoma, adenocarcinoma, enormous cell carcinoma. Death rate of lung cancer exceeds more than the other common cancers like colon and breast cancer (Yatabe *et al.*, 1998).

Etiology and Clinical Manifestation of Lung Carcinoma

The lung cancer impact may differ from male to female mostly lung cancer affects the male due to many various reasons and health factors such as smoking is one of the major factors which increases the risk of developing lung cancer than non- smokers (Peto, 2000). In early stages lung cancer doesn't show symptoms in anyone (NSCLC) non -smoke cell is the most common type of lung cancer.

Huff coughing, Chest pain, shortness of breath, wheezing, coughing up blood, pain while breathing frequent lung infections such as pneumonia or bronchitis. Cell carcinoma is a type of skin cancer which invades and starts developing in lungs may also cause paraneoplastic syndrome (Urden *et al.*, 1112).

Targeted Cell of Lung Cancer

NSCLC with wild type EGFR

Epidermal Growth Factor receptor tyrosine kinase inhibitor (EGFR-TKIs) are approved for second line treatment of EGFR wild type. (EGFR-w t) no small cell lung cancer (NSCLC) (Yagishita *et al.*, 2015). Mutation of EGFR protein leads to the development of small cell lung cancer. EGFR tyrosine kinase, the inhibitor blocks the mutation of protein in cancerous cells which alternately stops the growth and division of cancerous cells in the lungs (Chmielecki *et al.*, 2011).

Anti-EGFR Monoclonal Antibodies

Monoclonal antibodies are produced to inhibit the growth and development of cancerous cells in the lungs such antibodies are known as Anti-EGFR monoclonal antibodies. Antibodies binds with EGFR and block the action of epidermal growth factor in cancerous cells (Martinelli *et al.*, 2009). Anti-EGFR monoclonal antibodies are erlotinib, gefitinib and lapatinib are some of antibodies that work as anti-EGFR (Johnston *et al.*, 2006).

Braf Proto Kinase Inhibitor

BRAF is a proto-oncogene, which is a directed sign transduction serine/ threonine protein kinase that can advance cell multiplication and endurance (Tran *et al.*, 2016). BRAF substantial changes have been found in 1-4% of all NSCLC, most normally in patients with adenocarcinomas. These changes are all the more ordinarily connected with previous / current smokers (Shabnam, 2018).The kinase space areas of BRAF transformations in lung malignant growth patients vary from BRAF changes in bosom disease patients. An extraordinary greater part of BRAF changes have been seen the non-covering with other oncogenic transformations in NSCLC (EGFR changes, ALK modifications, and so forth) (Sánchez-Torres *et al.*, 2013).

CONCLUSIONS

Cell line treatment can drag out endurance, whitewash disease- related side effects, and improve personal satisfaction contrasted and best strong consideration in patients with NSCLC. Blends of treatments, particularly those acting by means of various systems, hold guarantee for enhancements in endurance, however exhaustive testing is required—and is without a doubt under way—to decide the ideal mixes of accessible medications and where new medications fit into the armamentarium. Targeting agents could give better treatment choices, regardless of whether utilized alone or in mix with standard cell line therapy. Also, different prognostic elements are beginning to rise to give hints about which patients would benefit from outside assistance by explicit operators. For instance, non-smokers and those with EGFR changes have a superior possibility of reacting to EGFR TKIs. This examination is keeping, attracting us nearer and nearer to the objective of successful, individualized treatment for NSCLC. The data and chart is very clear that lung cancer and breast cancer is estimated to be the most common cancer cases that arise worldwide. Whereas lung cancer is proven to be a more fatal and delicate case, the chance of survival is much less compared to other cancer types. Colon cancer also has a minimal chance of survival.

Conflict of Interest

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