

"Repurposing Avastin drug for detection of lung cancer and to study it's effects on pneumonocytes"

PROJECT WORK

Submitted in partial fulfilment of the requirements for the award of
Bachelor of Technology degree in Biotechnology

By

Mathuvarshini (40230054)



**DEPARTMENT OF BIOTECHNOLOGY
SCHOOL OF BIO AND CHEMICAL ENGINEERING**

SATHYABAMA

**INSTITUTE OF SCIENCE AND TECHNOLOGY
(DEEMED TO BE UNIVERSITY)**

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**JEPPIAAR NAGAR, RAJIV GANDHISALAI,
CHENNAI - 600119**

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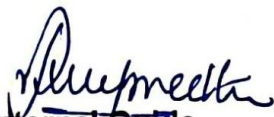
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BONAFIDE CERTIFICATE

This is to certify that this Project Report is the bonafide work of Mathuvarshini (40230054) who carried out the project entitled "Repurposing eugenol to study its effects on breast cancer cells and to study its potential as an anti-cancer drug" under our supervision from January 2024 to March 2024.


Internal Guide

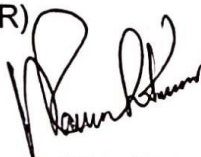
Mrs. JESIA PERSIS PREETHI
MTech (Pir


External Guide

DR. V. BAVANILATHA, Ph.D.

MBA (HR)

MBA (HR)



Head of the Department

ARESH KUMAR M.Phil., Ph.D.,

va voce Examination held on 06. 04. 2024



Inter:

(Dr. J. Theborel)

External Examiner

(Dr. J. Theborel)

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ABSTRACT

Cancer is a complex and diverse group of diseases characterized by the uncontrolled growth and spread of abnormal cells in the body. These cells can form tumors, disrupt normal bodily functions, and potentially invade other tissues and organs, leading to serious health problems.

Cancer can occur in

virtually any part of the body and can manifest in various forms, each with its unique characteristics. Lung cancer is a significant global health concern, and the statistics surrounding this disease highlight its impact on individuals and

society. Lung cancer is one of the most commonly diagnosed cancers worldwide. It accounts for a significant portion of all cancer cases. The incidence of lung cancer is influenced by factors such as smoking rates, air pollution, and occupational exposures. Lung cancer is the leading cause of cancer-related

deaths in both men and women. It is responsible for a higher number of deaths than other common cancers, including breast, colorectal, and prostate cancer.

The global burden of lung cancer is substantial, with millions of new cases diagnosed each year. It is a major public health issue in many countries,

particularly those with high smoking rates. Smoking tobacco is the primary risk factor for developing lung cancer. It is estimated that the majority of lung cancer cases are directly linked to tobacco. While smoking is the most significant risk factor, a significant number of non-smokers also develop lung cancer. This

includes individuals exposed to second-hand smoke, occupational carcinogens, and environmental pollutants. Lung cancer is often diagnosed at advanced stages, which significantly reduces survival rates. Early detection through

screening methods like low-dose CT scans can improve the chances of successful treatment.

The survival rates for lung cancer vary depending on the stage at

diagnosis. The overall five-year survival rate for lung cancer is relatively low compared to other cancers. However, when detected at an early stage, the chances of survival are significantly better. Avastin, also known as Bevacizumab, plays a significant role in the treatment of lung cancer, particularly in certain

types and stages of the disease. Avastin is classified as an anti-angiogenic drug. It works by inhibiting angiogenesis, the process of forming new blood vessels. In the context of cancer, this is essential because tumors need a blood supply to

grow and spread. By blocking angiogenesis, Avastin helps to "starve" the tumor, limiting its growth and ability to metastasize to other parts of the body. Avastin

is used in combination with chemotherapy for the treatment of advanced-stage, non-squamous non-small cell lung cancer (NSCLC).

1. INTRODUCTION

Cancer is a disease in which some of the body's cells grow uncontrollably and spread to other parts of the body.

Cancer can start almost anywhere in the human body, which is made up of trillions of cells. Normally, human cells grow and multiply (through a process called cell division) to form new cells as the body needs them. When cells grow old or become damaged, they die, and new cells take their place.

Sometimes this orderly process breaks down, and abnormal or damaged cells grow and multiply when they shouldn't. These cells may form tumors, which are lumps of tissue. Tumors can be cancerous or not cancerous (benign).

Cancerous tumors spread into, or invade, nearby tissues and can travel to distant places in the body to form new tumors (a process called metastasis). Cancerous tumors may also be called malignant tumors. Many cancers form solid tumors, but cancers of the blood, such as leukemia, generally do not.

Benign tumors do not spread into, or invade, nearby tissues. When removed, benign tumors usually don't grow back, whereas cancerous tumors sometimes do. Benign tumors can sometimes be quite large, however. Some can cause serious symptoms or be life threatening, such as benign tumors in the brain.



Cancer is a genetic disease—that is, it is caused by changes to genes that control the way our cells function, especially how they grow and divide.

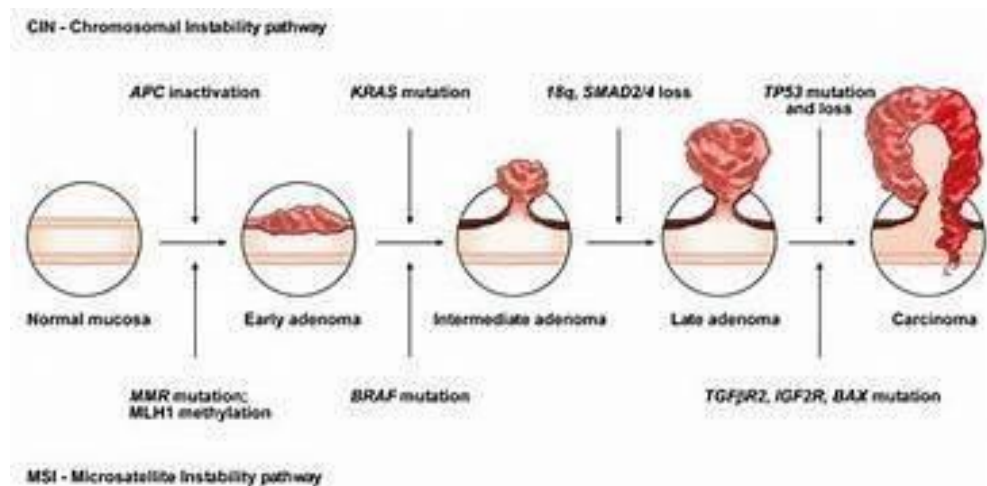
Genetic changes that cause cancer can happen because:

- of errors that occur as cells divide.

- of damage to DNA caused by harmful substances in the environment, such as the chemicals in tobacco smoke and ultraviolet rays from the sun. (Our Cancer Causes and Prevention section has more information.)
- they were inherited from our parents.

The body normally eliminates cells with damaged DNA before they turn cancerous. But the body's ability to do so goes down as we age. This is part of the reason why there is a higher risk of cancer later in life.

Each person's cancer has a unique combination of genetic changes. As the cancer continues to grow, additional changes will occur. Even within the same tumor, different cells may have different genetic changes.



The genetic changes that contribute to cancer tend to affect three main types of genes—proto-oncogenes, tumor suppressor genes, and DNA repair genes. These changes are sometimes called “drivers” of cancer.

Proto-oncogenes are involved in normal cell growth and division. However, when these genes are altered in certain ways or are more active than normal, they may become cancer-causing genes (or oncogenes), allowing cells to grow and survive when they should not.

DNA repair genes are involved in fixing damaged DNA. Cells with mutations in these genes tend to develop additional mutations in other genes and changes in their chromosomes, such as duplications and deletions of chromosome parts. Together, these mutations may cause the cells to become cancerous.

As scientists have learned more about the molecular changes that lead to cancer, they have found that certain mutations commonly occur in many types of cancer. Now there are many cancer treatments available that target gene mutations found in

cancer. A few of these treatments can be used by anyone with a cancer that has the targeted mutation, no matter where the cancer started growing.

1.1 LUNG CANCER

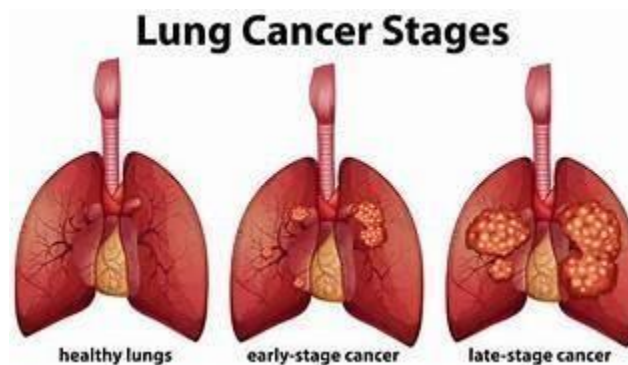
Lung cancer, also known as **lung carcinoma**, is a malignant tumor that begins in the lung. Lung cancer is caused by genetic damage to the DNA of cells in the airways, often caused by cigarette smoking or inhaling damaging chemicals. Damaged airway cells gain the ability to multiply unchecked, causing the growth of a tumor. Without treatment, tumors spread throughout the lung, damaging lung function. Eventually lung tumors metastasize, spreading to other parts of the body.



Early lung cancer often has no symptoms and can only be detected by medical imaging. As the cancer progresses, most people experience nonspecific respiratory problems: coughing, shortness of breath, or chest pain. Other symptoms depend on the location and size of the tumor. Those suspected of having lung cancer typically undergo a series of imaging tests to determine the location and extent of any tumors. Definitive diagnosis of lung cancer requires a biopsy of the suspected tumor be examined by a pathologist under a microscope. In addition to recognizing cancerous cells, a pathologist can classify the tumor according to the type of cells it originates from. Around 15% of cases are small-cell lung cancer, and the remaining 85% (the nonsmall-cell lung cancers) are adenocarcinomas, squamous-cell carcinomas, and largecell carcinomas. After diagnosis, further imaging and biopsies are done to determine the cancer's stage based on how far it has spread.

Treatment for early stage lung cancer includes surgery to remove the tumor, sometimes followed by radiation therapy and chemotherapy to kill any remaining

cancer cells. Later stage cancer is treated with radiation therapy and chemotherapy alongside drug treatments that target specific cancer subtypes. Even with treatment, only around 20% of people survive five years on from their diagnosis. Survival rates are higher in those diagnosed at an earlier stage, diagnosed at a younger age, and in women compared to men.



Most lung cancer cases are caused by tobacco smoking. The remainder are caused by exposure to hazardous substances like asbestos and radon gas, or by genetic mutations that arise by chance. Consequently, lung cancer prevention efforts encourage people to avoid hazardous chemicals and quit smoking. Quitting smoking both reduces one's chance of developing lung cancer and improves treatment outcomes in those already diagnosed with lung cancer.

Lung cancer is the most diagnosed and deadliest cancer worldwide, with 2.2 million cases in 2020 resulting in 1.8 million deaths. Lung cancer is rare in those younger than 40; the average age at diagnosis is 70 years, and the average age at death 72. Incidence and outcomes vary widely across the world, depending on patterns of tobacco use. Prior to the advent of cigarette smoking in the 20th century, lung cancer was a rare disease. In the 1950s and 1960s, increasing evidence linked lung cancer and tobacco use, culminating in declarations by most large national health bodies discouraging tobacco use.

Avastin (Bevacizumab) is a medication that has been used in the treatment of certain types of lung cancer, primarily non-small cell lung cancer (NSCLC). Avastin is classified as an anti-angiogenic drug. It works by inhibiting the activity of vascular endothelial growth factor (VEGF), a protein that promotes the formation of new blood vessels. In cancer, blocking VEGF can inhibit the growth of blood vessels that supply tumors, thereby limiting their growth and ability to spread. The effectiveness of Avastin may be

influenced by specific biomarkers, particularly VEGF expression. Biomarker testing may be performed to determine if a patient is a suitable candidate for Avastin treatment. In some cases, Avastin may be used as a maintenance therapy. After a patient has received a set number of cycles of initial chemotherapy, Avastin alone may be continued as maintenance therapy to prolong progression-free survival.

2. REVIEW OF LITERATURE

1. Lung Cancer Overview:

Lung cancer is a diverse disease with two primary subtypes: Non-Small Cell Lung Cancer (NSCLC) and Small Cell Lung Cancer (SCLC). NSCLC accounts for approximately 85% of all lung cancer cases, while SCLC is more aggressive.

Epidemiologically, lung cancer is a leading cause of cancer-related deaths worldwide. Risk factors include smoking, exposure to carcinogens, family history, and genetic mutations.

Staging of lung cancer is crucial in determining prognosis and treatment options, with Stage I having the best prognosis, while Stage IV indicates metastatic disease with limited treatment options.

Early lung cancer often has no symptoms. When symptoms do arise they are often nonspecific respiratory problems – coughing, shortness of breath, or chest pain – that can differ from person to person. Those who experience coughing tend to report either a new cough, or an increase in the frequency or strength of a pre-existing cough. Around one in four cough up blood, ranging from small streaks in the sputum to large amounts. Around half of those diagnosed with lung cancer experience shortness of breath, while 25–50% experience a dull, persistent chest pain that remains in the same location over time. In addition to respiratory symptoms, some experience systemic symptoms including loss of appetite, weight loss, general weakness, fever, and night sweats.

Several lung cancer types are subclassified based on the growth characteristics of the cancer cells. Adenocarcinomas are classified as lepidic (growing along the surface of intact alveolar walls), acinar and papillary, or micropapillary and solid pattern.

Lepidic adenocarcinomas tend to be least aggressive, while micropapillary and solid pattern adenocarcinomas are most aggressive.

2. Importance of Early Detection:

Early detection significantly improves the chances of survival in lung cancer patients. Late-stage diagnosis often results in a poor prognosis.

Early detection is of paramount importance in the battle against lung cancer. Lung cancer is often referred to as the "silent killer" because it frequently remains asymptomatic in its early stages, only manifesting symptoms when it has reached an advanced and less treatable phase. This makes early detection a critical lifesaver. When lung cancer is identified in its earlier stages, it offers patients a significantly higher chance of successful treatment and improved outcomes. Moreover, it allows for less aggressive and more focused treatment approaches, reducing the need for extensive surgeries or toxic chemotherapy regimens.

Early detection also lessens the emotional and financial burdens on individuals and their families, sparing them from the devastating consequences of late-stage diagnoses. Screening methods like low-dose CT scans can identify lung cancer at an earlier, more treatable stage, making them indispensable tools in the fight against this deadly disease. Ultimately, early detection is a powerful weapon that not only saves lives but also enhances the quality of life for those impacted by lung cancer. Current diagnostic methods include chest X-rays, computed tomography (CT) scans, bronchoscopy, sputum cytology, and biomarker testing. However, there remains a need for more reliable and less invasive early detection techniques.

3. Repurposing Existing Drugs:

Drug repurposing, also known as drug repositioning, offers a promising approach to drug development, as it leverages existing drugs for new therapeutic applications. This strategy can expedite the approval process and reduce costs.

Repurposing Avastin for lung cancer detection aligns with the growing interest in identifying new applications for existing pharmaceuticals.

The concept of repurposing existing drugs for lung cancer represents a beacon of hope in the quest to find more effective and accessible treatments for this devastating disease. Traditional drug development is a lengthy and costly process, but repurposing offers a shortcut by leveraging the safety

profiles and known mechanisms of established drugs. Repurposing not only accelerates the path to potential treatments but also opens up a treasure trove of possibilities. These drugs, originally designed for entirely different purposes, may possess untapped potential against lung cancer. This approach not only holds the promise of more cost-effective treatments but can also reduce the burden on patients and healthcare systems.

Furthermore, it underscores the versatility and adaptability of pharmacological science, potentially transforming familiar medications into life-saving assets in the ongoing battle against lung cancer.

4. Avastin (Bevacizumab):

Bevacizumab, marketed under the brand name Avastin, is a monoclonal antibody designed to inhibit vascular endothelial growth factor (VEGF). Its primary application has been in the treatment of various cancers, particularly colorectal, lung, and breast cancer, by suppressing angiogenesis, which is crucial for tumor growth and metastasis.

Avastin has shown effectiveness in extending progression-free survival and overall survival in certain cancers, but its applicability in early cancer detection remains an open question.

Classified as an anti-angiogenic drug, it operates by disrupting the formation of new blood vessels in the body, a process known as angiogenesis. Avastin's primary target is vascular endothelial growth factor (VEGF), a protein that plays a pivotal role in the development of blood vessels that nourish tumors. By inhibiting VEGF, Avastin starves cancer cells of their blood supply, effectively stifling their growth and metastatic potential. Avastin has gained prominence in the treatment of various cancers, including colorectal, lung, and breast cancers, often used in combination with chemotherapy to augment its efficacy. It has demonstrated its potential not only in slowing disease progression but also in extending survival rates, marking a turning point in cancer therapeutics.

However, the role of Avastin is not confined to its anti-angiogenic properties; it has opened new avenues of research, exploring its potential application in cancer diagnostics and the repurposing of this drug to serve dual roles in

both treatment and early detection. Avastin's story exemplifies the multifaceted nature of pharmaceutical science and its transformative impact on the landscape of cancer care, providing both hope and healing to countless patients around the world.

5. Avastin in Cancer Treatment:

Previous studies have explored Avastin's role in cancer treatment, demonstrating its ability to shrink tumors, prevent the formation of new blood vessels that supply the tumor, and increase the effectiveness of chemotherapy.

However, the application of Avastin in cancer diagnostics is a relatively unexplored avenue, with potential as a tool for identifying early-stage lung cancer through its interaction with VEGF.

The effects of Avastin (Bevacizumab) on lung cancer have been a subject of intense research and clinical exploration, particularly in the context of nonsmall cell lung cancer (NSCLC). As an anti-angiogenic drug, Avastin

disrupts the process of angiogenesis, which is the formation of new blood vessels that supply tumors with essential nutrients. In NSCLC, where it is frequently used in combination with chemotherapy, Avastin has shown the potential to inhibit the growth of blood vessels feeding the tumor, thus constraining its expansion. This action can slow the progression of the disease and, in some cases, lead to more extended periods of progression-free survival. Avastin's effects are not limited to its role in tumor blood vessel inhibition; it also has implications for the overall well-being of patients.

However, it is vital to acknowledge that Avastin is not a cure for lung cancer, and its effectiveness can vary depending on the patient's specific characteristics and the stage of their disease. This underscores the importance of individualized treatment plans, close patient monitoring, and ongoing research into the role of Avastin in lung cancer therapy, with the ultimate goal of improving patient outcomes and the quality of life for those living with this challenging disease.

6. Effects of Avastin on Pneumonocytes:

Pneumonocytes are specialized lung cells responsible for maintaining alveolar structure and function. There is limited information on how Avastin affects pneumonocytes.

Investigating the effects of Avastin on these cells is essential to understanding the safety and potential side effects of repurposing this drug for lung cancer detection.

Research into the effects of Avastin (Bevacizumab) on pneumonocytes, the specialized cells of the lung responsible for maintaining alveolar structure and function, is a critical aspect of understanding the safety and potential side effects of this drug in lung cancer treatment. While Avastin's primary role is to inhibit angiogenesis, its potential impact on lung cells has raised important questions.

Pneumonocytes, as vital components of lung health, play a crucial role in ensuring proper gas exchange and overall respiratory function. However, their vulnerability to potential drug-induced damage is a concern. Some studies have suggested that Avastin may have adverse effects on pneumonocytes, leading to concerns about possible impacts on lung function and the development of respiratory complications.

Further research is required to delve deeper into the specific effects of Avastin on pneumonocytes, including understanding the mechanisms through which these effects occur. This knowledge is essential to assess the safety and long-term implications of using Avastin in lung cancer treatment comprehensively. As we strive to improve lung cancer therapies, striking a balance between the benefits of this anti-angiogenic drug and its potential impact on lung cells remains a critical challenge, underscoring the need for ongoing investigations into this complex interaction.

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MATHU VARSHINI

(Full Name of the Applicant)



09 Nov 2001

(D.O.B)

Female

(Gender)

OBC-NCL

(Category)

Indian

National

+91-9500814829

(Parent/Guardian's Mobile Number)

VARALAKSHMI

(Parent/Guardian's Name)

Communication Address

No.26 Immanuel street, Mahalakshmi Nagar
Selayur, Chennai - 600073
CHENNAI
Tamil Nadu 600073
+91-9344063562 (Mobile No.)
mathuvarshini04@gmail.com

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