Molecular Characterisation of Bacterial Infection in Respiratory Cancer Patients

[1]Ravi Shankar Mishra, [1]CBS Dangi

[1]RKDF University

ABSTRACT

Worldwide, respiratory disorders provide enormous difficulties to healthcare systems and play a large role in the morbidity and death of the entire population. In fact lung cancer is one of the leading cancers worldwide as well as in India. A number of respiratory disorders including cancer can be attributed to smoking habits but bacterial infections are equally responsible for respiratory diseases. With the advent of advanced molecular technique like 16S RNA sequencing methods, molecular characterization of pathogens can be done much faster throwing light to their identification and mechanism of infection and targets for medications. It is a cost-effective tool to identify simpler to complex microbial strains at species level. In fact these molecular have transformed diagnostic microbiology as it is much faster than the conventional microbiological methods. It is also useful in detection of antimicrobial resistance genes and their characterization by genotyping. The present review will look into the various studies done to detect bacterial infections prevalent in respiratory cancers and the impact of molecular characterization of these bacteria for faster and better cancer management.

Keywords: Bacteria, molecular methods, 16S RNA sequencing, respiratory cancer

INTRODUCTION:

Molecular microbiology is the fastest growing discipline which plays significant role for the detection and characterization of microorganism. Rapid detection of microorganism by using these molecular methods has revolutionized routine diagnostic microbiology. Microorganisms which are fastidious, slow growing, non-viable, and non-cultivable may not be detected by conventional culture technique but can be identified by using molecular technique. The introduction of these molecular techniques and their automation was introduced in the form of PCR technology. And these automation when applied to various stages of DNA or RNA extraction, amplification and product detection

together with real-time PCR further increase the utility of molecular detection in the clinical microbiology laboratory by making it more efficient and cost-effective.[1] This paper will provide an overview of the some basic molecular technique and clinical applications of molecular methods for infectious diseases.

LINK BETWEEN BACTERIAL INFECTION AND LUNG CANCER

Although the main causes of lung cancer are attributed to environmental stressors like chemical pollution or smoking habits, genetic as well as nutritional variables and their interactions, microbial infections have also been linked to certain respiratory cancers including lung cancers (M.C. Poirier *et al.,* 2000, S.A. Sheweita *et al.,* 2000.)

As to the possible mechanism by which respiratory pathogens can induce lung cancer in a patient, it is suggested that it include systemic inflammatory pathways as a result of microbial persistence in the lung that can then lead to the development of lung carcinogenesis. Tumor development in lung cancer is known to be associated with chronic inflammation which in turn is associated with lung infection (Budisan *et al.,* 2021).

Some other studies that support the link between lung infections and lung cancer by inflammatory pathways include histology studies done by Cukie *et al.,* in 2017 and earlier by Liang et al. in 2009 that demonstrated connection between Mycobacterium tuberculosis induced fibrosis and lung cancer.

Similarly infections caused by *Haemophilus influenzae, Moraxella catarrhalis, Streptococcus pneumoniae, Haemophilus parainfluenzae, Staphylococcus aureus,* and *Pseudomonas aeruginosa* are all linked to chronic lung inflammation that can develop into lung cancer (S. Sthi *et al.,* 2001).

MOLECULAR CHARACERIZATION OF BACTERIA

With the advancement of molecular techniques, identification of bacteria have also become faster and more efficient. Studies have been done to molecularly characterize bacteria found in lung cancer patients to understand its pathophysiology and mechanism as lung cancer is the most prevalent cancer in the world and it's responsible for 1-7

million deaths annually. In a study done by Thahira *et. al.*, 2018, molecular characterization of bacteria isolated from lung cancer patients and bronchiectasis patients were done and the study confirmed that Gram-negative species patients harbour bacterial species m their lungs.

In another study, scientists evaluated the potential use of microbiome as biomarkers for the early detection of NSCLC. They used droplet digital PCR to analyze 25 NSCLC-associated bacterial genera in lung cancer patients. The study demonstrated that Sputum microbiome might provide non-invasive biomarkers for the early detection and classification of NSCLC.

Aquino *et al.,* in 1917 molecularly characterized some pathogenic bacteria from cystic fibrosis (CF) patients from their respiratory tract. The techniques used were standard microbiological techniques for culture along with 16S rRNA gene sequencing and MALDI-TOF mass spectrometry for molecular characterization. The most prevalent bacteria identified were *Pseudomonas aeruginosa* followed by *Staphylococcus aureus*, Pseudomonas spp and *Klebsiella oxytoca.*

Several studies have linked lung infections with development of lung cancer in the last several years one such study is a study done by Nakachi K *et al.,* in the year 1999 in which a correlation between TB infection, HPV infection and fungal infection like *Microsporum canis* and lung cancer in the area was demonstrated.

In view of the correlation seen between long term bacterial infection and lung cancer development, the microbiome can be regarded as a powerful diagnostic as well as therapeutic indicator. Lee *et al.,* in 2016 demonstrated the difference between the microbiomes of patients with benign and malignant cancers by using high-throughput NGS sequencing of 16S rRNA technique. They found that the genera Veillonella and Megasphaera can serve as potential lung cancer biomarkers

Other potential lung cancer biomarkers include the genera Capnocytophaga, Selenomonas, Veillonella, and Neisseria in small-cell carcinoma (SCC) and adenocarcinoma as demonstrated by Yan *et al.,* in 2015 by doing 16S RNA sequencing of saliva samples of cancer patients as well as healthy subjects.

The presence of bacterial load in sputum cancer patients can be regarded as biomarker of cancer stage and status as well as demonstrated by Cameron *et al.,* 2017. They did a pilot-

sized study to evaluate the potential of the sputum microbiome as a source of non-invasive bacterial biomarkers for lung cancer status and stage.

IMPACT ON TREATMENT OF LUNG CANCER

Immunotherapy has emerged as a very powerful anticancer treatment modality in recent years. The identification and molecular profiling of bacterial prevalent in cancers such as lung cancer can thus hugely benefit the therapeutic scene by explaining the role of immunity in cancer development as well as its cure. In this direction, numerous studies have been conducted to throw light in the understanding of microbiome and how anticancer immunotherapy works.

A study done by Kedarbahi *et al.,* in 2017 demonstrat5ed how antibiotics can affect teh treatment and management of non-small-cell lung cancer. They demonsrated the us of Nivolumab in the treatment of non-small-cell lung cancer.

On the other hand, antibiotic use in cancer treatment may also increase tumor progression by disrupting the commensal balanced microbiome as gut microbiota have a role to play in helping an individual's immunity and in eliminating pathogens and in preventing cancer development. Thus, gut microbiota impacts the efficacy of chemotherapy treatment. There is a delicate balance and homeostasis that needs to be maintained because gut microbiota can help in cancer prevention as well as cancer development (Akbar *et al.,* 2022). To enhance the effectiveness of chemotherapy like cisplatin, administration of pro-biotics can be very helpful as demonstrated by Gui *et al.,* 2015.

Thus it can be said that more and more research in this field by characterizing microflora by molecular technique will help in the better understanding of their role in carcinogenesis and will help in better management and prevention of cancer by impacting the treatment plan.

Various studies done in the last decade have shown a strong correlation between bacterial infections and carcinogenesis, but only a small number of cancers are actually linked to bacterial oncogeny. Cancer development is a multistep, multi-factorial and complex process and there still exists a lot of gap in our knowledge of this process. Molecular techniques have a huge potential in identification of pathogens and also in understanding their mechanism of action that contribute to cellular transformation. There is every

reason to believe that persistent and long term infections can actually disrupt the regulation of cells in the body leading to cancer development. The molecular characterization of pathogens can thus throw light in this aspect of cancer development and it will also impact the treatment and management of cancer and therefore, this field has become a highlighted area in cancer research and is bound to generate a huge data that will be beneficial to the medical fraternity and cancer patients in the future.

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