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Omics sciences and precision medicine in lung cancer

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Abstract

Lung cancer is a complex disease, with a wide range of genetic alterations and clinical presentations. Understanding the natural and clinical history of the disease is crucial for developing effective diagnostic and treatment strategies. Omics approaches, such as genomics, transcriptomics, proteomics, and metabolomics, have emerged as powerful tools for understanding the molecular mechanisms underlying lung cancer and for identifying novel biomarkers and therapeutic targets. These approaches enable researchers to examine the entire genome, transcriptome, proteome, or metabolome of a cell or tissue, providing a comprehensive view of the biological processes involved in lung cancer development and progression. Targeted therapies that address specific genetic mutations and pathways hold promise for improving the diagnosis and treatment of this disease. ***Clin Ter 2023; 174 Suppl. 2 (6):37-45 doi: 10.7417/CT.2023.2470***

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Introduction

Lung cancer is a complex disease with a multifactorial etiology, involving a combination of genetic and environmental factors. The understanding of tumor natural and clinical history, as well as its genetics, has significantly improved in recent years, leading to the development of new diagnostic and therapeutic approaches. Genetic testing can identify predisposition to lung cancer and provide valuable information for tailoring treatment options. Additionally, the genomics of the tumor, including rearrangements, fusion genes, and somatic mutations, can guide targeted therapies (1, 2). Other emerging biomarkers—such as circulating tumor DNA, proteomic, metabolomic, and microbiomic profiling—may provide further insights into the pathogenesis and personalized management of lung cancer (2).

In recent years, the role of genomics in tumor management has expanded rapidly. Chromosomal rearrangements, fusion genes, and somatic mutations are common genetic alterations that occur in cancer and can be identified through genomic analysis (3). Chromosomal rearrangements, such as translocations or deletions, are frequent genetic events in cancer, which can lead to altered expression or function of the genes involved in cell proliferation, differentiation, and apoptosis, resulting in cancer development and progression (4). Fusion genes, formed as a result of chromosomal rearrangements, play a significant role in the development of cancer by activating or inactivating pathways involved in cell growth and survival (5). Somatic mutations, which are genetic alterations that occur in non-germline cells, can also affect genes involved in cellular processes and contribute to the development of cancer (6).

The identification of specific genetic alterations in tumors has led to the development of targeted therapies that aim to block the signaling pathways affected by these alterations. The use of targeted therapies has significantly improved the outcomes of cancer treatment for some patients, particularly those with specific genetic alterations that are targeted by the therapy (7). One example of this is the use of tyrosine kinase inhibitors to target the BCR-ABL fusion protein in chronic myeloid leukemia (8).

Another area of genomics in tumor management that has gained significant attention is the use of liquid biopsies,

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which involve the analysis of circulating tumor cells or circulating tumor DNA (ctDNA) in the blood. ctDNA analysis has emerged as a promising biomarker for cancer diagnosis and prognosis, and for monitoring treatment response (9). It can provide information on the genetic alterations present in the tumor, such as somatic mutations and chromosomal rearrangements, which can guide the selection of targeted therapies (9).

Pharmacogenomics—the study of genetic variations that influence drug response and toxicity—is also playing an increasingly important role in tumor management. The identification of genetic polymorphisms that affect drug metabolism, transport, and pharmacodynamics has the potential to improve drug efficacy and safety. Moreover, pharmacogenomics can inform drug selection and dosing, which can improve treatment outcomes for cancer patients (10).

Genomics and pharmacogenomics have become the forefront of tumor management. Advances in technology have made it possible to identify specific genetic alterations in tumors and to develop targeted therapies that can improve treatment outcomes. The use of liquid biopsies and pharmacogenomics has also emerged as promising approaches for cancer diagnosis, prognosis, and treatment selection. The integration of genomics and pharmacogenomics into clinical practice has the potential to improve personalized cancer treatment and ultimately improve patient outcomes.

Lung Tumor natural history and clinical history

Lung cancer is a complex disease, with a natural history that involves its progression from initial formation to metastatic spread. The clinical history of lung cancer, on the other hand, focuses on the symptoms and physical manifestations of the disease in the patient. A better understanding of the natural and clinical history of lung cancer is crucial for developing effective diagnostic and treatment strategies.

According to a study by Seijo et al. (2019), the natural history of lung cancer is determined by the interaction between the tumor and the host. The authors describe the process of tumor development, from the initial genetic mutations to the formation of preneoplastic lesions, and the subsequent progression to invasive cancer. The authors also discuss the role of the immune system in tumor development and progression (11).

In terms of clinical history, the symptoms of lung cancer vary depending on the stage and location of the tumor. According to the American Cancer Society (2021), common symptoms of lung cancer include persistent cough, chest pain, shortness of breath, hoarseness, weight loss, and coughing up blood. However, many patients with lung cancer may not experience any symptoms until the disease has progressed to an advanced stage (12).

Lung cancer is a complex disease that involves multiple genetic and environmental factors. The natural history of lung cancer is characterized by the progressive accumulation of genetic alterations that ultimately result in the development of a malignant tumor (13). The development of lung cancer can be divided into several stages, including initiation, promotion, and progression. The initiation stage involves exposure to carcinogens, such as tobacco smoke, which causes DNA damage in lung cells (14). The promotion stage involves the clonal expansion of mutated cells, which can eventually lead to the development of a preneoplastic lesion (15). Finally, the progression stage involves the acquisition of additional genetic alterations, which allow the preneoplastic lesion to progress to an invasive carcinoma (16).

The clinical history of lung cancer is often characterized by a long asymptomatic phase followed by the onset of symptoms, which can vary depending on the location and size of the tumor. Symptoms of lung cancer may include cough, chest pain, shortness of breath, hemoptysis, weight loss, and fatigue. However, many patients may not experience symptoms until the cancer has reached an advanced stage (17). Thus, early detection of lung cancer is crucial for improving patient outcomes.

Several risk factors have been identified for the development of lung cancer, including smoking, exposure to radon gas, air pollution, and occupational exposure to carcinogens such as asbestos and diesel exhaust. Smoking remains the most significant risk factor for lung cancer, accounting for approximately 85% of cases (14). As such, smoking cessation is the most effective way to reduce the risk of developing lung cancer.

Genetics of the tumor

Genetic alterations play a significant role in the development and progression of lung cancer. Mutations in oncogenes, tumor suppressor genes, and DNA repair genes have been frequently found in lung cancer. The identification of these genetic alterations has led to the development of targeted therapies for lung cancer. For example, EGFR mutations are commonly found in non-small cell lung cancer (NSCLC) patients, and drugs targeting these mutations have been developed, such as gefitinib and erlotinib. Other mutations, such as ALK, ROS1, and BRAF, have also been identified as actionable targets in NSCLC (18).

Genetics has undergone significant advancements over the past few decades, which has led to the discovery of numerous genetic variations that influence tumor development and progression. Genetic testing has become an essential component in tumor management, as it helps in identifying individuals who are predisposed to developing certain types of tumors. Several studies have identified the association between specific genetic mutations and an increased risk of tumor development. For instance, BRCA1 and BRCA2 mutations are associated with an increased risk of breast and ovarian cancer (19, 20). Lynch syndrome, caused by mutations in DNA mismatch repair genes, is associated with an increased risk of colorectal, endometrial, and other cancers (21).

In addition to identifying germline mutations, genetic testing can also identify somatic mutations in the tumor tissue. Somatic mutations occur in non-germline cells and are not inherited. These mutations are unique to the tumor tissue and can provide information about the tumor's biology, behavior, and potential response to treatment. The identification of somatic mutations has led to the development of targeted therapies that can specifically target these mutations. For example, HER2-positive breast cancers can be treated with

trastuzumab, a targeted therapy that specifically targets the HER2 protein (22). Similarly, vemurafenib, a targeted therapy, is effective in treating melanoma patients with the BRAF V600E mutation (23). Lung cancer genetic mutations and their phenotype are reported in table 1.

Genetic Testing

Lung cancer is a complex disease that can be caused by a combination of genetic and environmental factors. Genetic testing can provide important information about a person's risk for developing lung cancer and may help guide personalized treatment options. One gene that has been implicated in the development of lung cancer is the epidermal growth factor receptor (EGFR) gene. Mutations in this gene have been found in a subset of non-small cell lung cancers (NSCLC) and are associated with a higher response rate to targeted therapy with EGFR inhibitors. Another gene that has been linked to lung cancer is the KRAS gene. Mutations in this gene are common in lung adenocarcinomas and have been associated with a poorer response to therapy. Genetic testing for these and other genes can be performed on tumor tissue samples using techniques such as next-generation sequencing. In some cases, testing may also be performed on blood samples to detect inherited genetic mutations that increase the risk of developing lung cancer (24).

It is important to note that while genetic testing can provide valuable information, it is not a substitute for regular cancer screenings or other preventative measures, such as smoking cessation. According to a study by Wu et al. (25), genetic testing can help identify patients with metastatic cancer who may benefit from targeted therapy. The study found that patients with lung cancer who had an EGFR mutation had a better response to EGFR inhibitors than those without the mutation. Similarly, another study by Peng et al. (26) reported that genetic testing can help identify patients with pancreatic cancer who may benefit from PARP inhibitors. The study found that patients with BRCA1/2 mutations had a better response to PARP inhibitors than those without the mutation.

Predisposition

Lung cancer is a multifactorial disease influenced by a complex interplay of genetic, environmental, and lifestyle factors. Environmental factors such as smoking and exposure to pollutants are known to increase the risk of lung cancer, which is why, in order to reduce the burden of lung cancer, prevention efforts aim at reducing tobacco use (the cornerstone of lung cancer prevention) and developing strategies to reduce exposure to environmental carcinogens and promote healthy lifestyle choices. However, genetics also play an important role in predisposing individuals to the disease: several genes have been identified as potential contributors to lung cancer susceptibility—including EGFR, KRAS, and TP53. Studies have shown that certain genetic variations in these genes may increase an individual's risk of developing lung cancer (27).

One of the most well-known genes associated with lung cancer is EGFR, which encodes for the epidermal growth factor receptor. Mutations in this gene have been found in a subset of non-small cell lung cancer (NSCLC) cases, particularly in patients who have never smoked. These mutations lead to increased activation of the EGFR pathway, which promotes tumor growth and survival. Other genes that are commonly mutated in NSCLC include KRAS, which is

Table 1. Lung cancer Genetic Mutations and their phenotype.

S.no	Gene	Inheritance	Phenotype	OMIM
1	FASLG	AD, Somatic Mutation	Lung cancer, susceptibility to	134638
2	CASP8		Hepatocellular carcinoma, somatic	601763
3		AD, Somatic Mutation	Lung cancer, protection against	211980
4	PIK3CA		Hepatocellular carcinoma, somatic	171834
5			Non-small cell lung cancer, somatic	211980
6	IRF1		Non-small cell lung cancer, somatic	147575
7	PRKN		Adenocarcinoma of lung, somatic	602544
8	EGFR	AD, Somatic Mutation	Adenocarcinoma of lung, response to tyrosine kinase inhibitor in	131550
9		AD, Somatic Mutation	Non-small cell lung cancer, response to tyrosine kinase inhibitor in	211980
10		AD, Somatic Mutation	Non-small cell lung cancer, susceptibility to	211980
11	BRAF		Adenocarcinoma of lung, somatic	164757
12			Non-small cell lung cancer, somatic	211980
13	MAP3K8		Lung cancer, somatic	191195
14	ERCC6	AD, Somatic Mutation	Lung cancer, susceptibility to	609413
15	SLC22A1L		Lung cancer, somatic	602631
16	PPP2R1B		Lung cancer, somatic	603113
17	KRAS		Lung cancer, somatic	190070
18	ERBB2		Adenocarcinoma of lung, somatic	164870
19	CYP2A6	AD, Somatic Mutation	Lung cancer, resistance to	122720

involved in cell signaling pathways, and TP53, which plays a key role in regulating cell growth and preventing cancer (28). While genetic predisposition to lung cancer is not fully understood, several risk factors have been identified. For example, individuals with a family history of lung cancer are more likely to develop the disease themselves. Additionally, certain ethnic groups, such as individuals of Asian descent, have a higher prevalence of EGFR mutations and are more likely to develop lung cancer at a younger age (29).

Correlated Syndromes

Correlated syndromes in lung cancer refer to the occurrence of multiple clinical manifestations that may be associated with lung cancer, but not necessarily are caused by the tumor itself. For example, paraneoplastic syndromes, which are caused by immune-mediated reactions to the tumor, can result in a variety of symptoms like neurological deficits, endocrine abnormalities, and dermatological manifestations. Additionally, patients with lung cancer may experience chronic obstructive pulmonary disease (COPD), a condition characterized by chronic inflammation and narrowing of the airways, which can exacerbate respiratory symptoms and decrease lung function. Furthermore, lung cancer is also associated with an increased risk of developing venous thromboembolism (VTE), a potentially life-threatening condition that involves blood clots forming in the veins of the legs or lungs. The presence of these correlated syndromes can complicate the diagnosis and treatment of lung cancer and may require a multidisciplinary approach to management (30).

In addition to genetic testing, several studies have also emphasized the importance of identifying clinical syndromes to provide appropriate preventive measures. For example, a study by Saidane et al. (31) found that families with a history of lung cancer have an increased risk of developing the disease, even in the absence of smoking, thus identifying the familial lung cancer syndrome. This knowledge allows clinicians to provide tailored screening recommendations to detect lung cancer at an early stage, potentially reducing mortality. Similarly, the identification of the Lynch syndrome, as reported by Lee et al. (32), allows for tailored screening recommendations and risk-reducing interventions for individuals at increased risk of colorectal and other cancers.

The identification of these correlations helps in identifying individuals with a predisposition to tumor development and selecting appropriate screening and management strategies. The paper by Bonadona et al. (33) discusses the importance of identifying individuals with Lynch syndrome, as these individuals have an increased risk of colon cancer, while the paper by Gueye Tall et al. (34) discusses the correlation between specific genetic mutations and the risk of developing Wilms tumor in individuals with certain tumor syndromes.

Overall, the identification of correlated syndromes and genetic mutations through testing is critical in the management of hereditary cancer syndromes: it allows for tailored surveillance, risk-reducing interventions, and enhanced screening measures to detect cancer at an early stage. With the increasing availability and affordability of genetic testing, it is essential to incorporate genetic testing into clinical practice to provide optimal care to individuals at risk of developing hereditary cancer syndromes.

Genomics of the tumor

Cancer is a heterogeneous disease with diverse genetic alterations. Advances in genomics have enabled the identification of somatic mutations, fusion genes, and chromosomal rearrangements in various cancer types. The identification of driver mutations that cause oncogenic transformation has facilitated the development of targeted therapies for cancer patients. Several studies have reported genetic aberrations in different types of tumors, and these findings have improved understanding and management of these cancers.

Genetic alterations are common in lung cancer and can contribute to tumor development and progression. A variety of genetic mutations have been identified in lung cancer, including mutations in the EGFR, KRAS, and TP53 genes. EGFR mutations, in particular, are associated with a subset of non-small cell lung cancers (NSCLC) and can be targeted by certain drugs, such as EGFR tyrosine kinase inhibitors (TKIs). Other mutations, such as KRAS and TP53, are associated with a more aggressive form of NSCLC and are less responsive to targeted therapies. Understanding the genetic makeup of lung tumors can help guide treatment decisions and improve outcomes for patients (35).

Rearrangements

Chromosomal rearrangements are common in lung cancer and can result in the activation of oncogenes or the inactivation of tumor suppressor genes. One well-known example is the EML4-ALK fusion gene, which is found in about 5% of non-small cell lung cancer cases. This fusion gene results from a chromosomal inversion that brings together the EML4 gene on chromosome 2 and the ALK gene on chromosome 2. This fusion leads to constitutive activation of the ALK protein, which can drive tumor growth and survival. Other chromosomal rearrangements that have been identified in lung cancer include the RET fusions, ROS1 fusions, and NTRK fusions (36).

In addition to the EML4-ALK fusion gene, numerous other chromosomal rearrangements were identified in lung cancer. For example, RET fusions result from a fusion between the RET gene and various other partner genes. These rearrangements are found in approximately 1-2% of non-small cell lung cancer cases and can lead to constitutive activation of the RET protein, which plays a role in cell growth and survival. Similarly, ROS1 fusions and NTRK fusions have also been identified in a subset of lung cancers and can result in the activation of the ROS1 and NTRK proteins, respectively (37). The identification of these chromosomal rearrangements has led to the development of targeted therapies for lung cancer. For example, crizotinib is a drug that targets ALK, ROS1, and MET, and has been shown to be effective in patients with EML4-ALK or ROS1 fusions. Similarly, drugs targeting RET and NTRK are currently under development and have shown promise in early clinical trials (38).

Overall, chromosomal rearrangements play an important role in the development of lung cancer and have provided new targets for the development of targeted therapies. Further research is needed to fully understand the role of these rearrangements in lung cancer and to develop more effective treatments for this devastating disease.

Fusion genes

Fusion genes are common in lung cancer and result from chromosomal rearrangements that bring together two previously separate genes, resulting in a hybrid gene. These fusion genes can drive tumorigenesis by altering normal cellular functions, such as signal transduction, gene expression, and cell cycle regulation. One well-known example of a fusion gene in lung cancer is the EML4-ALK fusion gene, which is found in a subset of non-small cell lung cancer cases. The fusion gene results from an inversion of the short arm of chromosome 2, leading to the fusion of the EML4 gene with the ALK gene. This fusion results in the constitutive activation of the ALK protein, leading to increased cell proliferation and survival (39).

In addition to the EML4-ALK fusion gene, other fusion genes have also been identified in lung cancer. For example, the ROS1 fusion gene, which results from rearrangements involving the ROS1 gene, is found in approximately 1-2% of non-small cell lung cancer cases. This fusion gene leads to the constitutive activation of the ROS1 protein, which can drive tumor growth and survival. Other fusion genes that have been identified in lung cancer include RET fusions, NTRK fusions, and MET fusions (40).

The identification of fusion genes in lung cancer has led to the development of targeted therapies that specifically target these genetic abnormalities. For example, crizotinib—a drug targeting ALK, ROS1, and MET—has been shown to be effective in patients with EML4-ALK or ROS1 fusions. Similarly, drugs targeting RET and NTRK fusions are currently under development and have shown promise in early clinical trials (41).

Fusion genes play an important role in the development of lung cancer, and their identification has provided new targets for the development of targeted therapies. Further research is needed to fully understand the role of fusion genes in lung cancer and to develop more effective treatments for this devastating disease.

Somatic mutations

Somatic mutations in lung cancer have been widely studied, as they are thought to play a crucial role in the development and progression of the disease. One of the most frequently mutated genes in lung cancer is TP53, which encodes for the tumor suppressor protein p53. In a study by Vogelstein et al. (2013), it was found that TP53 mutations were present in 50-70% of lung adenocarcinomas and were associated with poorer overall survival. Another commonly mutated gene in lung cancer is EGFR, which encodes for the epidermal growth factor receptor (42). In a study by Paez et al. (2004), EGFR mutations were found associated with increased sensitivity to tyrosine kinase inhibitors. Other frequently mutated genes in lung cancer, among others, include KRAS, BRAF, and ALK. Overall, these studies highlight the importance of somatic mutations in lung cancer, both as prognostic markers and as potential targets for therapy (43). Several studies have also shown that somatic mutations in genes such as TP53, KRAS, and EGFR are common in lung cancer patients. The identification of these somatic mutations has led to the development of targeted therapies that can selectively inhibit the growth of cancer cells. For example, EGFR mutations have been found in about 10-15% of non-small cell lung cancer (NSCLC) patients, and drugs targeting these mutations, such as gefitinib and erlotinib, have been developed and approved for clinical use. Other mutations, such as those in ALK, ROS1, and BRAF, have also been identified as actionable targets in NSCLC (44).

Circulating tumor

Circulating tumor DNA (ctDNA) is fragmented DNA released into the bloodstream by tumor cells undergoing apoptosis or necrosis, which has emerged as a promising biomarker for lung cancer diagnosis and monitoring. In fact, ctDNA analysis through liquid biopsy offers a non-invasive approach to detect and track disease progression. Several studies have also shown the potential of ctDNA in identifying genetic alterations like EGFR mutations and ALK rearrangements in non-small cell lung cancer (NSCLC) patients, which can guide targeted therapy selection and improve patient outcomes (45).

In addition to its potential for diagnosis and monitoring of lung cancer, ctDNA also showed promise in predicting treatment response and disease recurrence. Studies have demonstrated that ctDNA levels can be used as a predictor of response to therapy, with patients who experience a reduction in ctDNA after treatment having a higher likelihood of a positive treatment response (46). Furthermore, ctDNA analysis has the potential to detect minimal residual disease (MRD), which refers to the presence of small amounts of cancer cells that remain in the body after treatment and can lead to disease recurrence (47). By monitoring ctDNA levels over time, clinicians can identify patients at high risk of recurrence and adjust treatment accordingly, thus potentially improving patient outcomes. Overall, the use of ctDNA as a biomarker for lung cancer holds great promise for improving both diagnosis and treatment strategies, ultimately leading to better patient outcomes.

Pharmacogenomics

Pharmacogenomics is the study of genetic variations that influence drug response and toxicity. The identification of genetic polymorphisms that affect drug metabolism, transport, and pharmacodynamics has the potential to improve drug efficacy and safety. Moreover, pharmacogenomics can also inform drug selection and dosing, leading to personalized treatment options. In lung cancer treatment, pharmacogenomics can help identify patients who are likely to experience adverse drug reactions or who may not respond to certain therapies due to their genetic makeup. Several genetic variations, including those in the EGFR and ALK

genes, have been identified as predictive biomarkers for targeted therapy in non-small cell lung cancer (NSCLC) patients. Moreover, pharmacogenomics-guided dosing of chemotherapy drugs has been shown to improve patient outcomes by reducing toxicity and improving efficacy (48). For instance, in breast cancer, the presence of CYP2D6 polymorphisms is associated with altered metabolism of tamoxifen, a drug commonly used in the treatment of estrogen receptor-positive breast cancer. Patients with reduced CYP2D6 activity may have a lower response to tamoxifen and a higher risk of recurrence (49). Similarly, in colorectal cancer, the presence of KRAS mutations is associated with resistance to anti-EGFR therapy (50). Therefore, the use of pharmacogenomic testing can identify patients who are likely to benefit from a particular treatment and avoid the use of ineffective or harmful therapies in others.

Plasma and tissue proteomic biomarkers

Lung cancer is a highly aggressive and heterogeneous disease that often manifests non-specific symptoms, thus leading to late diagnosis and poor prognosis. Therefore, it is critical to identify non-invasive biomarkers that can improve the diagnosis and prognosis of lung cancer.

Plasma and tissue proteomics have emerged as promising tools for the discovery and validation of lung cancer biomarkers. Plasma proteomics enables the identification of circulating proteins that reflect the pathophysiological changes associated with lung cancer, while tissue proteomics provides insights into the molecular mechanisms underlying lung cancer development and progression. Several studies have demonstrated the potential of plasma and tissue proteomic biomarkers for lung cancer diagnosis, prognosis, and treatment monitoring (51, 52). For instance, a study by Chen et al. (2019) identified a panel of plasma proteins that could distinguish lung cancer patients from healthy controls with high sensitivity and specificity (53). Similarly, a study by Tang et al. (2018) identified tissue proteomic biomarkers that were associated with lung cancer prognosis and response to treatment (54). Overall, plasma and tissue proteomics represent valuable approaches for the identification and validation of lung cancer biomarkers, which have the potential to improve the management and outcomes of lung cancer patients.

Plasma and tissue metabolomics and microbiomics

As mentioned above, genetic predisposition aside, lung cancer is also influenced by environmental factors. Recent advances in technology have enabled the study of lung cancer using metabolomics and microbiomics approaches. Metabolomics is the study of small molecules, such as metabolites, that are produced by cells and tissues, while microbiomics focuses on the study of the microbial communities that inhabit different environments. In the context of lung cancer, plasma and tissue metabolomics and microbiomics have been used to identify potential biomarkers for early detection, prognosis, and treatment response.

Several studies have investigated the role of plasma metabolomics in lung cancer. For example, a study by Li et al. (2020) used liquid chromatography-mass spectrometry (LC-MS) to analyze the plasma metabolome of lung cancer patients and healthy controls. The study identified a panel of metabolites that could distinguish between lung cancer patients and controls with high accuracy. Similarly, tissue metabolomics has also been used to identify potential biomarkers for lung cancer (55). A study by Wang, H., et al 2018 used gas chromatography-mass spectrometry (GC-MS) to analyze the metabolome of lung cancer tissues and adjacent normal tissues. The study identified several metabolites that were significantly altered in lung cancer tissues, including amino acids and fatty acids. Microbiomics has also been studied in the context of lung cancer (56). A study by Jin et al. (2020) used 16S rRNA gene sequencing to analyze the lung microbiome of lung cancer patients and healthy controls. The study found that the composition of the lung microbiome was significantly different between lung cancer patients and controls, and that certain microbial taxa were associated with better or worse prognosis (57). Another study by Jin et al. (2021) used metagenomic sequencing to analyze the lung microbiome of lung cancer patients before and after treatment with immune checkpoint inhibitors. The study found that changes in the lung microbiome were associated with treatment response, suggesting that the lung microbiome may be a potential biomarker for predicting treatment response (26).

Plasma and tissue metabolomics and microbiomics are valuable tools for studying lung cancer. These approaches have the potential to identify new biomarkers for early detection, prognosis, and treatment response, and to improve our understanding of the underlying biology of this complex disease. Metabolites and biomarkers for lung cancer are reported in Table 2.

It's worth noting that this is not an exhaustive list, and there are many other metabolites and biomarkers that may be relevant for lung cancer diagnosis and prognosis. Additionally, the sensitivity and specificity of these markers may vary depending on the specific context and population being studied (58, 59).

Personalized and Tailored therapy

Personalized and tailored therapy is an emerging approach to cancer treatment that aims to provide individualized treatment plans based on the patient's unique molecular and genetic characteristics. This approach has shown great promise in the treatment of lung cancer, as it allows for more targeted and effective therapies that are tailored to the individual patient's needs (60).

One example of personalized therapy for lung cancer is the use of molecular testing to identify specific genetic mutations or abnormalities in the cancer cells. These mutations can be targeted with specific drugs that block the growth and spread of the cancer cells. For example, the drug crizotinib targets the ALK gene mutation, which is found in about 5% of non-small cell lung cancers. Similarly, the drug osimertinib targets the EGFR gene mutation, which is found in about 10% of non-small cell lung cancers (61).

Table 2. Metabolites and biomarkers for lung cancer.

Metabolite/Biomarker	Type	Importance
CEA	Biomarker	Elevated levels associated with lung cancer diagnosis and prognosis
Cyfra 21-1	Biomarker	Elevated levels associated with lung cancer diagnosis and prognosis
miRNA-21	Biomarker	Overexpression associated with lung cancer development and progression
miRNA-126	Biomarker	Downregulation associated with lung cancer development and poor prognosis
NSE	Biomarker	Elevated levels associated with small cell lung cancer diagnosis and prognosis
LDH	Biomarker	Elevated levels associated with advanced stage lung cancer and poor prognosis
Glutathione	Metabolite	Decreased levels associated with lung cancer development and progression
Tryptophan	Metabolite	Decreased levels associated with lung cancer development and poor prognosis
Proline	Metabolite	Increased levels associated with lung cancer development and progression

In addition to molecular testing, other factors such as the patient's age, overall health, and other medical conditions can also be considered when developing a personalized treatment plan. For example, elderly patients or those with other medical conditions may not be candidates for aggressive chemotherapy or surgery and may benefit more from less invasive treatments such as radiation therapy or targeted therapy. Personalized and tailored therapy for lung cancer is a rapidly evolving field, with new discoveries and treatments being developed all the time. As more is learned about the genetic and molecular characteristics of lung cancer, it is likely that even more targeted and effective therapies will be developed. This approach has the potential to revolutionize the treatment of lung cancer, allowing for more precise and effective treatment plans that improve outcomes and quality of life for patients (62).

Several studies have shown the benefits of tailored therapy in cancer treatment. For example, a study on non-small cell lung cancer patients found that those who received tailored therapy had a higher response rate and longer progression-free survival than those who received standard therapy (63). Another study found that breast cancer patients who received targeted therapy based on their tumor's genetic profile had better overall survival than those who received standard therapy (64).

Conclusions

In conclusion, the natural history and clinical history of lung cancer, along with its genetic and genomic profile, provide valuable information for its diagnosis, prognosis, and treatment. Genetic testing and predisposition analysis can identify individuals who are at a higher risk of developing lung cancer. Circulating tumor DNA analysis and pharmacogenomics can help determine the best treatment strategy for each lung cancer patient. Proteomic and metabolomic biomarkers offer insights into the metabolic and protein changes that occur in lung cancer cells, and tailored therapy provides a personalized approach to lung cancer treatment. The integration of these approaches has the potential to improve lung cancer diagnosis and treatment outcomes.

Overall, the research papers included in this review provide valuable insights into the various aspects of lung cancer research, including genetics, genomics, proteomics, metabolomics, and tailored therapy. While there is still much to learn about lung cancer biology, these studies represent important steps towards developing personalized and effective lung cancer treatments.

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Conflicts of interest statement

Authors declare no conflict of interest.

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