Research Article

Immunohistochemical Analysis of Lung Cancer: Mini Review

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Abstract

Lung cancer is one of the most prevalent cancers, but it is usually lately discovered. The main objective of this study was to review the literature about the use of biomarkers applying immunohistochemistry on tissues. Reviewing literature showed the need to use biomarkers to help in both diagnosing and assessing the clinical status of lung cancer. To choose the best course of treatment, it is essential to diagnose and distinguish Lung Adenocarcinoma (LUAD) from Lung Squamous Cell Carcinoma (LUSC), as recent targeted medicines demand precise subtyping Nonsmall-cell Lung Cancer (NSCLCs). Several biomarkers that could be used to distinguish between LUAD and LUSC, but they are less sensitive, specific, and clinically useful. LUSC expressed more SPATS2 and CLCA2 than LUAD. The expression of ST6GALNAC1 and Adipophilin was hfigher fin LUAD than LUSC (P=0.001). The CLCA2, SPATS2, ST6GALNAC1, and Adipophilin test has a 100% sensitivity and specificity for appropriate subtyping and diagnosis. Taken together, searching for the discovery of biomarkers and their applications in lung cancer is an ongoing process to cope with challenges in diagnosis and assessment of lung cancer.

Keywords: Lung cancer; Imuunohistochemistry; Biomarkers; Lung adenocarcinoma;

Introduction

Lung cancer accounted for 11.4 percent of the 19.3 million cases and remained the top cause of cancer death with 1.8 million fatalities, according to GLOBOCAN predictions of its incidence and mortality in 2020[1]. Small cell lung cancer (SCC), which makes up 80%–85% of cases, and Non-Small Cell Lung Cancer (NSCLC) are the two types (SCLC). Despite the fact that smoking is the main cause of lung cancer, up to 40% of Asians and 15% of Caucasians with the disease do not smoke. In non-smokers, risk factors and illness genesis are still largely unclear. NSCLC is typically not identified until the disease has progressed to an advanced stage[2].

Non-Small Cell Lung Cancer (NSCLC), which accounts for 80% of lung cancer subtypes, is the most frequent cause of cancer mortality in the world. For patients with locally advanced non-small cell lung cancer, immediate surgical intervention may be an option. The overall 5-year survival rate is, however, 59%. Adjuvant Chemotherapy (ACT), which was extensively researched to increase survival, revealed a general benefit in survival at 5 years of 7%. More than 25% of patients with stage IA/B cancers will relapse, although the evaluation of recurrence risk and subsequent requirement for ACT is only dependent on tumor stage (TNM classification). For EGFRmutated resected NSCLC, adjuvant targeted therapy has just been licensed, and trials are assessing various targeted therapies and immunotherapies in adjuvant settings. Costs, length of therapy, the creation of resistant clones, and side effects highlight the need for better patient selection. To more accurately stratify individuals who might benefit from adjuvant therapy, prognostic and theranostic markers must be identified and validated. In this review, we list the most recent validated clinical, pathological, and molecular prognostic biomarkers that affect resected NSCLC outcomes. We also discuss molecular biomarkers that are currently being studied and may become practical tools for ACT in resected NSCLC[3].

High morbidity and mortality are brought on by the very aggressive nature of lung cancer. Lung cancer is becoming more common, especially in India. Small cell lung carcinoma and non-small cell lung carcinoma are no longer the only types of lung cancer recognized today (NSCLC). The care and prognosis of patients are directly impacted by the accurate subtyping of poorly differentiated NSCLC into adenocarcinoma and squamous cell carcinoma. With this context, numerous compounds are being researched for the creation of targeted treatments. One such biomarker thought to be helpful in targeted therapy for adenocarcinoma is Epidermal Growth Factor Receptor (EGFR). Adenocarcinoma made up 55% of NSCLC, with a peak incidence between 61 and 70 years old and a male predominance. In 89% of the adenocarcinomas, EGFR was expressed. Conclusions: Immunohistochemical markers can subtype poorly differentiated non-small cell carcinoma, which

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directly affects the present therapy approaches[4].

Discussion

The most common type of cancer that results in mortality is lung cancer. An estimated 1 million people every year pass away from cancer[5]. Adenocarcinoma is the most common histologic form, and Non-small Cell Lung Carcinoma (NSCLC) makes 80–85 percent of all lung carcinomas. Despite the enhanced therapy choices available, the prognosis for these individuals remains poor, with an overall 5-year survival rate of fewer than 15%[6].

To choose the best course of treatment, it is essential to diagnose and distinguish Lung Adenocarcinoma (LUAD) from Lung Squamous Cell Carcinoma (LUSC), as recent targeted medicines demand precise subtyping of nonsmall-cell lung cancer (NSCLCs). Currently, there are several biomarkers that could be used to distinguish between LUAD and LUSC, but they are less sensitive, specific, and clinically useful. LUSC expressed more SPATS2 and CLCA2 than LUAD. The expression of ST6GALNAC1 and Adipophilin was higher in LUAD than LUSC (P=0.001).The CLCA2, SPATS2, ST6GALNAC1, and Adipophilin test has a 100% sensitivity and specificity for appropriate subtyping and diagnosis. Only the survival rate between patients with negative and positive CLCA2 expression was observed to differ significantly (P=0.038 and P=0.019, respectively). With the best sensitivity and specificity possible, a diagnosis of lung cancer may be made using a combination of the biomarkers CLCA2, SPATS2, ST6GALNAC1, and Adipophilin[7].

Nearly 89% of lung malignancies are Non-Small Cell Lung Cancers (NSCLC). They are further divided into the two main histological subtypes of lung cancer, Lung Adenocarcinoma (LUAD) and Lung Squamous Cell carcinoma (LUSC), which make up roughly 45 percent and 25 percent of cases, respectively[8]. To choose the best course of treatment, it is essential to make an accurate histopathological diagnosis and distinguish LUAD from LUSC because recently developed targeted therapies call for exact sub-typing of NSCLCs. The molecular profiling and histological characteristics of LUAD and LUSC differ greatly, but small biopsies with few tumor cells and tumors with ambiguous structures brought on by poor differentiation or necrosis make it challenging to make a precise diagnosis based solely on the standard histopathological evaluation. Consequently, immunohistochemistry is now strongly advised in clinical settings[8]. There are now a number of biomarkers that have undergone immunohistochemical evaluation and were found to be helpful in distinguishing LUAD from LUSC, although they have lower clinical relevance, sensitivity, and specificity[9].

Clinical and prognostic impact of p53 co-playing 50 -Nucleotidase Domain-Containing Protein 2 (NT5DC2) protein expression in 252 NSCLC patients was evaluated using Immuno Histo Chemistry (IHC) on Tissue Microarrays (TMA). Gene expression database. 1925 NSCLC patients' NT5DC2 mRNA was studied. High NT5DC2 protein expression reduced Overall Survival (OS) in stage I-III adenocarcinoma (p=0.026, HR 2.04 (1.08–3.87)) but not in squamous cell carcinoma (p=0.514, HR 0.87 (0.57–1.33)). Gene expression analysis in ADC and SCC confirmed OS findings (p 0.001, HR 1.64 (1.30–2.08)). NT5DC2 mRNA was higher in SCC than ADC (p 0.001) and pN2 tumors than pN0/1 (p=0.001). High-grade SCC has NT5DC2 protein expression. NT5DC2 expression was positively correlated with p53 (p=0.018) and TP53 (p<0.001), and its survival effect was p53-dependent. NT5DC2 expression was insignificantly higher in SMA+CAFs than p53 expression (p=0.065)[10].

Lung cancer causes the most cancer-related deaths globally[11]. It is important to distinguish between two types of lung cancer for analysis and prognosis. Small Cell Lung Cancer (SCLC) causes 14% of cases, but NSCLC causes 85%[12]. NSCLC has targetable oncogenic driver mutations[13], such as Kirsten Rat Sarcoma (KRAS), Epidermal Growth Factor Receptor (EGFR), Anaplastic Lymphoma Kinase (ALK), Serine/threonine-protein kinase B-rapidly Accelerated Fibrosarcoma (BRAF), Rearranged During Transfection (RET), and Proto-oncogene tyrosineprotein. Recent research has focused on co-mutations of multiple oncogenic and/or tumor-suppressing pathways in NSCLC, as treatment and prognostic implications may vary[14,15]. Targeting oncogenic drivers is promising, but tumor suppressors are difficult, and the clinical and therapeutical implications of co-mutations are unclear. In SCLC, >90% of patients have TP53 gene mutations, but in NSCLC, >25% do, and >30% in ALK, ROS1 and RET mutated patients[16]. TP53 has not been therapeutically addressed in NSCLC due to Loss Of Function (LoF), but its protein p53 may sensitize to specific treatment strategies[17]. Up- and down-regulators of p53, such as NT5DC2, may be targetable and are needed for biological and prognostic understanding of NSCLC[10].

Lin conducted a study taking into consideration that Tumor Node Metastasis (TNM) stage cannot predict pulmonary Squamous Cell Carcinoma Prognosis (SQCC)[18]. They evaluated Immunohistochemical (IHC) classifiers in patients with pulmonary SQCC who underwent complete surgery resection. 556 SQCC patients who underwent radical resection from 2010 to 2014 were included. Discovery (n=334) and validation (n=222) groups were created. Using LASSO, they extracted IHCs associated with Progression-Free Survival (PFS) and built classifiers. Clinicopathological variables and IHC-based classifiers were analyzed using logistic regression. The PFS nomogram was validated using bootstrap resampling. LASSO regression identified 4 IHC markers for PFS. IHC-based classifiers helped them divide patients into high- and low-risk groups. Low-risk discovery and validation groups had better PFS than high-risk groups. Multivariate analysis showed IHC-based classifiers independently predicted SQCC PFS. Clinically useful nomogram performance was evaluated. Combining IHC-based classification and clinicopathology improved prognostic assessment of SQCC patients after surgery, which can inform postoperative patient management[19,20].

Conclusion

The use of immunohistochemistry to investigate the expression

and localization of biomarkers in lung cancer can help in the diagnosis and assessment of lung cancers in terms of cancer type and severity.

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