Clinical & Experimental Pathology

Editorial Open Access

Molecular Pathology of Lung Cancer

Troxell LM*

Department of Pathology, Oregon Health & Science University, Knight Cancer Institute, Oregon Health & Science University, Beaverton, USA.

Pathology Insight of Lung Cancer

Lung cancer is the leading cause of deaths in worldwide. The high mortality associated with this disease is due primarily to the fact that most of the lung cancers are diagnosed advanced stages when the options for treatment are mostly palliative [1]. When diagnosed, most patients have either locally advanced unrespectable lung cancer (44%) or meta-static lung cancer (35%), for which chemotherapy is the standard treatment [2,3]. Accurate pathologic classification of lung cancer is essential for patients. From Histopathologic and biological perspectives, lung cancer is a highly complex neoplasm. Lung cancer comprises several histological types, Most frequently occurring being small-cell lung carcinoma [4] (SCLC, 15%) and the non-small-cell lung carcinoma (NSCLC) types squamous cell carcinoma (30%), adenocarcinoma (including the non-invasive type of bronchial-alveolar carcinoma, BAC; 45%), and large-cell carcinoma (9%) [5,6]. Advances in molecular technologies are providing insight the biology involved in the pathogenesis of lung cancer. Recent findings indicate that clinically evident lung cancers are the result of the accumulation of numerous genetic and epigenetic changes, including abnormalities of the inactivation of tumor-suppress organs and the activation of oncogenes [7]. All these molecular abnormalities involve the hallmarks of cancer, including abnormalities in self-sufficiency of growth signals, insensitivity to anti-growth signals, sustained angiogenesis, evading apoptosis, limitless replicative potential, and tissue invasion and metastasis. Molecular advances have provided unique opportunities for rational targeted therapies for lung cancer that have led to an emerging and exciting new area of therapy, which takes advantage of cancer-specific molecular defects that render the cancer cells to respond specific agents.

Molecular Examination

In this setting, the analysis of molecular abnormalities of lung cancers is becoming increasingly important and represents an interesting challenge for adequate integration of routine pathological and molecular examination for the diagnosis, classification, and choice of therapy options [8]. Although many molecular abnormalities have been described in clinically evident lung cancers, relatively little is known about the molecular events preceding the development of lung carcinomas and the underlying genetic basis of lung carcinogenesis. Several studies have provided information regarding the molecular characterization of the pre-neoplastic changes involved in the pathogenesis of lung cancer in last decade, especially squamous cell carcinoma and adenocarcinoma. Many molecular changes have been detected in histologically normal respiratory mucosa of smokers.

Genetic Abnormalities

The genetic abnormalities of lung adenocarcinomas include point mutations of dominant oncogenes, K-rash, BRAF, and EGFR, and tumour-suppressor genes TP53 and p16Ink4 [2, 46 ± 49]. In lung cancer, activating K-transmutations preferentially target adeno-carcinoma histology (20 ± 30%). Most K-transmutations lung cancer are G->T transversions and they affect exons 12 (~90% of mutations). These types of K-transmutation have been associated with tobacco related cancer. Activation of BRAF gene mutations, a Raf serine-threonine kinase pathway component, has also been detected in lung adeno-carcinoma cell lines (11%) and primary tumors (3%). Recently, a body of evidence has indicated that EGFR mutations affecting the tyrosine kinase domain of the gene (exons 18 ± 21) are present in approximately 20 ± 55% of adenocarcinomas that they are almost entirely absent in other types of lung cancer. EGFR mutations are somatic in origin, and they occur significant more frequently in adenocarcinomas in patients who have never smoked (51 ± 68%), women (42 ± 62%), and patients from countries in East Asia (30 ± 50%) [48,51 ± 54]. In addition, although infrequent t (3%), HER-2/Neogene mutations have been detected predominantly in lung adenocarcinoma histology and patients with an East Asian ethnic background. The remarkable similarities of mutations in EGFR and HER2/aneugens involving adenocarcinoma histology type, mutation type, gene location (tyrosine kinase do-main), and the specific patient subpopulations targeted are unprecedented and suggest similar etiologic factors. Of great interest EGFR, HER2/neu, and K-transmutations mutually exclusive, suggesting different pathways to lung cancer in smokers and never smokers. TP53 mutations are frequent in lung adenocarcinomas, with different patterns detected depending upon gender and smoking status.

References

1. Jemal A, Murray T, Ward E (2005) Cancer statistics. Ca Cancer J Clin 55: 10-30.
2. Minna JD, Gazdar A (2002) Focus on lung cancer. Cancer Cell 1: 49-50.
3. Hanahan D, Weinberg RA (2000) The hallmarks of cancer. Cell 100: 57-70.
4. Fong KM, Sekido Y, Gazdar AF, Minna JD (2003) Molecular Biology of Lung Cancer: Clinical Implications. Thorax 58: 892-900.
5. Herbst RS, Sandler AB (2004) Overview of the status of human epidermal growth factor receptor inhibitors in lung cancer. Clin Lung Cancer 6: 7.
6. Herbst RS, Onn A, Sandler A (2005) Angiogenesis and lung cancer: prognostic and therapeutic implications. J Clin Oncol 23: 3243-3249.
7. Wistuba II, Mao L, Gazdar AF (2002) Smoking molecular damage in bronchial epithelium. Oncogene 21: 7298-7306.
8. Westra WH (2000) Early glandular neoplasia of the lung. Respir Med 1:3.

***Corresponding author:** Troxell LM, Department of Pathology and Knight Cancer Institute, Oregon Health & Science University, USA, E-mail: troxllm@ohsu.edu

Received: November 10, 2020; **Accepted:** November 24, 2020; **Published:** December 02, 2020

Citation: Troxell LM (2020) Molecular Pathology of Lung Cancer. J Clin Exp Pathol S2. e002.