

The chemical elements in lung tissue and lung cancer subtypes

Ryosuke Chiba¹, Naoto Morikawa¹, Koichiro Sera², Takako Hosokawa³,
Satoshi Moriguchi¹, Heisuke Saito¹, Wataru Shigeeda⁴, Hiroyuki Deguchi⁴,
Makoto Tomoyasu⁴, Tatsuo Tanita⁴, Kazuyuki Ishida⁵, Tamotsu Sugai⁵,
Kohei Yamauchi¹ and Makoto Maemondo¹

¹Division of Pulmonary Medicine, Allergy and Rheumatology, Department of Internal Medicine,
School of Medicine, Iwate Medical University
19-1 Uchimaru, Morioka, Iwate 020-8505, Japan

²Cyclotron Research Center, Iwate Medical University
348-58 Tomegamori, Takizawa, Iwate 020-0603, Japan

³Nishina Memorial Cyclotron Center, Japan Radioisotope Association
348-58 Tomegamori, Takizawa, Iwate 020-0603, Japan

⁴Department of Respiratory Surgery, School of Medicine, Iwate Medical University
19-1 Uchimaru, Morioka, Iwate 020-8505, Japan

⁵Department of Molecular Diagnostic Pathology, School of Medicine, Iwate Medical University
19-1 Uchimaru, Morioka, Iwate 020-8505, Japan

Abstract

Background: The cause and mechanism of lung cancer in “never smokers” are still unclear. Additionally, the onset of driver mutations (e.g., *EGFR*, *ALK*) and the mechanism of their ethnic difference are unclear. Several studies have suggested that some trace elements may affect the onset of lung cancer. However, the effect of trace elements on lung cancer carcinogenesis is poorly understood. The aim of this study was to assess if trace elements may be the cause of carcinogenesis in lung cancer tissues of patients with lung cancer with a non-smoking history, driver mutations, or histology.

Methods: The study included patients with non-small cell lung cancer who had undergone surgical resection. For the measurement of trace elements, surgically resected formalin-fixed paraffin-embedded lung cancer samples were studied using particle induced X-ray emission analysis. In total, 54 elements were investigated in each sample. *EGFR* mutation and *ALK* rearrangement were assessed using commercially available CLIA testing. Based on the pathology and driver mutation status, samples were classified into the following groups: lung adenocarcinoma (LADC) with *EGFR* mutation (LADC *EGFR*m+); LADC without *EGFR* mutation and *ALK* rearrangement (LADC wt); and lung squamous cell carcinoma (SCC). Tissues from 20 patients with a non-malignant disease (e.g., pneumothorax) were also analyzed for trace elements as controls.

Results: In total, 60 patients with non-small cell lung cancer were included. The median patient age was 70years. Of the 60 patients, 27 (45%) were males. Cobalt was increased in the LADC wt group. Iron was increased in the LADC EGFRm+ group. Phosphorus and Sulfur were increased in the LADC group. In patients with squamous cell carcinoma, the amount of strontium in the tissue was significantly decreased.

Conclusion: Trace elements may play a role in the pathology and molecular signature of lung cancer.