Advances in
Biotechnology & Microbiology
ISSN 2474-7637

Juniper Publishers
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Mini Review
Volume 6 Issue 1 – August 2017
DOI: 10.19080/AIBM.2017.06.555677

Adv Biotech & Micro

Non Small Cell Lung (Nscl) Cancer Search for Biomarkers from Body Fluids to Microarrays

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Submission: August 08, 2017**; Published:** August 30, 2017

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Introduction

Lung and bronchus cancers are still one of the most common cancers worldwide, and the estimated numbers of new cases and deaths are more than 2.2 and 1.5 million respectively in the United States in 2013. Despite multi-model treatment strategies, including surgery, radiotherapy, chemotherapy and targeted therapy are used, the death rate of lung cancer is still the first leading cause of cancer-related death both in the World and in the America. The 5-year survival rate of lung cancer, predominantly NSCLC, remains as low as 15%. Therefore, improvements in diagnostics (marker associated with different degrees of malignancy and the consequent clinical behaviour of lung tumors) and treatments are urgently needed. Serological markers such as CEA, NSE (neuron-specific enolase) and Cyfra 21-1 are included in the diagnosis and management of lung cancer, but their diagnostic and prognostic value is still being debated and currently the usefulness of tumor associated antigenic biomarkers in the care of patients with lung cancer is limited. Panel of markers has gained widespread acceptance as a diagnostic test, as a prognostic indicator, or as a monitor of the treatment response. In fact, no useful marker for the screening of asymptomatic patients has been identified to date. Ideally, a biomarker should have one strategy of potentially increase both sensitivity and specificity parameters combining several biomarkers into a prognostic panel. Identification of lung cancer-specific biomarkers, together with other noninvasive methods, may allow for much needed further refinement of lung cancer screening to reduce mortality [1,2].

Tumor liberated protein (TLP) has been previously described as a TAA (complex) present in the sera from lung cancer patients with early stage disease [3,4]. Since early detection improves overall survival in lung cancer, identification of screening biomarkers for patients at risk for the development of this disease represents an important target. Starting from the peptide epitope RTNKEASI previously isolated from TLP complexes, we generated a rabbit anti-RTNKEASI serum. This antiserum detected and immuno precipitated a 55kDa protein band in the lysate of the lung cancer cell line A549. This protein band was identified as aldehyde dehydrogenase isoform 1A1 through mass spectrometry, revealing the molecular nature of at least one component of the previously described TLP complex. Next, we screened a cohort of 29 lung cancer patients (all histologies), 17 patients with non-neoplastic lung pathologies and 9 healthy donors for the presence of serum ALDH1A1 and global serum ALDH by enzyme-linked immunosorbent assay [5,6]. This analysis indicated that the presence of ALDH was highly restricted to patients with lung cancer. Interestingly, the global ALDH test detected more lung cancer patients compared to the ALDH1A1-specific test, suggesting that other ALDH isoforms might add to the sensitivity of the assay. Our data suggest that ALDH levels may therefore be evaluated as part of a marker panel for lung cancer screening [7]. Finally, the ability of the immune system to recognize a TAA, enables the development of a vaccine approach for preventive and therapeutic application and represents a main target of this field of research [4].

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DOI: 10.19080/AIBM.2017.06.555677

How to cite this article: Giulio T. Non Small Cell Lung (Nscl) Cancer Search for Biomarkers from Body Fluids to Microarrays. Adv Biotech & Micro. 2017; 6(1): 555677. DOI: 10.19080/AIBM.2017.06.555677