High aldehyde dehydrogenase levels are detectable in the serum of patients with lung cancer and may be exploited as screening biomarker

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ABSTRACT

Objectives: Since early detection improves overall survival in lung cancer, identification of screening biomarkers for patients at risk represents an area of intense investigation. Tumor liberated protein (TLP) has been previously described as a tumor-associated antigen (complex) present in the sera from lung cancer patients. Here, we set out to identify the nature of TLP to develop this as a potential biomarker for lung cancer screening.

Materials and Methods: Beginning from the peptide epitope RTNKEASI previously identified from TLP complex, we produced a rabbit anti-RTNKEASI serum and evaluated it in the lung cancer cell line A549 by means of immunoblot and peptide completion assay (PCA). The TLP sequence identification was conducted by mass spectrometry. The detected protein was, then, analyzed in patients with non small cell lung cancer (NSCLC), benign lung pathologies and healthy donors, by ELISA.

Results: The anti-RTNKEASI antiserum detected and immunoprecipitated a 55kDa protein band in the lysate of A549 cells identified as aldehyde dehydrogenase isoform 1A1, revealing the molecular nature of at least one component of the previously described TLP complex. Next, we screened blood samples from a non-tumor cohort of 26 patients and 45 NSCLC patients with different disease stages for the presence of ALDH1A1 and global ALDH. This analysis indicated that serum positivity was highly restricted to patients with NSCLC (ALDH $p<0.001$; ALDH1A1 $p=0.028$). Interestingly, the global ALDH test resulted positive in more NSCLC samples compared to the ALDH1A1 test, suggesting that other ALDH isoforms might add to the sensitivity of the assay.

Conclusion: Our data indicate that ALDH levels are elevated in the sera of NSCLC patients, even with early stage disease, and may thus be evaluated as part of a marker panel for non-invasive detection of NSCLC.

Keywords: non-small cell lung cancer (NSCLC), lung cancer, aldehyde dehydrogenase (ALDH), serological biomarkers, tumor liberated protein (TLP).