

Peptide arrays in lung cancer diagnostics: a novel platform for both diagnosis and differential diagnosis

Mehis Pold, Anu Pold, Jarrod Provins, Brian Gardner, Jenny Mao, Toomas Veidebaum, Steven Dubinett, Mats Estonius and Toomas Neuman
CeMines, Inc. 11099 North Torrey Pines Road, La Jolla, CA 92037;
National Institute for Health Development, Research Center, 42 Hiiu, Tallinn 11619, Estonia; Lung Cancer Research Program at Jonsson Comprehensive Cancer Center, University of California Los Angeles, Los Angeles, California 90095; Karolinska Institutet and Hospital, Stockholm 171-77, Sweden

Numerous studies indicate that cancer is accompanied by altered autoimmunity as detected by the appearance of cancer-related autoantibodies (aAB). Utilizing both protein and peptide arrays, we and others have shown that altered plasma and serum aAB-patterns could be used in cancer diagnostics. Using the gene expression and Cancer Immunome databases we have generated a library of 1,500 synthetic, potentially immunogenic peptides representing aberrantly expressed proteins in a variety of epithelial cancers. A subset of peptides from this library, exhibiting strong immunoreactivity with lung cancer sera was then used to produce peptide arrays for detection of aAB patterns in lung cancer and non-cancer control individuals. A study involving 80 lung cancer patients and 126 at-risk individuals (smokers and former smokers with at least 20 pack years smoking history), demonstrated that altered autoimmunity can be used for both lung cancer diagnosis and differential diagnosis. Specifically, stepwise logistic regression was used to construct multivariate models to differentiate (1) lung cancer from non-cancer control, and (2) non-small cell lung cancer (NSCLC) from small cell lung cancer (SCLC). A model discriminating between lung cancer and non-cancer control was based on 14 markers and produced an ROC curve yielding the maximum sum of sensitivity (S_E) and specificity (S_P) with $S_E = 0.79$ and $S_P = 0.77$. A model discriminating between NSCLC and SCLC was based on 6 markers and produced an ROC curve yielding the maximum sum of (S_E) and specificity (S_P) with $S_E = 0.78$ and $S_P = 0.78$. In addition, a separate series of experiments on 87 NSCLC and 74 benign lung tumor serum samples revealed aAB patterns, which differentiated between NSCLC and benign lung tumor. In conclusion, our studies employing peptide micro-arrays demonstrate that minimally invasive blood-based lung cancer tests can potentially be used in future cancer diagnostics including early detection and monitoring of lung cancer.