LUNG CANCER DIOAGNOSTICS R&D: FAST TRANSLATION OF BIOMARKERS TO DIAGNOSTICS VIA MONOCLONAL ANTIBODY BIOCHIP TECHNOLOGY:

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Introduction: Mortality of lung cancer is 84%, the five-year survival only 16%. Diagnosis of the early stage lung cancer would increase five-year survival to 50-60% according to several publications, which would also have high individual and social impact. Due to the cost, irradiation dose and logistics, lung cancer screening via spiral CT scan is impractical. Thus, there is a high demand for a non-invasive, simple blood test, which could decrease the number of necessary CT scans. It is the goal of numerous researh groups to develop such a test, however, today there is no sufficiently sensitive and specific product available on the market. Here, we report a paradigm for efficient translational R&D of a lung cancer test via monoclonal antibody proteomics mediated epitome profiling.
Methods: In order to obtain plasma epitome specific libraries (The QuantiPlasma series), mAb-s were produced to normalized human plasma in mouse using the patented technology of BSI. Selected BSI mAbs were printed on Randox platform: QuantiPlasma 69 (QP69) and QuantiPlasma 300 (QP300) biochip arrays. Plasma samples of healthy, COPD control and lung cancer bearing individuals were tested against biotinylated plasma tracers in an inhibition assay on the Randox Evidence Investigator Platform. Different statistical methods such as hypothesis testing, random forest analysis, logistic regression modelling, and support vector machines were tested. ROC analysis was applied on the entire data set to determine the minimal number of mAbs/ epitopes for optimal power to distinguish between control and lung cancer patients' plasma.
Results: Plasma samples were screened on QP69 biochips (detects 69 epitopes) in three experimental set (128, 127 and 133 clinical samples). Hypothesis testing found 90, 37, 27 of significantly discriminating variables. The 12 common variables were used then in logistic regression model building and found 3-3-3 variables, which as an optimal panel able to distinguish between the two populations. Variable selection with random forest analysis was also done followed by logistic regression. In this case 2 out of 3 mAbs were the same, which included in this model. Quality of each models were evaluated in ROC analysis. Classical tumour markers along with BSI markers were also tested as input variables. On QP300 biochips (detect 300 epitopes) two different cohort were screened. Results confirmed high accuracy (> 0.95 AUC of ROC). Low complexity (<25 epitopes) Lung cancer chips were built and being tested.
Conclusion: QP69 and QP300 mAb biochips developed by BSI and Randox are useful screening tools for candidate variable selection for ultimate disease specific diagnostic tool development. The process presented here is more efficient, less costly and faster

than translation that of hypothesis driven affinity reagent or MS proteomics based candidates.

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