

Project proposal

-Objective

To validate the diagnostic ability of IDH1 in lung cancer using multi-center samples and further assess its value for early detection of lung cancer.

-Resource available

- Research findings

We detected 12 pairs of lung cancer tumor tissues and adjacent normal tissues using 2D-DIGE, and 11 up-regulated and 17 down-regulated proteins were successfully identified. Among them, 5 proteins with important biological functions were selected and their expression levels were validated in an independent set of 15 pairs of tissues by RT-PCR and Western blot. Among the proteins found to be upregulated, IDH1 is involved in redox regulation and plays a critical role as an antioxidant allowing mammalian cells to resist oxidative damage. Next, we detected the expression level of IDH1 in tumor tissues and paired normal tissues of another 137 lung cancer patients by immunohistochemistry. The expression of IDH1 was significantly elevated in squamous cell carcinoma and adenocarcinoma tissues compared to normal tissues. The lung cancer patients with higher expression of IDH1 showed shorter overall survival after surgery, and multivariate Cox regression analysis indicated that overexpression of IDH1 is an independent prognostic factor for lung cancer patients. To investigate the blood level of IDH1, we enrolled 943 lung cancer patients (454 ADC and 489 SCC) and 479 age/sex matched healthy individuals, and detected their IDH1 level by ELISA. We also examined Cyfra21-1, CEA and CA125 level of the same samples by Elecsys immunoassay. The samples were randomly divided to a training set and a test set, and the following analysis was done in both the training and test sets to improve the reliability. IDH1 is significantly elevated in lung cancer patients compared with healthy individuals, and the IDH1 level is significantly higher in ADC than in SCC. The diagnostic efficacy of IDH1 was analyzed using receiver operating characteristic curves. The area under the curve of IDH1 is greater than 0.8 both in training set and test set, which is significantly higher than CEA, cyfra21-1 and CA125. With a cut-off value of 2.19 U/L, the sensitivity and specificity for ADC diagnosis is 56% and 95% respectively. In SCC, CYFRA21-1 displayed highest AUC among examined markers, IDH1 shows moderate efficacy. In all NSCLC, IDH1

exhibits optimal diagnostic efficacy, higher than cyfra21-1. Furthermore, we use binary logistic regression to analyze the diagnostic ability of combinations of these biomarkers, in lung adenocarcinoma, an algorithm combining IDH1, CEA, CA125 and cyfra21-1 yield optimal diagnostic efficacy with every single marker. In SCC and total NSCLC, the combination of IDH1, CYFRA21-1 and CA125 represents more efficient diagnosis than IDH1 or Cyfra21-1 alone. The IDH1 level is higher in patients with advanced T stage than in early T stage, in ADC patients this difference is significant, which indicates that IDH1 correlated with tumor burden and could be potentially useful for patient surveillance. We also found IDH1 levels are significantly elevated in TNM stage I patients compared with normal individuals, which implies IDH1 is a potential early detection biomarker.

- Resource available

The National Cancer Screening Program in Urban China will provide us with valuable resources for validating early detection giving us access to biomarkers to evaluate the value of IDH1 in the early detection of lung cancer.

- The pre-operation blood samples of patients with lung cancer who received a thoracic operation in our hospital, our tumor tissue bank routinely collects and stores this plasma and white blood cells.
- The blood of healthy people who get a physical examination in the Department of Cancer Prevention of our hospital.
- In order to evaluate biomarkers for cancer recurrence, we have collected hundreds of blood samples from postoperative follow-up lung cancer patients.

-Contact person:

Zhaoli Chen

Associate professor

Laboratory of Thoracic Surgery, CICAMS

No. 17, Panjiayuannanli, Chaoyang District, Beijing, 100021

Tel: 8610-87788798

Email: chenzhaoli2007@gmail.com