NOVEL BIOMARKERS TO DISCRIMINATE BETWEEN PRIMARY LUNG SQUAMOUS CELL CARCINOMA AND ADENOCARCINOMA IDENTIFIED BY THE CAP ANALYSIS OF GENE EXPRESSION (CAGE) METHOD

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Aim: In recent years, the use of targeted therapies focused on the molecular and histological features of cancer types has entered standard practice. In the context of non-small cell lung cancers, it is necessary to discriminate between squamous cell carcinoma (Sq) and adenocarcinoma (Ad) in order to select the most effective treatment regimen. However, this is sometime challenging to the pathologist in small biopsy specimens, especially for distinguishing poorly differentiated (P/D) Sq from Ad without a lepidic growth component (BAC).

Methods: Cap Analysis of Gene Expression (CAGE) is a method that can be used to quantify the transcription initiation reflecting the gene expression levels across the whole genome by determining the 5’ ends of capped RNA molecules using high-throughput sequencers. We performed CAGE on 97 frozen tumor tissue samples of surgically resected lung cancers (Sq, N = 22; Ad, N = 75), including P/D Sq and Ad without BAC. We subsequently explored whether there were novel biomarkers that could be used to discriminate the two types of cancers.

Results: (1) We confirmed that the expression levels of existing molecular markers used in the immunohistochemical (IHC) analysis of Sq (CK5, CK6, p40 and desmoglein-3) and Ad (TTF-1 and napsin A) were significantly different between P/D Sq (N = 3) and Ad without BAC (N = 12) in our CAGE data, but the performance to discriminate the two types of cancers were insufficient. (2) We identified four novel biomarkers, consisting of two protein coding genes and two non-coding RNAs, which showed better performance for discrimination than the existing markers. (3) Of the two protein coding genes, the expression level of SPATS2 was higher in Sq than in Ad, regardless of the extent of tumor differentiation. (4) The expression level of ST6GALNAC1, the other protein coding gene, was higher in Ad than in Sq, regardless of the presence of BAC.

Conclusions: We identified four biomarkers, including SPATS2 and ST6GALNAC1, protein coding genes, which may be useful to discriminate Sq from Ad by using CAGE. While further validation will be needed, our data indicated the performance of these markers to discriminate Sq from Ad is superior to that of the existing markers, leading to the more accurate selection of targeted therapies for non-small cell lung cancers.

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