ST45. Paxillin Expression and Amplification in Preneoplastic Lung Lesions of High Risk Patients, Lung Adenocarcinoma, and Metastasis

A.C. Mackinnon[1], M. Tretiakova[1], L. Joseph[1], L. Henderson[2], B. Yan[1], T. Krausz[1], A. Husain[1], R. Salgia[2]
[1]Pathology, University of Chicago Medical Center, Chicago, IL; [2]Medicine, University of Chicago Medical Center, Chicago, IL.

Background: The focal adhesion molecule Paxillin localizes to cell adhesion sites where it mediates interactions between the actin cytoskeleton and the extracellular matrix. We previously demonstrated that Paxillin was overexpressed in lung cancer compared to normal lung. We also identified somatic Paxillin mutations in 9% of lung cancer cases. A murine in vivo xenograft model the Paxillin mutation (A127T) showed increased cell proliferation and invasive tumor growth suggesting an important role for Paxillin in the devlopment of lung cancer. **Method:** To examine Paxillin during lung cancer development and progression, we analyzed Paxillin expression using immunohistochemistry in two populations: 279 transbronchial biopsy specimens from 93 high risk patients, and 44 cases of adenocarcinoma (12 cases of pure bronchioloalveolar carcinoma (BAC), 27 cases of adenocarcinoma with BAC pattern, 3 cases of adenocarcinoma, and 2 cases of adenocarcinoma with lymph node metastases). We used fluorescence in-situ hybridization (FISH) to analyze Paxillin gene copy number in the 44 lung adenocarcinomas. Since KRAS and EGFR can be mutated in lung cancer, and KRAS (12p12.1) and Paxillin (12q24) are located near the centromere on chromosome 12, we correlated changes in Paxillin gene copy number with somatic mutations in KRAS or EGFR in a subset of samples. **Results:** Paxillin was overexpressed in premalignant areas of hyperplasia, squamous metaplasia, and goblet cell metaplasia and was strongly overexpressed in areas of SD/CIS. Paxillin expression was associated with cigarette smoking and COPD. Increased Paxillin gene copy number was observed in both pure BAC (25%) and adenocarcinoma (34%), and adenocarcinoma greater than 1 cm demonstrate the greatest incidence of Paxillin amplification (6 of 11 cases). Both cases of adenocarcinoma with lymph node metastases displayed increased Paxillin gene copy number. **Conclusion:** Paxillin is overexpressed in premalignant lung lesions from patients that are high-risk for developing lung cancer suggesting paxillin plays a role in injury-repair process that may be important for progression to lung cancer. Our FISH analysis demonstrated that we could more easily detect increases in Paxillin gene copy number in adenocarcinoma compared with squamous cell carcinom. These findings suggest that amplification of Paxillin may be an underlying mechanism for increased Paxillin activity and promote the development of lung cancer.