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LUNG ALERT

Role of *EGFR* mutations in the pathogenesis of lung adenocarcinomas

▲ Tang X, Shigematsu H, Bekele BN, et al. *EGFR* tyrosine kinase domain mutations are detected in histologically normal respiratory epithelium in lung cancer patients. *Cancer Res* 2005;65:7568–72

The epidermal growth factor receptor (EGFR) is found in 40–80% of non-small cell lung cancers (NSCLC). Somatic mutations of the tyrosine kinase domain of *EGFR* have been reported in patients with NSCLC who had clinical responses to treatment with tyrosine kinase inhibitors targeted against *EGFR*. However, little is known about the early pathogenesis of lung adenocarcinomas and whether *EGFR* mutations are involved in this process.

The authors obtained surgically resected tissue specimens from 20 patients with adenocarcinomas and one with adenosquamous carcinoma, all with *EGFR* gene mutations. Most patients were women and never or former smokers. They also obtained tissue specimens from 16 patients with adenocarcinomas without *EGFR* mutation as a control group. Microdissection was done to obtain multiple foci of normal epithelium within the tumour and from adjacent normal lung tissue. DNA was extracted from cells obtained from these foci and analysed for *EGFR* mutation (axons 19 and 21).

Nine of the 21 patients with mutant lung adenocarcinomas (43%) were found to have identical *EGFR* mutations in normal epithelium foci within the tumour. However, none of the 16 patients in the control group (without tumour *EGFR* mutations) had mutations in the normal respiratory epithelium. Interestingly, *EGFR* mutations in normal respiratory epithelium were more frequent within the tumour (43%) than in adjacent sites (24%).

The findings of *EGFR* mutations in histologically normal epithelium have not been reported before and provide a new insight into the possible mechanisms involved in initiation of peripheral airway tumours such as lung adenocarcinoma. This may provide a future target for detection or treatment.

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