

Letter to the Editor

Comparable rate of EGFR kinase domain mutation in lung adenocarcinomas from Chinese male and female never-smokers

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Lung cancer patients with the epidermal growth factor receptor (EGFR) kinase domain mutations frequently show good responses to small molecule tyrosine kinase inhibitors, including Iressa and Tarceva, in clinical studies^[1-3]. Previous studies have demonstrated that EGFR kinase domain mutations are commonly observed in lung adenocarcinomas, never-smokers, East Asian, and females [4-8]. In contrast to caucasion females, most East Asian females do not smoke, while tobacco smoking is very common in the male population. This gender-associated tobacco usage may bias the EGFR mutation incidence in lung adenocarcinoma patients. Here we analyzed the EGFR mutation rate together with gender and smoking status in Chinese lung adenocarcinoma patients. Interestingly, our results showed a comparable rate of EGFR kinase domain mutations in lung adenocarcinomas from Chinese male and female never-smokers.

We have sequenced the EGFR kinase domain using cDNA extracted from 224 lung adenocarcinomas continuously collected from September 2007 to October 2009 at Shanghai Cancer Hospital, Fudan University, with patient consent. Clinical information including age, smoking history, stage and lung tumor differentiation status is listed in Table 1. All patients were Chinese; they came from Shanghai and 10 other provinces. About 62% (139/224) of the lung adenocarcinomas were from never-smokers, and about 38% (85/224) were from ever-smokers (Table 1). Only 2 of 110 Chinese females smoked, while 83 of 114 males were ever-smokers. About 63% (142/224) of lung adenocarcinomas harbored EGFR kinase domain mutations. Without considering gender-associated

We then analyzed the association of EGFR kinase domain mutations with gender in never-smokers and ever-smokers separately. About 55% (46/83) of male ever-smokers had EGFR mutations (Table 1). The only two female smokers had no EGFR mutations. Interestingly, a comparable EGFR kinase domain mutation rate was found in both male neversmokers (70.97%; 22/31) and female never-smokers (76.85%; 83/108) (Table 1). These data clearly showed that gender did not influence EGFR kinase domain mutation rates in neversmoker patients with lung adenocarcinomas. The low rate of EGFR mutations in males could possibly be ascribed to the low number/percentage of male never-smoker patients with lung adenocarcinomas.

Similar conclusion has been drawn using Japanese clinical samples^[9, 10]. Although Chinese and Japanese patients are both from East Asia, it has not been conclusively demonstrated that Japanese lung cancer patients are biologically the same as Chinese lung cancer patients. Our study using 224 lung adenocarcinoma specimens mainly from eastern China extends previous studies^[6, 7] and corroborates the notion that gender does not play a significant role in the distribution of EGFR mutations in lung adenocarcinoma. Further studies to include other areas in China and that significantly increase the patient number will be very helpful to solidify and extend our results. The status of EGFR kinase domain mutation has been proposed as one of most important factors used for Iressa or Tarceva treatment decision-making in clinic^[11]. Based on our findings in this study, not only Chinese female never-smokers

tobacco usage, our data were similar to those of previous reports^[4,5]. EGFR kinase domain mutations tended to occur in never-smokers (75.54%) more frequently than in ever-smokers (43.53%), and female patients had a higher mutation rate of the EGFR kinase domain (75.45%) than did male patients (51.75%) (P < 0.01).

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Table 1. No gender influence on EGFR kinase domain mutation rates in Chinese never-smokers with lung adenocarcinomas.

Lung adenocarcinoma	Total	Male	Female	P value
Patients, No	224	114	110	
Median age, year±sd	58.09±9.90	58.35±9.78	57.82±10.06	0.691
Smoking history, No (%)				
Never-smoker	139(62.05%)	31 (27.19%)	108 (98.18%)	< 0.001
Ever-smoker	85(37.95%)	83 (72.81%)	2 (1.82%)	
Differentiation, No (%)				
Well	37	13	24	0.001
Moderate	118	53	65	
Poor	69	48	21	
Stage, No (%)				
1	100 (44.64%)	42 (36.84%)	58 (52.73%)	0.102
II	21 (9.38%)	13 (11.40%)	7 (6.36%)	
III	94 (41.96%)	53 (46.49%)	40 (36.36%)	
IV	9 (4.02%)	6 (5.26%)	5 (4.55%)	
EGFR, No (%)				
Wild type	82 (36.61%)	55 (48.25%)	27 (24.55%)	< 0.001
Mutated	142 (63.39)	59 (51.75%)	83 (75.45%)	
Never-smoker, No (%)				
EGFR wild type	34 (24.46%)	9 (29.03%)	25 (23.15%)	0.502
EGFR mutation	105 (75.54%)	22 (70.97%)	83 (76.85%)	
Ever-smoker, No (%)				
EGFR wild type	48 (56.47%)	46 (55.42%)	2 (100%)	0.505
EGFR mutation	37 (43.53%)	37 (44.58%)	0 (0%)	

Never-smoker: less than 100 cigarettes in life time.

but also male never-smokers are likely to benefit from EGFRtargeted therapy.

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