Rac1 overexpression is correlated with Epithelial-Mesenchymal Transition and predicts poor prognosis of non-small cell lung cancer

Yujuan Zhou[1#](Hunan Cancer Hospital, China), Qianjin Liao[1#](Hunan Cancer Hospital, China), Jing Zhang[1](Hunan Cancer Hospital, China), Hang Ling[1](Hunan Cancer Hospital, China), Yaqian Han[1](Hunan Cancer Hospital, China), Zhigang Liu[1](Hunan Cancer Hospital, China), Wenjuan Yang[1](Hunan Cancer Hospital, China), Jie Chen[1](Hunan Cancer Hospital, China), Hui Wang[1*](Hunan Cancer Hospital, China), Bingqiang Hu[1*](Hunan Cancer Hospital, China)
[#] These authors contributed equally to this work.
* Corresponding authors.

BACKGROUND: Rac1 and epithelial-mesenchymal transition (EMT) is an important target in new cancer treatment strategies. However, the clinical significance of Rac1 and markers of EMT expression and the possible association between Rac1 expression and EMT phenotype remains unclear in non-small cell lung cancer (NSCLC).

HYPOTHESIS: Rac1 may promote NSCLC progression and metastasis by involving EMT program, which may be considered a potential therapeutic target in NSCLC.

METHODS: Immunohistochemistry was used to assess the expressions of Rac1, Snail1, Twist1, N-cadherin(N-cad), Vimentin (Vim), and E-cadherin (E-cad) in 153 NSCLC paraffin-embedded specimens and 45 tumor-adjacent normal specimens. The association of Rac1 and EMT markers with clinicopathological characteristics and relationships between the protein levels and progression free survival (PFS) and overall survival(OS) were analyzed.

RESULTS: Compared with non-tumorous tissues, Rac1, Snail1, Twist1, N-cad, Vim levels were markedly increased in NSCLC tissues, whereas decreased E-cad levels were observed ($P < 0.05$). Based on immunohistochemical evaluation, the statistical analysis suggested that Rac1 and EMT markers aberrant expression were significantly associated with TNM stage and metastasis ($P < 0.05$). Patients who displayed high expression of Rac1 may achieve a poorer OS and PFS, compared to those with low expression of Rac1($P<0.001$ and $P=0.004$). Furthermore, significant correlations were observed between every EMT markers' expression levels and OS or PFS($P<0.01$). In addition, among the clinicopathologic characteristics, multi-variate analysis indicated Rac1, Snail1, Twist1, N-cad, Vim, and E-cad expression respectively could be as an independent prognostic factor in NSCLC. Interestingly, correlation analysis suggested Rac1 expression was positively correlated with Snail1, Twist1, N-cad, Vim levels ($r=0.563$, $r=0.440$, $r=0.247$ $r=0.536$, $P<0.01$, respectively) and negatively correlated with E-cadherin amounts ($r=-0.464$, $P<0.001$) in NSCLC tissues.