Aim: The cancer stem cell (CSC) hypothesis asserts that only a small subset of cells within a tumor is capable of both tumor initiation and sustenance. CSCs may be naturally resistant to the cytotoxic effect of radio-chemotherapy because of slow cell cycling, lower proliferation, and increased expression of DNA repair and antiapoptotic genes. Although many CSC markers have been reported, the clinicopathological implications in lung cancer are controversial. The aim of this study is to investigate the expression and clinical significance of representative CSC markers in non-small cell lung cancer (NSCLC).

Methods: A total of 449 surgically resected NSCLC specimens including 253 adenocarcinomas (ADC) and 163 squamous cell carcinomas (SqCC) were enrolled. Immunohistochemistry for CD133, CD44, aldehyde dehydrogenase 1 (ALDH1), nanog, Octamer-4 (OCT4), sex-determining region Y-box 2 (SOX2), CXCR4, CD117 (C-kit) was performed using tissue microarray. Correlations between the expression of CSC markers and clinicopathologic, molecular features and survival analysis were performed.

Results: High expression of CD133, ALDH1 and CD44 was correlated with the lower pathologic stage (p = 0.008, 0.037 and 0.024, respectively), absence of lymphovascular invasion (p = 0.004, <0.001 and 0.021, respectively) and absence of pleural invasion (p = 0.011, for CD133) in ADC. Increased expression of CD133 and ALDH1 was associated with intact expression of E-cadherin (p = 0.014 and 0.014, respectively). On the contrary, high nanog expression was associated with presence of lymphatic invasion (p = 0.01). In multivariate analysis, high nanog expression was an independent poor prognostic factor in ADC (progression-free survival: hazard ratio [HR] 1.541; 95% confidence interval [CI] 1.043–2.278; p = 0.03; overall survival: HR, 1.700; 95% CI 1.048–2.760; p = 0.032). In SqCC, CD133 was never expressed but, SOX2 was frequently expressed compared with ADC. All the CSC markers were not associated with clinicopathologic parameters in SqCC.

Conclusions: Lung ADC and SqCC showed distinct expression profiles and prognostic significance of CSC markers. High nanog expression was an independent poor prognostic marker in lung ADC, which may present a new therapeutic target for lung ADC patients.

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