Study of the methylation patterns of the EGFR gene promoter in non-small cell lung cancer

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ABSTRACT. We investigated the methylation state of the epidermal growth factor receptor (EGFR) gene promoter in non-small cell lung cancer (NSCLC) and analyzed its effect on tumor biology. We enrolled 120 patients with NSCLC who had been confirmed by pathologic diagnosis and had been operated on. The methylation states of the EGFR gene promoter were detected and analyzed and a prognosis was given. NSCLC cell lines and nude mice were used to study the treatment reactivity of gefitinib (an EGFR inhibitor) with or without 5-aza-2'-deoxycytidine (5-aza-CdR) intervention. EGFR expression was high when the methylation degree was lower in patients with adenocarcinoma and poor pathological differentiation of tumor than in patients with squamous cell carcinoma and good pathological differentiation. NSCLC cells with low expression of EGFR and high methylation in the promoter region were insensitive to EGFR-targeted therapy. However, apoptosis and proliferation inhibition of cancer cells were even more pronounced when 5-aza-CdR was used to inhibit methylation. An in vivo study confirmed that methylation
adjuvant therapy can improve the sensitivity of cancer to EGFR-targeted therapy. Application of a demethylating agent could be an important supplement for improving EGFR inhibition in the treatment of NSCLC, especially in those who are insensitive to the use of an EGFR inhibitor alone.

**Key words:** Non-small cell lung cancer; EGFR gene promoter; Epidermal growth factor receptor; Methylation