Abstract:

Cancer-associated fibroblasts (CAFs) are important components in the tumor microenvironment, and we sought to identify effective therapeutic targets in CAFs for non-small cell lung cancer (NSCLC). In this study, we established fibroblast cell lines from the cancerous and non-cancerous parts of surgical lung specimens from patients with NSCLC and evaluated the differences in behaviors towards NSCLC cells. RNA sequencing analysis was performed to investigate the differentially expressed genes between normal fibroblasts (NFs) and CAFs, and we identified that the expression of periostin (POSTN), which is known to be overexpressed in various solid tumors and promote cancer progression, was significantly higher in CAFs than in NFs. POSTN increased cell proliferation via NSCLC cells' ERK pathway activation and induced epithelial-mesenchymal transition (EMT), which improved migration *in vitro*. In addition, POSTN knockdown in CAFs suppressed these effects, and *in vivo* experiments demonstrated that the POSTN knockdown improved the sensitivity of EGFR-mutant NSCLC cells for osimertinib treatment. Collectively, our results showed that CAF-derived POSTN is involved in tumor growth, migration, EMT induction, and drug resistance in NSCLC. Targeting CAF-secreted POSTN could be a potential therapeutic strategy for NSCLC.

・Keywords: lung cancer, periostin, cancer-associated fibroblasts, tumor microenvironment