**The Role of EGFR-TKI in Regulating the Effector Function of T Cells**

範 例

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**EGFR-TKI在調控T細胞效應功能中的角色**

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**Background:** Lung cancer remains the leading cause of cancer-related deaths worldwide. EGFR tyrosine kinase inhibitors (EGFR-TKI) are standard first-line treatments for lung cancer with EGFR mutations, significantly improving survival and quality of life. Recent research emphasizes combining EGFR-TKIs with immune checkpoint blockade (ICB) to enhance efficacy. However, the immunomodulatory effects of EGFR-TKIs remain poorly understood, warranting further investigation into their role in regulating antitumor immunity.

**Aim:** This study investigates how EGFR-TKI regulates T cell effector function and antitumor response, its impact on ICB efficacy, and the underlying molecular targets mediating T cell suppression.

**Methods:** EGFR-TKI inhibited T cell activation and effector function by *in vitro* treatment experiments. In tumor-bearing mice treated with EGFR-TKI, T cells showed reduced activity. Combination therapy with ICB revealed suppressed antitumor immunity. Mass spectrometry identified Ko-1 as a target mediating EGFR-TKI’s immunomodulatory effects.

**Results:** Our findings revealed that EGFR-TKI inhibited IFNγ, IL-2, and granzyme B expression in T cells, regardless of activation status. EGFR-TKI reduced proliferation and mildly affected apoptosis. Adoptively transferred, EGFR-TKI-treated T cells showed reduced function and frequency in tumors. Mechanistically, Ko-1 was identified as a target mediating this immunosuppressive effect.

**Conclusions:** EGFR-TKI suppresses T cell activation, proliferation, and cytotoxic function, and reduces IFNγ production even when combined with anti-PD-1 therapy. Ko-1 was identified as a key target mediating this immunosuppressive effect. These findings suggest that EGFR-TKI impairs T cell-mediated antitumor responses, offering valuable insights for the development of more effective therapeutic strategies.

**Keywords**

EGFR-TKI, lung cancer, NSCLC, immune checkpoint blockade, Ko-1.