Poster

[P25-10] P25-10: Oncologic drugs (2)

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[P25-10-9] Loss of tumor suppressor CYLD sensitizes oral squamous cell carcinoma cells to EGFR-TKI

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Background

The long-term survival of patients with oral squamous cell carcinoma (OSCC) remains low. Anti-EGFR therapy is the only targeted therapy approved for OSCC treatment. Effective methods for potentiation and selection of the sensitive tumors of anti-EGFR therapy are urgently awaited. Although cylindromatosis (CYLD) is thought as a potent tumor suppressor, its biological significances in OSCC is largely unknown. The aim of this study was to clarify roles of CYLD in OSCC progression and its involvement in response to anti-EGFR treatment.

Methods

We investigated CYLD expression in normal oral mucosa and OSCC tissues including carcinoma in situ (CIS) and invasive tumors by immunohistochemistry. Effects of CYLD knockdown by siRNA on cell cycle, proliferation, migration, invasion, and global gene expression in OSCC cells and non-malignant HaCaT keratinocytes were investigated. Furthermore, we assessed sensitivity to cisplatin, EGFR-TKIs (gefitinib and AG1478) or anti-EGFR antibody (cetuximab) after CYLD knockdown.

Results

CYLD expression was significantly reduced at invasive lesion in OSCC tissues and correlated with poor prognosis. CYLD knockdown led to EMT-like changes in OSCC cell lines and HaCaT cells. In addition, CYLD repression led to resistance to cisplatin with G0/G1 cell cycle arrest. However, despite resistance to cetuximab was also induced, CYLD knockdown significantly increased susceptibility to EGFR-TKI-inducible apoptosis.

Conclusions

Downregulation of CYLD promotes cell invasion and resistance to anti-cancer drugs in OSCC leading to a poor prognosis. However, sensitivity to EGFR-TKIs was increased by loss of CYLD possibly through the mechanisms regulating sensitivity to anti-EGFR antibody. Further studies may enhance the *development of more effective treatments* for OSCC and enable prospective identification of individuals who will benefit from *EGFR* inhibition.