



COP9 signalosome in regulating EGFR oncogenic signals

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Abstract

The constitutive photomorphogenesis 9 signalosome (CSN) regulates the stability of tumor suppressor and oncogenic proteins via proteasome-mediated protein degradation. The detailed regulatory mechanisms of CSN subunit expression in tumorigenesis remain to be illustrated. We demonstrated several important biological functions of CSN6: p53 signal transduction, neddylation regulation of Cullin, F-box protein ubiquitination, and Myc stability regulation. Biochemical studies demonstrated that CSN6 is involved in cell cycle regulator stability function and various cancer signaling pathways, including epidermal growth factor receptor (EGFR) pathway. We show that CSN6 overexpression is frequently observed in human colorectal cancers, which leads to drug resistance in anti-EGFR treatment and is correlated with poor clinical survival. We present a mechanism for the role of CSN6 in ERK signaling cascade and provide new insights into the functional role of CSN6 deregulation during tumorigenesis.

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Keywords

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References