High expression of RAD18 promotes invasion and metastases in esophageal squamous cell carcinoma

Shitao Zou[1], Jundong Zhou[1], Jinchang Wu[1]

[1]The Core Laboratory of Suzhou Cancer Center and Department of Radio-Oncology, Suzhou Municipal Hospital, P.R. China,

Abstract (300 word limit)

Statement of the Problem: Esophageal cancer is one of the most virulent malignant diseases and a major cause of cancer-related deaths worldwide. Poor outcomes in patients with esophageal cancer are related to propensity for metastases. The E3 ligase RAD18 is a key regulator for the lesion bypass pathway, which plays an important role in genomic stability, as well as cancer metastasis. Our previous studies identified the elevated expression of RAD18 in human esophageal cancer tissues. However, the function of RAD18 remains unclear in esophageal cancer. The present study aimed to investigate the role of RAD18 in esophageal cancer metastasis and the molecular mechanism by which RAD18 enhances the metastasis of esophageal cancer cells. Findings: We found that the expression of RAD18 was higher in esophageal cancers with T3-T4 stages compared to those with T1-T2 stages. Kaplan-Meier analysis revealed a negative correlation between the expression of RAD18 and patients' prognosis. Furthermore, the expression of matrix metalloproteinase-2(MMP-2) and matrix metalloproteinase-9(MMP-9), both being essential regulators for cells invasion, were associated with that of RAD18 in esophageal cancer tissue samples. The CCK-8 and transwells assay revealed that over-expression of RAD18 enhances prolificacy and invasiveness of esophageal cancer cells. In vivo, up-regulation of RAD18 promoted the metastasis of esophageal cancer cells in the lung. Signaling pathway analysis showed that RAD18 induces the expression of MMP-2/9 and enhances the esophageal cancers progression via JNK pathway. Conclusion & Significance: Our finding demonstrated the underlying mechanism by which RAD18 promotes esophageal cancers' development.

Recent Publications (minimum 5)

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3. Despras E, Sittewelle M, Pouvelle C, et al. Rad18-dependent SUMOylation of human specialized DNA polymerase eta is required to prevent under-replicated DNA. Nat Commun. 2016; 7:13326
4. Wong RP, Aguissa-Tourᅠé AH, Wani AA, et al. Elevated expression of Rad18 regulates melanoma cell proliferation. Pigment Cell Melanoma Res. 2012; 25(2):213-81.
5. Zou ST, Shang ZF, Zhou J, et al. DNA polymerase iota (Pol ι) promotes invasion and metastasis of esophageal squamous cell carcinoma. Oncotarget. 2016; 7(22):32274-85.

Email: sdzoushitao@126.com