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Small GTPase RBJ promotes cancer progression by mobilizing MDSCs via IL-6

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RBJ has been identified to be dysregulated in gastrointestinal cancer and promotes tumorigenesis and progression by mediating nuclear accumulation of active MEK1/2 and sustained activation of ERK1/2. Considering that nuclear accumulation and constitutive activation of MEK/ERK not only promotes tumor progression directly but also induces chronic inflammation, we wonder whether and how RBJ impairs host immune-surveillance via chronic inflammation and consequently supports tumor progression. Here, we report that higher expression of RBJ in human breast cancer tissue has been significantly correlated with poorer prognosis in breast cancer patients. The forced expression of RBJ promotes tumor growth and metastasis both *in vitro* and *in vivo*. In addition, more accumulation of immune suppressive cells but less anti-tumor immune cell sub-populations were found in spleen and tumor tissue derived from RBJ force-expressed tumor-bearing mice. Furthermore, forced RBJ expression significantly promotes tumor cell production of pro-inflammatory cytokine IL-6 by constitutive activating MEK/ERK signaling pathway. Accordingly, RBJ knockdown significantly decreases tumor growth and metastasis *in vitro* and *in vivo* with markedly reduced production of IL-6. Administration of anti-IL-6 neutralizing antibody could reduce MDSCs accumulation in tumor tissue *in vivo*. Therefore, our results demonstrate that RBJ-mediated nuclear constitutive activation of ERK1/2 leads to persistent production of IL-6 and increase of MDSCs recruitment, contributing to promotion of tumor growth and metastasis. These results suggest that RBJ contributes to tumor immune escape, maybe serving a potential target for design of antitumor drug.

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