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#### **ACCEPTED MANUSCRIPT**

# PAG1 promotes the inherent radioresistance of laryngeal cancer cells via activation of STAT3

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#### **Abstract**

Phosphoprotein associated with glycosphingolipid-enriched microdomains 1(PAG1) is a ubiquitous protein that is essential for the development and progression of various malignancies. A previous study in our laboratory confirmed that PAG1 plays an important role in modulating the inherent radioresistance of laryngeal cancer cells, but the underlying mechanisms are still poorly defined. In this study, we found that PAG1 was significantly increased in laryngeal cancer tissues compared to adjacent non-tumor tissues (P < 0.05). The expression of PAG1 was positively correlated with lymph node metastasis (P < 0.05) and TNM stage (P < 0.05). High expression of PAG1 also predicted a poor prognosis in patients with laryngeal cancer. Moreover, gain-of-function and loss-of-function studies showed that PAG1 overexpression was able to promote growth, increase migration and invasion, and enhance inherent radioresistance of laryngeal cancer cells. Mechanistic investigations revealed that the activation of STAT3 was required for PAG1-mediated inherent radioresistance of laryngeal cancer. Inhibition of

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