Rap-1A is a poor prognosis factor in oral squamous cell carcinoma and its expression promotes tumor cell motility via Aurora-A modulation

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Background: Oral cancer is the sixth most common neoplasm in human, occurring with an increasing frequency worldwide. Although several well-known markers correlated with poor metastasis/prognosis in oral cancer patients was reported, the functions of Rap-1A in oral carcinogenesis are mainly unknown. In this study, we examined the expression of Rap-1A at different malignant stages of oral cavity squamous cell carcinoma.

Materials and Methods: By using semi-quantitative-RT-PCR, Q-RT-PCR and Western blotting approaches, we evaluate Rap-1A mRNA and protein expressions in paired oral cavity squamous cell carcinoma (OCSCC) patient specimens. Human oral cancer cell lines with overexpressing-Rap-1A /Aurora-A or Rap-1A-mediated-siRNA were generated by transfection. Transwell chamber, wound healing, western blot, indirect immunofluorescence and immunohistochemical assays were done to evaluate the signaling pathways that were involved.

Results: Strong Rap-1A expression was a significantly prognostic marker and predictor of aggressive OCSCC. The overall and disease-specific 5-year survival rates were significantly correlated with strong expression of Rap-1A (p<0.001). Functionally, overexpressed Rap-1A could promote oral cancer cells motility by Transwell chambers and wound healing assay. Conversely, the inhibition of Rap-1A expression using Rap-1A-mediated-siRNA was sufficient to decrease cell motility. Furthermore, we found that Aurora-A not only could induce mRNA and protein expressions of Rap-1A for enhancing cancer cell motility, but also co-localize and form a complex with Rap-1A in oral cancer cell line. Finally, by using immunohistochemical, indirect immunofluorescence, and Western blotting analysis, Rap-1A and Aurora-A expression showed a significant positively correlation in human aggressive OCSCC specimens.

Conclusions: Our results suggest that Aurora-A/Rap-1A pathway is associated with survival, tumor progression and metastasis of OCSCC patients.