CORRIGENDUM

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by

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request to replace section Discussion in paper

EXPRESSION OF CAVEOLIN-2 IN PATIENTS WITH ORAL CANCER AND CORRELATIONS WITH CLINICOPATHOLOGICAL PARAMETERS

by

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DISCUSSION

Among head and neck cancers, oral cancer tends to occur in younger patients in recent years, and it is characterized by fairly high proliferation activity, invasiveness and metastases. Oral cancer is one of the most common malignant tumors in humans and a serious global public health problem. Therefore, seeking for pathological changes in oral cancer and potential molecular markers that can accurately indicate the prognosis of patients is particularly important for the early diagnosis, prevention of the disease and intervention, as well as for the improvement of patient's survival rate.

Existing clinical data and experiments have corroborated that the pathological process of oral cancer involves the combined action of multiple genes and protein molecules, as well as epigenetic factors (POPOVIC *et al.*, 2010; ELJABO *et al.*, 2018). SUMITA *et al.* (2018) reported that the abnormal expressions of homeobox A3 and sex-determining region Y box 9 were highly associated with the poor prognosis of oral cancer patients, while JELOVAC *et al.* (2015) found that c-erb-B2 amplification in oral cancer margins was associated with tumor recurrences and significantly lower survival of patients.

CAV2 gene with 8940 bp and three exons is located on human chromosome 7q31.2. Its product caveolin-2 participates in endocytosis, mechanical protection, metabolism and other

physiological processes in the cells. It was reported in the study of ARIANA *et al.* (2018) that CAV2 exhibited high expressions in invasive breast tumors. A comparative study of adenocarcinomas and squamous cell carcinomas concluded that CAV2 expression has a different function and clinical significance, depending on cancer type (FU *et al*., 2017 doi: 10.2147/OTT.S123912). In the present study, the data of CAV2 expression in oral cancer were extracted from the online Human Protein Atlas Database, and the results revealed that CAV2 extensively existed in oral mucosa and other tissues in oral cavity. Besides, CAV2 was also highly expressed in oral cancer, and the patients with a high CAV2 expression had remarkably lower survival rate and survival curves than those with a low CAV2 expression. In subsequent basic experiments on clinical tissue specimens, qPCR and immunohistochemistry confirmed that the mRNA and protein expression levels of CAV2 were significantly lower in paracancerous tissues compared to oral cancer tissues. Furthermore, the Kaplan-Meier survival curve analysis indicated that both OS and RFS of patients with a high CAV2 expression were significantly shorter than those of patients with a low CAV2 expression (P=0.001). GERSTENBERGER *et al.* (2018) pointed out that the expression of CAV2 was related to the grade of lung squamous cell carcinoma, and the expression of CAV2 was raised with the increase of histopathological grade. PRIETO-VILA *et al.* (2019) discovered that the CAV2 expression had a close correlation with the clinical stage of luminal B breast cancer. Based on the statistical analysis of 173 patients with oral cancer in this study, the patients who had a higher clinical stage were more prone to early cancer metastasis and a lower differentiation degree, and it was more likely to detect the high expression of CAV2 in primary tumor tissues. The univariate and multivariate analyses demonstrated that the patients with highly expressed CAV2 exhibited a shorter postoperative survival time and a higher relapse rate than those with low expression of CAV2. Additionally, the ROC curve analysis revealed that the expression level of CAV2 had high sensitivity and specificity in predicting the OS and RFS of patients with oral cancer. CAV2 can act as an independent indicator for the evaluation of prognosis of oral cancer patients and could help in determining the optimal clinical treatment protocols.

However, the pathway through which CAV2 is implicated in the development and progression of oral cancer remains to be explored more deeply and systemically. Besides, there are some limitations in this study. For example, the differences in surgical approaches and postoperative nursing were not considered in this study, so the prognosis of patients varied.

In conclusion, CAV2 is highly expressed in oral cancer. The higher the CAV2 expression level is, the shorter the survival time of patients will be, and the higher the relapse risk will be, suggesting a poor prognosis for the patients.