中文題目：JMJD3 抑制舌鱗狀細胞癌的腫瘤生長

英文題目：JMJD3 Functions as Tumor Suppressor in Oral Tongue Squamous Cell Carcinoma

作　　者：高子訓[1] 陳彥豪[2]

服務單位：[1]高雄長庚紀念醫院內科部, [2]高雄長庚紀念醫院內科部血液腫瘤科

***Background*:** Head and neck squamous cell carcinoma is one of the most aggressive malignancies and ranks the fifth leading cause of cancer mortality; oral tongue squamous cell carcinoma (OTSCC) is the largest form of tongue cancer, and recently, the incidence has been persistently increasing. Surgical resection is the gold standard for operable disease; however, local recurrence and distant metastasis are the most critical factors that contribute to poor outcome and impaired quality of life. Jumonji domain-containing-3 (JMJD3) is reported to be a histone H3 lysine 27 (H3K27) demethylase and a tumor suppressor gene. The present study designed to investigate the crucial role of JMJD3 in OTSCC patients who received surgical resection.

***Methods*:** Between January 2007 and December 2016, a total of 1,143 OTSCC patients treated at Kaohsiung Chang Gung Memorial Hospital were retrospectively reviewed. We excluded patients who had a history of any second primary malignancy, distant metastasis or those who received neoadjuvant chemotherapy, radiotherapy, or chemoradiotherapy. Finally, we enrolled 156 OTSCC patients receiving surgical resection, including 73 patients (47%) with high expression of JMJD3 and 83 patients (53%) harboring low expression of JMJD3. Two OTSCC cell lines, SAS and Cal 27, were used to explore the modulation of cancer. Chi-square test was performed to examine between-group differences in categorical variables; the Kaplan–Meier method was used to investigate survival outcome in univariate analysis, and the Cox regression model was used for multivariate analysis.

***Results*:** In the current study, the median follow-up period was 87.9 months for the 71 living survivors and 59.2 months for all 156 patients. The five-year disease-free survival (DFS) and overall survival (OS) rates were 46.2% and 50.0%, respectively. Patient with high expression of JMJD3 was significantly associated with superior DFS (87.9 months versus 13.3 months, P=0.001) and OS (not reach versus 20.6 months, P=0.001) compared to those with low expression of JMJD3 in the univariate analyses. Multivariate analysis showed high expression of JMJD3 was the independent prognostic factors of better DFS (P=0.011) and OS (P=0.013). In addition, these two OTSCC cell lines were transfected with JMJD3 siRNA. Western blotting analysis showed that the protein expressions of JMJD3, E-cadherin, Rb and p21 were

downregulation, but H3K27me3 status, N-cadherin, Twist1, CDK4 and cyclin D1 were upregulation in JMJD3-knockdown cell lines compared to that in the control cells. These data revealed inhibition of JMJD3 promoted cell cycle and epithelial-mesenchymal transition.

***Conclusion*:** Our study showed that JMJD3 plays a crucial role in OTSCC, and high expression of JMJD3 is a good prognostic factor in OTSCC patients who underwent surgical resection.