

Senescence Associated Stemness in the Epithelium of Oral Submucous Fibrosis

W.A.M.U.L Abeyasinghe^{1*}, M.W.S Perera², P.R Jayasooriya¹

¹*Faculty of Dental Sciences, University of Peradeniya, 20400, Sri Lanka*

²*Faculty of Medicine, Sabaragamuwa University of Sri Lanka, 70140, Sri Lanka*

**udariabey@dental.pdn.ac.lk*

Cellular senescence and stemness play a key role in the pathogenesis and malignant transformation (MT) of oral submucous fibrosis (OSF), a fibrotic disease of the mouth found among betel chewers in Asia. Senescence is a long term, stable cell cycle arrest while stemness refers to the degree at which cells possess the ability to self-renew, differentiate, and proliferate. The aim of the present study was to evaluate the expression of senescence and stemness in the OSF epithelium. One hundred and six formalin fixed-paraffin embedded OSF tissue samples were selected from the Oral Pathology archives, Faculty of Dental Sciences. Serial sections of the tissues were immunostained with the senescent marker, DEP-1 and the stem cell marker Bmi-1 antibodies separately. To analyze the relationship between DEP-1 and Bmi-1, the marker intensity in the OSF epithelium was recorded as negative or positive. The effect of epithelial senescence on epithelial stemness was analyzed using binary logistic regression. Statistical analysis was performed considering $p < 0.05$. Twenty-eight cases were negative for both markers, 32 cases were positive for both markers, 11 cases were positive for Bmi-1 and negative for DEP-1 and 35 cases were positive for DEP-1 and negative for Bmi-1. OSF cases expressing epithelial senescence had 2.3 times higher odds (95% CI [0.998, 5.425], Wald $\chi^2(1) = 3.827$, $p = 0.05$) to express stemness than the OSF lesions that did not express epithelial senescence, indicating that senescence may elicit stemness. It was also observed that OSF with atrophic epithelium expressed DEP-1 but not Bmi-1. There were 30.2% ($n = 32/106$) of OSF lesions which showed positivity in epithelial cells for both senescence and stemness. In conclusion, it is reasonable to speculate that stemness in the epithelium could be induced by senescence which should be explored further to elucidate the MT mechanism of OSF.

Keywords: Oral Submucous Fibrosis, Senescence Associated Stemness

Acknowledgement: Financial assistance from National Science Foundation (RG/HS/2017/001) is gratefully acknowledged.