# ROLE OF TGF BETA-1, MMP-1, TIMP-1 AND PCNA IN PATHOGENESIS AND MALIGNANT TRANSFORMATION OF ORAL SUBMUCOUS FIBROSIS

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## Introduction

Oral submucous Fibrosis (OSF) is a potentially malignant fibrotic oral disease. There is strong epidemiological evidence to suggest the association of OSF with the habit of chewing areca quid (AQ) which consists mainly of areca nut, betel leaves, slaked lime and tobacco. A primary ingredient of AQ, areca nut was classified as a group I carcinogen by the World Health Organization in 2004. Recent studies showed that malignancy develops in about 13% of OSF lesions (Tilakaratne et al., 2006). The carcinogenesis of OSF into OSCC is still unclear although a variety of approaches have been applied to analyze the carcinogenic process. It is likely that in OSF, the normal regulatory mechanism of the extracellular matrix (ECM) is either down- or up- regulated, causing imbalance in the normal equilibrium of collagen deposition and breakdown (Tilakaratne et al., 2006). Therefore, the present study aims to elucidate the ECM remodeling process and fibrosis in OSF and their influence on the malignant transformation of the OSF epithelium into oral squamous cell carcinoma.

## Materials and Methods

Forty- two archival specimens in the form of paraffin blocks which had been histologically diagnosed as OSF were selected from the Department of Oral Pathology of Faculty of Dental Sciences, University of Peradeniya together with eight normal oral mucosa (NOM) specimens from patients who have neither pathological mucosal lesions nor habits of smoking and/or betel chewing. The clinically diagnosed patients of OSF for this study were 36 men (86%) and 6 women (14%), ranging in ages from 21 to 65 years, with an average age of 40 years.

We compared the expressions of TGF Beta-1, TIMP-1, MMP-1, PCNA in OSF and NOM by immunohistochemistry. For each slide, 10 non-overlapping fields were randomly selected (5 fields for epithelium and 5 fields for connective tissue) and photographed using light microscopy with a digital camera (Olympus, BX51T, Tokyo, Japan x 200). Sections were considered either negative or positive according to the absence or presence of brown staining in epithelial or stromal cells. The positive cases were graded into three