Head & Neck Oncology



Poster presentation



# Integrin αvβ6 promotes TGF-β1-dependent myofibroblastic transdifferentiation in oral submucous fibrosis

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## Introduction

Oral submucous fibrosis (OSF) is a chronic progressive fibrosing disorder of the oral cavity. Commonly in fibrosis, TGF-β1 promotes the transdifferentiation of fibroblasts into α-smooth muscle actin (SMA)-secreting myofibroblasts. Integrin αvβ6 is not detectable on normal oral keratinocytes but is upregulated during tissue remodelling. αvβ6 is a key activator of TGF-β1 through its interaction with its latency associated peptide.

## Objective

To investigate the role of αvβ6 integrin in the pathogenesis of OSF.

## Methods

αvβ6 expression was examined in 41 OSF cases compared with 14 cases of fibroepithelial hyperplasia by immunohistochemistry. TGF-β1 activation assays were carried out using a keratinocyte cell line expressing high levels of αvβ6 (VB6). VB6 cells were co-cultured with HFFF2 fibrblasts and SMA expression examined by Western blotting and confocal microscopy.

## Results and conclusion

αvβ6 was highly expressed in 54% of OSF cases. αvβ6 activated TGF-β1, which was significantly reduced by antibody blockade. Co-culture experiments revealed markedly increased SMA expression by fibroblasts, indicating myofibroblast transdifferentiation, which was αvβ6-dependent. *In vitro* findings were confirmed by immunochemistry, which demonstrated SMA-. pSmad2 and Smad4-positive myofibroblasts in OSF connective tissue. Finally, treating oral keratinocytes with the areca nut alkaloid arecoline upregulated αvβ6 expression. In summary, we show that αvβ6 integrin is strongly expressed in OSF, and that it promotes myofibroblast transdifferentiation by activating TGF-β1. These data suggest a possible mechanism for the chronic fibrosis seen in OSF.