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## Monospecies and polymicrobial biofilms differentially regulate the phenotype of genotype-specific oral cancer cells

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### Abstract

Oral cancer isolate *C.albicans*, *A.naeslundii* and *S.mutans* formed biofilms in flow environment which differentially modulated the malignant phenotype of oral keratinocytes in a paracrine manner.

Abstract Microbial infection has been shown to involve in oral carcinogenesis; however, the underlying mechanisms remain poorly understood. The present study aimed to characterize the growth of oral microorganisms as both monospecies and polymicrobial biofilms and determine the effects of their products on oral keratinocytes. *Candida albicans* (ALC3), *Actinomyces naeslundii* (AN) and *Streptococcus mutans* (SM) biofilms or a combination of these (TRI) were grown in flow-cell system for 24 h. The biofilms were subjected to fluorescent in situ hybridization using species-specific probes and analysed using confocal laser scanning microscopy. The effluent derived from each biofilm was collected and incubated with malignant (H357) and normal (OKF6) oral keratinocytes to assess extracellular matrix adhesion, epithelial-mesenchymal transition (EMT) and cytokines expression. Incubation of OKF6 with ALC3 and TRI effluent significantly decreased adhesion of the oral keratinocyte to collagen I, whereas incubation of H357 with similar effluent increased adhesion of the oral keratinocyte to laminin I, significantly when compared with incubation with artificial saliva containing serum-free medium (NE;  $P < 0.05$ ). In OKF6, changes in E-cadherin and vimentin expression were not consistent with EMT although there was evidence of a mesenchymal to epithelial transition in malignant oral keratinocytes incubated with AN and SM effluent. A significant increase of pro-inflammatory cytokines expression, particularly interleukin (IL)-6 and IL-8, was observed when H357 was incubated with all biofilm effluents after 2- and 24-h incubation when compared with NE ( $P < 0.05$ ). In conclusion, *C.albicans*, *A.naeslundii* and *S.mutans* form polymicrobial biofilms which differentially modulate malignant phenotype of oral keratinocytes.

### Keywords

**KeyWords Plus:** CANDIDA-ALBICANS; STREPTOCOCCUS-MUTANS; INFLAMMATION; EXPRESSION; CYTOKINE; BACTERIA; CADHERIN; MATRIX

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