Effect of phenotype switched *Candida auris* mono-culture and co-culture biofilms on the morphology, viability, and adhesion of hTERT TIGKs and ORL-48 cell lines

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Abstract Objectives: This study aims to determine the paracrine effects of Candida auris phenotypic switching in mono-and co-culture with Staphylococcus aureus on oral epithelial homeostasis and oncogenic progression in phenotypically normal (hTERT TIGKs) and malignant (ORL-48) oral keratinocytes. Design: C. auris switched phenotype was scored using Phloxine B, and mono-and co-culture biofilms with S. aureus were developed. hTERT TIGKs and ORL-48 cell lines were independently seeded into 6-well and 96-well plates for dispase and viability test, respectively. The oral cell lines were exposed to phenotypically switched C. auris mono-and co-culture biofilm test cell growth medium (TCGM) for 24 h. Outcomes included cell morphology, metabolic activity/viability (CCK-8), and cell-cell adhesion (dispase assay). Results: Microscopic observation revealed that the biofilm induced damage and disrupted epithelial cell integrity in a paracrine manner. The mono-and co-culture TCGM suppressed the growth of normal cells while promoting the metabolic activity of cancer cells. The adhesion analysis of hTERT TIGKs indicated a strong intercellular cohesion, while ORL-48 cells downregulated intercellular adhesion and compromised cell-cell cohesion. Conclusion: C. auris biofilms promote the development of a malignant phenotype by regulating cell viability, promoting epithelial-mesenchymal transition, and adhesion in a switched generation-dependent manner.

Keywords **Author Keywords:** Candida auris; Staphylococcus aureus; Phenotype switch; Biofilm; HTERT TIGKs; ORL-48; EMT; Interkingdom interaction; Oral carcinogenesis
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