unilocular radiolucency at the apex of tooth #28. Owing to the increasing size and nonhealing nature of the lesion after root canal therapy, an incisional biopsy was performed. Histopathologic examination revealed an epithelial malignant neoplasm of odontogenic origin consistent with PIOC. The patient was treated with anterior mandibulectomy followed by reconstruction with a fibula free flap. In addition to a comprehensive literature review, we discuss the diagnostic criteria and clinical, histopathologic, therapeutic and prognostic features of PIOC.


Adenosquamous carcinoma (ASC) is a rare and aggressive malignant neoplasm with a poor prognosis. It arises from both the surface and the salivary ductal epithelium, with histologic features of both squamous cell carcinoma and adenocarcinoma. The most common site in the upper aerodigestive tract is the larynx, followed by the oral cavity. An exhaustive literature search revealed <20 documented cases of intraoral ASC. The most common intraoral locations are the tonsillar pillars, floor of the mouth, and posterior tongue. We report a case of ASC on the palate of a 72-year-old edentulous patient, who presented with a chief complaint of pain and soreness of 3 weeks’ duration under the denture. Clinically, the lesion presented as a thick diffuse leukoplakia extending from the right vestibule to the alveolar ridge and the hard and soft palate, with cratered ulceration of the left side of the hard palate. An incisional biopsy was performed. The microscopic examination displayed squamous cell carcinoma and adenocarcinoma, favoring a diagnosis of ASC. The patient opted for treatment with chemotherapy and radiation only, without extensive surgery. The clinical and histopathologic features of ASC, differential diagnosis, and review of literature are presented.


Leukoplakia is the most frequently occurring oral lesion with malignant potential: a clinical entity defined by the World Health Organization as “white plaques of questionable risk having exclusion of these benign frictional and otherwise reactive keratotic conditions, this study found the proportion of cases of true leukoplakia that represent atypia, dysplasia, carcinoma-in-situ, and invasive squamous cell carcinoma to be 43.2%, twice that previously reported.

P38 REGULATES INTERLEUKIN-12–MEDIATED CYTOKINE SECRETION IN HEAD AND NECK SQUAMOUS CELL CARCINOMA. R. Vander Broek, E. van Tubergen, K. Kirkwood, N. D. Silva. U Michigan School of Dentistry, Ann Arbor, Medical U South Carolina School of Dentistry, Charleston.

Background. Cytokines and proinflammatory factors are critical mediators of head and neck squamous cell carcinoma (HNSCC). RNA-binding proteins, such as tristetraprolin (TTT), target cytokine mRNA for degradation and decrease cytokine production. However, during an inflammatory response, TTP is functionally inactivated by phosphorylation through p38 activity, leading to increased expression of cytokines. A constitutively active p38 pathway is implicated in tumor survival and interleukin (IL) 6 production. Previously, we showed that increased IL-6 in HNSCC is prognostic for poor disease-specific survival and higher probability of tumor recurrence. Therefore, an active p38 mitogen-activated protein kinase pathway may inactivate TTP and contribute to tumor progression.

Objective. The aim of this study was to delineate the role of p38 activity in regulating cytokine secretion in HNSCC.

Study design. p38 activation was optimized with an IL-12 dose curve. UM-SCC-11A and –81B were transfected with small interfering (si) RNA nontarget (NT) and p38. Conditioned medium was collected from cells transfected with siNT or si-p38 in the presence of IL-12. IL-6, vascular endothelial growth factor, and prostaglandin E2 secretion were quantified by ELISA.

Results. p38 is activated in HNSCC cell lines. IL-12 mediates p38 activation in HNSCC cell lines maximally at 10 ng/mL. p38 knockdown was verified by immunoblot analysis. Maximal knockdown of p38 occurred at 72 hours post transfection. p38 knockdown reduced cytokine secretion even in the presence of IL-12 at 72 hours after transfection.

Conclusions. These findings support the potential for targeting regulators of cytokine secretion, such as p38 or downstream targets of p38, as a practical means for limiting the progression of HNSCC. Future studies will elucidate the mechanisms of p38 regulation of TTP activity in HNSCC. (UMich School of Dentistry and National Institute of Dental and Craniofacial Research grant nos. R01 DE018512 and K02 DE019513)


In head and neck squamous cell carcinoma (SCC) samples, we observed the intimate association of myeloid dendritic cells (DC) with SCC cells in both primary tumors and their lymph node metastases. In vitro videomicroscopy studies showed that the direct interactions between monocyte-derived DC and SCC cells produced a significant effect on SCC cell migration. Our current research further examines the influence of monocyte-
derived DC on the properties of SCC cells. Because monocytes are precursors of mucosal DC, we used peripheral blood monocytes differentiated in vitro into DC by standard methods, which produces a nonadherent population of immature DC (naDC) and a population of adherent cells (aDC). Because in vitro–differentiated DC are used in tumor immunotherapy studies, we examined both aDC and naDC, aDC and naDC were phenotyped by flow cytometry and individually cocultured with 2 SCC cell lines. All cocultures produced floating and attached mixed DC–SCC cell populations which were analyzed for viability, chemokine receptor expression, morphology, and ability to reestablish colonies. SCC populations caused the up-regulation of DC differentiation marker CD1a, lymph-node homing chemokine receptor CCR7, and tissue-migration receptor CXCRA and down-regulation of DC maturation marker CD86 on aDC and naDC, with more pronounced influence on aDC. On the other hand, the floating SCC cells in cocultures with aDC and naDC were enriched for viable cells and expressed more CCR7. Repleted DC–SCC floaters were capable of establishing new colonies. Quantification of the migratory abilities of DC and SCC cells and the functional characterization of detached SCC cells are under investigation.


Background. Animal models of oral carcinogenesis are critical for development of noninvasive optical imaging diagnostic tests.

Objective. The aim of this study was to describe the optical imaging data in a mouse model of tongue carcinogenesis and correlate them with histologic and molecular features.

Study design. Two inbred strains (CBA and C57BL/6) of mice were given 4NQO (100 μg/mL) in drinking water for 16-weeks. Mice were killed 8 and 18 weeks after initiation of 4NQO treatment, and their tongues were imaged and then used for histologic and molecular studies. The tongues were imaged after topical application of the following fluorescently tagged contrast agents: fluorescent deoxyglucose analog 2-NBDG (to assess metabolic activity), epidermal growth factor (EGF) peptide, and proflavine (DNA-binding dye). Tissue sections were stained with antimouse EGF receptor (EGFR), phosphorylated EGFR (p-EGFR), CD147, cyclin D1, and p63 antibodies.

Results. Autofluorescence imaging of experimental tongues revealed multifocal loss of autofluorescence, whereas control tongues revealed normal autofluorescence. Images obtained with contrast agents revealed higher fluorescence intensity in experimental tongues compared with control tongues. The experimental tongue mucosa revealed epithelial dysplasia at 8 weeks and oral squamous cell carcinoma at 18 weeks. Confocal imaging of fresh tissue slices incubated with 2-NBDG and EGF revealed increased binding in experimental compared with control tongues. Proflavine staining displayed dysplastic cells with enlarged nuclei throughout the entire epithelium. Immunohistochemistry revealed increased expression of EGFR, p-EGFR, CD147, cyclin D1, and p63 in the experimental tongue sections.

Conclusions. The 4NQO-induced mouse tongue carcinogenesis closely mimics the key optical imaging, histologic, and molecular features of human oral cancers and its precursors.

DISCOID LUPUS ERYTHEMATOSUS IN THE ORAL CAVITY: CLINICAL CHARACTERISTICS AND TREATMENT. E. Gagari, E. Georgakopoyloy, T. Danciu. U Athens School of Medicine, Greece.

Discoid lupus erythematosus (DLE) is a chronic skin disease that mainly affects the skin of the face and other sun-exposed areas. It is distinctly rare in the oral cavity, and there are few evidence-based studies that document its treatment. We present a case series of 9 patients with oral DLE that have been followed for the past 2 years in the oral medicine clinic of the A. Syggros Hospital. The mean age of the patients was 52 years (range 40-75 years) and the majority (8/9) female. The oral lesions presented mainly as painful lichenoid mucositis with desquamative gingivitis and bullae formation being an occasional finding. Oral lesions responded initially well to treatment with oral prednisolone, but presented with frequent relapses. All of the patients demonstrated skin lesions characteristic of DLE and received different treatment for the skin lesions, which appeared to cause less discomfort to the patients. Serologic findings indicative of systemic lupus erythematosus were found to be negative in all of the cases examined.


Background. Twist1/2 are members of the bHLH family of transcription factors that are implicated in carcinogenesis and play essential roles during development. Despite their significant roles, the mechanisms that regulate the function of these factors remains poorly understood. We have identified 2 putative Akt phosphorylation sites in Twist1 that are conserved across species. Because both Akt and Twist1 are implicated in tumor initiation and progression, we tested expression and colocalization of Twist1 and active (phosphorylated) Akt (p-Akt) in samples of human oral squamous cell carcinoma (OSCC). Study design. Twenty-five cases of paraffin-embedded tissues were selected from the oral and maxillofacial biopsy service at University of Michigan (UM) School of Dentistry. Immunohistochemistry was performed to localize Twist1 and p-Akt. reverse-transcription polymerase chain reaction was used to detect mRNA expression of Twist1 in OSCC cell lines isolated and characterized at UM; immunoblotting was used to detect p-Akt in these cells.

Results. In epithelium from normal patients, p-Akt and Twist1 staining was negative. In biopsy specimens of patients with OSCC, there was significant variability in Twist1 staining, ranging from <10% of the tumor cells being positive to >50%. There was a greater tendency for Twist1 positivity to be localized in the nucleus of poorly differentiated tumors. Similarly, there was variability in p-Akt staining and localization. All of the OSCC cell lines expressed p-Akt, whereas Twist1 levels were variable.

Conclusion. This preliminary work unveils a potential role for Twist1 in OSCC and its possible regulation by p-Akt in this malignancy. Future studies aimed at clarifying the role of Twist1 and Akt in the prognosis of patients with OSCC will be conducted in our laboratory.