cytoplasm. Three cell lines demonstrated lower growth potential under inhibition of the expression of LAD1 by using siRNA. Although early adhesion to the plates was not affected, cleaved-caspase-3 positive and TUNEL positive cell ratio were increased in LAD1-knockdown cells. Furthermore, cell motility of LAD1-knockdown cells was significantly suppressed in wound scratch assay.

Conclusions: LAD1 is potentially involved in modulation of actin dynamics in oral SCC cells, affecting their motility and proliferation at the interface between cancer and non-cancerous tissue.

INTERLEUKIN 1 RECEPTOR ANTAGONIST (IL-1RA) BIOLOGY IN ORAL EPITHELIUM, ORAL DYSPLASIA AND ORAL SQUAMOUS CELL CARCINOMA.

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Objectives: Knowledge of molecular biology of oral dysplasia (OD) and oral squamous cell carcinoma (OSCC) is essential in order to find novel biological markers that could serve as predictor markers for malignant transformation. IL-1 receptor antagonist (IL-1RA), IL-1 natural inhibitor, is encoded by the IL1RN gene and has been reported to be downregulated in head and neck squamous cell carcinoma, but the effects of its downregulation in OSCC and OD are largely unknown. Thus, the aim of this research was to study the role of IL-1RA in oral carcinogenesis and oral keratinocyte senescence.

Findings: IL1RN, specifically intracellular IL-1RA type 1 (icIL-1RA1), is constitutively expressed in normal oral epithelium, but is downregulated, both in vitro and in vivo, in OD and OSCC cell lines. We also found an upregulation of IL-1R1 (IL-1 agonist receptor) in OSCC and OD cell lines. Using confocal microscopy, we have found that both proteins, IL-1RA and IL-1R1, are able to localize inside the nucleus, which suggests a new possible ways of interactions of intra-nuclear IL-1α in oral keratinocytes. Transient transfection in OSCC and OD cell lines with a plasmid encoding for icIL-1RA1, showed no or limited effects on cell migration (by cell exclusion and transwell assay), cell proliferation (by EDU incorporation) and IL-6 and IL-8 secretion (by ELISA). Preliminary data suggests an increase of IL-1 alpha and a decrease of icIL1-RA mRNA expression as primary oral keratinocytes and mortal OD cells senesce.

Conclusions: IL1RN is downregulated in oral dysplasia and oral cancer. How this downregulation favours oral carcinogenesis it is not yet known, but might be related with the oral senescence program.

EXTRAPARENCHYMAL EXTENSION, LYMPH NODE INVOLVEMENT, AND A HIGHER KI67 INDEX WERE HIGH RISK FACTORS FOR WORSE PROGNOSIS IN CONVENTIONAL MAMMARY ANALOGUE SECRETORY CARCINOMA.

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Objective: The prognostic factors of salivary gland (mammary analogue) secretory carcinoma (SC) are unclear because of the rarity of the tumors. Here we presented the largest case series to investigate the prognosis related clinicopathological factors in salivary conventional SC.

Findings: The study was based on a retrospective cohort of patients whose sections were reviewed and newly diagnosed as SC by the detection of ETV6 rearrangement from 1993 to 2015. The clinicopathological features were analysed as the primary predictors and patients' final outcome was collected. Survival analysis was performed in conventional SC by using Kaplan-Meier method and Cox proportional hazards regression model. In our study, totally sixty-two cases of SC were confirmed. Fifty-nine out of 62 cases were conventional SC with a mean age of 43.2 years, showing significant male predilection (49/59, 83.1%) and mostly occurred in parotid glands (49/59, 83.1%). Additional 3 cases were identified as SC with high-grade transformation (HG-SC), with a mean age of 20 years older than that of patients with conventional SC. Lymph node metastasis and Ki67 expression $\geq$10% were related to poor recurrence-free survival (RFS), distant disease-free survival (DDFS) and disease-free survival (DFS) in conventional SC. Significantly decreased RFS and DFS were seen in patients with extraparenchymal extension. T3/T4 stage, age greater than 44 years and markedly hyalinized fibrous septa were associated with worse DDFS. By using multivariate analysis, the Ki67 index was found to be an independent prognostic factor for RFS ($p = 0.008$) and DFS ($p = 0.003$) in conventional SC. Much more worse RFS and DFS were presented in HG-SC due to its aggressive behaviour.

Conclusion: In conventional SC, patients with extraparenchymal extension, lymph node involvement, and higher Ki67 index exhibited poor clinical outcome. Moreover, Ki67 was a potential predictor of RFS and DFS of conventional SC.

THE EXPRESSION OF MAML2 GENE REARRANGMENT IN CASES OF GLANDULAR ODONTOGENIC CYSTS AND MUCOEPIDERMOID CARCINOMAS WITH OVERLAPPING HISTOLOGIC FEATURES.

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Objectives: MAML2 expression has been demonstrated in the majority of mucoepidermoid carcinomas (MEC) arising in the salivary glands. MEC may also arise intraosseously in the jawbone (IMEC). Glandular odontogenic cyst (GOC) is an odontogenic cyst with some histologic overlap with IMEC. MAML2 expression has not been extensively studied in IMEC or in GOC. This study will test the reliability of MAML2 in distinguishing cases of IMEC from GOC that share similar histologic features.

Methods: An IRB-approved retrospective search of IMEC, GOC, and IMEC with prior history of GOC was performed within the archives of the UF Oral Pathology Biopsy Service from 1994-2017. Eight cases from four patients were selected with diagnoses of either IMEC with earlier GOC, GOC with IMEC features, or IMEC with GOC features. Tissue was available for six out of the eight cases, on which break apart fluorescent in situ hybridization (FISH) analysis was performed for the presence of MAML2 rearrangement.

Findings: Lesions from two of the patients were negative for the MAML2 gene rearrangement while lesions from the other two patients were positive for the MAML2 gene rearrangement.

Conclusion: Although it can be concluded that the two patients with positive translocation for MAML2 had a diagnosis of IMEC, the same conclusion could not be drawn for the two patients with negative translocation. Whether the cases that were negative for the translocation are GOCs with MEC-like islands or MAML2 negative IMEC could not be ascertained. Therefore, MAML2 gene rearrangement is not always dependable in differentiating IMECs and GOCs that share similar histologic overlap. The limited nature of the study due to small sample size precludes a more definitive conclusion. Collaboration vis-à-vis cases and data exchanges between oral and maxillofacial pathology centers may help achieve a better understanding of two uncommon, but clinically impactful, entities.

TUMOR ASSOCIATED MACROPHAGES: TAGGING AGGRESSIVENESS IN ORAL SQUAMOUS CELL CARCINOMA.

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Introduction: A tumor cannot progress independently of its micro-environment-the stromal cells, tumor associated inflammation, metabolic alterations and extracellular matrix remodeling is significant in disease progression, evolution and metastasis. Bi-directional interactions between the tumor cells and stromal elements determine individual tumor behavior as reflected in the prognostic variability of cases within the same histological grade.
However, pivotal findings relating to the tumor micro-environment (TME) in Oral Squamous Cell Carcinoma (OSCC) still remain unaccounted for in the standard grading and staging systems. Thus evaluation of the TME could provide a more robust and accurate predictive assessment of OSCC.
Tumor Associated Macrophages (TAM) constitute the major inflammatory cell population of the TME, with a prominent role in stromal modulation and tumor progression. TAMs have also been regarded as suitable demonstrators of the "seed and soil theory" of metastasis.

Objective: To correlate the presence and role of TAMs in OSCC with the STNMP staging system.

Findings: Immunohistochemical evaluation revealed a definitive presence of TAMs at the advancing front of the tumor. The density of cells escalated from STNMP stage-1 to stage-4. A statistically significant, strong positive correlation was noted between-TAMs, tumor stage, tumor size and nodal status. A poor correlation between TAMs and tumor grade was noted.

Conclusion: In India, of the 77,003 new cases of OSCC registered annually, 67.7% of the patients are lost to the disease. While tumor grade is indicative of the degree of differentiation of OSCC, it is inadequate as a sole predictor of tumor behavior and prognosis. A holistic evaluation of tumors and their TME may be the remedy. Thus, it has emerged that TAMs being dynamic cells of the TME, could be utilized as indicators of tumor behavior and aggressiveness.

PLAQUE-TYPE LICHEN PLANUS OR LEUKOPLAKIA WITH LYMPHOCYTIC HOST RESPONSE?.

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Introduction: Oral epithelial dysplasia (OED) and oral squamous cell carcinomas (SCCAs) often exhibit a lymphocytic host response (LHR) present as a band at the epithelium-connective tissue interface. Because these are often diagnosed as dysplasia with lichenoid mucositis or lichenoid dysplasia, clinicians assume that such lesions represent dysplasia or SCCA arising within lesions of oral lichen planus (OLP). If the clinical lesion is a solitary plaque, the diagnosis of plaque-type OLP may be made. Lichenoid lymphocytic reactions are not specific to OLP and may be seen in drug-induced, contact hypersensitivity reactions and other conditions. The objective of this study is to review cases of leukoplakia with a lichenoid LHR.

Materials and Methods: Cases diagnosed as OED with lichenoid features or lichenoid mucositis that represented biopsies from solitary white lesions were identified from the files of one laboratory from January 2013 to December 2018.

Results: There were 13 males and 11 females (1.2:1 male to female ratio), and the median age was 61 (range 37–90). All lesions were unilateral and the two most common locations were the tongue (12 cases, 50.0%) and the gingiva (5 cases, 20.8%). Hyperkeratosis and/or parakeratosis and epithelial atrophy was present in 23 (95.8 %) and 10 cases (41.6%) respectively while degeneration of the basal cells was present in 7 cases (29.1%) only. OED was present in 13 (54.1%) of the cases (5 mild, 5 moderate, 2 severe, and 1 carcinoma-in-situ); 36.3% of the cases that showed epithelial atrophy also showed OED. A lymphocytic band was present in 24 cases (100%).

Conclusion: These lichenoid lesions were solitary plaques located most commonly on the tongue and gingiva, common sites for leukoplakia with 54.1% exhibiting OED. As such, these lesions more likely represent leukoplakia with a LHR rather than OLP. Clinicopathologic correlation is essential for accurate diagnosis.

COMPARATIVE ASSESSMENT OF P16 PROTEIN EXPRESSION IN NORMAL AND DYSPLASTIC ORAL MUCOSAL EPITHELIUM.

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Objective: Expression of the protein marker p 16INK4a is used as a surrogate for human papillomavirus (HPV) infection in biopsies of oral and tonsillar mucosa. While HPV infection accounts for <5% of oral cavity cancers, its association with oral epithelial dysplasia (OED) is unclear, with prevalence estimates ranging from zero to greater than 90%. In this study, the expression of p 16INK4a was examined in archived biopsy specimens by immunohistochemistry within three groups: control mucosa (CM), low-grade dysplasia (LGD) and high-grade dysplasia (HGD). Tissue samples were age-, sex-and site-matched with 24 cases in each group. Grading of p16 expression was performed according to the criteria of intensity and proportion of cells as described by Grobe et al.

Findings: Fifteen of the 24 HGDs (62.5%), fourteen of the 24 LGDs (58.3%) and four of the 24 CMs (16.6%) were positive for p 16INK4a expression. The difference in p16 expression between HGD versus CM and LGD versus CM were analyzed by Wilcoxon signed rank test and statistically significantly different at level with p-values of 0.0001 and 0.0009, respectively. Greater p16 expression was noted in HGDs compared to LGDs (p-value = 0.01960, which was significant at level). A step-down