Materials and Methods: 10 cases each of AEP, IPH and PSCC were retrieved from the University of Florida, Oral Pathology Biopsy Service archive and stained with Anti-KMT6/EZH2 antibody. The cases were reviewed and the extent and pattern of EZH2 expression were assessed. The results were analyzed for statistical significance using Fischer's exact test.

Results: The pattern and intensity of EZH2 expression in AEP and PSCC demonstrated statistically significant differences when compared to IPH (p=0.002). In addition, the basal cell layer showed EZH2 expression in all the cases of AEP (100%) and PSCC (100%) but only 3 out of 10 (30%) in IPH (p=0.000), comparable to normal oral epithelial control tissue.

Conclusion: EZH2 expression in AEP is more similar to malignant processes than benign lesions. The pattern of basal cell layer expression of EZH2 could be a potential prognostic indicator of malignant transformation risk in oral AEP lesions. A subsequent study by our group to assess EZH2 expression with respect to clinical outcome in AEP lesions is ongoing.

INTER-OBSERVER VARIABILITY AMONG PATHOLOGISTS IN THE INTERPRETATION OF LESIONS OF PROLIFERATIVE VERRUCOUS LEUKOPLAKIA SPECTRUM: A COLLABORATIVE PILOT STUDY.

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Objective: The use of diverse terminology may lead to inconsistency in the diagnosis and subsequent treatment of lesions within the proliferative verrucous leukoplakia (PVL) spectrum. The objective of this study was to determine inter-observer variability between pathologists in the diagnosis of PVL spectrum lesions.

Methods: Digitally scanned slides of 40 PVL lesions of varying stages were diagnosed by six oral pathologists (OP) and six head and neck pathologists (HNP) at multiple institutions. Inter-observer agreement on diagnoses was evaluated by Fleiss' kappa analysis using Microsoft Excel 2013 and IBM SPSS version 25 software.

Results: The responses provided were grouped into five broad categories. Category 1, simple hyperkeratosis with/without low-grade dysplasia; category 2, verrucous hyperplasia/keratosis with/without low-grade dysplasia; category 3, high-grade dysplasia or carcinoma-in-situ with/without verrucous surface change; category 4, verrucous carcinoma (VC) or atypical epithelial proliferation suggestive of but not fulfilling criteria of VC or squamous cell carcinoma (SCC) and; category 5, papillary or conventional SCC. The overall level of agreement between all pathologists for all cases as measured by Fleiss' kappa (KF) was 0.270, considered fair agreement. Amongst OP the KF was 0.225, whereas amongst HNP the KF was 0.344. The best agreement between pathologists was on category 5 lesions (KF=0.650) followed by category 1 (KF=0.312). The least agreement was within categories 2 (KF=0.150), 3 (KF=0.192) and 4 (KF=0.156).

Conclusion: This study reflects the lack of standardized diagnostic criteria and terminology for lesions in the PVL spectrum. We recommend that standardized criteria and terminology be proposed and established by an expert panel position paper, which would assist pathologists and clinicians to uniformly diagnose and manage PVL spectrum lesions more effectively.

SALIVARY GLAND ANLAGE TUMOR: MOLECULAR PROFILING SHEDS LIGHT ON A MORPHOLOGIC QUESTION.

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Objectives: The salivary gland anlage tumor (SGAT), previously referred to as a "congenital pleomorphic adenoma" or a "squamous proliferative lesion," is a rare, benign entity which presents within the first few months of life. It occurs almost exclusively in the nasopharynx or the posterior nasal cavity, and affected neonates typically present with respiratory distress and difficulty feeding. Despite this ominous clinical picture, the SGAT can be easily treated by surgical excision, with no recurrence reported in the limited cases available in the literature. Histologic examination of this lesion reveals a distinct biphasic composition containing both epithelial and mesenchymal elements. Although the clinical and histologic features of the SGAT are well-described, the etiology of this entity is still poorly understood. The SGAT is currently believed to be a hamartoma rather than a true neoplasm due to its benign nature and lack of reported recurrence following treatment, however molecular studies have yet to be performed to verify this claim.

Findings: We present three new cases of SGAT on which whole exome sequencing has been performed. Specific attention was given to variants affecting 964 cancer-related genes compiled from five sources: the Cancer Gene Census, Oncomine, and the targets of the cancer panels designed by the Columbia Combined Cancer Panel, Memorial Hospital for Cancer and Allied Diseases, and Foundation Medicine. In the current study, examination of the entire exome from the three cases shows no plausible sequence-level driver mutations.

Conclusions: Our demonstration of apparently normal exome sequences from the three cases provides molecular support for the concept of SGAT as a non-neoplastic process. These results enhance the characterization and understanding of this tumor, and illustrate the manner in which molecular studies may contribute to resolution of morphologic debates and impasses.

AMELOBLASTOMA ARISING IN ODONTOGENIC KERATOCYST: REPORT OF FOUR RARE CASES, IMMUNOHISTOCHEMICAL ANALYSIS AND REVIEW OF LITERATURE.

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Odontogenic keratocyst (OKC) is a developmental cyst of the gnathic bones arising from the rests of dental lamina. This cyst demonstrates propensity for aggressive behavior and a

relative high rate of recurrence compared to the other odontogenic cysts. Ameloblastoma is a benign neoplasm of odontogenic epithelium. It is the most common clinically significant odontogenic tumor that may demonstrate a locally aggressive clinical behavior. Ameloblastoma may theoretically arise de novo from the rests of dental lamina as well as a developing enamel organ or from the epithelial lining of a pre-existing odontogenic cyst. Rare cases of ameloblastoma arising in the wall of dentigerous cyst, calcifying odontogenic cyst, glandular odontogenic cyst, radicular cyst, and residual cyst have been previously documented in the existing literature. Furthermore, ameloblastomatous changes of cysts in nevoid basal cell carcinoma syndrome (NBCCS) have been previously reported. To our knowledge, only one case of ameloblastoma combined with an OKC in a non-syndromic patient has been reported in the English language literature so far. Here we report four additional and extremely rare instances of ameloblastoma arising in combination with an OKC. Microscopically, all the cases exhibit the distinctive histopathologic features of OKC and ameloblastoma. Immunohistochemical staining for CD56, which has been reported to stain the peripheral layer of ameloblastomas and calretinin was performed on all cases. Additionally, two OKCs were stained with both markers as controls. No case demonstrated calretinin positivity, including in the obvious ameloblastic islands. CD56 highlighted only the ameloblastic areas while the areas of OKC were negative. The lack of staining in the areas typical of OKC help highlight the combined nature of the lesions. These findings suggest that much may still be unknown about the biologic potentials of OKC and that the pluripotentiality of the odontogenic epithelium may be the driving force behind such rare findings.

CLINICAL ORAL PATHOLOGY CONSULTS IN A US DENTAL SCHOOL: A RETROSPECTIVE ANALYSIS OF UTILIZATION AND EFFICACY.

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Introduction: Chairside clinical oral pathology consultations are frequently provided in most dental schools; however, the outcome and efficacy of those consults remains largely unanalyzed. We designed a retrospective study to assess the utilization of consults by Oral and Maxillofacial Pathology (OMP) providers at the UF College of Dentistry (UFCOD).

Materials and Methods: With IRB approval, the clinical record system (AxiUm) at the UFCOD was searched from January 1, 2011 until July 1, 2017 for oral pathology consultations. The following information was collected for these consults: year of consult, requesting clinic, reason/clinical impression, presumptive diagnosis, recommended plan of action, and outcome (follow up).

Results: A total of 418 consults were included in this study, of which 11 were repeat consults on the same lesion on different occasions. The most frequent clinics requesting consults were in decreasing order: undergraduate DMD clinics, followed by faculty practice, graduate prosthodontics, graduate periodontics clinic, with other clinics requesting consults infrequently. The most common reasons consults were requested in descending order were: white lesions, ulcerations, nodules, pigmented lesions, swellings/enlargements, and erythematous lesions. Radiographic consults were uncommon in our study as at UFCOD, these are usually assigned or reassigned to oral radiology. The disposition of the consults resulted in the following recommendations: 35% for observation/re-evaluation (ORE) in original clinic, 24% referred for biopsy, 19% treatment in original clinic followed by ORE, 12% referral to specialty clinic for treatment, and 10% multiple recommendations/lesions. In terms of outcome, biopsy and referral compliance was relatively reasonable, however ORE remained problematic.

Conclusions: This study illustrates the scope and difficulties associated with clinical consults in dental school and identifies areas of potential improvement.

HPV DOWN-REGULATES THE STEM CELL MARKER CD44 IN VIRAL-RELATED ORAL EPITHELIAL DYSPLASIA AND HNSCC.

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Objective: Head and Neck Squamous Cell Carcinoma (HNSCC) represents the sixth most common malignancy worldwide and is characterized by dismal prognosis and poor patient survival. More than 75% of HNSCCs arise on a precancerous lesion. CD44 is a membrane bound glycoprotein stem-cell marker strongly expressed in normal oral mucosal epithelium. Upregulated in HNSCC, CD44 participates in key cell functions including cell division, migration and adhesion, and is recognized as a negative prognosticator for the disease. In addition, HPV(+) tumors show decreased CD44 levels when compared to HPV(-) neoplasms. We aimed to investigate the role of HPV infection in the regulation of CD44 expression in oral epithelial dysplasia (OED) and invasive HNSCC.

Methods: Formalin fixed, paraffin embedded specimens of HPV(+) OED (N=16), HPV(-) OED (N=15) and HNSCC (N=29) were evaluated by immunohistochemistry for CD44. Among the carcinoma specimens, five were HPV(+) and 24 HPV(-); 13 well-differentiated (WD), 5 moderately-differentiated (MD) and 6 poorly-differentiated (PD). HPV positivity was confirmed by immunohistochemistry for the surrogate marker p16. CD44 immunoreactivity was semi-quantitatively evaluated. Statistical analysis was performed using one-way ANOVA.

Results: HPV(+) OEDs (mean expression=1.74) showed significantly lower CD44 membranous immunoexpression than HPV(-) OEDs (mean expression=2.42, $p<0.01$). Similarly, HPV(+) HNSCCs (mean expression=0.98) exhibit prominent loss of CD44 expression when compared to HPV(-) cancers (mean expression=2.99, $p<0.01$). Interestingly, CD44 expression appeared to associate with tumor differentiation since WD and MD specimens collectively (mean expression=3.18) display higher CD44 positivity than PD (mean expression=2.10, $p<0.05$).

Conclusions: Lower CD44 expression in HPV(+) OEDs and HNSCCs may reflect decreased numbers of stem cells in HPV-driven lesions. The latter, can explain the limited frequency of malignant transformation in HPV(+) OEDs and better survival rates for patients with HPV(+) tumors.