pathway through other mechanisms is present in ameloblastomas in Taiwan and how frequent sonic hedgehog (SHH) pathway coexistence with BRAF mutation, we aimed to examine the expression of Gli1, the key transcription factor in SHH pathway, in ameloblastomas.

Methods: Thirty formalin fixed paraffin embedded ameloblastoma tissue sections were used for macro-dissection of tumor component and DNA and RNA extraction. Sanger sequencing was performed to detect the BRAF(V600E) and SMO(L412F and W535L) mutations. Real-time RT-PCR was performed to investigate the expression of Gli1. Four radicular cysts and one calcifying odontogenic cyst were used as controls. The relationship between Gli1 expression in ameloblastomas and clinicopathological parameters were also evaluated.

Results: Among 30 ameloblastoma cases, twenty-six cases harbored BRAF(V600E) mutation and none had SMO mutations. Either BRAF(V600) nor SMO mutations were identified in controls. The expression of Gli1 was significantly higher in ameloblastomas than controls ($p<0.01$), especially in follicular type ameloblastomas with acanthomatous changes. Multicystic/ Solid ameloblastomas showed higher Gli1 expression than unicystic ameloblastomas ($p<0.05$). The expression of Gli1 was higher in patients >50 year-old than <50 year-old ($p<0.05$). We observed a trend that higher Gli1 expression in BRAF wild type than BRAF mutant cases (P=0.24), however, analysis of a larger cohort is needed to substantiate this finding. No statistical significance was identified between Gli1 expression level with gender, root resorption, bone perforation, and recurrence.

Conclusion: Frequent coexistence of Gli1 overexpression and BRAF(V600E) mutation in ameloblastomas was noted. This finding suggested that inhibition of both SHH pathway and BRAF-MAPK pathway might be required for future target therapy in ameloblastomas.

CANCER ASSOCIATED FIBROBLASTS (CAFS) INFLUENCE TISSUE INVASION ON SALIVARY GLAND MUCOEPIDERMOID CARCINOMA (MEC) CELLS.

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Objectives: MEC is the most common salivary gland malignancy. Although prognosis is mostly based on TNM status, histologic grade is also used as a parameter to determine treatment. CAFs have been reported to influence worse behavior in several malignancies including head and neck squamous cell carcinoma. We noticed the presence of CAF-like cells, displaying immunohistochemical positivity for alpha smooth muscle actin, in some MECs with bad outcome and we hypothesize that CAFs may influence MEC aggressiveness. Therefore, we investigated tissue invasion using the organotypic 3D human leiomyoma model and cell migration using the Incucyte® system with a gel derived from human leiomyomas (myogel). MEC cell lines HMC2 and UTMUC1, derived from high grade tumors, were cultivated alone or co-cultured with CAFs in order to evaluate if CAFs would influence MEC cells invasion and migration. Cells were cultivated on top of human leiomyoma discs for 14 days to allow invasion. Discs were fixed in 10% buffered formalin, processed and 3 micrometer tissue slices were prepared and submitted to immunohistochemical reaction with a pan-cytokeratin antibody (clone AE1/AE3). The number of invasive cells was determined by counting invasive cells under light microscope. Invasion was studied using a wound scratch assay coupled with a live camera and data obtained was analyzed using software provided by the manufacturer.

Findings: Both MEC cell lines (HMC2 and UTMUC1) displayed a significant increase in tissue invasion when co-cultured with CAFs compared to when they were cultured alone. Only HMC2 cell line presented a significant increase in migration when co-cultured with CAFs.

Conclusion: CAFs significantly increase MEC cell lines invasion and migration. The presence of CAFs deserves further investigation in MEC tumor samples and it may correlate with tumor behavior and clinical outcome.

SYNCHRONOUS ORAL SALIVARY GLAND TUMORS: REPORT OF THREE NEW CASES AND REVIEW OF THE LITERATURE.

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Multiple synchronous or metachronous salivary gland tumors, benign or malignant, are rare yet more likely to occur in the major salivary glands compared to involvement of the minor salivary glands. In this poster we present three new cases of synchronous oral salivary gland tumors in minor salivary glands and review the previously reported cases.

All three patients were female. Two of the patients aged 55 and 85, presented with submucosal nodules of the upper lip and left buccal mucosa, respectively. Histopathologically, both cases exhibited two separate encapsulated tumors identified as pleomorphic adenoma and canalicular adenoma presenting as a single nodule in the first case, but as two separated nodules in the second. The third patient was a 46-year old who presented with a grayish-blue, non-ulcerated, and painful nodule on the left soft palate. Histopathologic examination showed a nodule composed of two adjacent, yet separate tumors diagnosed as polymorphous adenocarcinoma demonstrating significant perineural invasion, and low-grade mucoepidermoid carcinoma.

Conclusion: Intraoral multiple synchronous salivary gland tumors are rare and unusual, with only a few cases reported in the literature. The diagnosis of such tumors would be significant from treatment, management, and prognostic standpoints. Cytogenetic studies might be useful in further clarification of these entities.

DISSEMINATED METASTATIC MELANOMA OF UNKNOWN ORIGIN FIRST DIAGNOSED IN THE ORAL CAVITY WITH NEAR RESOLUTION AFTER IMMUNOTHERAPY AND SUBSEQUENT IMMUNE-RELATED SEQUALAE.

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Herein, we report an atypical clinicopathological presentation of amelanotic melanoma first diagnosed in the oral cavity of a 68-year-old man. The tumor was immunopositive for HMB45 and S-100, and weakly positive to Melan A. PET (positron emission tomography) and CT (computed tomography) scans demonstrated widespread organ and bone metastases, obviating surgical intervention. Standard immunotherapy was instituted with ipilimumab and nivolumab. At 3-weeks, near resolution of the oral lesion was evident and repeat imaging showed resolution of the left lung lesions and marked reductions in size of other affected sites. The patient subsequently experienced and recovered from multiple immune-related adverse events, including autoimmune carditis, which was managed with steroid administration. Following subsequent immunoregimens and 4 months since the initial diagnosis, the patient succumbed to sudden apparent cardiac arrest. Historically, surgery, chemotherapy, and radiotherapy to manage mucosal melanoma have yielded poor long-term outcomes, necessitating alternative efforts to improve patient care. Immunotherapy is an emerging modality for management of late-stage melanoma and has shown promising results to extend overall survival.

DOES THE GERMLINE DEFICIENCY IN TOLL-LIKE RECEPTOR (TLR)2 AFFECT THE 4-NITROQUINOLONE N-OXIDE (4-NQO)-INDUCED CARCINOGENESIS IN THE UPPER AERODIGESTIVE TRACT?

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TLR2 is implicated in the development and/or progression of several cancer types. We showed recently that activated TLR2 in human TLR2-high oral squamous carcinoma cells (OSCC) directly promote their growth and survival via the extracellular regulated kinases (ERK)1/2 signaling, among other functions (Palani et al, Oncotarget 2018;9:6814-29). However, most of the mechanisms of TLR2 function in squamous carcinogenesis remain unknown.

Objectives & Approach: To develop protocols and cell lines for targeted studies of squamous carcinogenesis in upper aerodigestive tract (UADT), we used an established (Protocol #1) and a modified (Protocol #2) 4-NQO carcinogenesis models in wild-type, TLR2-/- and TLR4-/- mice. Protocol #1 included carcinogen alone x 10 weeks, followed by 10% ethanol for 26 wks total. Protocol #2 included carcinogen and 5% ethanol x 19 weeks total. The study was approved by AU IACUC.

Results: Both protocols produced epithelial dysplasia and SCC in the oral and esophageal mucosae. In Protocol #1, fewer SCC developed in the absence of TLR2 than in the WT hosts (p=0.03). In contrast, Protocol #2 produced somewhat fewer SCC in WT hosts than in either TLR2-/- or TLR4-/- hosts (difference not significant). Moreover, there was marked intraepithelial exocytosis of leukocytes throughout the UADT in Protocol #2, irrespective of TLR expression. This contrasted with minimal exocytosis induced by Protocol #1. The characterization of the mucosal inflammation is ongoing. In addition, two OSCC cell lines were established for use in orthotopic models.

Conclusions: 1) The two protocols induced UADT SCC, but differed in the levels of mucosal inflammation. 2) TLR2 may have contributed to carcinogenesis in Protocol #1, but not in Protocol #2. 3) The specific roles of TLR in mucosal squamous carcinogenesis may depend upon additional factors, such as inflammation.

EPSTEIN-BARR- VIRUS (EBV)-NEGATIVE PLASMABLASTIC LYMPHOMA: A CASE REPORT.

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Plasmablastic lymphoma is an aggressive neoplasm with poor response to therapeutic management. It is commonly associated with HIV infection and it is strongly associated with Epstein-Bairr virus (EBV) in most of the cases, although negative cases to EBV can be ocassionaly identified. The aim of this report is to describe an original case of a 52-year old male patient referred to our department due to maxillary swelling causing facial asymmetry of the right side. His medical history was positive for HIV infection. The extraoral examination revealed hemifacial edema on the right side, involving the middle and lower thirds of the face, while intraoral exam showed an ulcerated swelling extending through the hard and soft palate on the right side, involving the buccal vestibule. CT scan revealed the presence of a hypodense image destroying the maxilla, involving the maxillary sinus, floor of the orbit and the nasal cavity. Incisional biopsy was done revealing a sheet-like proliferation of atypical large cells with plasmablastic appearance. Individually, these cells had eosinophilic cytoplasm with high nuclear-to-cytoplasmic ratio. Centrally and eccentrically cellular nuclei, with vesicular chromatin and evident nucleoli, with a starry-sky appearance were found. Immunohistochemistry was positive for CD138, EMA and MUM1, negative for CD20 and LCA, demonstrating monoclonality to lambda light chain. EBER was negative and final dignosis was rendered as EBV-negative plasmablastic lymphoma. Unfortunately, the patient died two months after diagnosis.

ORAL IATROGENIC KAPOSI'S SARCOMA: CASE REPORT.

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